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(54) Titre : NOUVELLES PROTEINES ET ACIDES NUCLEIQUES CODANT LESDITES PROTEINES  
(54) Title: PROTEINS NAMED FCTR X AND NUCLEIC ACIDS ENCODING SAME

(57) **Abrégé/Abstract:**

Disclosed herein are novel human nucleic acid sequences which encode polypeptides. Also disclosed are polypeptides encoded by these nucleic acid sequences, and antibodies which immunospecifically-bind to the polypeptide, as well as derivatives, variants, mutants, or fragments of the aforementioned polypeptide, polynucleotide, or antibody. The invention further discloses therapeutic, diagnostic and research methods for diagnosis, treatment, and prevention of disorders involving any one of these novel human nucleic acids and proteins.



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(54) Title: NOVEL PROTEINS AND NUCLEIC ACIDS ENCODING SAME

(57) Abstract: Disclosed herein are novel human nucleic acid sequences which encode polypeptides. Also disclosed are polypeptides encoded by these nucleic acid sequences, and antibodies which immunospecifically-bind to the polypeptide, as well as derivatives, variants, mutants, or fragments of the aforementioned polypeptide, polynucleotide, or antibody. The invention further discloses therapeutic, diagnostic and research methods for diagnosis, treatment, and prevention of disorders involving any one of these novel human nucleic acids and proteins.



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## NOVEL PROTEINS AND NUCLEIC ACIDS ENCODING SAME

### BACKGROUND OF THE INVENTION

The invention relates generally to polynucleotides and polypeptides, as well as vectors, host cells, antibodies, and recombinant methods for producing these nucleic acids and polypeptides.

### SUMMARY OF THE INVENTION

The invention is based in part upon the discovery of novel nucleic acid sequences encoding novel polypeptides. The disclosed FCTR1, FCTR2, FCTR3, FCTR4, FCTR5, FCTR6 and FCTR7 nucleic acids and polypeptides encoded therefrom, as well as derivatives, homologs, analogs and fragments thereof, will hereinafter be collectively designated as “FCTR” nucleic acid or polypeptide sequences.

In one aspect, the invention provides an isolated FCTR nucleic acid molecule encoding a FCTR polypeptide that includes a nucleic acid sequence that has identity to the nucleic acids disclosed in SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24. In some embodiments, the FCTR nucleic acid molecule will hybridize under stringent conditions to a nucleic acid sequence complementary to a nucleic acid molecule that includes a protein-coding sequence of a FCTR nucleic acid sequence. The invention also includes an isolated nucleic acid that encodes a FCTR polypeptide, or a fragment, homolog, analog or derivative thereof. For example, the nucleic acid can encode a polypeptide at least 80% identical to a polypeptide comprising the amino acid sequences of SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25. The nucleic acid can be, for example, a genomic DNA fragment or a cDNA molecule that includes the nucleic acid sequence of any of SEQ ID NOS: 1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24.

Also included in the invention is an oligonucleotide, *e.g.*, an oligonucleotide which includes at least 6 contiguous nucleotides of a FCTR nucleic acid (*e.g.*, SEQ ID NOS: 1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24) or a complement of said oligonucleotide.

Also included in the invention are substantially purified FCTR polypeptides (SEQ ID NO: 2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25). In certain embodiments, the FCTR polypeptides include an amino acid sequence that is substantially identical to the amino acid sequence of a human FCTR polypeptide.

The invention also features antibodies that immunoselectively-binds to FCTR<sub>X</sub> polypeptides, or fragments, homologs, analogs or derivatives thereof.

In another aspect, the invention includes pharmaceutical compositions that include therapeutically- or prophylactically-effective amounts of a therapeutic and a pharmaceutically-acceptable carrier. The therapeutic can be, *e.g.*, a FCTR<sub>X</sub> nucleic acid, a FCTR<sub>X</sub> polypeptide, or an antibody specific for a FCTR<sub>X</sub> polypeptide. In a further aspect, the invention includes, in one or more containers, a therapeutically- or prophylactically-effective amount of this pharmaceutical composition.

In a further aspect, the invention includes a method of producing a polypeptide by culturing a cell that includes a FCTR<sub>X</sub> nucleic acid, under conditions allowing for expression of the FCTR<sub>X</sub> polypeptide encoded by the DNA. If desired, the FCTR<sub>X</sub> polypeptide can then be recovered.

In another aspect, the invention includes a method of detecting the presence of a FCTR<sub>X</sub> polypeptide in a sample. In the method, a sample is contacted with a compound that selectively binds to the polypeptide under conditions allowing for formation of a complex between the polypeptide and the compound. The complex is detected, if present, thereby identifying the FCTR<sub>X</sub> polypeptide within the sample.

The invention also includes methods to identify specific cell or tissue types based on their expression of a FCTR<sub>X</sub>.

Also included in the invention is a method of detecting the presence of a FCTR<sub>X</sub> nucleic acid molecule in a sample by contacting the sample with a FCTR<sub>X</sub> nucleic acid probe or primer, and detecting whether the nucleic acid probe or primer bound to a FCTR<sub>X</sub> nucleic acid molecule in the sample.

In a further aspect, the invention provides a method for modulating the activity of a FCTR<sub>X</sub> polypeptide by contacting a cell sample that includes the FCTR<sub>X</sub> polypeptide with a compound that binds to the FCTR<sub>X</sub> polypeptide in an amount sufficient to modulate the activity of said polypeptide. The compound can be, *e.g.*, a small molecule, such as a nucleic acid, peptide, polypeptide, peptidomimetic, carbohydrate, lipid or other organic (carbon containing) or inorganic molecule, as further described herein.

Also within the scope of the invention is the use of a Therapeutic in the manufacture of a medicament for treating or preventing disorders or syndromes including, *e.g.*, Colorectal cancer, adenomatous polyposis coli, myelogenous leukemia, congenital neonatal alloimmune thrombocytopenia, multiple human solid malignancies, malignant ovarian tumours particularly at the interface between epithelia and stroma, malignant brain tumors, mammary tumors,

human gliomas, astrocytomas, mixed glioma/astrocytomas, renal cells carcinoma, breast adenocarcinoma, ovarian cancer, melanomas, renal cell carcinoma, clear cell and granular cell carcinomas, autocrine/paracrine stimulation of tumor cell proliferation, autocrine/paracrine stimulation of tumor cell survival and tumor cell resistance to cytotoxic therapy, paranechmal and basement membrane invasion and motility of tumor cells thereby contributing to metastasis, tumor-mediated immunosuppression of T-cell mediated immune effector cells and pathways resulting in tumor escape from immune surveillance, neurological disorders, neurodegenerative disorders, nerve trauma, familial myelodysplastic syndrome, Charcot-Marie-Tooth neuropathy, demyelinating Gardner syndrome, familial myelodysplastic syndrome; mental health conditions, immunological disorders, allergy and infection, asthma, bronchial asthma, Avellino type eosinophilia, lung diseases, reproductive disorders, male infertility, female reproductive system disorders, male and female reproductive diseases, hemangioma, deafness, glycoprotein Ia deficiency, desmoid disease, turcot syndrome, liver cirrhosis, hepatitis C, gastric disorders, pancreatic diseases like diabetes, *Schistosoma mansoni* infection, Spinocerebellar ataxia, *Plasmodium falciparum* parasitemia, Corneal dystrophy - Groenouw type I, Corneal dystrophy - lattice type I, and Reis-Bucklers corneal dystrophy. The Therapeutic can be, *e.g.*, a FCTR<sub>X</sub> nucleic acid, a FCTR<sub>X</sub> polypeptide, or a FCTR<sub>X</sub>-specific antibody, or biologically-active derivatives or fragments thereof.

The invention further includes a method for screening for a modulator of disorders or syndromes including, *e.g.*, Also within the scope of the invention is the use of a Therapeutic in the manufacture of a medicament for treating or preventing disorders or syndromes including, *e.g.*, Colorectal cancer, adenomatous polyposis coli, myelogenous leukemia, congenital neonatal alloimmune thrombocytopenia, multiple human solid malignancies, malignant ovarian tumours particularly at the interface between epithelia and stroma, malignant brain tumors, mammary tumors, human gliomas, astrocytomas, mixed glioma/astrocytomas, renal cells carcinoma, breast adenocarcinoma, ovarian cancer, melanomas, renal cell carcinoma, clear cell and granular cell carcinomas, autocrine/paracrine stimulation of tumor cell proliferation, autocrine/paracrine stimulation of tumor cell survival and tumor cell resistance to cytotoxic therapy, paranechmal and basement membrane invasion and motility of tumor cells thereby contributing to metastasis, tumor-mediated immunosuppression of T-cell mediated immune effector cells and pathways resulting in tumor escape from immune surveillance, neurological disorders, neurodegenerative disorders, nerve trauma, familial myelodysplastic syndrome, Charcot-Marie-Tooth neuropathy, demyelinating Gardner syndrome, familial myelodysplastic syndrome; mental health conditions, immunological

disorders, allergy and infection, asthma, bronchial asthma, Avellino type eosinophilia, lung diseases, reproductive disorders, male infertility, female reproductive system disorders, male and female reproductive diseases, hemangioma, deafness, glycoprotein Ia deficiency, desmoid disease, turcot syndrome, liver cirrhosis, hepatitis C, gastric disorders, pancreatic diseases like diabetes, *Schistosoma mansoni* infection, Spinocerebellar ataxia, *Plasmodium falciparum* parasitemia, Corneal dystrophy - Groenouw type I, Corneal dystrophy - lattice type I, and Reis-Bucklers corneal dystrophy. The method includes contacting a test compound with a FCTR<sub>X</sub> polypeptide and determining if the test compound binds to said FCTR<sub>X</sub> polypeptide. Binding of the test compound to the FCTR<sub>X</sub> polypeptide indicates the test compound is a modulator of activity, or of latency or predisposition to the aforementioned disorders or syndromes.

Also within the scope of the invention is a method for screening for a modulator of activity, or of latency or predisposition to an disorders or syndromes including, *e.g.*, Also within the scope of the invention is the use of a Therapeutic in the manufacture of a medicament for treating or preventing disorders or syndromes including, *e.g.*, Colorectal cancer, adenomatous polyposis coli, myelogenous leukemia, congenital neonatal alloimmune thrombocytopenia, multiple human solid malignancies, malignant ovarian tumours particularly at the interface between epithelia and stroma, malignant brain tumors, mammary tumors, human gliomas, astrocytomas, mixed glioma/astrocytomas, renal cells carcinoma, breast adenocarcinoma, ovarian cancer, melanomas, renal cell carcinoma, clear cell and granular cell carcinomas, autocrine/paracrine stimulation of tumor cell proliferation, autocrine/paracrine stimulation of tumor cell survival and tumor cell resistance to cytotoxic therapy, paranechmal and basement membrane invasion and motility of tumor cells thereby contributing to metastasis, tumor-mediated immunosuppression of T-cell mediated immune effector cells and pathways resulting in tumor escape from immune surveillance, neurological disorders, neurodegenerative disorders, nerve trauma, familial myelodysplastic syndrome, Charcot-Marie-Tooth neuropathy, demyelinating Gardner syndrome, familial myelodysplastic syndrome; mental health conditions, immunological disorders, allergy and infection, asthma, bronchial asthma, Avellino type eosinophilia, lung diseases, reproductive disorders, male infertility, female reproductive system disorders, male and female reproductive diseases, hemangioma, deafness, glycoprotein Ia deficiency, desmoid disease, turcot syndrome, liver cirrhosis, hepatitis C, gastric disorders, pancreatic diseases like diabetes, *Schistosoma mansoni* infection, Spinocerebellar ataxia, *Plasmodium falciparum* parasitemia, Corneal dystrophy - Groenouw type I, Corneal dystrophy - lattice type I, and Reis-Bucklers corneal dystrophy by

administering a test compound to a test animal at increased risk for the aforementioned disorders or syndromes. The test animal expresses a recombinant polypeptide encoded by a FCTR<sub>X</sub> nucleic acid. Expression or activity of FCTR<sub>X</sub> polypeptide is then measured in the test animal, as is expression or activity of the protein in a control animal which recombinantly-expresses FCTR<sub>X</sub> polypeptide and is not at increased risk for the disorder or syndrome. Next, the expression of FCTR<sub>X</sub> polypeptide in both the test animal and the control animal is compared. A change in the activity of FCTR<sub>X</sub> polypeptide in the test animal relative to the control animal indicates the test compound is a modulator of latency of the disorder or syndrome.

In yet another aspect, the invention includes a method for determining the presence of or predisposition to a disease associated with altered levels of a FCTR<sub>X</sub> polypeptide, a FCTR<sub>X</sub> nucleic acid, or both, in a subject (*e.g.*, a human subject). The method includes measuring the amount of the FCTR<sub>X</sub> polypeptide in a test sample from the subject and comparing the amount of the polypeptide in the test sample to the amount of the FCTR<sub>X</sub> polypeptide present in a control sample. An alteration in the level of the FCTR<sub>X</sub> polypeptide in the test sample as compared to the control sample indicates the presence of or predisposition to a disease in the subject. Preferably, the predisposition includes, *e.g.*, Also within the scope of the invention is the use of a Therapeutic in the manufacture of a medicament for treating or preventing disorders or syndromes including, *e.g.*, Colorectal cancer, adenomatous polyposis coli, myelogenous leukemia, congenital neonatal alloimmune thrombocytopenia, multiple human solid malignancies, malignant ovarian tumours particularly at the interface between epithelia and stroma, malignant brain tumors, mammary tumors, human gliomas, astrocytomas, mixed glioma/astrocytomas, renal cells carcinoma, breast adenocarcinoma, ovarian cancer, melanomas, renal cell carcinoma, clear cell and granular cell carcinomas, autocrine/paracrine stimulation of tumor cell proliferation, autocrine/paracrine stimulation of tumor cell survival and tumor cell resistance to cytotoxic therapy, paranechmal and basement membrane invasion and motility of tumor cells thereby contributing to metastasis, tumor-mediated immunosuppression of T-cell mediated immune effector cells and pathways resulting in tumor escape from immune surveillance, neurological disorders, neurodegenerative disorders, nerve trauma, familial myelodysplastic syndrome, Charcot-Marie-Tooth neuropathy, demyelinating Gardner syndrome, familial myelodysplastic syndrome; mental health conditions, immunological disorders, allergy and infection, asthma, bronchial asthma, Avellino type eosinophilia, lung diseases, reproductive disorders, male infertility, female reproductive system disorders, male and female reproductive diseases, hemangioma, deafness,

glycoprotein Ia deficiency, desmoid disease, turcot syndrome, liver cirrhosis, hepatitis C, gastric disorders, pancreatic diseases like diabetes, *Schistosoma mansoni* infection, Spinocerebellar ataxia, *Plasmodium falciparum* parasitemia, Corneal dystrophy - Groenouw type I, Corneal dystrophy - lattice type I, and Reis-Bucklers corneal dystrophy. Also, the expression levels of the new polypeptides of the invention can be used in a method to screen for various cancers as well as to determine the stage of cancers.

In a further aspect, the invention includes a method of treating or preventing a pathological condition associated with a disorder in a mammal by administering to the subject a FCTR<sub>X</sub> polypeptide, a FCTR<sub>X</sub> nucleic acid, or a FCTR<sub>X</sub>-specific antibody to a subject (*e.g.*, a human subject), in an amount sufficient to alleviate or prevent the pathological condition. In preferred embodiments, the disorder, includes, *e.g.*, Also within the scope of the invention is the use of a Therapeutic in the manufacture of a medicament for treating or preventing disorders or syndromes including, *e.g.*, Colorectal cancer, adenomatous polyposis coli, myelogenous leukemia, congenital neonatal alloimmune thrombocytopenia, multiple human solid malignancies, malignant ovarian tumours particularly at the interface between epithelia and stroma, malignant brain tumors, mammary tumors, human gliomas, astrocytomas, mixed glioma/astrocytomas, renal cells carcinoma, breast adenocarcinoma, ovarian cancer, melanomas, renal cell carcinoma, clear cell and granular cell carcinomas, autocrine/paracrine stimulation of tumor cell proliferation, autocrine/paracrine stimulation of tumor cell survival and tumor cell resistance to cytotoxic therapy, paraneoplastic and basement membrane invasion and motility of tumor cells thereby contributing to metastasis, tumor-mediated immunosuppression of T-cell mediated immune effector cells and pathways resulting in tumor escape from immune surveillance, neurological disorders, neurodegenerative disorders, nerve trauma, familial myelodysplastic syndrome, Charcot-Marie-Tooth neuropathy, demyelinating Gardner syndrome, familial myelodysplastic syndrome; mental health conditions, immunological disorders, allergy and infection, asthma, bronchial asthma, Avellino type eosinophilia, lung diseases, reproductive disorders, male infertility, female reproductive system disorders, male and female reproductive diseases, hemangioma, deafness, glycoprotein Ia deficiency, desmoid disease, turcot syndrome, liver cirrhosis, hepatitis C, gastric disorders, pancreatic diseases like diabetes, *Schistosoma mansoni* infection, Spinocerebellar ataxia, *Plasmodium falciparum* parasitemia, Corneal dystrophy - Groenouw type I, Corneal dystrophy - lattice type I, and Reis-Bucklers corneal dystrophy.

In yet another aspect, the invention can be used in a method to identify the cellular receptors and downstream effectors of the invention by any one of a number of techniques

commonly employed in the art. These include but are not limited to the two-hybrid system, affinity purification, co-precipitation with antibodies or other specific-interacting molecules.

Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs. Although methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present invention, suitable methods and materials are described below. All publications, patent applications, patents, and other references mentioned herein are incorporated by reference in their entirety. In the case of conflict, the present specification, including definitions, will control. In addition, the materials, methods, and examples are illustrative only and not intended to be limiting.

Other features and advantages of the invention will be apparent from the following detailed description and claims.

### DETAILED DESCRIPTION

The invention is based, in part, upon the discovery of novel nucleic acid sequences that encode novel polypeptides. The novel nucleic acids and their encoded polypeptides are referred to individually as FCTR1, FCTR2, FCTR3, FCTR4, FCTR5, FCTR6, and FCTR7. The nucleic acids, and their encoded polypeptides, are collectively designated herein as "FCTR".

The novel FCTR nucleic acids of the invention include the nucleic acids whose sequences are provided in Tables 1A, 2A, 3A, 3C, 3E, 3F, 3G, 3H, 4A, 5A, 5C, 5E, 6A, 6C, and 7A inclusive ("Tables 1A - 7A"), or a fragment, derivative, analog or homolog thereof. The novel FCTR proteins of the invention include the protein fragments whose sequences are provided in Tables 1B, 2B, 3B, 3I, 4B, 5B, 5D, 6B, 6D, and 7B inclusive ("Tables 1B - 7B"). The individual FCTR nucleic acids and proteins are described below. Within the scope of this invention is a method of using these nucleic acids and peptides in the treatment or prevention of a disorder related to cell signaling or metabolic pathway modulation.

#### FCTR1

Novel FCTR1 is a growth factor ("FCTR") protein related to follistatin-like gene, and mac25. FCTR1 (also referred to by proprietary accession number 58092213.0.36) is a full-length clone of 771 nucleotides, including the entire coding sequence of a 105 amino acid protein from nucleotides 438 to 753. The clone was originally obtained from thyroid gland, kidney, fetal kidney, and spleen tissues.

The nucleotide sequence of FCTR1 as presently determined is reported in Table 1A. The start and stop codons are bolded and the 5' and 3' untranslated regions are underlined.

**Table 1A. FCTR1 nucleotide sequence (SEQ ID NO:1).**

5 GGTCCTCACCCCCTTCCTCTCTCCCAGCCTCGGTGTCTGGTTACGGCTCCTCTGCTCGCATTTGTGACTTTGGGCCAGGCTGGGG  
GAAATGACCCGGGAGGGTCCCATGCGGCTACATAAAATTGGCAGCCTTAGAACTAGTGGGAAGGCGGGTGCGCCAAGTCGAGGG  
GCGGAGAGAGGGGGCCGGAGGAGCTGCTTTCTGAATCCAAGTTCGTGGGCTCTCTCAGAAGTCCTCAGGACGGAGCAGAGGTGG  
CCGGCGGGCCCCGGCTGACTGCGCCTCTGCTTTCTTTCCATAACCTTTTCTTTCCGACTCGAATCACGGCTGCTGCGAAGGGTCT  
AGTTCGGGACACTAGGGCCCCAGATCGTGTACATCCATATGACACTTGAATGTGACAGGGCAGGATGTGATCTTTGGCTGTG  
AAGTGTTCCTACCCCATGGCCTCCATCGAGTGGAGGAAGGATGGCTTGGACATCCAGCTGCCAGGGGATGACCCCCACATCT  
10 CTGTGCAGTTTAGGGGTGGACCCAGAGGTTTGGAGTGACTGGCTGGCTGCAGATCCAGGCTGTGCGTCCCAGTGATGAGGGCA  
CTTACCGCTGCCTTGCCCGCAATGCCCTGGGTCAAGTGGAGGCCCTGCTAGCTTGACAGTGCTCACACCTGACCAGCTGAACT  
CTACAGGCATCCCCAGCTGCGATCACTAAACCTGGTTCTGAGGAGGAGGCTGAGAGTGAAGAGAATGACGATTACTACTAGG  
TCCAGAGCTCTGGCC

15 The predicted amino acid sequence of FCTR1 protein corresponding to the foregoing nucleotide sequence is reported in Table 1B. FCTR1 was searched against other databases using SignalPep and PSort search protocols. The protein is most likely located in the cytoplasm (certainty=0.6500) and seems to have no N-terminal signal sequence. The predicted molecular weight of FCTR1 protein is 11711.8 daltons.

20 **Table 1B. Encoded FCTR1 protein sequence (SEQ ID NO:2).**

MASIEWRKDGLDIQLPGDDPHISVQFRGGPQRFEVTGWLQIQAVRPSDEGTYRCLARNALGQVEAPASLTVLTPDQLNSTGIPQ  
 LRSNLNVPEEEAESEENDYY

25 FCTR1 was initially identified with a TblastN analysis of a proprietary sequence file for a follistatin-like probe or homolog which was run against the Genomic Daily Files made available by GenBank. A proprietary software program (GenScan™) was used to further predict the nucleic acid sequence and the selection of exons. The resulting sequences were further modified by means of similarities using BLAST searches. The sequences were then manually corrected for apparent inconsistencies, thereby obtaining the sequences encoding the  
 30 full-length protein.

In an analysis of sequence databases, it was found, for example, that the FCTR1 nucleic acid sequence has 31/71 bases (43%) identical and 46/71 bases positively alike to a *Mus Musculus* IGFBP-like protein (TREMBL Accession Number:BAA21725) shown in Table 1C. In all BLAST alignments herein, the "E-value" or "Expect" value is a numeric  
 35 indication of the probability that the aligned sequences could have achieved their similarity to the BLAST query sequence by chance alone, within the database that was searched. For example, as shown in Table 1C, the probability that the subject ("Sbjct") retrieved from the FCTR1 BLAST analysis, in this case the *Mus Musculus* IGFBP-like protein, matched the Query FCTR1 sequence purely by chance is  $1.2 \times 10^{-11}$ .

**Table 1C. BLASTP of FCTR1 against *Mus Musculus* IGFBP-like protein (SEQ ID NO:38)**

PTNR:REMTREMBL-ACC:BAA21725 IGFBP-LIKE PROTEIN - MUS MUSCULUS (MOUSE), 270 AA.  
LENGTH = 270

SCORE = 161 (56.7 BITS), EXPECT = 1.2E-11, P = 1.2E-11  
IDENTITIES = 31/71 (43%), POSITIVES = 46/71 (64%)

QUERY: 9 DGLDIQLPGDDPHISVQFRGGPQRFVETGWLQIQAVRPSDEGTYRCLARNALGQVEAPAS 68  
+|+ +|+|+ +|+|+ | | + | + | | | | | +|+ ++ +  
SBJCT: 191 EGLE-ELPGDHVNIQVVRGGPSDHETTSWILINPLRKEDEGVYHCHAANAIGEAQSHGT 249

QUERY: 69 LTVLTPDQLNS 79  
+|+ + + |  
SBJCT: 250 VTVLDLNRYS 260

The amino acid sequence of FCTR1 also had 26/58 bases (44%) identical, and 38/58 bases (65%) positive for *Mus Musculus* Follistatin-like Protein shown in Table 1D.

**Table 1D. BLASTP of FCTR1 against *Mus Musculus* Follistatin-like Protein (SEQ ID NO:39)**

PTNR:SPTREMBL-ACC:Q61581 FOLLISTATIN-LIKE 2 (FOLLISTATIN-LIKE PROTEIN) - MUS MUSCULUS (MOUSE), 238 AA.  
LENGTH = 238

SCORE = 149 (52.5 BITS), EXPECT = 1.5E-10, P = 1.5E-10  
IDENTITIES = 26/58 (44%), POSITIVES = 38/58 (65%)

QUERY: 15 LPGDDPHISVQFRGGPQRFVETGWLQIQAVRPSDEGTYRCLARNALGQVEAPASLTVL 72  
| | | + + + + | | | + + | | | | | + | | | + | +  
SBJCT: 165 LPGDRENLAIQTRGGPEKHEVTGWVLSPLSKEDAGEYECHASNSQGQASAAKITVV 222

The amino acid sequence of FCTR1 also had 26/58 bases (44%) identical, and 38/58 bases (65%) positive for *Homo sapiens* MAC25 protein shown in Table 1E.

**Table 1E. BLASTP of FCTR1 against *Homo sapiens* MAC25 protein (SEQ ID NO:40)**

PTNR:SPTREMBL-ACC:Q07822 MAC25 PROTEIN - HOMO SAPIENS (HUMAN), 277 AA.  
LENGTH = 277

SCORE = 149 (52.5 BITS), EXPECT = 3.2E-10, P = 3.2E-10  
IDENTITIES = 26/58 (44%), POSITIVES = 38/58 (65%)

QUERY: 15 LPGDDPHISVQFRGGPQRFVETGWLQIQAVRPSDEGTYRCLARNALGQVEAPASLTVL 72  
| | | + + + + | | | + + | | | | | + | | | + | +  
SBJCT: 209 LPGDRDNLAIQTRGGPEKHEVTGWVLSPLSKEDAGEYECHASNSQGQASASAKITVV 266

The amino acid sequence of FCTR1 also had 26/58 bases (44%) identical, and 38/58 bases (65%) positive for *Mus musculus* MAC25 protein shown in Table 1F.

**Table 1F. BLASTP of FCTR1 against *Mus musculus* MAC25 protein (SEQ ID NO:41)**

PTNR:SPTREMBL-ACC:O88812 MAC25 - MUS MUSCULUS (MOUSE), 281 AA  
 LENGTH = 281

SCORE = 149 (52.5 BITS), EXPECT = 3.4E-10, P = 3.4E-10  
 IDENTITIES = 26/58 (44%), POSITIVES = 38/58 (65%)

QUERY: 15 LPGDDPHISVQFRGGPQRFVETGWLQIQAVRPSDEGTYRCLARNALGQVEAPASLTVL 72  
 |||| ++++| ||||++ |||||+ + + | | | | | | + | | | + || +  
 SBJCT: 208 LPGDRENLAIQTRGGPEKHEVTGWVLVSPLSKEDAGEYECHASNSQGOASAAKITVV 265

The amino acid sequence of FCTR1 also had 26/58 bases (44%) identical, and 38/58 bases (65%) positive for *Homo sapiens* Prostacyclin-stimulating factor shown in Table 1G.

**Table 1G. BLASTP of FCTR1 against *Homo sapiens* Prostacyclin-stimulating factor (SEQ ID NO:42)**

PTNR:SPTREMBL-ACC:Q16270 PROSTACYCLIN-STIMULATING FACTOR - HOMO SAPIENS (HUMAN), 282 AA  
 LENGTH = 282

SCORE = 149 (52.5 BITS), EXPECT = 3.4E-10, P = 3.4E-10  
 IDENTITIES = 26/58 (44%), POSITIVES = 38/58 (65%)

QUERY: 15 LPGDDPHISVQFRGGPQRFVETGWLQIQAVRPSDEGTYRCLARNALGQVEAPASLTVL 72  
 |||| ++++| ||||++ |||||+ + + | | | | | | + | | | + || +  
 SBJCT: 209 LPGDRDNLAIQTRGGPEKHEVTGWVLVSPLSKEDAGEYECHASNSQGOASASAKITVV 266

The amino acid sequence of FCTR1 also had 18/44 bases (40%) identical, and 25/44 bases (56%) positive for rat Colorectal cancer suppressor shown in Table 1H.

**Table 1H. BLASTP of FCTR1 against rat Colorectal cancer suppressor (SEQ ID NO:43)**

PTNR:PIR-ID:B40098 COLORECTAL CANCER SUPPRESSOR DCC - RAT (FRAGMENTS)  
 LENGTH = 144

SCORE = 78 (27.5 BITS), EXPECT = 1.1E-05, SUM P(2) = 1.1E-05  
 IDENTITIES = 18/44 (40%), POSITIVES = 25/44 (56%)

QUERY: 33 FEVTGW--LQIQAVRPSDEGTYRCLARNALGQVEAPASLTVLTP 74  
 |++ | |++ | |||| |++ | | | ++ | | | |  
 SBJCT: 101 FQIVGGSNLRILGVVKSDEGFYQCVAENEAGNAQSSAQLIVPKP 144

SCORE = 37 (13.0 BITS), EXPECT = 1.1E-05, SUM P(2) = 1.1E-05  
 IDENTITIES = 8/19 (42%), POSITIVES = 12/19 (63%)

QUERY: 1 MASIEWRKDGLDIQL-PGD 18  
 | + | |++ | + |||  
 SBJCT: 30 MPTIHWQKNQQLTPNPGD 48

The amino acid sequence of FCTR1 also had 32/83 bases (38%) identical, and 45/83 bases (54%) positive to bases 55-137, and 24/68 bases (35%) identical, and 37/68 bases (54%) positive to bases 166-225 of *Homo sapiens* PTPsigma-(Brain) Precursor shown in Table 1I.

**Table 1I. BLASTP of FCTR1 against *Homo sapiens* PTPsigma-(Brain) Precursor (SEQ ID NO:44)**

PTNR:TREMBLNEW-ACC:AAD09360 PTPSIGMA-(BRAIN) PRECURSOR - HOMO SAPIENS (HUMAN), 1502 AA.

LENGTH = 1502

SCORE = 109 (38.4 BITS), EXPECT = 0.00010, P = 0.00010  
IDENTITIES = 32/83 (38%), POSITIVES = 45/83 (54%)

QUERY: 14 QLPGDD-PHISVQFRG---GPQRFVETGW-----LQIQAVR-PSDEGTYRCLARNALG 61  
| || | ++ +| ||| + |++| +| | || | |++|++|  
SBJCT: 55 QATGDPKPRVTWNKKGKKVNSQRFETIEFDESAGAVLRIQPLRTPRDENVYECVAQNSVG 114

QUERY: 62 QVEAPASLTVLTPDQLNSTGIPQL 85  
++ | ||| || | | | +  
SBJCT: 115 EITVHAKLTVLREDQLPS-GFPNI 137

SCORE = 77 (27.1 BITS), EXPECT = 0.25, P = 0.22  
IDENTITIES = 24/68 (35%), POSITIVES = 37/68 (54%)

QUERY: 4 IEWRKDGLDIQLPGDDPHISVQFRGGPQRFVETGWLQIQAVRPSDEGTYRCLARNALG-Q 62  
| | || | + || | | ++ +| ||++ +|+| | |+| | + | +  
SBJCT: 166 ITWFKDFLPV-----DPSAS---NGRIKQLR-SGALQIESSEETDQGYECVATNSAGVR 216

QUERY: 63 VEAPASLTV 71  
+||+| |  
SBJCT: 217 YSSPANLYV 225

The amino acid sequence of FCTR1 also had 32/83 bases (38%) identical, and 45/83 bases (54%) positive for amino acids 55-137 and 26/69 bases (37%) identical, and 38/69 (54%) positive for amino acids 166-234 of *Homo sapiens* Protein-Tyrosine Phosphatase Sigma shown in Table 1J.

**Table 1J. BLASTP of FCTR1 against *Homo sapiens* PTPsigma-(Brain) Precursor (SEQ ID NO:45)**

PTNR:SPTREMBL-ACC:Q13332 PROTEIN-TYROSINE PHOSPHATASE, RECEPTOR-TYPE, S PRECURSOR (EC 3.1.3.48) (PROTEIN-TYROSINE PHOSPHATASE SIGMA) (R-PTP-SIGMA) (PTPRS) - HOMO SAPIENS (HUMAN), 1948 AA.

LENGTH = 1948

SCORE = 109 (38.4 BITS), EXPECT = 0.00013, P = 0.00013  
IDENTITIES = 32/83 (38%), POSITIVES = 45/83 (54%)

QUERY: 14 QLPGDD-PHISVQFRG---GPQRFVETGW-----LQIQAVR-PSDEGTYRCLARNALG 61  
| || | ++ +| ||| + |++| +| | || | |++|++|  
SBJCT: 55 QATGDPKPRVTWNKKGKKVNSQRFETIEFDESAGAVLRIQPLRTPRDENVYECVAQNSVG 114

QUERY: 62 QVEAPASLTVLTPDQLNSTGIPQL 85  
++ | ||| || | | | +  
SBJCT: 115 EITVHAKLTVLREDQLPS-GFPNI 137

SCORE = 88 (31.0 BITS), EXPECT = 0.023, P = 0.022  
IDENTITIES = 26/69 (37%), POSITIVES = 38/69 (55%)

QUERY: 4 IEWRKDGLDIQLPGDDPHISVQFRGGPQRFVET---GWLQIQAVRPSDEGTYRCLARNAL 60  
| | || | + + | | | + || | |||++ +|+| | |+| | +  
SBJCT: 166 ITWFKDFLPVDPSASNGRIK-QLRS--ETFESTPIRGALQIESSEETDQGYECVATNSA 222

QUERY: 61 G-QVEAPASLTV 71  
| + +||+| |  
SBJCT: 223 GVRYSSPANLYV 234

A ClustalW analysis comparing the protein of the invention with related protein sequences is given in Table 1K, with FCTR1 shown on line 2. In the ClustalW alignment of the FCTR1 protein, as well as all other ClustalW analyses herein, the black outlined amino acid residues indicate regions of conserved sequence (*i.e.*, regions that may be required to preserve structural or functional properties), whereas non-highlighted amino acid residues are less conserved and can potentially be mutated to a much broader extent without altering protein structure or function.

Table 1K. ClustalW Analysis of FCTR1

- 10 1) Q07822 MAC25 PROTEIN. (SEQ ID NO:40)  
 2) Q16270 PROSTACYCLIN-STIMULATING FACTOR. (SEQ ID NO:42)  
 3) Q61581\_FOLLISTATIN-LIKE 2: FOLLISTATIN-LIKE 2 (FOLLISTATIN-LIKE PROTEIN) (SEQ ID NO:39)  
 4) BAA21725 IGF1P-LIKE PROTEIN (SEQ ID NO:38)  
 15 5) FCTR1 (SEQ ID NO:2)  
 6) B40098 COLORECTAL CANCER SUPPRESSOR DCC - RAT (FRAGMENTS) (SEQ ID NO:43)

|    |          |                                                               |
|----|----------|---------------------------------------------------------------|
| 20 | Q07822   | MERASLRALLFGPAGLLLLLLPLSSSSSSSDTCGPCEPASCPPLPPLGCLLGETRDACGCC |
|    | Q16270   | MERPSLRALLLGAAGLLLLLLPLSSSSSSSDTCGPCEPASCPPLPPLGCLLGETRDACGCC |
|    | Q61581   | MERP PRALLLGAAGLLLLLLPLSSSSSSSDACGR                           |
|    | BAA21725 | MPRLPLLLLLPLSLARGLGLRDAG RRHPECSPCQQDRCPAPSFCPAPWISARDECGCC   |
|    | FCTR1    |                                                               |
|    | B40098   |                                                               |
| 25 | Q07822   | PMCARGEGEPCCGGGAGRGYCAPGMECVKSRKRRRGKAGAAAGGPGVSGVCVCKSRVPVC  |
|    | Q16270   | PMCARGEGEPCCGGGAGRGYCAPGMECVKSRKRRRGKAGAAAGGPGVSGVCVCKSRVPVC  |
|    | Q61581   | RGHCAPGMECVKSRKRRRGKAGAAAGGPGATLAVCVCKSRVPVC                  |
|    | BAA21725 | ARCLGAEGASCG GPVGSRCGEGLVCA SR ASGTAPEG T GLCVCAQRGAVC        |
|    | FCTR1    |                                                               |
|    | B40098   | PLRFLSQTESIT                                                  |
| 35 | Q07822   | GSDGT TYPSCGQLRAASQRAESRGEKA ITQVSKGTCEQGPSIVTPPKDIWNVTGAQV   |
|    | Q16270   | GSDGT TYPSCGQLRAASQRAESRGEKA ITQVSKGTCEQGPSIVTPPKDIWNVTGAQV   |
|    | Q61581   | GSNGIT TYPSCGQLRAASLRAESRGEKP ITQVSKGTCEQGPSIVTPPKDIWNVTGAKV  |
|    | BAA21725 | GSDGRSYSSICALLRLRARHAPRAHHGH LHKARDGPECFAPVVLMPERDIHNVGTQV    |
|    | FCTR1    |                                                               |
|    | B40098   | AFMGDTVLLKCEVIGDPMPTIHWQKNQDLTPNPGDSRVVVPWFNLNHPNLYAYESMDT    |
| 40 | Q07822   | YLSCEVIGIPTPVLIIWNKVKGHYGVQRTTELLPGDRDNLAIQTRGGPEKHEVTGWVLVSP |
|    | Q16270   | YLSCEVIGIPTPVLIIWNKVKGHYGVQRTTELLPGDRDNLAIQTRGGPEKHEVTGWVLVSP |
|    | Q61581   | ELSCVIGIPTPVLIIWNKVGRDHSQVQRTTELLPGDRDNLAIQTRGGPEKHEVTGWVLVSP |
|    | BAA21725 | ELSCVIGIPTPVLIIWNKVKGHYGVQRTTELLPGDRDNLAIQTRGGPEKHEVTGWVLVSP  |
|    | FCTR1    | MASLEWRKDGLDIO.....LPGDDPHISVQFRGGPQRFVETGWLQIQQA             |
| 45 | B40098   | EFECVAVSGKEVPTVNNMKNQGDVVV.....ISDYFQIVGGSN.....LRILG         |
| 50 | Q07822   | LSKEDAGEYECHASNSQGOASASAKITVVDALHEIAS.....EKR....             |
|    | Q16270   | LSKEDAGEYECHASNSQGOASASAKITVVDALHEIPV.....KKGEGAE             |
|    | Q61581   | LSKEDAGEYECHASNSQGOASAAAKITVVDALHEIPV.....KKGEGAQ             |
|    | BAA21725 | LRKEDEGVYHCHAAANAIGEAQSHGTVTVLIDLNRYKSL.....YSSVPGD           |
|    | FCTR1    | VRPSDEGTYRCLARNALGOVEAPASLTIVLTPDQLNSTGIPQLRSLNLVPEEEAESEEND  |
|    | B40098   | VVKSDGEGFYQCVAENEAGNAQSSAQLIVPKP.....                         |
| 55 | Q07822   |                                                               |
|    | Q16270   | L.                                                            |
|    | Q61581   | L.                                                            |
|    | BAA21725 | LL                                                            |
|    | FCTR1    | YY                                                            |

IGFBP is expressed in neurostem cell and developing central nervous system. MAC-25, a follistatin like protein is a growth suppressor of osteosarcoma cells, and meningiomas. DCC is expressed in most normal tissues especially in colonic mucosa, but is deleted in colorectal cancers.

Since FCTR1 has similarity to these proteins (shown in BlastP, Tables 1C-1J, and in clustalW, Table 1K) it is likely that it has similar function. Therefore FCTR1 could function as on or more of the following: a tumor suppressor gene or regulator of neurological system development.

Based on the protein similarity and tissue expression, FCTR1 may be useful in the following diseases and uses:

- (i) Tissue regeneration in vitro and in vivo
- (ii) Neurological disorders, neurodegenerative disorders, nerve trauma
- (iii) Reproductive health
- (iv) Immunological disorders, allergy and infection
- (v) In cancer as a diagnostic and prognostic marker, as well as a protein therapeutic

## FCTR2

FCTR2 (alternatively referred to herein as AC012614\_1.0.123), is a growth factor bearing sequence similarity to human KIAA1061 protein and to genes involved in neuronal development and reproductive physiology (e.g., cell adhesion molecules, follistatin, roundabout and frazzled). FCTR2 is a full-length clone of 5502 nucleotides, including the entire coding sequence of a 815 amino acid protein. This sequence is expressed in glioma, osteoblast, other cancer cells, lung carcinoma, small intestine (This sequence maps to Unigene Hs.123420 which is expressed in brain, breast, kidney, pancreas, pooled tissue).

A FCTR2 ORF begins with an ATG initiation codon at nucleotides 420-422 and ends with a TGA codon at nucleotides 2865-2867. Putative untranslated regions upstream from the initiation codon and downstream from the termination codon are underlined in Table 2A, and the start and stop codons are in bold letters.

**Table 2A. FCTR2 Nucleotide Sequence (SEQ ID NO:3).**

CAATTTACACAGGAAACAGCTATGCCATGATTACGCAAGTTGGTACCGAGCTCGGATCCACTAGTAACGGCCGCCAGTG  
TGCTGGAATTCGGCTTACTCACTATAGGGCTCGAGCGGCTGCCCGGCAGGTCATTAATTCATTTCTTTTAGAGTATC  
ACAGCTTTCTCCTTCACTGACCACCCTTTGCTTCCTGTCAGAAAGCCCTGGACAGAAGCTCTCTGTGGGATTCTGCCCATG  
TTTCTGAGATATCGCCTCAATTGTCCTGGCTGGGCTGTCGGGTCTGCCCGTTTACAGATGGGCAGGAGTGGGAG  
TATCCGGGTGGCTTCCTCAGGCCTGCAGCTGGTGGAGCAGCTACTGAAACAATCAGGAGCCCAGAAGCTTTGAAGTCACA  
AGAAGAGAAGACTCCCAGAAATGCAGTGTGATGTTGGTGATGGACGCCTGTTTCGCCTTTCCTTAAACGTGCCCTTCCA  
GCTGCCCTGACCTCTTTGGGCTTTCCAGCCGCAACGAGCTGCTGGCCTCCTGCGGGAAGAAGTTCTGCAGCCGAGGGAGC  
CGTGCGTGCTCAGCAGGAAGACAGGGGAGCCGAATGCCAGTGCTGGAGGCATGCAGGCCAGCTACGTGCCTGTGTG  
CGGCTCTGATGGGAGGTTTTATGAAAACCACTGTAAGCTCCACCGTGCTGCTTGCCTCCTGGGAAAGAGGATCACCGTCA  
TCCACAGCAAGGACTGTTTCCTCAAAGGTGACACGTGCACCATGGCCGGCTACGCCCGCTGAAGAATGTCCTTCTGGCA

CTCCAGACCCGTCTGCAGCCACTCCAAGAAGGAGACAGCAGACAAGACCCTGCCTCCCAGAAGCGCCTCCTGGTGGAATC  
 TCTGTTTCAAGGACTTAGATGCAGATGGCAATGGCCACCTCAGCAGCTCCGAAGTGGCTCAGCATGTGCTGAAGAAGCAGG  
 ACCTGGATGAAGACTTACTTGGTTGCTCACCAGGTGACCTCCTCCGATTGACGATTACAACAGTGACAGCTCCCTGACC  
 CTCCGCGAGTTCTACATGGCCTTCCAAGTGGTTCAGCTCAGCCTCGCCCCGAGGACAGGGTCAGTGTGACCAGAGTGAC  
 5 CGTGGGGCTGAGCACAGTGCTGACCTGCGCCGTCCATGGAGACCTGAGGCCACCAATCATCTGGAAGCGCAACGGGCTCA  
 CCCTGAACTTCTGGACTTGAAGACATCAATGACTTTGGAGAGGATGATTCCCTGTACATCACCAAGGTGACCACCATC  
 CACATGGGCAATTACACCTGCCATGCTTCCGGCCACGAGCAGCTGTTCCAGACCCACGTCTGTCAGGTGAATGTGCCGCC  
 AGTCATCCGTGTCTATCCAGAGAGCCAGGCACAGGAGCCTGGAGTGGCAGCCAGCCTAAGATGCCATGCTGAGGGCATTC  
 CCATGCCCAGAATCACTTGGCTGAAAAACGGCGTGGATGTCTCAACTCAGATGTCCAAACAGCTCTCCCTTTTAGCCAAT  
 10 GGGAGCGAACTCCACATCAGCAGTGTTGCGGTATGAAGACACAGGGGCATACACCTGCATTGCCAAAAATGAAGTGGGTGT  
 GGATGAAGATATCTCCTCGCTCTTCATTGAAGACTCAGCTAGAAAGACCCTTGCAAACATCCTGTGGCGAGAGGAAGGCC  
 TCAGCGTGGGAAACATGTTCTATGTCTTCTCCGACGACGGTATCATCGTCATCCATCCTGTGGACTGTGAGATCCAGAGG  
 CACCTCAAACCCACGGAAGATTTTCATGAGCTATGAAGAAATCTGTCTCAAAGAGAAAAAATGCAACCCAGCCCTG  
 CCAGTGGGTATCTGCAGTCAATGTCCGGAACCGGTACATCTATGTGGCCAGCCAGCACTGAGCAGAGTCCTTGTGGTCTG  
 15 ACATCCAAGCCCAGAAAGTCTACAGTCCATAGGTGTGGACCCTCTGCCGGCTAAGCTGTCTTATGACAAGTCACATGAC  
 CAAGTGTGGGTCTGAGCTGGGGGGACGTGCACAAGTCCCGACCAAGTCTCCAGGTGATCACAGAAGCCAGCACCGGCCA  
 GAGCCAGCACCTCATCCGCACACCCTTTGCAGGAGTGGATGATTTCTTCATTCCCCAACAAACCTCATCATCAACCACA  
 TCAGGTTTGGCTTCATCTTCAACAAGTCTGATCCTGCAGTCCACAAGGTGGACCTGGAAACAATGATGCCCCCTCAAGACC  
 ATCGGCCTGCACCACCATGGCTGCGTGGCCCGAGGCCATGGCACACACCCACCTGGGCGGCTACTTCTTCATCCAGTGCCG  
 20 ACAGGACAGCCCCGCCTCTGCTGCCCCGACAGCTGCTCGTTGACAGTGTACAGACTCTGTGCTTGGCCCCAATGGTGATG  
 TAACAGGCACCCACACACATCCCCCGACGGGCGCTTCATAGTCAGTGCTGCAGCTGACAGCCCCTGGCTGCACGTGCAG  
 GAGATCACAGTGCGGGGCGAGATCCAGACCCTGTATGACCTGCAAATAAACTCGGGCATCTCAGACTTGGCCTTCCAGCG  
 CTCTTCACTGAAAGCAATCAATACAACATCTACGCGGCTCTGCACACGGAGCCGACCTGCTGTTCTGGAGCTGTCCA  
 CGGGGAAGGTGGGCATGCTGAAGAACTTAAAGGAGCCACCCGACGGGCCAGCTCAGCCCTGGGGGGGTACCCACAGAATC  
 25 ATGAGGGACAGTGGGCTGTTTGGACAGTACCTCCTCACACCAGCCGAGAGTCACTGTTCTCATCAATGGGAGACAAAA  
 CACGCTGCGGTGTGAGGTGTGAGGTATAAAGGGGGGACCACAGTGGTGTGGGTGGGTGAGGTATGAAGGGCCAGAGCA  
 GAGCCCTGGGCCAAGGAACACCCCTAGTCTGACACTGCAGCCTCAAGCAGGTACGCTGTACATTTTACAGACAAAAG  
 CAAAAACCTGTACTCGCTTTGTGGTTCAACACTGGTCTCCTTGCAAGTTTCTAGTATAAGGTATGCGCTGCTACCAAGA  
 TTGGGGTTTTTTCTGTTAGGAAGTATGATTTATGCCTTGAGCTACGATGAGAACATATGCTGCTGTGTAAAGGGATCATTT  
 30 CTGTGCCAAGCTGCACACCGAGTGACCTGGGGACATCATGGAACCAAGGGATCCTGCTCTCCAAGCAGACACCTCTGTCA  
 GTTGCCTTCACATAGTCATTGTCCCTTACTGCCAGACCCAGCCAGACTTTGCCCTGACGGAGTGGCCCCGAAGCAGAGGC  
 CGACCAGGAGCAGGGGCTCCCTCCCGAAGTGAAGGCCATCCGTCTCGCGTGGGACCGCATCTTCTCCCTCGCAGCTG  
 CTTCTTGCTTTTCTTTCCATTTGACTTGCTGTAAGCCTGAGGGAGAGCCAACAAGACTTACTGCATCTTGGGGGATGGGG  
 AAATCACTCACTTTATTTTGGAAATTTTGTATTAATAAATAAATTTTATAATCTCAAATGCTAGTAAGCAGAAAGATGCTC  
 35 TCCGAGGTCCAATATATCTTCCCTGCCTTAGGCCGAGTCTCGGGGGTGGTCAACAACCCACATCCCACAGCCAGAAAG  
 AACATGGTCACTCTGAGAATACTGGCCCTGTGACTATTGCCACCCTGCTTCTCCAAGAGCAGACCAGGCCACCTCATCC  
 GTAAGGACTCGGTTCTGTGTTGGGACCCCAAAAAACCAGAACAAGTCTGTGTGCTCCTTTTCAGCACAGAAGGGAGACA  
 TCTCATTAGTCAGGTCTGGTACCCAGATTTCAGGGCAGACTGGGCTTGCCCTGGCAAGGTATGGGTGGCCTCCAGGCTCAA  
 TGCAGAAACCCCAAGGACACGAGTGGGGCCAGGTGAGTTCTGAAGCTATACCTTTTCAAAACAGATTTTGTCTTCTTAC  
 40 CTGTGGCCCATCCACTCCTCTCTGGTACCCCATCCCGCATCAGCACTGCAGAGAGAACACATTTCCGGCAGGGTTTTCT  
 TACCCACATTTCCCAATCAATACACACACTGCAGAACCCAGAAGGCCACAGGCTGGCACTACTGCATTCTCCT  
 TATGTGTCTCAGGCTGTGGTGAATCTCACATGGGCATCGAAGAAGTACAACCCACATAGCCCTCTGGAGACCGCCTAGAT  
 CAGAGACTCAGCAAAAACAGGCTCGCCTTCCCTCTCCACATATGAGTGGAACTTACATGTGTCTGGTTTGAATGATCA  
 TTTTGCAAGCCACACGGGTGGGAGAGGTGGTCTCACCACAGACGTCTTTGCTAATTTGGCCACCTTCACCTACTGACAT  
 45 GACCAGGATTTTCTTTGCCATTAAGGAATGAACCTTTTCAAGGAGAGGAAACCCCTAGACTCTGTGTCACTCTCAACACA  
 CACAGCTCCTTTCACTCCTGCCTGACTGCCAAGCCACCTGCATCCCCCGCCCCAGATCTCATGAGATCAATCACTTGTAT  
 GTCTCACGCAACTTGGTCCACCAAACGCCTGTCCCCTGTAACCTCTAGGGGTGCGCCTAGACAGGTACGTCTGTTTTTTA  
 TTTTAAAGATATGCTATGTAGATATAAGTTGAGGAAGCTCACCTCAAAGCCTAGAATGCAGTTTCACAGTAGCTGGGA  
 TGCATGGATGACCCATCTCACCCTTTTTTTTTCTGCTCAATATCTTGATATGTTATGTTTACTCCCAATCTCCCAT  
 50 TTTTACCACTAAAATTCTCCAATTTTCATAAACTTTTTTTTTGGAAAAATTTCCATTGTATCAGCCCCTGACAGAAAAAGGA  
 TCTCTGAGCCTAAAGGAGGAAAAGTCCACCAACTACCAGACCAGAACACGAGCCCTCTGGGCAGCAGGATTCCTAAGT  
 CAAAGACCAGTTTGACCCAACTGGCCTTTTAAATAATCAGGAGTGACAGAGTCAACTTCTGCAGCACCTGCTTCTCCC  
 CCACTGTCCCTTCCATCTTGAATGTGTCTAAAAAAGCATAGCTGCCCTTTGCTGTCTCCTCAGAGTGCATTTCTTGGAGAC  
 55 GGCAGGCTTAGGTCTCACTGACAGCATGCCAGACAACTGAATCGAAGCAGGCCTGAAGCCTAGGTGAGGTTTCAGGA  
 GTCCAGCCCCAGGAGGCAAAGTCAACATGCAGGGAGGTAAATGCCTTTTGGCAGGAAAACCAATAGAGTTGGTTGGGTG  
 GGGAGTCAGGGGTGGGAGGAGAAGGAGGAAGAGGAGGAAGGCCAGACTGGCCTGCCCTTTCTCCCATACTTCACCCACAGC  
 AGAGGTTTCATGGGACACAGTTGGAAAGCCACTGGGAGGAAATGCCTCACTACAGGGGGGCTCCTGTAGCAAGCCAGCC  
 GGTAACTCCTCCTAATGAACCCACAAGGTCAATTCACAACCTGATATCTTAGCTATTAAAGAAGTACTGACTTTACCAAAAG  
 AATCATCAAGAAAGCTATTTATATAAACCCCTCAGTCATTTTGAATAAAATTAATTTTAC

The predicted amino acid sequence of FCTR2 protein corresponding to the foregoing nucleotide sequence is reported in Table 2B. FCTR2 was searched against other databases using SignalPep and PSort search protocols. The protein is most likely located in the

mitochondrial matrix space (certainty=0.4718) and seems to have no N-terminal signal sequence. The predicted molecular weight is 90346.9 Daltons.

**Table 2B. FCTR2 Protein Sequence (SEQ ID NO:4).**

5 MQCDVGDGRFLFRLSLKRALSSCPDLFGLSSRNELLASCGKKFCSRGSRVLSRKTGEPECCLEACRPSYVPVCGSDGRFYENH  
CKLHRAACLLGKRITVIHSDKCFLKGDTCTMAGYARLKNVLLALQTRLQPLQEGDSRQDPASQKRLLVESLFRDLADGNHLS  
SSELAQHVLKKQDLDEDLLGCSPGDLLRFDDYNSDSSLTLREFYMAFQVVQLSLAPEDRVSVTTVTVGLSTVLTCAVHGDLRPP  
IIWKRNGLTNLFLDLEDINDFGEDDSLYITKVTTIHMGNYTCHASGHEQLFQTHVLQVNVPPVIRVYPESQAQEPGVAASLRCH  
10 AEGIPMPRITWLKNGVDVSTQMSKQLSLLANGSELHISSVRYEDTGAYTCIAKNEVGVEDDISSLFIEDSARKTLANILWREEG  
LSVGNMFYVFSDDGIIIVHPVDCEIQRHLKPTTEKIFMSYEEICPQREKNATQPCQWVS AVNVRNRYIYVAQPALSRLVVDIQA  
QKVLQSIGVDPLPAKLSYDKSHDQVWVLSWGDVHKS RPSLQVITEASTGQSQH LIRTPFAGVDDFFIPPTNLIINHIREGFI FN  
KSDPAVHKVDLETMMPLKTIGLHHHGCVPQAMATHLGGYFFIQC RQDSFASAARQLLVDSVTD SVLGPNGDVTGT PHTSPDGR  
FIVSAAADSPWLHVQEITVRGEIQ TLYDLQINSGISDLAFQRSFTESNQYNIYAALHTEPDLLFLELSTGKVGMLKNLKEPPAG  
PAQPWGGTHRIMRDSGLFGQYLLTPARES LFLINGRQNTLRCEVSGIKGTTTVVWVGEV

In a BLASTN search it was also found that nucleotides 784-5502 of FCTR2 nucleic acid had 4672 of 4719 bases (99%) identical to *Homo sapiens* mRNA for KIAA1061 protein, partial cds (GenBank Acc:AB028984) (Table 2C).

**Table 2C. BLASTN of FCTR2 against *Homo sapiens* mRNA for KIAA1061 protein (SEQ ID NO:46)**

```

>GI|5689458|DBJ|AB028984.1|AB028984 HOMO SAPIENS MRNA FOR KIAA1061 PROTEIN, PARTIAL
CDS
      LENGTH = 4719

25  SCORE = 9075 BITS (4578), EXPECT = 0.0
    IDENTITIES = 4672/4719 (99%)
    STRAND = PLUS / PLUS

30  QUERY: 784   AGAATGTCCTTCTGGCACTCCAGACCCGTCTGCAGCCACTCCAAGAAGGAGACAGCAGAC 843
      |||
    SBJCT: 1     AGAATGTCCTTCTGGCACTCCAGACCCGTCTGCAGCCACTCCAAGAAGGAGACAGCAGAC 60

35  QUERY: 844   AAGACCCTGCCTCCCAGAAGCGCCTCCTGGTGAATCTCTGTTCAGGGACTTAGATGCAG 903
      |||
    SBJCT: 61    AAGACCCTGCCTCCCAGAAGCGCCTCCTGGTGAATCTCTGTTCAGGGACTTAGATGCAG 120

40  QUERY: 904   ATGGCAATGGCCACCTCAGCAGCTCCGAACTGGCTCAGCATGTGCTGAAGAAGCAGGACC 963
      |||
    SBJCT: 121   ATGGCAATGGCCACCTCAGCAGCTCCGAACTGGCTCAGCATGTGCTGAAGAAGCAGGACC 180

45  QUERY: 964   TGGATGAAGACTTACTTGTTGCTCACCAGGTGACCTCCTCCGATTTGACGATTACAACA 1023
      |||
    SBJCT: 181   TGGATGAAGACTTACTTGTTGCTCACCAGGTGACCTCCTCCGATTTGACGATTACAACA 240

50  QUERY: 1024  GTGACAGCTCCCTGACCCTCCGCGAGTTCTACATGGCCTTCCAAGTGGTTCAGCTCAGCC 1083
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    SBJCT: 241   GTGACAGCTCCCTGACCCTCCGCGAGTTCTACATGGCCTTCCAAGTGGTTCAGCTCAGCC 300

55  QUERY: 1084  TCGCCCCCGAGGACAGGGTCAGTGTGACCACAGTGACCGTGGGGCTGAGCACAGTGCTGA 1143
      |||
    SBJCT: 301   TCGCCCCCGAGGACAGGGTCAGTGTGACCACAGTGACCGTGGGGCTGAGCACAGTGCTGA 360

60  QUERY: 1144  CCTGCGCCGTCCATGGAGACCTGAGGCCACCAATCATCTGGAAGCGCAACGGGGCTCACCC 1203
      |||
    SBJCT: 361   CCTGCGCCGTCCATGGAGACCTGAGGCCACCAATCATCTGGAAGCGCAACGGGGCTCACCC 420

65  QUERY: 1204  TGAACTTCCTGGACTTGAAGACATCAATGACTTTGGAGAGGATGATTCCCTGTACATCA 1263
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    SBJCT: 420   TGAACTTCCTGGACTTGAAGACATCAATGACTTTGGAGAGGATGATTCCCTGTACATCA 1263

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SBJCT: 421 TGAACCTCCTGGACTTGGAAGACATCAATGACTTTGGAGAGGATGATTCCCTGTACATCA 480

QUERY: 1264 CCAAGGTGACCACCATCCACATGGGCAATTACACCTGCCATGCTTCCGGCCACGAGCAGC 1323  
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SBJCT: 481 CCAAGGTGACCACCATCCACATGGGCAATTACACCTGCCATGCTTCCGGCCACGAGCAGC 540

QUERY: 1324 TGTTCAGACCCACGTCCTGCAGGTGAATGTGCCGCCAGTCATCCGTGTCTATCCAGAGA 1383  
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SBJCT: 541 TGTTCAGACCCACGTCCTGCAGGTGAATGTGCCGCCAGTCATCCGTGTCTATCCAGAGA 600

QUERY: 1384 GCCAGGCACAGGAGCCTGGAGTGGCAGCCAGCCTAAGATGCCATGCTGAGGGCATTCCCA 1443  
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SBJCT: 601 GCCAGGCACAGGAGCCTGGAGTGGCAGCCAGCCTAAGATGCCATGCTGAGGGCATTCCCA 660

QUERY: 1444 TGCCCAGAATCACTTGGCTGAAAAACGGCGTGGATGTCTCAACTCAGATGTCCAAACAGC 1503  
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SBJCT: 661 TGCCCAGAATCACTTGGCTGAAAAACGGCGTGGATGTCTCAACTCAGATGTCCAAACAGC 720

QUERY: 1504 TCTCCCTTTTAGCCAATGGGAGCGAACTCCACATCAGCAGTGTTCGGTATGAAGACACAG 1563  
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SBJCT: 721 TCTCCCTTTTAGCCAATGGGAGCGAACTCCACATCAGCAGTGTTCGGTATGAAGACACAG 780

QUERY: 1564 GGGCATAACCTGCATTGCCAAAAATGAAGTGGGTGTGGATGAAGATATCTCCTCGCTCT 1623  
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SBJCT: 781 GGGCATAACCTGCATTGCCAAAAATGAAGTGGGTGTGGATGAAGATATCTCCTCGCTCT 840

QUERY: 1624 TCATTGAAGACTCAGCTAGAAAGACCCTTGCAAACATCCTGTGGCGAGAGGAAGGCCTCA 1683  
|||||

SBJCT: 841 TCATTGAAGACTCAGCTAGAAAGACCCTTGCAAACATCCTGTGGCGAGAGGAAGGCCTCA 900

QUERY: 1684 GCGTGGGAAACATGTTCTATGTCTTCTCCGACGACGGTATCATCGTCATCCATCCTGTGG 1743  
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SBJCT: 901 GCGTGGGAAACATGTTCTATGTCTTCTCCGACGACGGTATCATCGTCATCCATCCTGTGG 960

QUERY: 1744 ACTGTGAGATCCAGAGGCACCTCAAACCCACGGAAAAGATTTTCATGAGCTATGAAGAAA 1803  
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SBJCT: 961 ACTGTGAGATCCAGAGGCACCTCAAACCCACGGAAAAGATTTTCATGAGCTATGAAGAAA 1020

QUERY: 1804 TCTGTCTCTCAAAGAGNNNNNNNTGCAACCCAGCCCTGCCAGTGGGTATCTGCAGTCAATG 1863  
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SBJCT: 1021 TCTGTCTCTCAAAGAGAAAAAATGCAACCCAGCCCTGCCAGTGGGTATCTGCAGTCAATG 1080

QUERY: 1864 TCCGGAACCGGTACATCTATGTGGCCCAGCCAGCACTGAGCAGAGTCCTTGTGGTTCGACA 1923  
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SBJCT: 1081 TCCGGAACCGGTACATCTATGTGGCCCAGCCAGCACTGAGCAGAGTCCTTGTGGTTCGACA 1140

QUERY: 1924 TCCAAGCCCAGAAAGTCCTACAGTCCATAGGTGTGGACCCTCTGCCGGCTAAGCTGTCCT 1983  
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SBJCT: 1141 TCCAAGCCCAGAAAGTCCTACAGTCCATAGGTGTGGACCCTCTGCCGGCTAAGCTGTCCT 1200

QUERY: 1984 ATGACAAGTCACATGACCAAGTGTGGGTCTGAGCTGGGGGGACGTGCACAAGTCCCGAC 2043  
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SBJCT: 1201 ATGACAAGTCACATGACCAAGTGTGGGTCTGAGCTGGGGGGACGTGCACAAGTCCCGAC 1260

QUERY: 2044 CAAGTCTCCAGGTGATCACAGAAGCCAGCACCAGCCAGAGCCAGCACCTCATCCGCACAC 2103  
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SBJCT: 1261 CAAGTCTCCAGGTGATCACAGAAGCCAGCACCAGCCAGAGCCAGCACCTCATCCGCACAC 1320

QUERY: 2104 CCTTTGCAGGAGTGGATGATTTCTTCATTCCCCCAACAAACCTCATCATCAACCACATCA 2163  
|||||

SBJCT: 1321 CCTTTGCAGGAGTGGATGATTTCTTCATTCCCCCAACAAACCTCATCATCAACCACATCA 1380

QUERY: 2164 GGTTTGGCTTCATCTTCAACAAGTCTGATCCTGCAGTCCACAAGGTGGACCTGGAAACAA 2223  
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SBJCT: 1381 GGTTTGGCTTCATCTTCAACAAGTCTGATCCTGCAGTCCACAAGGTGGACCTGGAAACAA 1440

QUERY: 2224 TGATGCCCCCTCAAGACCATCGGCCTGCACCACCATGGCTGCGTGCCCCAGGCCATGGCAC 2283  
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SBJCT: 1441 TGATGCCCCCTCAAGACCATCGGCCTGCACCACCATGGCTGCGTGCCCCAGGCCATGGCAC 1500

QUERY: 2284 ACACCCACCTGGGCGGCTACTTCTTCATCCAGTGCCGACAGGACAGCCCCGCCTCTGCTG 2343  
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 SBJCT: 1501 ACACCCACCTGGGCGGCTACTTCTTCATCCAGTGCCGACAGGACAGCCCCGCCTCTGCTG 1560

5 QUERY: 2344 CCCGACAGCTGCTCGTTGACAGTGTACAGACTCTGTGCTTGGCCCCAATGGTGATGTAA 2403  
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 SBJCT: 1561 CCCGACAGCTGCTCGTTGACAGTGTACAGACTCTGTGCTTGGCCCCAATGGTGATGTAA 1620

10 QUERY: 2404 CAGGCACCCACACACATCCCCGACGGGCGCTTCATAGTCAGTGCTGCAGCTGACAGCC 2463  
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 SBJCT: 1621 CAGGCACCCACACACATCCCCGACGGGCGCTTCATAGTCAGTGCTGCAGCTGACAGCC 1680

15 QUERY: 2464 CCTGGCTGCACGTGCAGGAGATCACAGTGCAGGGCGAGATCCAGACCCTGTATGACCTGC 2523  
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 SBJCT: 1681 CCTGGCTGCACGTGCAGGAGATCACAGTGCAGGGCGAGATCCAGACCCTGTATGACCTGC 1740

20 QUERY: 2524 AAATAAACTCGGGCATCTCAGACTTGGCCTTCCAGCGCTCCTTCACTGAAAGCAATCAAT 2583  
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 SBJCT: 1741 AAATAAACTCGGGCATCTCAGACTTGGCCTTCCAGCGCTCCTTCACTGAAAGCAATCAAT 1800

25 QUERY: 2584 ACAACATCTACGCGGCTCTGCACACGGAGCCGGACCTGCTGTTCTGGAGCTGTCCACGG 2643  
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 SBJCT: 1801 ACAACATCTACGCGGCTCTGCACACGGAGCCGGACCTGCTGTTCTGGAGCTGTCCACGG 1860

30 QUERY: 2644 GGAAGGTGGGCATGCTGAAGAACTTAAAGGAGCCACCCGAGGGCCAGCTCAGCCCTNNN 2703  
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 SBJCT: 1861 GGAAGGTGGGCATGCTGAAGAACTTAAAGGAGCCACCCGAGGGCCAGCTCAGCCCTGGG 1920

35 QUERY: 2704 NNNNTACCCACAGAATCATGAGGGACAGTGGGCTGTTTGGACAGTACCTCCTCACACCAG 2763  
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 SBJCT: 1921 GGGGTACCCACAGAATCATGAGGGACAGTGGGCTGTTTGGACAGTACCTCCTCACACCAG 1980

40 QUERY: 2764 CCCGAGAGTCACTGTTCTCATCAATGGGAGACAAAACACGCTGCGGTGTGAGGTGTCAG 2823  
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 SBJCT: 1981 CCCGAGAGTCACTGTTCTCATCAATGGGAGACAAAACACGCTGCGGTGTGAGGTGTCAG 2040

45 QUERY: 2824 GTATAAANNNNNNNACCACAGTGGTGTGGGTGGGTGAGGTATGAAGGGCCCAGAGCAGAG 2883  
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 SBJCT: 2041 GTATAAAGGGGGGGACCACAGTGGTGTGGGTGGGTGAGGTATGAAGGGCCCAGAGCAGAG 2100

50 QUERY: 2884 CCCTGGGCCAAGGAACACCCCCTAGTCCTGACACTGCAGCCTCAAGCAGGTACGCTGTAC 2943  
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 SBJCT: 2101 CCCTGGGCCAAGGAACACCCCCTAGTCCTGACACTGCAGCCTCAAGCAGGTACGCTGTAC 2160

55 QUERY: 2944 ATTTTACAGACAAAAGCAAAAACCTGTACTCGCTTTGTGGTTCAACACTGGTCTCCTTG 3003  
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 SBJCT: 2161 ATTTTACAGACAAAAGCAAAAACCTGTACTCGCTTTGTGGTTCAACACTGGTCTCCTTG 2220

60 QUERY: 3004 CAAGTTTCCTAGTATAAGGTATGCGCTGCTACCAAGATTGGGGTTTTTTCGTTAGGAAGT 3063  
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 SBJCT: 2221 CAAGTTTCCTAGTATAAGGTATGCGCTGCTACCAAGATTGGGGTTTTTTCGTTAGGAAGT 2280

65 QUERY: 3064 ATGATTTATGCCTTGAGCTACGATGAGAACATATGCTGCTGTGTAAAGGGATCATTTCTG 3123  
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 SBJCT: 2281 ATGATTTATGCCTTGAGCTACGATGAGAACATATGCTGCTGTGTAAAGGGATCATTTCTG 2340

70 QUERY: 3124 TGCCAAGCTGCACACCGAGTGACCTGGGGACATCATGGAACCAAGGGATCCTGCTCTCCA 3183  
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 SBJCT: 2341 TGCCAAGCTGCACACCGAGTGACCTGGGGACATCATGGAACCAAGGGATCCTGCTCTCCA 2400

75 QUERY: 3184 AGCAGACACCTCTGTGAGTTGCCTTCACATAGTCATTGTCCCTTACTGCCAGACCCAGCC 3243  
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 SBJCT: 2401 AGCAGACACCTCTGTGAGTTGCCTTCACATAGTCATTGTCCCTTACTGCCAGACCCAGCC 2460

80 QUERY: 3244 AGACTTTGCCCTGACGGAGTGGCCCGGAAGCAGAGGCCGACCAGGAGCAGGGGCCTCCCT 3303  
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 SBJCT: 2461 AGACTTTGCCCTGACGGAGTGGCCCGGAAGCAGAGGCCGACCAGGAGCAGGGGCCTCCCT 2520

85 QUERY: 3304 CCCGAACTGAAAGCCCATCCGTCTCGCGTGGGACCGCATCTTCTCCCTCGCAGCTGCTT 3363  
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SBJCT: 2521 CCCGAAGTCAAAGCCCATCCGTCCTCGCGTGGGACCGCATCTTCTCCCTCGCAGCTGCTT 2580  
 QUERY: 3364 CTTGCTTTTCTTTCCATTTGACTTGCTGTAAGCCTGAGGGAGAGCCAACAAGACTTACTG 3423  
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 5 SBJCT: 2581 CTTGCTTTTCTTTCCATTTGACTTGCTGTAAGCCTGAGGGAGAGCCAACAAGACTTACTG 2640  
 QUERY: 3424 CATCTTGGGGGATGGGGAAATCACTCACTTTATTTTGGAAATTTTGGATTNNNNNNNNNT 3483  
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 10 SBJCT: 2641 CATCTTGGGGGATGGGGAAATCACTCACTTTATTTTGGAAATTTTGGATTAAAAAAAAT 2700  
 QUERY: 3484 TTTATAATCTCAAATGCTAGTAAGCAGAAAGATGCTCTCCGAGGTCCAACCTATATCCTTC 3543  
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 SBJCT: 2701 TTTATAATCTCAAATGCTAGTAAGCAGAAAGATGCTCTCCGAGGTCCAACCTATATCCTTC 2760  
 QUERY: 3544 CCTGCCTTAGGCCGAGTCTCGGGGGTGGTCACAACCCACATCCACAGCCAGAAAGAAC 3603  
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 15 SBJCT: 2761 CCTGCCTTAGGCCGAGTCTCGGGGGTGGTCACAACCCACATCCACAGCCAGAAAGAAC 2820  
 QUERY: 3604 AATGGTCATCTGAGAATACTGGCCCTGTGCGACTATTGCCACCCTGCTTCTCCAAGAGCAG 3663  
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 20 SBJCT: 2821 AATGGTCATCTGAGAATACTGGCCCTGTGCGACTATTGCCACCCTGCTTCTCCAAGAGCAG 2880  
 QUERY: 3664 ACCAGGCCACCTCATCCGTAAGGACTCGGTTCTGTGTTGGGACCCCAAAAACCAGAACA 3723  
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 25 SBJCT: 2881 ACCAGGCCACCTCATCCGTAAGGACTCGGTTCTGTGTTGGGACCCCAAAAACCAGAACA 2940  
 QUERY: 3724 AGTTCTGTGTGCCTCCTTTTCAGCACAGAAGGGAGACATCTCATTAGTCAGGTCTGGTACC 3783  
 |||||||||||||||||||||||||||||||||||||||||||||||||||||  
 30 SBJCT: 2941 AGTTCTGTGTGCCTCCTTTTCAGCACAGAAGGGAGACATCTCATTAGTCAGGTCTGGTACC 3000  
 QUERY: 3784 CCAGATTCAGGGCAGACTGGGCTTGCTGCGCAAGGTATGGGTGGCCTCCAGGCTCAATGC 3843  
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 SBJCT: 3001 CCAGATTCAGGGCAGACTGGGCTTGCTGCGCAAGGTATGGGTGGCCTCCAGGCTCAATGC 3060  
 QUERY: 3844 AGAAACCCCAAGGACACGAGTGGGGCCAGGTGAGTTCCTGAAGCTATACCTTTTCAAAAC 3903  
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 35 SBJCT: 3061 AGAAACCCCAAGGACACGAGTGGGGCCAGGTGAGTTCCTGAAGCTATACCTTTTCAAAAC 3120  
 QUERY: 3904 AGATTTTGTTCCTACCTGTGGCCCATCCACTCCTCTCTGGTACCCCATCCCCGCATCA 3963  
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 40 SBJCT: 3121 AGATTTTGTTCCTACCTGTGGCCCATCCACTCCTCTCTGGTACCCCATCCCCGCATCA 3180  
 QUERY: 3964 GCACTGCAGAGAGAACACATTTTCGGCGAGGGTTTCTTACCCACATTCCCAATCAATAC 4023  
 |||||||||||||||||||||||||||||||||||||||||||||||||||||  
 45 SBJCT: 3181 GCACTGCAGAGAGAACACATTTTCGGCGAGGGTTTCTTACCCACATTCCCAATCAATAC 3240  
 QUERY: 4024 ACACACACTGCAGAACCCAGAACAGAAGGCCACAGGCTGGCACTACTGCATTCTCCTTAT 4083  
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 50 SBJCT: 3241 ACACACACTGCAGAACCCAGAACAGAAGGCCACAGGCTGGCACTACTGCATTCTCCTTAT 3300  
 QUERY: 4084 GTGTCTCAGGCTGTGGTGACTCTCACATGGGCATCGAAGAAGTACAACCCACATAGCCCT 4143  
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 SBJCT: 3301 GTGTCTCAGGCTGTGGTGACTCTCACATGGGCATCGAAGAAGTACAACCCACATAGCCCT 3360  
 QUERY: 4144 CTGGAGACCGCCTAGATCAGAGACTCAGCAAAAACAGGCTCGCCTTCCCTCTCCACATA 4203  
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 55 SBJCT: 3361 CTGGAGACCGCCTAGATCAGAGACTCAGCAAAAACAGGCTCGCCTTCCCTCTCCACATA 3420  
 QUERY: 4204 TGAGTGGAACCTACATGTGTCCTGGTTTGAATGATCATTTTGCAAGCCACACGGGTGGG 4263  
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 60 SBJCT: 3421 TGAGTGGAACCTACATGTGTCCTGGTTTGAATGATCATTTTGCAAGCCACACGGGTGGG 3480  
 QUERY: 4264 AGAGGTGGTCTCACCACAGACGTCTTTGCTAATTTGGCCACCTTCACCTACTGACATGAC 4323  
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 65 SBJCT: 3481 AGAGGTGGTCTCACCACAGACGTCTTTGCTAATTTGGCCACCTTCACCTACTGACATGAC 3540  
 QUERY: 4324 CAGGATTTTCCTTTGCCATTAAGGAATGAACTCTTTCAAGGAGAGGAAACCCTAGACTCT 4383  
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 70 SBJCT: 3541 CAGGATTTTCCTTTGCCATTAAGGAATGAACTCTTTCAAGGAGAGGAAACCCTAGACTCT 3600

QUERY: 4384 GTGTCACTCTCAACACACACAGCTCCTTTCACTCCTGCCTGACTGCCAAGCCACCTGCAT 4443  
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SBJCT: 3601 GTGTCACTCTCAACACACACAGCTCCTTTCACTCCTGCCTGACTGCCAAGCCACCTGCAT 3660

5 QUERY: 4444 CCCCCGCCCCAGATCTCATGAGATCAATCACTTGTATGTCTCACGCAACTTGGTCCACCA 4503  
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SBJCT: 3661 CCCCCGCCCCAGATCTCATGAGATCAATCACTTGTATGTCTCACGCAACTTGGTCCACCA 3720

10 QUERY: 4504 AACGCCTGTCCCCTGTAACTCCTAGGGGTGCGCCTAGACAGGTACGTCTGTTTTTTATTT 4563  
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SBJCT: 3721 AACGCCTGTCCCCTGTAACTCCTAGGGGTGCGCCTAGACAGGTACGTCTGTTTTTTATTT 3780

15 QUERY: 4564 TAAAAGATATGCTATGTAGATATAAGTTGAGGAAGCTCACCTCAAAAGCCTAGAATGCAG 4623  
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SBJCT: 3781 TAAAAGATATGCTATGTAGATATAAGTTGAGGAAGCTCACCTCAAAAGCCTAGAATGCAG 3840

20 QUERY: 4624 TTTCACAGTAGCTGGGATGCATGGATGACCCATCTCACCCNNNNNNNNCCTGCCTCAA 4683  
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SBJCT: 3841 TTTCACAGTAGCTGGGATGCATGGATGACCCATCTCACCCCTTTTTTTTCTGCCTCAA 3900

25 QUERY: 4684 TATCTTGATATGTTATGTTTACTCCCAATCTCCATTTTTTACCCTAAAATTCTCCAAC 4743  
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SBJCT: 3901 TATCTTGATATGTTATGTTTACTCCCAATCTCCATTTTTTACCCTAAAATTCTCCAAC 3960

30 QUERY: 4744 TTCATAAACNNNNNNNNNGGAAAAATTTCCATTGTATCAGCCCCCTGACAGAAAAAGGATCT 4803  
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SBJCT: 3961 TTCATAAACCTTTTTTTTGGAAAAATTTCCATTGTATCAGCCCCCTGACAGAAAAAGGATCT 4020

35 QUERY: 4804 CTGAGCCTAAAGGAGGAAAAAGTCCCACCAACTACCAGACCAGAACACGAGCCCCTCTGGG 4863  
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SBJCT: 4021 CTGAGCCTAAAGGAGGAAAAAGTCCCACCAACTACCAGACCAGAACACGAGCCCCTCTGGG 4080

40 QUERY: 4864 CAGCAGGATTCTTAAGTCAAAGACCAGTTTGACCCAAACTGGCCTTTTAAAATAATCAGG 4923  
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SBJCT: 4081 CAGCAGGATTCTTAAGTCAAAGACCAGTTTGACCCAAACTGGCCTTTTAAAATAATCAGG 4140

45 QUERY: 4924 AGTGACAGAGTCAACTTCTGCAGCACCTGCTTCTCCCCACTGTCCCTTCCATCTTGGA 4983  
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SBJCT: 4141 AGTGACAGAGTCAACTTCTGCAGCACCTGCTTCTCCCCACTGTCCCTTCCATCTTGGA 4200

50 QUERY: 4984 TGTGTCTAAAAAAGCATAGCTGCCCTTTGCTGTCTCAGAGTGCATTTCTTGAGACGGC 5043  
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SBJCT: 4201 TGTGTCTAAAAAAGCATAGCTGCCCTTTGCTGTCTCAGAGTGCATTTCTTGAGACGGC 4260

55 QUERY: 5044 AGGCTTAGGTCTCACTGACAGCATGCCAGACACAACCTGAATCGAAGCAGGCCTGAAGCCT 5103  
|||||  
SBJCT: 4261 AGGCTTAGGTCTCACTGACAGCATGCCAGACACAACCTGAATCGAAGCAGGCCTGAAGCCT 4320

60 QUERY: 5104 AGGTCAGGGTTTCAGGAGTCCAGCCCCAGGAGGCAAAGTCACCAATGCAGGGAGGTAAAT 5163  
|||||  
SBJCT: 4321 AGGTCAGGGTTTCAGGAGTCCAGCCCCAGGAGGCAAAGTCACCAATGCAGGGAGGTAAAT 4380

65 QUERY: 5164 GCCTTTTGGCAGGAAAACCAATAGAGTTGGTTGGGTGGGGAGTCAGGGGTGGGAGGAGAA 5223  
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SBJCT: 4381 GCCTTTTGGCAGGAAAACCAATAGAGTTGGTTGGGTGGGGAGTCAGGGGTGGGAGGAGAA 4440

70 QUERY: 5224 GGAGGAAGAGGAGGAAGGCCAGACTGGCCTGCCCTTTCTCCCATACTTCACCCAGCAGA 5283  
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SBJCT: 4441 GGAGGAAGAGGAGGAAGGCCAGACTGGCCTGCCCTTTCTCCCATACTTCACCCAGCAGA 4500

75 QUERY: 5284 GGTTCATGGGACACAGTTGGAAAGCCACTGGGAGGAAATGCCTCACTACAGGGGGGCCTC 5343  
|||||  
SBJCT: 4501 GGTTCATGGGACACAGTTGGAAAGCCACTGGGAGGAAATGCCTCACTACAGGGGGGCCTC 4560

80 QUERY: 5344 CTGTAGCAAGCCCAGCCGGTAATCCTCCTAATGAACCCACAAGGTCAATTCACAACTGAT 5403  
|||||  
SBJCT: 4561 CTGTAGCAAGCCCAGCCGGTAATCCTCCTAATGAACCCACAAGGTCAATTCACAACTGAT 4620

85 QUERY: 5404 ATCTTAGCTATTAAAGAAGTACTGACTTTACCAAAAGAATCATCAAGAAAGCTATTTATA 5463  
|||||

5 SBJCT: 4621 ATCTTAGCTATTAAAGAAGTACTGACTTTACCAAAGAATCATCAAGAAAGCTATTTATA 4680

QUERY: 5464 TAAACCCCTCAGTCATTTTGAAATAAAATTAATTTTAC 5502

|||||

5 SBJCT: 4681 TAAACCCCTCAGTCATTTTGAAATAAAATTAATTTTAC 4719

The FCTR2 amino acid sequence has 473 of 810 amino acid residues (58%) identical to, and 616 of 810 residues (76%) positive with, the 850 amino acid residue proteins from *Homo sapiens* KIAA1263 Protein fragment (ptnr: TREMBLNEW-ACC:BAA86577) (SEQ ID NO:47) (Table 2D).

**Table 2D. BLASTP of FCTR2 against *Homo sapiens* KIAA1263 Protein fragment (SEQ ID NO:47)**

ptnr:TREMBLNEW-ACC:BAA86577 KIAA1263 PROTEIN - *Homo sapiens* (Human), 850 aa (fragment)

Length = 850

Score = 2573 (905.7 bits), Expect = 2.0e-267, P = 2.0e-267  
Identities = 473/810 (58%), Positives = 616/810 (76%)

20 QUERY: 10 LFRSLKRALSSCPDLFGLSSRNELLASCGKKFCSRGSRCVLSRKTGEPECQCLEACRPS 69

| || | + | ++ || | + | || | + | + | || | + | + |

5 SBJCT: 40 LMRLRHKEKNQESSRVKGFMIQDGFPGSCENKYCGLGRHCVTSRETGQAECACMDLCKRH 99

25 QUERY: 70 YVPVCGSDGRFYENHCKLHRAACLLGKRITVIHSDKDFLKGDTCTMAGYARLKNVLLALQ 129

| ||||| ||||| + + ||||| + + || + + || || | || + + || + || ||

5 SBJCT: 100 YKPVCSDGEFYENHCEVHRAACLLKQKITIVHNEDCFKGDCKKTTEYSKMNMLDLQ 159

30 QUERY: 130 TRLOPLQEGDSRQ-DPASQKRLLVESLFRDLADGNHLSSELAQHVLKKQDLDEDLIG 188

+ + || ++ | | + + || + + || || | + + || | + + + + | + ||

5 SBJCT: 160 NQKYIMQENENPNNGDDISRKLLVDQMFKYFDADSNGLVDINELTQ-VIKQEELGKDLFD 218

35 QUERY: 189 CSPGDLLRFDDYNSDSSLTLREFYMAFQVVQLSLAPEDRVSVTTVTVGLSTVLTCAVHGD 248

| + || + + || + + | | ||| ||| + ||| + + | | ||| | || + |

5 SBJCT: 219 CTLYVLLKYDDFNADKHLALEEFYRAFQVIQLSLPEDQKLSITAATVGQSAVLSCAIQGT 278

40 QUERY: 249 LRPPIIWKRNGLTLNFDLEDINDFGEDDSLYITKVTTIHMGNYTCHASGHEQLFQTHVL 308

||||| || + || ||||| ||| + ||||| ||| + ||||| ||| + ||||| ||| +

5 SBJCT: 279 LRPPIIWKRNIIILNLDLEDINDFGDDGSLYITKVTTTHVGNYTCYADGYEQVYQTHIF 338

45 QUERY: 309 QVNVPPVIRVYPESQAQEPGVAASLRCHAEGIPMPRITWLKNGVDVSTQMSKQLSLLANG 368

||||| ||||| + ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||

5 SBJCT: 339 QVNVPPVIRVYPESQAREPGVTASLRCHAEGIPKPQLGWLKNGIDITPKLSKQLTLQANG 398

50 QUERY: 369 SELHISSVRYEDTGAYTCIAKNEVGVEDISSLFIEDSARKTLANILWREEGLSVGNMFY 428

|| + || + ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||

5 SBJCT: 399 SEVHISNVRYEDTGAYTCIAKNEAGVEDISSLFVEDSARKTLANILWREEGLGIGNMFY 458

55 QUERY: 429 VFSDDGIIVIHFPVDCEIQRHLPTEKIFMSYEEICPQREKNATQPCQWVSAVNVRNRYIY 488

|| + |||| || + + || || + + || + + || + + || + + || + + || + + ||

5 SBJCT: 459 VFYEDGIKVIQPIECEFORHIKPSEKLLGFQDEVCPKAEGDEVQRCVWASAVNVKDKFIY 518

60 QUERY: 489 VAQPALSRVLVVDIQAQKVLSIGVDPLPAKLSYDKSHDQVWVLSWGDVHKSRLPSLQVIT 548

|||| | ||| + || + || + || + || + || + || ||||| ||||| ||||| |||||

5 SBJCT: 519 VAQPTLDRVLIVDVQSQKVVAQVSTDPVPVKLHYDKSHDQVWVLSWGTLEKTSPTLQVIT 578

65 QUERY: 549 EASTGQSQHILRT-----PEAGVDDFFIPPTNLIINHIFGFIENKSDPAVHKVDLETMM 603

|| | | | | ||||| | ||| | + |||| | + | + | + |||||

5 SBJCT: 579 LASGNVPHHTIHTQPVGKQFDRVDDFFIPTTTLIITHMRFGFILHKDEAALQKIDLETMS 638

70 QUERY: 604 PLKTIGLHHHGCVLPQAMATHLGGYFFIQCRQDSPASAAQQLLVDSVTDVSLGPNQDVTG 663

+ ||| | + |||| + || + ||||| + || | + || + + || + || ||||| + | ||||

5 SBJCT: 639 YIKTINLKDYKCVPSLAYTHLGGYFFIGCKPDSTGAVSPQVMVDGVTDVIGFNSDVTG 698

QUERY: 664 TPHTSPDGRFIVSAAADSPWLHVQEITVRGEIQTLYDLQINSGISDLAFQRFSTESNQYN 723  
 ||+ ||| ++|| + || ||+||| | |+ | ||||| |||++|||  
 SBJCT: 699 TPYVSPDGHYLVSIINDVKGLVRVQYITIRGEIQEAFDIYTNLHISDLAFQPSFTEAHQYN 758  
 5  
 QUERY: 724 IYAALHTEPDLLFLELSTGKVGMLKNLKEPPAGPAQPWGGTHRIMRDSGLFGQYLLTPAR 783  
 || + |+ |++|||+||| |++||| || |+|++|||++|||++  
 SBJCT: 759 IYGSSSTQTDVLFVELSSGKVKMIKSLKEPLKAEWPNRKNRQIQDSGLFGQYLMTPSK 818  
 10  
 QUERY: 784 ESLFLINGRQNTLRCEVSGIKGGTTVVWVGE 814  
 +|||+++|| | | ||++ ++ | ||+|||+  
 SBJCT: 819 DSLFILDGRNLNKLNCEITEVEKGNVTIVWVG 849

Amino acids 123-815 of FCTR2 also have 693 of 693 amino acid residues (100%)  
 15 identical to, the 693 amino acid residue protein fragment of KIAA1061 Protein from *Homo sapiens* (ptnr: TREMBLNEW-ACC: BAA83013) (SEQ ID NO:48) (Table 2E).

**Table 2E. BLASTP of FCTR2 against KIAA1061 Protein [Fragment] (SEQ ID NO:48)**

ptnr: TREMBLNEW-ACC: BAA83013 KIAA1061 PROTEIN - Homo sapiens (Human),  
 20 693 aa (fragment) .

Length = 693

Score = 3623 (1275.4 bits), Expect = 0.0, P = 0.0  
 Identities = 693/693 (100%), Positives = 693/693 (100%)

25  
 QUERY: 123 NVLLALQTRLQPLQEGDSRQDPASQKRLLVESLFRDLADGNHLSSELAQHVLKKQDL 182  
 |||||  
 SBJCT: 1 NVLLALQTRLQPLQEGDSRQDPASQKRLLVESLFRDLADGNHLSSELAQHVLKKQDL 60  
 30  
 QUERY: 183 DEDLLGCSPGDLLRFDDYNSDSSLTLREFYMAFQVVQLSLAPEDRVSVTTVTVGLSTVLT 242  
 |||||  
 SBJCT: 61 DEDLLGCSPGDLLRFDDYNSDSSLTLREFYMAFQVVQLSLAPEDRVSVTTVTVGLSTVLT 120  
 35  
 QUERY: 243 CAVHGDLRPPIIWKRNGLTNLFLDLEDINDFGEDDSLYITKVTTIHMGNYTCHASGHEQL 302  
 |||||  
 SBJCT: 121 CAVHGDLRPPIIWKRNGLTNLFLDLEDINDFGEDDSLYITKVTTIHMGNYTCHASGHEQL 180  
 40  
 QUERY: 303 FQTHVLQVNVPPVIRVYPESQAQEPGVAASLRCHAEGIPMPRITWLKNGVDVSTQMSKQL 362  
 |||||  
 SBJCT: 181 FQTHVLQVNVPPVIRVYPESQAQEPGVAASLRCHAEGIPMPRITWLKNGVDVSTQMSKQL 240  
 45  
 QUERY: 363 SLLANGSELHISSVRYEDTGAYTCIAKNEVGVEDISSLFIEDSARKTLANILWREEGLS 422  
 |||||  
 SBJCT: 241 SLLANGSELHISSVRYEDTGAYTCIAKNEVGVEDISSLFIEDSARKTLANILWREEGLS 300  
 50  
 QUERY: 423 VGNMFYVFSDDGIIVHPVDCEIQRHLKPTEKIFMSYEEICPQREKNATQPCQWVSAVNV 482  
 |||||  
 SBJCT: 301 VGNMFYVFSDDGIIVHPVDCEIQRHLKPTEKIFMSYEEICPQREKNATQPCQWVSAVNV 360  
 55  
 QUERY: 483 RNRYIYVAQPALSRLVVDIQAQKVLQSIGVDPLPAKLSYDKSHDQVWVLSWGDVHKSRLP 542  
 |||||  
 SBJCT: 361 RNRYIYVAQPALSRLVVDIQAQKVLQSIGVDPLPAKLSYDKSHDQVWVLSWGDVHKSRLP 420  
 60  
 QUERY: 543 SLQVITEASTGQSQHLIRTPFAGVDDEFFIPPTNLINHIRFGFIFNKSDPAVHKVDLETM 602  
 |||||  
 SBJCT: 421 SLQVITEASTGQSQHLIRTPFAGVDDEFFIPPTNLINHIRFGFIFNKSDPAVHKVDLETM 480  
 QUERY: 603 MPLKTIGLHHHGCVPQAMATHLGGYFFIQCRQDSPASAARQLLVDSVTDVSVLGPNGDVT 662  
 |||||  
 SBJCT: 481 MPLKTIGLHHHGCVPQAMATHLGGYFFIQCRQDSPASAARQLLVDSVTDVSVLGPNGDVT 540  
 QUERY: 663 GTPHTSPDGRFIVSAAADSPWLHVQEITVRGEIQTLYDLQINSGISDLAFQRFSTESNQY 722

SBJCT: 541 GTPHTSPDGRFIVSAAADSPWLHVQEITVRGEIQTLYDLQINSGISDLAFQRSFTESNQY 600  
 5 QUERY: 723 NIYAALHTEPDLLFLELSTGKVGMLKNLKEPPAGPAQPWGGTHRIMRDSGLFGQYLLTPA 782  
 SBJCT: 601 NIYAALHTEPDLLFLELSTGKVGMLKNLKEPPAGPAQPWGGTHRIMRDSGLFGQYLLTPA 660  
 QUERY: 783 RESLFLINGRQNTLRCEVSGIKGGTTVVWVGEV 815  
 10 SBJCT: 661 RESLFLINGRQNTLRCEVSGIKGGTTVVWVGEV 693

The amino acid sequence of the FCTR2 protein has 451 of 772 amino acid residues  
 (58%) identical to, and 586 of 772 residues (75%) positive with, the 773 amino acid residue  
 15 proteins hypothetical protein DKFZp566D234.1 from *Homo sapiens* (fragments) (ptnr:  
 SPTREMBL-ACC: CAB70877.1) (SEQ ID NO:49) (Table 2F).

**Table 2F. BLASTP of FCTR2 against hypothetical protein DKFZp566D234.1 (SEQ ID NO:49)**

20 >GI|11360192|PIR||T46283 HYPOTHETICAL PROTEIN DKFZP566D234.1 - HUMAN (FRAGMENTS)  
 GI|6808053|EMBL|CAB70877.1| (AL137695) HYPOTHETICAL PROTEIN [HOMO SAPIENS]  
 LENGTH = 773  
 SCORE = 911 BITS (2354), EXPECT = 0.0  
 IDENTITIES = 451/772 (58%), POSITIVES = 586/772 (75%), GAPS = 7/772 (0%)  
 25 QUERY: 49 CVLSRKTGEPECQCLEACRPSYVPVCGSDGRFYENHCKLHRAACLKGKRTVIHSDKDCFL 108  
 || ||+||+ || ||+ ||+ || ||||| |||||++||| ||+||+||+|||  
 SBJCT: 2 CVTSRETGQAECACMDLCKRHYKPVCGSDGEFYENHCEVHRAACLKKQKITIVHNEDCFF 61  
 30 QUERY: 109 KGDTCTMAGYARLKNVLLALQTRLQPLQEGDSRQ-DPASQKRLLVESLFRDLADGNGHL 167  
 ||| | +++||+|| || + +|| ++ | |+|||+ |+ + ||| | +  
 SBJCT: 62 KGDKCKTTECSKMKNMLLDLQNRQYIMQENENPNNGDDISRKKLLVDQMFKYFDADSNDLV 121  
 35 QUERY: 168 SSSELAQHVLKKQDLDEDLGCSPGDLLRFDDYNSDSSLTLREFYMAFQVVQLSLAPEDR 227  
 +|| | |+|+++| +|| |+ ||++||+|| | | ||| |||+||| + +  
 SBJCT: 122 DINELTQ-VIKQEELGKDLFDCTLYVLLKYDDFNADKHLALEEFYRAFOVIQLSLPEDQK 180  
 QUERY: 228 XXXXXXXXXXXXXXXCAVHGDLRPPIIWKRNGLTNLFLELDEINDFGEDDSLYITKVTTI 287  
 ||+ | ||||| ||| + || | |||||+| ||||| |||  
 40 SBJCT: 181 LSITAATVGQSAVLSCAIQGTLRPPIIWKRNNIILNNGLEDINDFGDDGSLYITKVTTT 240  
 QUERY: 288 HMGNYTCHASGHEQLFQTHVLQVNVPPVIRVYPESQAQEPGVAASLRCHAEGIPMPRITW 347  
 |+|||+| |+|++|||+ ||||| |||||+||| ||||| |||+|||  
 45 SBJCT: 241 HVGNYTCYADGYEQVYQTHIFQVNVPPVIRVYPESQAREPGVTASLRCHAEGIPKPQLGW 300  
 QUERY: 348 LKNGVDVSTQMSKQLSLLANGSELHISVRYEDTGAYTCIAKNEVGVEDISSLFIEDSA 407  
 |||+||+ ++|||+| |||+|||+||| ||||| |||||+|||  
 SBJCT: 301 LKNGIDITPKLSKQLTLQANGSEVHISNVRYEDTGAYTCIAKNEAGVEDISSLFVEDSA 360  
 50 QUERY: 408 RKTLANILWREEGLSVGNMFYVFSDDGIIVIHVPDCEIQRHLKPTEKIFMSYEEICPQRE 467  
 ||||| ||||| +||| || ||+|| ||+||+||+ +||| |  
 SBJCT: 361 RKTLANILWREEGLGIGNMFYVYEDGIKVIQPIECEFRHIKPSKLLGFQDEVCPPIAE 420  
 55 QUERY: 468 KNATQPCQWVASVNVNRNRYIYVAQPALSRVLVVDIQAQKVLQSIGVDPLPAKLSYDKSHD 527  
 + | | | |||||++++||| | |||+||+||+||+ ||+ || |||||  
 SBJCT: 421 GDEVQRCVWASAVNVKDKFIYVAQPTLDRVLIVDVQSQKVVQAVSTDPVPVKLHYDKSHD 480  
 QUERY: 528 QVWVLSWGDVHKSRLSLQVITEASTGQSQHLIRT-----PFAGVDDFFIPPTNLIINHIR 582  
 ||||| || + |+|+||| || | | | ||||| | ||| |+|  
 60 SBJCT: 481 QVWVLSWGTEKTSPTLQVITLASGNVPHHTIHTQPVGKQFDRVDDFFIPTTTLIITHMR 540  
 QUERY: 583 FGFIFNKSDPAVHKVDLETMMPLKTIGLHHHGCVPAQMAHHLGGYFFIQCRQDSPASAA 642  
 ||| +| + |+|+||| +|| | + |||++|+|||+|| |+ || + +

5 SBJCT: 541 FGFILHKDEAALQKIDLETMSYIKTINLKDYKCVPOQLAYTHLGGYYFIGCKPDSTGAVS 600

QUERY: 643 RQLLVDSVTDVSLGPNVDVTGTPHTSPDGRFIVSAAADSPWLHVQEITVRGEIQTLYDLQ 702  
 |++|| | | | | | + | | | | | | + | | | | ++|| + | | | | + | | | | + | +

10 SBJCT: 601 PQVMVDGVTDSVIGFNSDVTGTPYVSPDGHYLVSINDVKGLVRVQYITIRGEIQEAFDIY 660

QUERY: 703 INSGISDLAFQRSFTESNQYNIYAALHTEPDLLFLELSTGKVGMLKNLKEPPAGPAQPWG 762  
 | | | | | | | | | | ++ | | | | + | + | + | + | | + | | | | | | | |

10 SBJCT: 661 TNLHISDLAFQPSFTEAHQYNIYGSSSTQTDVLFVELSSGKVMIKSLKEPLKAEWPN 720

QUERY: 763 GTHRIMRDSGLFGQYLLTPARESLFLINGRQNTLRCEVSGIKGGTTVVWVGE 814  
 + | ++ | | | | | | | | | | + | + | + | + | | | | + | + | + | + | + | + | +

15 SBJCT: 721 RKNRQIQDSGLFGQYLMTPSKDSLFLDGRNLNCEITEVEKGNTVIWVG 772

15 The amino acid sequence of the FCTR2 protein has 61 of 194 amino acid residues (31%) identical to, and 90 of 194 residues (45%) positive with, the 306 amino acid residue protein Follastatin-Related Protein 1 Precursor from *Rattus Norvegicus* (ptnr: GenBank Acc:Q62632) (SEQ ID NO:50) (Table 2G).

20 **Table 2G. BLASTP of FCTR2 against Follastatin-Related Protein 1 Precursor from *Rattus Norvegicus* (SEQ ID NO:50)**

>GI|2498392|SP|Q62632|FRP RAT FOLLISTATIN-RELATED PROTEIN 1 PRECURSOR  
 GI|1083669|PIR||S51361 FOLLISTATIN-RELATED PROTEIN PRECURSOR - RAT  
 GI|536900|GB|AAA66063.1| (U06864) FOLLISTATIN-RELATED PROTEIN PRECURSOR [RATTUS NORVEGICUS]

25 LENGTH = 306

SCORE = 86.4 BITS (213), EXPECT = 1E-15  
 IDENTITIES = 61/194 (31%), POSITIVES = 90/194 (45%), GAPS = 26/194 (13%)

30 QUERY: 38 CGKKFCSRGSRCVLSRKTGEPECQCLEACRPSYVPVCGSDGRFYENHCKLHRAACLLGKR 97  
 | | | | | | | | ++ | | | | | | + | + | | | | + | + | | | | | | | +  
 SBJCT: 29 CANVFCGAGRECAVTEK-GEPTCLCIEQCKPHKRPVCGSNGKTYLNHCELHRDACLTGSK 87

35 QUERY: 98 ITVIHSKDCFLKGD-----TCTMAGYARLKNVLLA-LQTRLQPLQEGDSRQDPASQK 148  
 | | + | | | | | | | | + ++ | + + | | | | |  
 SBJCT: 88 IQVDYDGHCKEKKSVSPSASPVCYQANRDELRRRIIQWLEAEIIP----DGWFSKGSNY 143

40 QUERY: 149 RLLVESLFRDLADGNGHLSSSELAQHVLK-----KQDLDEDLLGCSPGDLLRF 197  
 +++ | + | + | + | | | | + | + | + ++ | | | +  
 SBJCT: 144 SEILDKYFKSFD-NGDSHLDSSEFLKFVEQNETAVNITAYPNQENNKLLRGLCVDALIEL 202

45 QUERY: 198 DDYNSDSSLTLREF 211  
 | | + | + + | |  
 SBJCT: 203 SDENADWKLSFQEF 216

The amino acid sequence of the FCTR2 protein has 61 of 194 amino acid residues (31%) identical to, and 89 of 194 residues (45%) positive with, the 306 amino acid residue protein Follastatin-Related Protein 1 Precursor from *Mus musculus* (GenBank Acc:Q62356) (SEQ ID NO:51) (Table 2H).

50 **Table 2H. BLASTP of FCTR2 against Follastatin-Related Protein 1 Precursor from *Mus musculus* (SEQ ID NO:51)**

>GI|6679871|REF|NP\_032073.1| FOLLISTATIN-LIKE [MUS MUSCULUS]  
 GI|2498391|SP|Q62356|FRP MOUSE FOLLISTATIN-RELATED PROTEIN 1 PRECURSOR (TGF-BETA-INDUCIBLE PROTEIN TSC-36)

GI|481186|PIR||S38251 FOLLISTATIN-RELATED PROTEIN - MOUSE  
 GI|349006|GB|AAC37633.1| (M91380) TGF-BETA-INDUCIBLE PROTEIN [MUS MUSCULUS]  
 LENGTH = 306

5 SCORE = 85.2 BITS (210), EXPECT = 3E-15  
 IDENTITIES = 61/194 (31%), POSITIVES = 89/194 (45%), GAPS = 26/194 (13%)

10 QUERY: 38 CGKKFCSRGSRCVLSRKTGEPECQCLEACRPSYVPVCGSDGRFYENHCKLHRAACLLGKR 97  
 | | | | ++ | | | | | + | + | | | | + | | | + | | | | +  
 SBJCT: 29 CANVFCGAGRECAVTEK-GEPTCLCIEQCKPHKRPVCGSNGKTYLNHCELHRDACLTGSK 87

15 QUERY: 98 ITVIHSKDCFLKGD-----CTMAGYARLKNVLLA-LQTRLQPLQEGDSRQDPASQK 148  
 | | + | | | | | + | + | + + | | | |  
 SBJCT: 88 IQVDYDGHCKEKKSSASPSASPVVCYQANRDELRRRLIQWLEAEIIP-----DGWFSKGSNY 143

20 QUERY: 149 RLLVESLFRDLADGNGHLSSSELAQHVLKK-----QDLDEDLLGCSPGDLLRF 197  
 +++ | + | + | + | | | + | + | + + | +  
 SBJCT: 144 SEILDYFYSFD-NGDSHLDSSEFLKFVEQNETAINITTYADQENNKLLRSLCVDALIEL 202

20 QUERY: 198 DDYNSDSSLTLREF 211  
 | | + | + + | |  
 SBJCT: 203 SDENADWKLSFQEF 216

25 The amino acid sequence of the FCTR2 protein has 63 of 193 amino acid residues  
 (32%) identical to, and 89 of 193 residues (45%) positive with, the 299 amino acid residue  
 protein Follastatin-Related Protein from the African Clawed Frog (GenBank Acc:JG0187)  
 (SEQ ID NO:52) (Table 2I).

**Table 2I. BLASTP of FCTR2 against Follastatin-Related Protein from the African  
 Clawed Frog (SEQ ID NO:52)**

30 >GI|7512162|PIR||JG0187 FOLLISTATIN-RELATED PROTEIN - AFRICAN CLAWED FROG  
 LENGTH = 299

35 SCORE = 81.8 BITS (201), EXPECT = 3E-14  
 IDENTITIES = 63/193 (32%), POSITIVES = 89/193 (45%), GAPS = 25/193 (12%)

40 QUERY: 38 CGKKFCSRGSRCVLSRKTGEPECQCLEACRPSYVPVCGSDGRFYENHCKLHRAACLLGKR 97  
 | | | | ++ | | + | | + | + | | | | + | | | + | | | | +  
 SBJCT: 28 CANVFCGAGRECAVTEK-GDPTCDIECKSHKRPVCGSNGKTYLNHCELHRDACLTGSK 86

45 QUERY: 98 ITVIHSKDCFLK-GDT-----CTMAGYARL-KNVLLALQTRLQPLQEGDSRQDPASQK 148  
 | | + | | | | | + + + | + | | + | | | |  
 SBJCT: 87 IQVDYDGHCKEKTSDTPAAVPVACYQSDRDEMRRRVHVLQTEITP-----DGWFSKGSNDY 142

50 QUERY: 149 RLLVESLFRDLADGNGHLSSSELAQHVLKKQDL-----DED-----LLGCSPGDLLRFD 198  
 +++ | + | | + | | + | + | | + | | + | +  
 SBJCT: 143 SEILDYFYSFD-DGDSHLDSAELOSFLEQSQSTNITTYKDEETNRMLKSLCVEALIELS 201

50 QUERY: 199 DYNSSDSSLTLREF 211  
 | | + | | | |  
 SBJCT: 202 DENADWKLNKNEF 214

55 The amino acid sequence of the FCTR2 protein has 59 of 194 amino acid residues  
 (30%) identical to, and 90 of 194 residues (45%) positive with, the 308 amino acid residue  
 protein Follistatin-Related Protein 1 Precursor from *Homo sapiens* (GenBank Acc:Q12841)  
 (SEQ ID NO:53) (Table 2J).

**Table 2J. BLASTP of FCTR2 against Follistatin-Related Protein 1 Precursor from *Homo sapiens* (SEQ ID NO:53)**

5 >GI|5901956|REF|NP\_009016.1| FOLLISTATIN-LIKE 1 [HOMO SAPIENS]  
 GI|2498390|SP|Q12841|FRP HUMAN FOLLISTATIN-RELATED PROTEIN 1 PRECURSOR  
 GI|1082372|PIR||S51362 FOLLISTATIN-RELATED PROTEIN - HUMAN  
 GI|536898|GB|AAA66062.1| (U06863) FOLLISTATIN-RELATED PROTEIN PRECURSOR [HOMO  
 SAPIENS]  
 GI|3184393|DBJ|BAA28707.1| (D89937) FOLLISTATIN-RELATED PROTEIN (FRP) [HOMO  
 SAPIENS]  
 10 GI|12652619|GB|AAH00055.1|AAH00055 (BC000055) FOLLISTATIN-LIKE 1 [HOMO SAPIENS]  
 LENGTH = 308

SCORE = 82.9 BITS (204), EXPECT = 1E-14  
 IDENTITIES = 59/194 (30%), POSITIVES = 90/194 (45%), GAPS = 26/194 (13%)

15 QUERY: 38 CGKKFCSRGRSVCVLSRKTGEPECQCLEACRPSYVPVCGSDGRFYENHCKLHRAACLLGKR 97  
 | || | | ++ | || | | + | + | ||| + | + | ||| + || | | +  
 SBJCT: 31 CANVFCGAGRECAVTEK-GEPTCLCIEQCKPHKRPVCGSNGKTYLNHCELHRDACLTGSK 89

20 QUERY: 98 ITVIHSDKCFLKGD-----TCTMAGYARLKNVLLA-LQTRLQPLQEGDSRQDPASQK 148  
 | | + | | | + | + ++ | + + | | |  
 SBJCT: 90 IQVDYDGHCKEKKSVSPSASPVVCYQSNRDELRRRIIQWLEAEIIP----DGWFSKGSNY 145

25 QUERY: 149 RLLVESLFRDLADGNHGLSSSELAQHVLKK-----QDLDEDLGCSPGDLLRF 197  
 +++ |++ | ++ | || | + | + | + ++ | | | +  
 SBJCT: 146 SEILDKYFKNFD-NGDSRLDSSEFLKEVEQNETAINITTPDQENNKLLRGLCVDALIEL 204

QUERY: 198 DDYNSDSSLTLREF 211  
 | | + | + + |  
 30 SBJCT: 205 SDENADWKLSFQEF 218

The amino acid sequence of the FCTR2 protein has 35 of 69 amino acid residues (50%) identical to, and 45 of 69 residues (64%) positive with, the 315 amino acid residue Flik protein [*Gallus gallus*] (EMBL Acc:CAB42968.1) (SEQ ID NO:54) (Table 2K).

**Table 2K. BLASTP of FCTR2 against Flik protein [*Gallus gallus*] (SEQ ID NO:54)**

35 >GI|4837645|EMB|CAB42968.1| (AJ238977) FLIK PROTEIN [GALLUS GALLUS]  
 LENGTH = 315

40 SCORE = 79.8 BITS (196), EXPECT = 1E-13  
 IDENTITIES = 35/69 (50%), POSITIVES = 45/69 (64%), GAPS = 1/69 (1%)

45 QUERY: 38 CGKKFCSRGRSVCVLSRKTGEPECQCLEACRPSYVPVCGSDGRFYENHCKLHRAACLLGKR 97  
 | || || + | ++ | || | | + | + | ||| + | + | ||| + || | | +  
 SBJCT: 31 CANVFCGRGAECAVTEK-GEPTCLCIEQCKPHGRPVCGSNGKTYLNHCELHRDACLTGSK 89

QUERY: 98 ITVIHSDKC 106  
 | | + |  
 SBJCT: 90 IQVDYDGHK 98

50 The amino acid sequence of the FCTR2 protein has 49 of 152 amino acid residues (32%) identical to, and 65 of 152 residues (42%) positive with a 272-420 amino acid fragment and, 31 of 83 residues (37%) identical to and 44 of 83 residues (52%) positive with a 248-329 amino acid fragment, both of the 1375 amino acid residue Frazzled gene protein [*Drosophila melanogaster*] (GenBankAcc:T13822) (SEQ ID NO:55) (Table 2L).

**Table 2L. BLASTP of FCTR2 against Frazzled gene protein [*Drosophila melanogaster*]  
(SEQ ID NO:55)**

>GI|7511861|PIR|T13822 FRAZZLED GENE PROTEIN - FRUIT FLY (DROSOPHILA MELANOGASTER)  
GI|1621115|GB|AAC47314.1| (U71001) FRAZZLED [DROSOPHILA MELANOGASTER]  
LENGTH = 1375

SCORE = 69.4 BITS (169), EXPECT = 2E-10  
IDENTITIES = 49/152 (32%), POSITIVES = 65/152 (42%), GAPS = 4/152 (2%)

QUERY: 243 CAVHGDLRPPIIWKRNLTLNFDLEDINDFGEDDSLYITKVTTIHMGNYTCHASGH-EQ 301  
| +| +| | | |||+ |+| ||+ || |+ | ||| | || +  
SBJCT: 272 CVANGVPKPQIKWLRNGMDLDFNDLDSRFSIVGTGSLQISSAEDIDSGNYQCRASNTVDS 331

QUERY: 302 LFQTHVLQVNVPPVIRVYPESQAQEPGVAASLRCHAEGIPMPRITWLKNGVDVSTQMSKQ 361  
| +|| || |+ |+| | | | |||| ++ |  
SBJCT: 332 LDAQATVQVQEPKPKFIKAPKDTTAHEKDEPELKCDIWGKPKPVIRWLKNGDLITPNDYMQ 391

QUERY: 362 LSLLANGSELHISSVRYEDTGAYTCIAKNEVG 393

| +| | | + | | + |+ | |  
SBJCT: 392 ---LVDGHNLIKILGLLNSDAGMFQCVGTNAAG 420

SCORE = 52.9 BITS (126), EXPECT = 1E-05  
IDENTITIES = 31/83 (37%), POSITIVES = 44/83 (52%), GAPS = 2/83 (2%)

QUERY: 311 NVPPVIRVYPESQAQEPGVAASLRCHAEGIPMPRITWLKNGVDVS-TQMSKQLSLLANGS 369  
+| | | | + | +| | | |+| |+| ||+||+|+ + + |++ ||  
SBJCT: 248 SVAPSFLVGPSPKTVREGDVTLDLCVANGVPKPQIKWLRNGMDLDFNDLDSRFSIVGTGS 307

QUERY: 370 ELHISSVRYEDTGAYTCIAKNEV 392

| ||| |+| | | | | |  
SBJCT: 308 -LQISSAEDIDSGNYQCRASNTV 329

The amino acid sequence of the FCTR2 protein has 53 of 177 amino acid residues (29%) identical to, and 78 of 177 residues (43%) positive with a 366-539 amino acid fragment, 51 of 170 residues (30%) identical to and 74 of 170 residues (43%) positive with a 276-438 amino acid fragment, 46 of 165 amino acid residues (27%) identical to, and 74 of 165 amino acid residues positive with a 185-341 amino acid fragment, 48 of 167 amino acid residues (28%) identical to and 70 of 167 amino acid residues (41%) positive with a 77-243 amino acid fragment, and 28 of 84 amino acid residues (33%) and 37 of 84 amino acid residues positive with a 56-139 amino acid fragment all of the protein 1395 residue Roundabout 1 protein [*Drosophila melanogaster*] (GenBankAcc:AAC38849.1) (SEQ ID NO:56) (Table 2M).

**Table 2M. BLASTP of FCTR2 against Roundabout 1 protein [*Drosophila melanogaster*]  
(SEQ ID NO:56)**

>GI|2804782|GB|AAC38849.1| (AF040989) ROUNDABOUT 1 [DROSOPHILA MELANOGASTER]  
LENGTH = 1395

SCORE = 69.8 BITS (170), EXPECT = 1E-10  
IDENTITIES = 53/177 (29%), POSITIVES = 78/177 (43%), GAPS = 11/177 (6%)

QUERY: 243 CAVHGDLRPPIIWKRNL-TLNFDLEDINDF-GEDDSLYITKVTTIHMGNYTCHA---- 296  
| |+ | + | + |+| | + + | |+| || | | | |  
SBJCT: 366 CMASGNPPPSVFEWTKEGVSTLMFPNSSHGRQYVAADGTLQITDVRQEDEGYYVCSAFSVV 425

QUERY: 297 --SGHEQLFQTHVLQVNVPPVIRVYPESQAQEPGVAASLRCHAEGIPMPRITWLKNGVDV 354  
| | + |||++ | +| | |+| | | | | || | +| |

SBJCT: 426 DSSTVRVFLQVSSVDERPPPIIQIGPANQTLPKGSVATLPCRATGNPSPRIKWFHDGHAV 485  
 QUERY: 355 STQMSKQLSLLANGSELHISSVRYEDTGAYTCIAKNEVGVDDEDISSLFIEDSARKTL 411  
 | + |++ || | + ++ |++ || | | | ++ | + | + |  
 5 SBJCT: 486 --QAGNRYSTII-QGSSLRVDDLQLSDSGTYTCTASGERGETSWAATLTVEKPGSTSL 539  
 SCORE = 56.3 BITS (135), EXPECT = 1E-06  
 IDENTITIES = 51/170 (30%), POSITIVES = 74/170 (43%), GAPS = 12/170 (7%)  
 10 QUERY: 243 CAVHGDRLRPPIIWKRNGLTNLNFDLEDINDEGEDDSLYITKVTTIHMGNYTCHASGH-EQ 301  
 |++ | | | ++ |++ + ++ | + | | | + + | | | + |  
 SBJCT: 276 CSVGGDPPPKVLWKKEEGNIPVSRARILHD---EKSLEISNITPTDEGTYVCEAHNNVGQ 332  
 15 QUERY: 302 LEQTHVLQVNVPPVIRVYPESQAQEPGVAASLRCHAEGIPMPRITWLKNGVDVSTQM--- 358  
 + | | + | | | ++ | | | | | + | | | | | | |  
 SBJCT: 333 ISARASLIVHAPPNETKRPSNKKVGLNGVVQLPCMASGNPPPSVFWTKEG--VSTLMFPN 390  
 QUERY: 359 -SKQLSLLANGSELHISSVRYEDTGAYTCIAKNEVGVDDEDISSLFIEDSA 407  
 | + | | | + | | | | | + | | + |++ | +  
 20 SBJCT: 391 SSHGRQYVAADGTLQITDVRQEDEGYYVCSAFSV--VDSSTVRVFLQVSS 438  
 SCORE = 51.7 BITS (123), EXPECT = 3E-05  
 IDENTITIES = 46/165 (27%), POSITIVES = 74/165 (43%), GAPS = 20/165 (12%)  
 25 QUERY: 251 PPIIWKRNGLTNLNFDLEDINDEG-----EDDSLYITKVTTIHMGNYTCHASG----- 298  
 | + | | ++ | + | + | | + ++ | | + + | | | | | |  
 SBJCT: 185 PTLIWIKDGVPLD--DLKAMS-FGASSRVRIVDGGNLLISNVEPIDEGNYKCIAQNLVGT 241  
 30 QUERY: 299 HEQLFQTHVLQVNVPPVIRVYPESQAQEPGVAASLRCHAEGIPMPRITWLKNGVDVSTQM 358  
 | + ++ | | | | + | | | + | | | |++ | | ++  
 SBJCT: 242 RESSYAKLIVQVK--PYFMKEPKDQVMLYGQTATFHCSVGGDPPPKVLWKKEEGNIPVSR 299  
 QUERY: 359 SKQLSLLANGSELHISSVRYEDTGAYTCIAKNEVGVDDEDISSLFI 403  
 ++ + | + | |++ | | | | | | | + | | +  
 35 SBJCT: 300 AR---ILHDEKSLEISNITPTDEGTYVCEAHNNVGQISARASLIV 341  
 SCORE = 44.0 BITS (103), EXPECT = 0.007  
 IDENTITIES = 48/167 (28%), POSITIVES = 70/167 (41%), GAPS = 13/167 (7%)  
 40 QUERY: 243 CAVHGDRLRPPIIWKRNGLTNLNFDLEDINDEGEDDSLYITKVTTIHM----GNYTCHASG 298  
 | | | | | | ++ | ++ + + + | + | + + | | | |  
 SBJCT: 77 CKVEGKPEPTIEWFKDGEPVSTNEKKSHRVQFKDGALFFYRTMQGKKEQDGGEYWCVAKN 136  
 45 QUERY: 299 H-EQLFQTHV-LQVNV-PPVIRVYPESQAQEPGVAASLRCH-AEGIPMPRITWLKNGVDV 354  
 | | | | | | + | | | + | | | | + | | | | + | + | + | +  
 SBJCT: 137 RVGQAVSRHASLQIAVLRDDFRVEPKDTRVAKGETALLECGPPKGIPEPTLIWIKDGVPL 196  
 QUERY: 355 STQMSKQLSL-----LANGSELHISSVRYEDTGAYTCIAKNEVGVD 396  
 + + + | | | + | | | | | + | | |  
 50 SBJCT: 197 DDLKAMSFGASSRVRIVDGGNLLISNVEPIDEGNYKCIAQNLVGTRE 243  
 SCORE = 42.9 BITS (100), EXPECT = 0.014  
 IDENTITIES = 28/84 (33%), POSITIVES = 37/84 (43%), GAPS = 4/84 (4%)  
 55 QUERY: 314 PVIRVYPESQAQEPGVAASLRCHAEGIPMPRITWLKNGVDVSTQMSKQLSLLANGSELH- 372  
 | | + | + | + | | | | | | + | | | | + |  
 SBJCT: 56 PRIIEHPTDLVVKKNEPATLNCKVEGKPEPTIEWFKDGEPVSTNEKKSHRVQFKDGALFF 115  
 60 QUERY: 373 ---ISSVRYEDTGAYTCIAKNEVG 393  
 + + + | | | + | | | |  
 SBJCT: 116 YRTMQGKKEQDGGEYWCVAKNRVG 139

The amino acid sequence of the FCTR2 protein has 55 of 157 amino acid  
 residues (35%) identical to, and 75 of 157 residues (47%) positive with a 620-775 amino acid  
 65 fragment, 49 of 163 residues (30%) identical to and 71 of 163 residues (43%) positive with a

335-492 amino acid fragment, 32 of 85 amino acid residues (37%) identical to, and 48 of 85 amino acid residues (55%) positive with a 1305-1388 amino acid fragment, 37 of 143 amino acid residues (25%) identical to and 60 of 143 amino acid residues (41%) positive with a 183-319 amino acid fragment, 43 of 174 amino acid residues (24%) and 70 of 174 amino acid residues (39%) positive with a 711-884 amino acid fragment, and 46 of 165 residues (27%) identical to and 69 of 165 residues positive with a 831-884 amino acid fragment all of the protein 1395 residue Down Syndrome Cell Adhesion Molecule Precursor (CHD2) from *Homo Sapiens* (GenBankAcc:O60469) (SEQ ID NO:57) (Table 2N).

**Table 2N. BLASTP of FCTR2 against Down Syndrome Cell Adhesion Molecule Precursor (SEQ ID NO:57)**

```
>gi|12643619|sp|O60469|DSCA HUMAN DOWN SYNDROME CELL ADHESION MOLECULE PRECURSOR
(CHD2)
GI|6740013|GB|AAF27525.1|AF217525_1 (AF217525) DOWN SYNDROME CELL ADHESION MOLECULE
[HOMO SAPIENS]
      LENGTH = 2012

      SCORE = 70.6 BITS (172), EXPECT = 6E-11
      IDENTITIES = 55/157 (35%), POSITIVES = 75/157 (47%), GAPS = 7/157 (4%)

QUERY: 245 VHGDLRPPPIIWKRNGLTLNFLDLEDINDFGEDDSLYITKVTTIHMGNYTCHASGHEQLFQ 304
      | ||| | |+++| + |++ || | + ++ + | |||| | | +
SBJCT: 620 VSGDLPITITWQKGRPIPGSLGVTIDNIDFTSSLRISNLSLMHNGNYTCIARNEAAAVE 679

QUERY: 305 THV-LQVNVPPVIRVYPESQAQEPGVAASLRCHAEGIPMPRITW-LKNGVDVST----QM 358
      | | ||| | | | | | | || | + | | | | | +
SBJCT: 680 HQSQLIVRVPPKFVVQPRDQDGIYGKAVILNCSAEGYPVPTIVWKFSKGAGVPQFQPIAL 739

QUERY: 359 SKQLSLLANGSELHISSVRYEDTGAYTCIAKNEVGVD 395
      + ++ + | + || | | | | | + | | | | + | | |
SBJCT: 740 NGRIQVLSNGS-LLIKHVVEEDSGYYLCKVSNDVGAD 775

      SCORE = 50.6 BITS (120), EXPECT = 7E-05
      IDENTITIES = 49/163 (30%), POSITIVES = 71/163 (43%), GAPS = 16/163 (9%)

QUERY: 243 CAVHGDLRPPPIIWKRNGLTLNFLDLEDINDFGEDDSLYITKVTTIHMGNYTCHASGHEQL 302
      | + | | + | ||| || | | | ++ | + + | | | +
SBJCT: 335 CSVGTGTEDQELSWYRNGEILNPGKNVRITGINHEN-LIMDHMVKSDGGAYQCVRKDKLS 393

QUERY: 303 FQTH---VLQVNVPPVIRVYPESQAQEPGVAASLRCHAEGIPMPRITW-----LKNGV 352
      | + ||+ | + | + | | | | + + | + | ||| | | |
SBJCT: 394 AQDYVQVVLEDGTPKIISAFSE-KVVSAPAEVSLMCNVKGTPLPTITWTLDLDDPILKGG- 451

QUERY: 353 DVSTQMSKQLSLLAN-GSELHISSVRYEDTGAYTCIAKNEVG 394
      | ++ | + ++ | | | + ||| + | | | | | | | |
SBJCT: 452 --SHRISQMITSEGNVVSYLNISSSQVRDGGVYRCTANNSAGV 492

      SCORE = 47.9 BITS (113), EXPECT = 5E-04
      IDENTITIES = 32/85 (37%), POSITIVES = 48/85 (55%), GAPS = 6/85 (7%)

QUERY: 333 LRCHAEGIPMPRITWLK--NGVDVSTQMSKQLSLLANGSELHISSVRYEDTGAYTCIAKN 390
      | | | | | | + | + | | | + + | + + ||| + | + | + ||| |
SBJCT: 1305 LPCKAVGDPSPAVKWMKDSNGTSPSLVTIDGRRSIFSNGSFI-IRTVKAEDSGYYSIANN 1363

QUERY: 391 EVGVDEDISSLFIE---DSARKTLA 412
      | || | + | ++ | | | ++
SBJCT: 1364 NWGSDEIILNLQVQVPPDQPRLTVS 1388

      SCORE = 42.9 BITS (100), EXPECT = 0.015
      IDENTITIES = 37/143 (25%), POSITIVES = 60/143 (41%), GAPS = 6/143 (4%)
```

5  
 QUERY: 270 INDFGEDDSLYITKVTTIHMGNITCHASGHEQLFQTHVLQVNVPPVIRVYPESQAQEPGV 329  
 | | + | | + | | | + | | | + + |  
 SBJCT: 183 IKDVQNEEDGLYNYRCITRHRYTGETRQNSARLFVSD--PANSAPSILDGFDHRKAMAGQ 240

10  
 QUERY: 330 AASLRCHAEGIPMPRITWLKNGVDVSTQMSKQLSLLANGSELHISSVRYEDTGAYTCIAK 389  
 | | | | | | |||+ ++ ++| + | | | ++| |++| |  
 SBJCT: 241 RVELPCKALGHPEPDYRWLKD--NMPLELSGRFQKTVTG--LLIENIRPSDSGSYVCEVS 296

15  
 SCORE = 41.3 BITS (96), EXPECT = 0.047  
 IDENTITIES = 43/174 (24%), POSITIVES = 70/174 (39%), GAPS = 11/174 (6%)

20  
 QUERY: 243 CAVHGDRLRPPIIWK--RNGLTNLNFDLEDINDFGEDDSLYITKVTTIHMGNITCHASG 298  
 |+ | | |++| + | + | + || | | | | |  
 SBJCT: 711 CSAEGYPVPTIVWKFSGAGVPQFQPIALNGRIQVLSNGSLLIKHVVEEDSGYYLCKVSN 770

25  
 QUERY: 357 QMSKQLSLLANGSELHISSVRY-----EDTGAYTCIAKNEVGVEDISSLFIED 405  
 +|++ | | |++| |++| ++| | | | | | | |++  
 SBJCT: 831 EMARYLVSTKEVGEEVISTLQILPTVREDSGFFSCHAINS YGEDRGIIQLTVQE 884

30  
 SCORE = 40.6 BITS (94), EXPECT = 0.074  
 IDENTITIES = 46/165 (27%), POSITIVES = 69/165 (40%), GAPS = 7/165 (4%)

35  
 QUERY: 243 CAVHGDRLRPPIIWKRNGLTNLNFDLEDINDFGEDDSLYITKVTT-IHMGNITCHASGHEQ 301  
 | | | | | + | | + | + + | ++ | + | | | + |  
 SBJCT: 525 CRVIGYPYYSIKWYKNSNLLPFNHRQVA--FENNGTLKLSDVQKEVDEGEYTCNVLVQPQ 582

40  
 QUERY: 302 LFQTHVLQVN--VPPVIRVYPESQAQEPGVAASLRCHAEGIPMP-RITWLKNGVDVSTQM 358  
 | + + | | | | + + | | + | + | | | | + +  
 SBJCT: 583 LSTSQSVHVTVKVPPFIQPF-EFPFRSIGQRFVPCVVVSGDLPITITWQKDGRPIPGSL 641

40  
 QUERY: 359 SKQLSLLANGSELHISSVRYEDTGAYTCIAKNEVGVEDISSLFI 403  
 + + | | |++ | | | | | + | | | +  
 SBJCT: 642 GVTIDNIDFTSSLRISNLSLMHNGNYTCIARNEAAVEHQSQLIV 686

45 The amino acid sequence of the FCTR2 protein has 55 of 194 amino acid residues  
 (28%) identical to, and 86 of 194 residues (44%) positive with Limbic System-Associated  
 Membrane Protein Precursor (LSAMP) from *Homo sapiens* (SWISSPROT Acc:Q13449)  
 (SEQ ID NO:58) (Table 2O).

**Table 2O. BLASTP of FCTR2 against Limbic System-Associated Membrane Protein  
 Precursor (SEQ ID NO:58)**

50 PTNR:SWISSPROT-ACC:Q13449 LIMBIC SYSTEM-ASSOCIATED MEMBRANE PROTEIN  
 PRECURSOR (LSAMP) - HOMO SAPIENS (HUMAN), 338 AA.

LENGTH = 338

55 SCORE = 191 (67.2 BITS), EXPECT = 6.7E-12, P = 6.7E-12  
 IDENTITIES = 55/194 (28%), POSITIVES = 86/194 (44%)

The amino acid sequence of the FCTR2 protein has 68 of 190 amino acid residues  
 (35%) identical to, and 92 of 190 residues (48%) positive with Putative Neuronal Cell

Adhesion Molecule, Short Form from *Mus musculus* (SPTREMBL Acc:O70246) (SEQ ID NO:59) (Table 2P).

**Table 2P. BLASTP of FCCTR2 against Putative Neuronal Cell Adhesion Molecule, Short Form from *Mus musculus* (SEQ ID NO:59)**

5 PTNR:SPTREMBL-ACC:O70246 PUTATIVE NEURONAL CELL ADHESION MOLECULE (PUNC)  
(PUTATIVE NEURONAL CELL ADHESION MOLECULE, SHORT FORM) - MUS MUSCULUS  
(MOUSE), 793 AA  
LENGTH = 793

10 SCORE = 203 (71.5 BITS), EXPECT = 7.0E-12, SUM P(2) = 7.0E-12  
IDENTITIES = 68/190 (35%), POSITIVES = 92/190 (48%)

The amino acid sequence of the FCCTR2 protein has 58 of 199 amino acid residues (29%) identical to, and 91 of 199 residues (45%) positive with CHLAMP, G11-Isoform Precursor from *Gallus gallus* (SPTREMBL Acc: O02869) (SEQ ID NO:60) (Table 2Q).

**Table 2Q. BLASTP of FCCTR2 against CHLAMP, G11-Isoform Precursor from *Gallus gallus* (SEQ ID NO:60)**

20 PTNR:SPTREMBL-ACC:O02869 CHLAMP, G11-ISOFORM PRECURSOR - GALLUS GALLUS  
(CHICKEN), 350 AA.  
LENGTH = 350

SCORE = 191 (67.2 BITS), EXPECT = 7.7E-12, P = 7.7E-12  
IDENTITIES = 58/199 (29%), POSITIVES = 91/199 (45%)

25 The amino acid sequence of the FCCTR2 protein has 55 of 194 amino acid residues (28%) identical to, and 86 of 194 residues (44%) positive with Limbic System-Associated Membrane Protein Precursor (LSAMP) from *Rattus norvegicus* (SWISSPROT Acc:Q62813) (SEQ ID NO:61) (Table 2R).

**Table 2R. BLASTP of FCCTR2 against Limbic System-Associated Membrane Protein Precursor (LSAMP) from *Rattus norvegicus* (SEQ ID NO:61)**

30 PTNR:SWISSPROT-ACC:Q62813 LIMBIC SYSTEM-ASSOCIATED MEMBRANE PROTEIN  
PRECURSOR (LSAMP) - RATTUS NORVEGICUS (RAT), 338 AA.  
LENGTH = 338

35 SCORE = 188 (66.2 BITS), EXPECT = 1.5E-11, P = 1.5E-11  
IDENTITIES = 55/194 (28%), POSITIVES = 86/194 (44%)

40 FCCTR2 protein has similarity to cell adhesion molecules, follistatin, roundabout and frazzled (see BlastP results). These genes are involved in neuronal development and reproductive physiology. Frazzled encodes a *Drosophila* member of the DCC immunoglobulin subfamily and is required for CNS and motor axon guidance (Cell 87:197-204(1996)). Characterization of a rat C6 glioma-secreted follistatin-related protein (FRP) and

cloning and sequence of the human homologue is described in Eur. J. Biochem. 225:937-946(1994). This protein may modulate the action of some growth factors on cell proliferation and differentiation. FRP binds heparin. The follistatin-related protein is a secreted protein and has one follistatin-like domain. The cloning and early dorsal axial expression of Flik, a chick  
 5 follistatin-related gene and evidence for involvement in dorsalization/neural induction is presented in Dev. Biol. 178:327-342(1996). Roundabout controls axon crossing of the CNS midline and defines a novel subfamily of evolutionarily conserved guidance receptors, as shown in Cell 92:205-215(1998). cDNA cloning and structural analysis of the human limbic-system- associated membrane protein (LAMP) is described in Gene 170:189-195(1996).  
 10 LAMP, a protein of the OBCAM family that contains three immunoglobulin-like C2-type domains, mediates selective neuronal growth and axon targeting. LAMP contributes to the guidance of developing axons and remodeling of mature circuits in the limbic system. This protein is essential for normal growth of the hippocampal mossy fiber projection. LAMP is attached to the membrane by a GPI-Anchor. It is expressed on limbic neurons and fiber tracts  
 15 as well as in single layers of the superior colliculus, spinal chord and cerbellum. Characterization of the human full-length PTK7 cDNA encoding a receptor protein tyrosine kinase-like molecule closely related to chick KLG is disclosed in J. Biochem. 119:235-239(1996). Based upon homology, FCTR2 proteins and each homologous protein or peptide may share at least some activity.

#### 20 **Functions and therapeutic uses:**

The OMIM gene map has identified this region which the invention maps to (5q21-5q31) as associated with susceptibility to the following diseases (OMIM Ids are underlined):

- Allergy and asthma
- Hemangioma,
- 25 • capillary infantile Schistosoma mansoni infection, susceptibility/resistance to Spinocerebellar ataxia
- Bronchial asthma
- Plasmodium falciparum parasitemia,
- intensity of Corneal dystrophy, Groenouw type I, 121900; Corneal dystrophy, lattice type I, 122200;
- 30 • Reis-Bucklers corneal dystrophy; Corneal dystrophy, Avellino type Eosinophilia, familial Myelodysplastic syndrome;

- Myelogenous leukemia, Acute Cutis laxa, recessive, type I, Deafness, autosomal dominant nonsyndromic sensorineural, 1 Contractural arachnodactyly, Congenital Neonatal alloimmune thrombocytopenia;
- Glycoprotein Ia deficiency Male infertility;
- 5 • Charcot-Marie-Tooth neuropathy, Demyelinating Gardner syndrome ;
- Adenomatous polyposis coli;
- Colorectal cancer;
- Desmoid disease, hereditary, 135290;
- Turcot syndrome, 276300;
- 10 • Adenomatous polyposis coli, attenuated
- Colorectal cancer

Therefore the invention is implicated in at least all of the above mentioned diseases and may have therapeutic uses for these diseases.

15 This sequence has similarity to cell adhesion molecules, follistatin, roundabout and frazzled (see BlastP results). These genes are involved in neuronal development and reproductive physiology. Therefore the invention is also implicated in disorders such as or therapeutic uses for:

- Neurodegenerative disorders, nerve trauma, epilepsy, mental health conditions
- 20 • Tissue regeneration in vivo and in vitro

Female reproductive system disorders and pregnancy

### FCSTR3

FCSTR3, is an amino acid type II membrane, neurestin-like protein. The FCSTR3a  
 25 nucleic acid of 1430 nucleotides (also designated 10129612.0.118) is shown in Table 3A. An ORF was identified beginning with an ATG initiation codon at nucleotides 69-71 and ending with a TAG codon at nucleotides 1212-1214. A putative untranslated region upstream from the initiation codon and downstream from the termination codon is underlined in Table 3A, and the start and stop codons are in bold letters.

30 **Table 3A. FCSTR3a Nucleotide Sequence (SEQ ID NO:5)**

35 AAAAAAGGCGGGGGGTGGACTTAGCAGTGTAATTGAGACCGGTGGTAAGGATTGGAGCGAGCTAGAGATGCTGCACGCTGCTA  
ACAAGGGAAGGAAGCCTTCAGCTGAGGCAGGTCGTCCCATTCCACCTACATCCTCGCCTAGTCTCCTCCCATCTGCTCAGCTGC  
CTAGCTCCCATATCCTCCACAGTTAGCTGCCAGATGCCATTGCTAGACAGCAACACCTCCCATCAAATCATGGACACCAACC  
CTGATGAGGAATTCTCCCCAATTCATACCTGCTCAGAGCATGCTCAGGGCCCCAGCAAGCCTCCAGCAGTGGCCCTCCGAACC  
ACCACAGCCAGTCGACTCTGAGGCCCCCTCTCCACCCCCCTCACAACCACACGCTGTCCCATCACCCTCGTCCGCCAACTCCC  
TCAACAGGAACTCACTGACCAATCGGCGGAGTCAGATCCACGCCCCGGCCCCAGCGCCCAATGACCTGGCCACCACACAGAGT  
CCGTCAGCTTCAGGACAGCTGGGTGCTAAACAGCAACGTGCCACTGGAGACCCGGCACTTCCTCTTCAAGACCTCCTCGGGGA

GCACACCCCTTGTTTCAGCAGCTCTTCCCCGGGATACCCCTTTGACCTCAGGAACGGTTTACACGCCCCCGCCCCGCTGCTGCCCCA  
 GGAATACTTTCTCCAGGAAGGCTTTCAAGCTGAAGAAGCCCTCCAAATACTGCAGCTGGAAATGTGCTGCCCTCTCCGCCATTG  
 CCGCGGCCCTCCTCTTGCTATTTTGCTGGCGTATTTTCATAGTGCCCTGGTCTTGAAAAACAGCAGCATAGACAGTGGTGAAG  
 CAGAAGTTGGTCGGCGGGTAACACAAGAAGTCCACCAGGGGTGTTTTGGAGGTCACAAATTCACATCAGTCAGCCCCAGTTCT  
 5 TAAAGTTCAACATCTCCCTCGGGAAGGACGCTCTCTTTGGTGTTCACATAAGAAGAGGACTTCCACCATCTCATGCCCAGTATG  
 ACTTCATGGAACGTCTGGACGGGAAGGAGAAGTGGAGTGTGGTTGAGTCTCCAGGGAACGCCGGAGCATAACAGACCTTGGTTC  
 AGAATGAAGCCGTGTTTGTGCAGTACCTGGATGTGGGCCTGTGGCATCTGGCCTTCTACAATGATGGAAAAGACAAAGAGATGG  
 TTTCCTTCAATACTGTTGTCTAGATGGGACCATCTAGTTGCAGAAAAACAAGCTCAGGGCGCCCACTGATTTGACATTATGAT  
 10 TCAGTGCAGGACTGTCCACGTAACCTGCCATGGGAATGGTGAATGTGTGTCCGGGGTGTGTCACTGTTTCCAGGATTTCTAGGA  
 GCAGACTGTGCTAAGACCTTCCTGCCTTGACTTTCTGCAAGACAATCATTATAAAGCTGCTCTGTAAATACTAAAAAAA  
 CA

The FCTR3 polypeptide (SEQ ID NO:5) encoded by SEQ ID NO:5 is 381 amino acid residues and is presented using the one-letter code in Table 3B.

### 15 Table 3B. Encoded FCTR3a protein sequence (SEQ ID NO:6).

MLHAANKGRKPSAEAGRPIPPPTSSPSLLPSAQLPSSHNPPVSCQMPLLDSNTSHQIMDTNPDEEFSPNSYLLRACSGPQQASS  
 SGPPNHHSQSTLRPPLPPPHNHTLSHHHSSANS LNRS LNRRSQIHAPAPAPNDLATTPESVQLQDSWVLNSNVPLETRHFLF  
 KTSSGSTPLFSSSSPGYPLTSGTVYTPPPRLLPRNTFSRKAFLKPKSKYCSWKCAALSAIAAALLAILLAYFIVPWSLKNSS  
 20 IDSGEAEVGRRTQEVPPGVFWRQIHSQPQFLKENISLGKDALFGVYIRGLPPSHAQYDFMERLDGKEKWSVVE SPRERS  
 IQTLVQNEAVFVQYLDVGLWHLAFYNDGKDKEMVSENTVVLDTI

In an alternative embodiment, the 5' end of the FCTR3a nucleic acid could be extended as it is in the 9826bp FCTR3b (also referred to herein as 10129612.0.405) shown in Table 3C. An ORF was identified beginning with an ATG initiation codon at nucleotides 280-  
 25 282 and ending with a TAA codon at nucleotides 8479-8481. A putative untranslated region upstream from the initiation codon and downstream from the termination codon is underlined in Table 3C, and the start and stop codons are in bold letters. Italicized bases 1-201 refer to a variable 5' region that will be further discussed below.

### Table 3C. FCTR3b Nucleotide Sequence (SEQ ID NO:7)

30 TTTAAATCCTCATACCTTAAAGGAGATGTGTATATAAGGGAGTTGGAACCAGCATTAGATGAGTTGACAAAAATGCAGTT  
TCAGTTCTAGAGGTCTGGGAAGTCCAAGAACAAGGTGCTGGCAGATTGGATTCCCCGTGAGGGCTTTCTTCTGGCTTGA  
AGTTGGCTGCTTCTCTGCTGAGACTTCTCATGGCAGAGACTGAGGGTGGCAAAGTGACAAGTGCCAAACTCAGGCCTGA  
CTTTTCTGAAAACATCAGCATTCTGCCATATCTGGAATAATGGATGTAAAGGACCGGCGACACCGCTCTTTGACCAGAGG  
 35 ACGCTGTGGCAAAGAGTGTGCTACACAAGCTCCTCTCTGGACAGTGAGGACTGCCGGGTGCCACACAGAAATCCTACA  
 GCTCCAGTGAGACTCTGAAGGCCTATGACCATGACAGCAGGATGCACTATGGAAACCGAGTCACAGACCTCATCCACCGG  
 GAGTCAGATGAGTTTCTAGACAAGGAACCAACTTCACCCTTGCCGAAGTGGGCATCTGTGAGCCCTCCCCACACCGAAG  
 CGGCTACTGCTCCGACATGGGGATCCTTCACCAGGGCTACTCCCTTAGCACAGGGTCTGACGCCGACTCCGACACCGAGG  
 GAGGGATGTCTCCAGAACACGCCATCAGACTGTGGGGCAGAGGGATAAAATCCAGGCGCAGTTCCGGCCTGTCCAGTCGT  
 40 GAAAACTCGGCCCTTACCCTGACTGACTCTGACAACGAAACAAATCAGATGATGAGAACGGTCTGCCATTCCACCTAC  
 ATCCTCGCCTAGTCTCCTCCCATCTGCTCAGCTGCCTAGCTCCATAATCCTCCACAGTTAGCTGCCAGATGCCATTGC  
 TAGACAGCAACACCTCCCATCAAATCATGGACACCAACCCTGATGAGGAATTCTCCCCCAATTACATACCTGCTCAGAGCA  
 TGCTCAGGGCCCCAGCAAGCCTCCAGCAGTGGCCCTCCGAACCACACAGCCAGTCTGAGTCTGAGGCCCTCTCCCACC  
 CCTCACAACCACAGCTGTCCCATCACCCTCGTCCGCCAACTCCCTCAACAGGAACTCACTGACCAATCGGCGGAGTC  
 45 AGATCCACGCCCCGGCCCCAGCGCCCAATGACCTGGCCACCACACAGAGTCCGTTGAGCTTCAGGACAGCTGGGTGCTA  
 AACAGCAACGTGCCACTGGAGACCCGGCACTTCTCTTCAAGACCTCCTCGGGGAGCACACCCTTGTTGAGCAGCTCTTC  
 CCGGGGATACCCTTTGACCTCAGGAACGGTTTACACGCCCCCGCCCCGCTGCTGCCAGGAATACTTTCTCCAGGAAGG  
 CTTTCAAGCTGAAGAAGCCCTCCAAATACTGCAGCTGGAAATGTGCTGCCCTCTCCGCCATTGCCGCGGCCCTCCTCTTG  
 GCTATTTTGCTGGCGTATTTTCATAGTGCCCTGGTCTTGAAAAACAGCAGCATAGACAGTGGTGAAGCAGAAGTTGGTCG  
 50 GCGGGTAACACAAGAAGTCCCACCAGGGGTGTTTTGGAGGTCACAAATTCACATCAGTCAGCCCCAGTTCTTAAAGTTCA  
 ACATCTCCCTCGGGAAGGACGCTCTCTTTGGTGTTCACATAAGAAGAGGACTTCCACCATCTCATGCCCAGTATGACTTC  
 ATGGAACGTCTGGACGGGAAGGAGAAGTGGAGTGTGGTTGAGTCTCCAGGGAACGCCGGAGCATAACAGACCTTGGTTCA  
 GAATGAAGCCGTGTTTGTGCAGTACCTGGATGTGGGCCTGTGGCATCTGGCCTTCTACAATGATGGAAAAGACAAAGAGA  
 TGGTTTCTTCAATACTGTTGTCTAGATTAGTGCAGGACTGTCCACGTAACCTGCCATGGGAATGGTGAATGTGTGTCC  
 GGGGTGTGTCACTGTTTCCAGGATTTCTAGGAGCAGACTGTGCTAAAGCTGCCTGCCCTGTCTGTGCAGTGGGAATGG  
 55 ACAATATTCTAAAGGGACGTGCCAGTGCTACAGCGGCTGGAAAGGTGCAGAGTGCAGCGTGGCCATGAATCAGTGCATCG

ATCCTTCCTGCGGGGGCCACGGCTCCTGCATTGATGGGAACTGTGTCTGCTCTGCTGGCTACAAAGGCGAGCACTGTGAG  
 GAAGTTGATTGCTTGGATCCCACCTGCTCCAGCCACGGAGTCTGTGTGAATGGAGAATGCCTGTGCAGCCCTGGCTGGGG  
 TGGTCTGAACTGTGAGCTGGCGAGGGTCCAGTGCCAGACCACTGTCAGTGGGCATGGCACGTACCTGCCTGACACGGGCC  
 TCTGCAGCTGCGATCCCACTGGATGGGTCCCGACTGCTCTGTTGAAGTGTGCTCAGTAGACTGTGGCACTCACGGCGTC  
 5 TGCATCGGGGGAGCCTGCCGCTGTGAAGAGGGCTGGACAGGCGCAGCGTGTGACCAGCGCGTGTGCCACCCCCGCTGCAT  
 TGAGCACGGGACCTGTAAAGATGGCAAATGTGAATGCCGAGAGGGCTGGAATGGTGAACACTGCACCATTGGTAGGCAAA  
 CGGCAGGCACCGAAACAGATGGCTGCCCTGACTTGTGCAACGGTAACGGGAGATGCACACTGGGTGAGAACAGCTGGCAG  
 TGTGTCTGCCAGACCGGCTGGAGAGGGCCCCGGATGCAACGTTGCCATGGAACTTCCTGTGCTGATAACAAGGATAATGA  
 10 GGGAGATGGCCTGGTGGATTGTTTGGACCTGACTGCTGCCTGCAGTCAGCCTGTGAGAACAGCCTGCTCTGCCGGGGGT  
 CCGGGGACCACTGGACATCATTCAGCAGGGCCAGACGGATTGGCCCCGAGTGAAGTCTTCTATGACCGTATCAAGCTC  
 TTGGCAGGCAAGGATAGCACCCACATCATTCCTGGAGAGAACCCTTTCAACAGCAGCTTGGTTTCTCTCATCCGAGGCCA  
 AGTAGTAACACAGATGGAACCTCCCTGGTCGGTGTGAACGTGTCTTTTGTCAAGTACCCAAAATACGGCTACACCATCA  
 CCGCCAGGATGGCACGTTGACCTGATCGCAAATGGAGGTGCTTCCTTGACTCTACACTTTGAGCGAGCCCCGTTTCATG  
 15 AGCCAGGAGCGCACTGTGTGGCTGCCGTGGAACAGCTTTTACGCCATGGACACCCTGGTGATGAAGACCGAGGAGAACTC  
 CATCCCCAGCTGTGACCTCAGTGGCTTTGTCCGGCCTGATCCAATCATCATCTCCTCCCCACTGTCCACCTTCTTTAGTG  
 CTGCCCCCTGGGCAGAAATCCCATCGTGCCTGAGACCCAGGTTCTTCATGAAGAAATCGAGCTCCCTGGTTCCAATGTGAAA  
 CTTGCTATCTGAGCTCTAGAACTGCAGGGTACAAGTCACTGCTGAAGATCACCATGACCCAGTCCACAGTCCCCCTGAA  
 CCTCATTAGGGTTACCTGATGGTGGCTGTGAGGGGGCATCTCTCCAGAAGTCATTCCAGGCTTCTCCCAACCTGGCCT  
 20 CCACCTTCATCTGGGACAAGACAGATGCGTATGGCCAAAGGGTGATGGACTCTCAGATGCTGTTGTGTCTGTGCGGGTTT  
 GAATATGAGACCTGTCCCAGTCTAATTCTCTGGGAGAAAAGGACAGCCCTCCTTCAGGGATTTCGAGCTGGACCCCTCCAA  
 CCTCGGTGGCTGGTCCCTAGACAAACACCACATCCTCAATGTTAAAAGTGAATCCTACACAAAGGCACTGGGGAAAACC  
 AGTTCCTGACCCAGCAGCCTGCCATCATCACCAGCATCATGGGCAATGGTCCGCCCGGAGCATTTCTGTCCCAGCTGC  
 AACGGCCTTGCTGAAGGCAACAAGCTGCTGGCCCCAGTGGCTCTGGCTGTTGGAATCGATGGGAGCCTCTATGTGGGTGA  
 CTTCAATTACATCCGACGCATCTTTCCCTCTCGAAATGTGACCAGCATCTTGAGATTACGAAATAAAGAGTTTAAACATA  
 25 GCAACAACCCAGCACACAAGTACTACTTGGCAGTGGACCCCGTGTCCGGCTCGCTCTACGTGTCCGACACCAACAGCAGG  
 AGAATCTACCGCGTCAAGTCTCTGAGTGGAACCAAAGACCTGGCTGGGAATTCGGAAGTTGTGGCAGGGACGGGAGAGCA  
 GTGTCTACCCTTTGATGAAGCCCGCTGCGGGGATGGAGGGAAGGCCATAGATGCAACCCTGATGAGCCCGAGAGGTATTG  
 CAGTAGACAAGAATGGGCTCATGTACTTTGTGATGCCACCATGATCCGGAAGGTTGACCAGAATGGAATCATCTCCACC  
 CTGCTGGGCTCCAATGACCTCACTGCCGTCCGGCCGCTGAGCTGTGATTCCAGCATGGATGTAGCCAGGTTCTGTCTGGA  
 30 GTGGCCAAACAGACCTTGCTGTCAATCCCATGGATAACTCCTTGATGTTCTAGAGAAATGTATCCTTCGAATCACCG  
 AGAACCACCAAGTCAGCATCATTCGCGGACGCCCCATGCACTGCCAAGTTCTGGCATTGACTACTCACTCAGCAAATA  
 GCCATTCACTCTGCCCTGGAGTCAGCCAGTGCCATTGCCATTTCTCACACTGGGGTCTCTACATCACTGAGACAGATGA  
 GAAGAAGATTAACCGTCTACGCCAGGTAACAACCAACGGGGAGATCTGCCTTTTAGCTGGGGCAGCCTCGGACTGCGACT  
 GCAAAAACGATGTCAATTGCAACTGCTATTTCAGGAGATGATGCCCTACGCGACTGATGCCATCTTGAATTCCCCATCATCC  
 35 TTAGCTGTAGCTCCAGATGGTACCATTACATTGCAGACCTTGGAATATTTCGGATCAGGGCGGTGAGCAAGAACAAGCC  
 TGTTCTTAATGCCTTCAACCAGTATGAGGCTGCATCCCCCGGAGAGCAGGAGTTATATGTTTTCAACGCTGATGGCATCC  
 ACCAATACTGTGAGCCTGGTGACAGGGGAGTACTTGTACAATTTACATATAGTACTGACAATGATGTCACTGAATTG  
 ATTGACAATAATGGGAATTCCTGAAGATCCGTCCGGACAGCAGTGGCATGCCCCGTCACCTGCTCATGCCTGACAACCA  
 GATCATCACCCCTCACCGTGGGCACCAATGGAGGCCCTCAAAGTCGTGTCCACACAGAACCTGGAGCTTGGTCTCATGACCT  
 40 ATGATGGCAACACTGGGCTCCTGGCCACCAAGAGCGATGAAACAGGATGGACGACTTTCTATGACTATGACCACGAAGGC  
 CGCCTGACCAACGTGACGCGCCCCACGGGGGTGGTAACCAGTCTGCACCGGGAATGGAGAAATCTATTACCATTGACAT  
 TGAGAACTCCAACCGTGATGATGACGTCACTGTATCACCACCTCTCTTCAGTAGAGGCCCTCTACACAGTGGTACAAG  
 ATCAAGTTCGGAACAGCTACCAGCTCTGTAATAATGGTACCCTGAGGGTGATGTATGCTAATGGGATGGGTATCAGCTTC  
 CACAGCGAGCCCCATGTCTAGCGGGCACCATCACCCCCACCATTTGGACGCTGCAACATCTCCCTGCCTATGGAGAATGG  
 45 CTTAAACTCCATTGAGTGGCGCCTAAGAAAGGAACAGATTAAAGGCAAAGTCACCATCTTTGGCAGGAAGCTCCGGGTCC  
 ATGGAAGAAATCTCTTGTCCATTGACTATGATCGAAATATTTCGGACTGAAAAGATCTATGATGACCACCGGAAGTTCAAC  
 CTGAGGATCATTTATGACCAGGTGGGCGCCCCCTTCTCTGGCTGCCAGCAGCGGGCTGGCAGCTGTCAACGTGTCTATA  
 CTTCTTCAATGGGCGCCTGGCTGGGCTTCAGCGTGGGGCCATGAGCGAGAGGACAGACATCGACAAGCAAGGCCGCATCG  
 50 TGTCCCGCATGTTGCTGACGGGAAAGTGTGGAGTACTCCTACCTTGACAAGTCCATGGTCTCCTGCTTCAGAGCCAA  
 CGTCAGTATATATTGAGTATGACTCCTCTGACCGCCTCCTTGCCGTACCATGCCAGCGTGGCCCGGCACAGCATGTC  
 CACACACACCTCCATCGGCTACATCCGTAATATTTACAACCCGCTGAAAGCAATGCTTCGGTCATCTTTGACTACAGTG  
 ATGACGGCCGCATCCTGAAGACCTCCTTTTTTGGGCACCGGACGCCAGGTGTTCTACAAGTATGGGAACTCTCCAAGTTA  
 TCAGAGATTGTCTACGACAGTACCGCCGTACCTTCGGGTATGACGAGACCACTGGTGTCTTGAAGATGGTCAACCTCCA  
 AAGTGGGGGCTTCTCCTGCACCATCAGGTACCGGAAGATTGGCCCCCTGGTGGACAAGCAGATCTACAGGTTCTCCGAGG  
 55 AAGGCATGGTCAATGCCAGGTTTACTACACCTATCATGACAACAGCTTCCGCATCGCAAGCATCAAGCCCGTCATAAGT  
 GAGACTCCCCTCCCCGTTGACCTCTACCGCTATGATGAGATTTCTGGCAAGGTGGAACACTTTGGTAAGTTTGGAGTCAT  
 CTATTATGACATCAACCAGATCATCACCCTGCGGTGATGACCTCAGCAAACACTTCGACACCCATGGGCGGATCAAGG  
 AGGTCCAGTATGAGATGTTCCGGTCCCTCATGTACTGGATGACGGTGCAATATGACAGCATGGGCAGGGTGATCAAGAGG  
 GAGCTAAAACCTGGGGCCCTATGCCAATACCACGAAGTACACCTATGACTACGATGGGGACGGGCAGCTCCAGAGCGTGGC  
 60 CGTCAATGACCGCCGACCTGGCGCTACAGCTATGACCTTAATGGGAATCTCCACTTACTGAACCCAGGCAACAGTGTGC  
 GCCTCATGCCCTTGCGCTATGACCTCCGGGATCGGATAACCAGACTCGGGGATGTGCAGTACAAAATTGACGACGATGGC  
 TATCTGTGCCAGAGAGGGTCTGACATCTTCGAATAACAATTCCAAGGGCTCCTAACAAGAGCCTACAACAAGGCCAGCGG  
 GTGGAGTGTCCAGTACCGCTATGATGGCGTAGGACGGCGGGCTTCTACAAGACCAACCTGGGCCACCACCTGCAGTACT  
 TCTACTCTGACCTCCACAACCCGACGCGCATCACCCATGTCTACAATCACTCCAACCTCGGAGATTACCTCACTGTACTAC  
 65 GACCTCCAGGGCCACCTCTTTGCCATGGAGAGCAGCAGTGGGGAGGAGTACTATGTTGCCTCTGATAACACAGGGACTCC  
 TCTGGCTGTGTTGAGCATCAACGGCCTCATGATCAAACAGCTGCAGTACACGGCCTATGGGGAGATTTATTATGACTCCA  
 ACCCGACTTCCAGATGGTCATTGGCTTCCATGGGGGACTCTATGACCCCTGACCAAGCTGGTCCACTTCACTCAGCGT  
 GATTATGATGTGCTGGCAGGACGATGGACCTCCCCAGACTATACCATGTGGAAAAACGTGGGCAAGGAGCCGGCCCCCTT  
 70 TAACCTGTATATGTTCAAGAGCAACAATCCTCTCAGCAGTGAGCTAGATTTGAAGAACTACGTGACAGATGTGAAAAGCT  
 GGCTTGTGATGTTTGGATTTCAGCTTAGCAACATCATTCCTGGCTTCCCGAGAGCCAAAATGTATTTCTGTCCTCCTCCC

TATGAATTGTCAGAGAGTCAAGCAAGTGAGAATGGACAGCTCATTACAGGTGTCCAACAGACAACAGAGAGACATAACCA  
 GGCCTTCATGGCTCTGGAAGGACAGGTCACTACTAAAAAGCTCCACGCCAGCATCCGAGAGAAAGCAGGTCACTGGTTTG  
 CCACCACCACGCCCATCATTGGCAAAGGCATCATGTTTGCCATCAAAGAAGGGCGGGTGACCACGGGCGTGTCCAGCATC  
 5 GCCAGCGAAGATAGCCGCAAGGTGGCATCTGTGCTGAACAACGCCTACTACCTGGACAAGATGCACTACAGCATCGAGGG  
 CAAGGACACCCACTACTTTTGTGAAGATTGGCTCAGCCGATGGCGACCTGGTCACACTAGGCACCACCATCGGCCGCAAGG  
 TGCTAGAGAGCGGGGTGAACGTGACCGTGTCCCAGCCCACGCTGCTGGTCAACGGCAGGACTCGAAGGTTACGAACATT  
 GAGTTCAGTACTCCACGCTGCTGCTCAGCATCCGCTATGGCCTCACCCCGACACCTGGACGAAGAGAAGGCCCGCGT  
 CCTGGACCAGGCGAGACAGAGGGCCCTGGGCACGGCCTGGGCCAAGGAGCAGCAGAAAGCCAGGGACGGGAGAGAGGGGA  
 10 GCGCCTGTGGACTGAGGGCGAGAAGCAGCAGCTTCTGAGCACCGGGCGCGTGCAAGGGTACGAGGGATATTACGTGCTT  
 CCCGTGGAGCAATACCCAGAGCTTGCAGACAGTAGCAGCAACATCCAGTTTAAAGACAGAATGAGATGGGAAAGAGGTA  
 ACAAATAATCTGCTGCCATTCTTGTCTGAATGGCTCAGCAGGAGTAAGTGTATCTCCTCTCCTAAGGAGATGAAGAC  
 CTAACAGGGGCACTGCGGCTGGGCTGCTTTAGGAGACCAAGTGGCAAGAAAGCTCACATTTTTTGTAGTTCAAATGCTACT  
 GTCCAAGCGAGAAGTCCCTCATCCTGAAGTAGACTAAAGCCCGCTGAAAATTCGAGGAAAACAAAACAAACGAATGAA  
 15 TGAACAGACACACACAATGTTCCAAGTTCCTTAAATATGACCCACTTGTCTGGGTCTACGCAGAAAAGAGACGCAAA  
 GTGTCCAAAAGGAACAAAAGAACAAAACGAATAAGCAAAGAAGAAACAAAACAAAACAAAACAAACACACGGA  
 CCGATAAACAAAGAAGCGAAGATAAGAAAGAAGGCCTCATATCCAATTACCTCACTCATTACATGTGAGCGACACGCAG  
 ACATCCCGGAGGGCCAGCGTCACCAGACCAGCTGCGGGACAAACCACTCAGACTGCTTGTAGGACAAATACTTCTGACAT  
 TTTCTGTTTAAAGCAAATACAGCTGCATTTAAACACGACTTTGGGGGTGATTTGTGTGTAGCGCCTGGGGAGGGGGGATAA  
 20 AAGAGGAGGAGTGAGCACTGGAAATACTTTTTAAAGAAAAAAAACATGAGGGAATAAAGAAATTCCTATCAAAAATCA  
 AAGTGAAATAATACCATCCAGCACTTAAGTCTCAGGTCCCACTAAGTCTGGCCTGAGCTAATTTATTTGAGCGCAGAGT  
 GTAAAATTTAATTCAAATGGTGGCTATAATCACTACAGATAAATTTCACTACTCTTTTGTCTTTGGAGATTCCATTGTGG  
 ACAGTAATACGCAGTTACAGGGGTAGTCTGTTTAGATTCCGTAGTTCTGTTGGGTATCAGTTTCGGTAGAGGTGCAGCATC  
 GTGACACTTTTGTACAGGTACCACTTCTGATCACCTGTACATACATGAGCCGAAAGGCACAATCACTGTTTCAGATT  
 25 TAAATTTATTAGTGTGTTTGTGTTGGTCCAGAACTGAGACAATCACATGACAGTCACCACGAGGAGAGAAAATTTAAAAA  
 ATAAAAATAAAAAACAAAAAAATTTTAAAAATTAAAAAACAAAAATAAAGTCTAATAAGAACTTTGGTACAGGAATTT  
 TTTGTAATATACATGTATGAATTGTTTCATCGAGTTTATATTAATTTAATTTGCTGCTAAGCAAAGACTAGGGACAGG  
 CAAAGATAATTTATGGCAAAGTGTAAATTGTTTATACATAAATAAAGTCTCTAAACTCCTGTG

The FCTR3b polypeptide (SEQ ID NO:8) encoded by SEQ ID NO:7 is 2733 amino  
 30 acid residues and is presented using the one-letter code in Table 3D. The protein has a  
 predicted molecular weight of 303424.3 daltons.

**Table 3D. Encoded FCTR3b protein sequence (SEQ ID NO:8).**

MDVKDRRHRSLTRGRCGKECRYTSSSLDSEDCRVPTQKSYSSSETLKAYDHDSRMHYGNRVTDLIHRESDEFPRQGTNETLAEL  
 GICEPSPHRSGYCSMDGILHQYSLSTGSDADSDTEGGMSPEHAIRLWGRGIKSRSSGLSSRENSALTITDSDNENKSDDENG  
 35 RPIPTSSPSLLPSAQLPSSHNPVSCQMLLDSTSHQIMDTNPDEEFSPNSYLLRACSGPQQASSSGPPNHHSQSTLRPPL  
 PPPHNHTLSHHHSSANS LNRS LNRRSQIHAPAPAPNDLATTPESVQLQDSWVLNSNVPLETRHFLFKTSSGSTPLFSSSSPG  
 YPLTSGTVYTPPPRLLPRNTFSRKAFLKKPSKYCSWKCAALSAIAAALLAILLAYFIVPWSLKNSSIDSGEAEVGRVTVQEV  
 PPGVFWRSQIHISQPOFLKFNISLGKDALFGVYIRGLPPSHAQYDFMERLDGKEKWSVVEsprerrsiQTLVQNEAVFVQYLD  
 40 VGLWHLAFYNDGKDKEMVSENTVVLDSVQDCPRNCHNGECVSGVCHCFPGFLGADCAKAACPVLCSGNGQYSKGTCCQYSGWK  
 GAECDVPMNQCIDPSCGGHSGCIDGNCVCSAGYKGEHCEEVDCLDPTCSSHGVCVNGECLCSPGWGGLNCELARVQCPDQCSGH  
 GTYLPDTGLCSCDPNWMGPDCSVEVCSVDCGTHGVCIGGACRCEEGWTGAACDQRVCHPRCIEHGTCKDGKCECREGWNHEHCT  
 IGRQTAGTETDGCPLDLCNGNGRCTLGQNSWQCVCQTGWRGPGCNVAMETSCADNKDNEGDGLVDCLDPDCLQSACQNSLLCRG  
 SRDPLDI IQQGQTDWPAVKSFYDRIKLLAGKDSHTIIPGENPFNSLVSLIRGQVVTDDGTPLVGVNVSFVKYPKYGYTITRQD  
 45 GTFDLIANGGASLTLHFERAPFMSQERTVWLPWNSFYAMDTLVMKTEENSIPSCDLSGFVRPDPIIISSPLSTFFSAAPGQNPI  
 VPETQVLHEEIELPGSNVKLRYLSSRTAGYKSLKITMTQSTVPLNLRVHLMVAVEGHLFQKSFQASPNLASTFIWDKTDAYG  
 QRVYGLSDAVVSVGFYETCPSLILWEKRTALLQGFELDSPNLGGWSLDKHHILNVKSGILHKGTGENQFLTQOPAIITSIMGN  
 GRRRSISCPSCNGLAEGNKLLAPVALAVGIDGSLYVGDFNYIRRIIPSRNVT SILELRNKEFKHSNNPAHKYYLAVDPVSGSLY  
 VSDTNSRRIYRVKSLSGTKDLAGNSEVVAGTGEQCLPFDEARCGDGGKAIDATLMSPRGIAVDKNGLMYFVDATMIRKVDQNGI  
 50 ISTLLGSNDLTAVRPLSCDSSMDVAQVRLEWPTDLAVNPMDNSLYVLENNVILRITENHQVSIIAGRPMHCQVPGIDYSLSKLA  
 IHSALASASAIASHTGVLYITETDEKKINRLRQVTTNGEICLLAGAASDCDCKNDVNCNCYSGDDAYATDAILNSPSSLAVAP  
 DGTIYIADLGNIRIRAVSKNKPVLNAFNQYEAASPGEQELYVFNADGIHQYTVSLVTGEYLYNFTYSTDNDVTELIDNNGNSLK  
 IRRDSSGMPRHLLMPDNQIITLTVTGNGGLKVSTQNLGLMTYDNGTGLLATKSDETGWTTFYDYDHEGRLTNVTRPTGVVT  
 SLHREMEKSITIDIENSNRDDVTITNLSSVEASYTVVQDQVRNSYQLCNGNGLRVMYANGMGISFHSEPHVLAGTITPTIGR  
 CNISLPMENGLNSIEWRLRKEQIKGKVTIFGRKLRVHGRNLLSIDYDRNIRTEKIYDDHRKFTLRIIYDQVGRPFLLWLPSSGLA  
 55 AVNVSYFFNGRLAGLQRGAMSERDIDKQGRIVSRMFADGKVWSYSYLDKSMVLLQLSQRYIFEYDSSDRLLAVTMPVARHS  
 MSTHTSIGYIRNIYNPPESNASVIFDYSDDGRILKTSFLGTGRQVFYKYGKLSKLSEIVYDSTAVTFGYDETTGVLKMNVLQSG  
 GFSCITIRYRKIGPLVDKQIYRFSEEGMVNARFDYTYHDNSFRIASIKPVISETPLPVDLYRYDEISGKVEHFGKFGVIYYDINQ  
 IITTAVMTLSKHFDTHGRIKEVQYEMFRSLMYWMTVQYDSMGRVIKRELKLGPYANTTKYTYDYDGDGQLQSVAVNDRPTWRY  
 60 YDLNGLNHLNPGNSVRIMPLRYDLRDRITRLGDVQYKIDDDGYLCQRGSDIFFEYNSKGLLTRYNKASGWSVQYRYDGVGRRRA  
 SYKTNLGHHLQYFYSDLHNPTRITHVYNHSNSEITSLYYDLQGHLFAMESSSGEEYYVASDNTGTPLAVFSINGLMIKQLQYTA  
 YGEIYYDSNPDFQMVIGFHGGLYDPLTKLVHFTQRDYDVLAGRWTSPDYTMWKNVGKEPAPFNLYMFKSNNPLSSELDLKNYVT  
 DVKSWLVMFGFQLSNIIPGFPRAKMYFVPPPYELSESQASENGQLITGVQQTTERHNQAFMALEGQVITKKLHASIREKAGHWF  
 ATTTPIIGKIMFAIKEGRVTTGVSSIASEDSRKVASVLNNAYYLDKMHYSIEGKDTHYFVKIGSADGDLVTLGTTIGRKVLES

GVNVTVSQPTLLVNGRTRRFTNIEFQYSTLLLSIRYGLTPDTLDEEKARVLDQARQRALGTAWAKEQQKARDGREGSRLWTEGE  
KQQLLSTGRVQGYEGYYVLPVEQYPELADSSSNIQFLRQNMKGKR

In further alternative embodiments the italicized bases in the 5' end of the FCTR3b sequence in table 3C is a variable region. This region can be substituted for in other embodiments of FCTR3. The nucleotide sequence for 9823bp FCTR3c (also referred to herein as 10129612.0.154) has the same nucleotide sequence as FCTR3b except that the italicized region is replaced with the 201 base sequence shown in Table 3E. An ORF for the total FCTR3c nucleotide sequence was identified beginning with an ATG initiation codon at nucleotides 277-280 and ending with a TAG codon at nucleotides 8473-8475. This is the same open reading frame that is shown in Table 3C, with the corresponding base numbers for FCTR3c. This open reading frame will translate the same amino acid sequence as shown in Table 3C for FCTR3b.

**Table 3E. Encoded FCTR3c 5'end nucleotide sequence (SEQ ID NO:9).**

GCTCCAAAGCGAGCTGGGACCGAAGACTCTAGGCTAAGTTATCTATGTAGATGGTGTGAGGGAGCGAAGCTACTGACCGA  
GCTGCTGTTACATCCAGCTTTTTTAATTGCCTAAGCGGTCTGGGGCTTGCTTCGTCATTTGGCTTTGCTGTGGAGCACTCC  
TGTAAGCCAGCTGAATTGTACATCGAAGATCCACCCTTT

In yet another embodiment, the italicized region shown in the 5' end of the sequence in Table 3C can be replaced with the sequence shown in Table 3F to form 9823bp FCTR3d (also referred to herein as 10129612.0.67). An ORF was identified beginning with an ATG initiation codon at nucleotides 277-280 and ending with a TAG codon at nucleotides 8473-8475. This is the same open reading frame that is shown in Table 3C, with the corresponding base numbers for FCTR3d. This open reading frame will translate the same amino acid sequence as shown in Table 3D for FCTR3b.

**Table 3F. Encoded FCTR3d 5'end nucleotide sequence (SEQ ID NO:10).**

GCTCCAAAGCGAGCTGGGACCGAAGACTCTAGGCTAAGTTATCTATGTAGATGGTGTGAGGGAGCGAAGCTACTGACCGA  
GCTGCTGTTACATCCAGCTTTTTTAATTGCCTAAGCGGTCTGGGGCTTGCTTCGTCATTTGGCTTTGCTGTGGAGCACTCC  
TGTAAGCCAGCTGAATTGTACATCGAAGATCCACCCTTT

In yet another embodiment, the italicized region shown in the 5' end of the sequence in Table 3C can be replaced with the sequence shown in Table 3G to form 9765 bp FCTR3e (also referred to as 10129612.0.258). An ORF was identified beginning with an ATG initiation codon at nucleotides 210-212 and ending with a TAG codon at nucleotides 8408-8410. This is the same open reading frame that is shown in Table 3C, with the corresponding base numbers for FCTR3e. This open reading frame will translate the same amino acid sequence as shown in Table 3D for FCTR3b.

**Table 3G. Encoded FCTR3e 5'end nucleotide sequence (SEQ ID NO:11).**

CCAGCATTAGATGAGTTGACAAAAATGCAGTTTCAGCTCTGAAGGTCTGAAAGATTCTGCTGCAACTAAAGCTCTGAAGA  
TTCTGCTACAACTATGACATCCATTTTCTCCCACTTCAGACAGGATGAATACAAAGGTGGCAAAGTGACAAGTGCCAAAAC

5 In yet another embodiment another FCTR3a homolog, FCTR3f (also referred to as  
10129612.0.352) was found having the 9729bp sequence shown in Table 3H. An ORF was  
identified beginning with an ATG initiation codon at nucleotides 210-212 and ending with a  
TAG codon at nucleotides 8382-8384. A putative untranslated region upstream from the  
initiation codon and downstream from the termination codon is underlined in Table 3G, and  
10 the start and stop codons are in bold letters.

**Table 3H. Encoded FCTR3f nucleotide sequence (SEQ ID NO:12).**

CCAGCATTAGATGAGTTGACAAAAATGCAGTTTCAGCTCTGAAGGTCTGAAAGATTCTGCTGCAACTAAAGCTCTGAAGA  
TTCTGCTACAACTATGACATCCATTTTCTCCCACTTCAGACAGGATGAATACAAAGGTGGCAAAGTGACAAGTGCCAAAAC  
TCAGGCCTGACTTTCCTGAAAACATCAGCATTCTGCCATATCTGGAATAATGGATGTAAAGGACCGGCGACACCGCTCTT  
15 TGACCAGAGGACGCTGTGGCAAAGAGTGTGCTACACAAGCTCCTCTCTGGACAGTGAGGACTGCCGGGTGCCACACAG  
AAATCCTACAGCTCCAGTGAGACTCTGAAGGCCTATGACCATGACAGCAGGATGCACTATGGAAACCGAGTCACAGACCT  
CATCCACCGGGAGTCAGATGAGTTTCTAGACAAGGAACCAACTTCACCCTTGCCGAAGTGGGCATCTGTGAGCCCTCCC  
CACACCGAAGCGGCTACTGCTCCGACATGGGGATCCTTCACCAGGGCTACTCCCTTAGCACAGGGTCTGACGCCGACTCC  
GACACCGAGGGAGGGATGTCTCCAGAACACGCCATCAGACTGTGGGGCAGAGGGATAAAATCCAGGCGCAGTTCGGGCCT  
20 GTCCAGTCGTGAAAACCTCGGCCCTTACCCTGACTGACTCTGACAACGAAAACAAATCAGATGATGAGAACGGTCGTCCCA  
TTCCACCTACATCCTCGCCTAGTCTCCTCCCATCTGCTCAGCTGCCTAGCTCCCATATCCTCCACCAGTTAGCTGCCAG  
ATGCCATTGCTAGACAGCAACACCTCCCATCAAATCATGGACACCAACCTGATGAGGAATTCTCCCCAATTCATACCT  
GCTCAGAGCATGCTCAGGGCCCCAGCAAGCCTCCAGCAGTGGCCCTCCGAACCACACAGCCAGTCGACTCTGAGGCCCC  
CTCTCCCACCCCTCACAACCACACGCTGTCCCATCACCACCTCGTCCGCCAACTCCCTCAACAGGAACTCACTGACCAAT  
25 CGGCGGAGTCAGATCCACGCCCCGGCCCCAGCGCCCAATGACCTGGCCACCACACCAGAGTCCGTTTCTGCTTCAGGACAG  
CTGGGTGCTAAACAGCAACGTGCCACTGGAGACCGGCACTTCCTCTTCAAGACCTCCTCGGGGAGCACACCCTTGTTCA  
GCAGCTCTTCCCCGGGATACCCTTTGACCTCAGGAACGGTTTACACGCCCCCGCCCCGCTGCTGCCAGGAATACTTTC  
TCCAGGAAGGCTTTCAAGCTGAAGAAGCCCTCCAAATACTGCAGCTGGAATGTGCTGCCCTCTCCGCCATTGCCGCGGC  
CCTCCTCTTGCTATTTTGGTGGCGTATTTTATAGTGCCCTGGTGGTGAAGGAGTGCAGCATAGACAGTGGTGAAGCAG  
30 AAGTTGGTTCGGCGGGTAACACAAGAAGTCCCACCAGGGGTGTTTGGAGGTACAAATTCACATCAGTCAGCCCCAGTTC  
TTAAAGTTCAACATCTCCCTCGGGAAGGACGCTCTCTTTGGTGTTCACATAAGAAGAGGACTTCCACCATCTCATGCCCA  
GTATGACTTCATGGAACGTCTGGACGGGAAGGAGAAGTGGAGTGTGGTTGAGTCTCCAGGGGAACGCCGAGCATAACAGA  
CCTTGGTTTCAAGATGAAGCCGTGTTTGTGTCAGTACCTGGATGTGGGCTGTGGCATCTGGCCTTCTACAATGATGGA  
35 GACAAAGAGATGGTTTCTTCAATACTGTTGTCTAGATTGAGTGCAGGACTGTCCACGTAAGTCCCATGGGAATGGTGA  
ATGTGTGTCCGGGTGTGTCACTGTTTCCCAGGATTTCTAGGAGCAGACTGTGCTAAAGCTGCCTGCCCTGTCTGTGCA  
GTGGGAATGGACAATATTCTAAAGGGACGTGCCAGTGTACAGCGGCTGGAAAGGTGCAGAGTGGACGTGCCCATGAAT  
CAGTGCATCGATCCTTCTGCGGGGGCCACGGCTCCTGCATTGATGGGAAGTGTGTCTGCTCTGCTGGCTACAAAGGCGA  
GCACTGTGAGGAAGTTGATTGCTTGGATCCCACCTGCTCCAGCCACGGAGTCTGTGTGAATGGAGAATGCCTGTGCAGCC  
CTGGCTGGGGTGGTCTGAACTGTGAGCTGGCGAGGGTCCAGTGGCCAGACCAGTGCAGTGGGCATGGCACGTACCTGCCT  
40 GACACGGGCTCTGCAGCTGCGATCCCACTGGATGGGTCCGACTGCTCTGTTGAAGTGTGCTCAGTAGACTGTGGCAC  
TCACGGCGTCTGCATCGGGGAGCCTGCCGCTGTGAAGAGGGCTGGACAGGCGCAGCGTGTGACCAGCGCGTGTGCCACC  
CCCGCTGCATTGAGCATGGGACCTGTAAAGATGGCAAATGTGAATGCCGAGAGGGCTGGAATGGTGAACACTGCACCAT  
GATGGCTGCCCTGACTTGTGCAACGGTAACGGGAGATGCACACTGGGTGAGAACAGCTGGCAGTGTGTCTGCCAGACCGG  
CTGGAGAGGGCCCGGATGCAACGTTGCCATGGAACTTCCTGTGCTGATAACAAGGATAATGAGGGAGATGGCCTGGTGG  
45 ATTGTTTGGACCTGACTGCTGCCTGCAGTCAGCCTGTGAGAACAGCCTGCTCTGCCGGGGTCCCGGGACCCACTGGAC  
ATCATTACAGCAGGGCCAGACGGATTGGCCCGCAGTGAAGTCTTCTATGACCGTATCAAGCTCTTGGCAGGCAAGGATAG  
CACCCACATCATTCCTGGAGAGAACCCTTTCAACAGCAGCTTGGTTTCTCTCATCCGAGGCCAAGTAGTAAGTACAGATG  
GAACTCCCCTGGTCGGTGTGAACGTGTCTTTGTCAAGTACCCAAAATACGGCTACACCATCACCCGCCAGGATGGCAGC  
TTTCAGCTGATCGCAAATGGAGGTGCTTCTTGAAGTCTACACTTTGAGCGAGCCCCGTTTATGAGCCAGGAGCGCACTGT  
50 GTGGCTGCCGTGGAACAGCTTTTACGCCATGGACACCCTGGTGTGAAGACCGAGGAGAACTCCATCCCCAGCTGTGACC  
TCAGTGGCTTTGTCCGGCCTGATCCAATCATCATCTCCTCCCCACTGTCCACCTTCTTTAGTGCTGCCCTGGGCAGAAAT  
CCCATCGTGCCTGAGACCCAGGTTCTTCATGAAGAAATCGAGCTCCCTGGTTCCAATGTGAACTTCGCTATCTGAGCTC  
TAGAACTGCAGGGTACAAGTCACTGCTGAAGATCACCATGACCCAGTCCACAGTGGCCCTGAACCTCATTAGGGTTTACC  
TGATGGTGGCTGTGAGGGGCATCTCTCCAGAAGTCATTCCAGGCTTCTCCCAACCTGGCCTCCACCTTCATCTGGGAC  
55 AAGACAGATGCGTATGGCCAAAGGGTGTATGGACTCTCAGATGCTGTTGTGTCTGTGCGGGTTTGAATATGAGACCTGTCC  
CAGTCTAATTCTCTGGGAGAAAAGGACAGCCCTCCTTCAGGGATTTCAGAGCTGGACCCCTCCAACCTCGGTGGCTGGTCCC  
TAGACAAACACCACATCCTCAATGTTAAAAGTGAATCCTACACAAAGGCACTGGGGAAAACAGTTTCTGACCCAGCAG  
CCTGCCATCATCACCAGCATCATGGGCAATGGTCCGCCCGGAGCATTTCCTGTCCAGCTGCAACGGCCTTGCTGAAGG  
CAACAAGCTGCTGGCCCCAGTGGCTCTGGCTGTTGGAATCGATGGGAGCCTCTATGTGGGTGACTTCAATTACATCCGAC  
60 GCATCTTCCCTCTCGAAATGTGACCAGCATCTTGAGTTACGAAATAAAGAGTTTAAACATAGCAACAACCCAGCACAC

AAGTACTACTTGGCAGTGGACCCCGTGTCCGGCTCGCTCTACGTGTCCGACACCAACAGCAGGAGAATCTACCGCGTCAA  
 GTCTCTGAGTGGAACCAAAGACCTGGCTGGGAATTCGGAAGTTGTGGCAGGGACGGGAGAGCAGTGTCTACCCTTTGATG  
 AAGCCCGCTGCGGGGATGGAGGGAAGGCCATAGATGCAACCTGATGAGCCCGAGAGGTATTGCAGTAGACAAGAATGGG  
 CTCATGTACTTTGTTCGATGCCACCATGATCCGGAAGGTTGACCAGAATGGAATCATCTCCACCCTGCTGGGCTCCAATGA  
 5 CCTCACTGCCGTCCGGCCGCTGAGCTGTGATTCCAGCATGGATGTAGCCAGGTTTCGTCTGGAGTGGCCAACAGACCTTG  
 CTGTCAATCCCATGGATAACTCCTTGTATGTTCTAGAGAACAATGTCATCCTTCGAATCACCGAGAACCACCAAGTCAGC  
 ATCATTGCGGGACGCCCCATGCACTGCCAAGTTCCTGGCATTGACTACTCACTCAGCAAACCTAGCCATTCACTCTGCCCT  
 GGAGTCAGCCAGTGCCATTGCCATTTCTCACACTGGGGTCTCTACATCACTGAGACAGATGAGAAGAAGATTAACCGTC  
 10 TACGCCAGGTAACAACCAACGGGGAGATCTGCCTTTTAGCTGGGGCAGCCTCGGACTGCGACTGCAAAAACGATGTCAAT  
 TGCAACTGCTATTTCAGGAGATGATGCCTACGCGACTGATGCCATCTTGAATTCCTCATCATCTTAGCTGTAGCTCCAGA  
 TGGTACCATTTACATTGCAGACCTTGGAATATTTCGGATCAGGGCGGTGAGCAAGAACAAGCCTGTTCTTAATGCCTTCA  
 ACCAGTATGAGGCTGCATCCCCCGGAGAGCAGGAGTTATATGTTTTCAACGCTGATGGCATCCACCAATACACTGTGAGC  
 CTGGTGACAGGGGAGTACTTGTACAATTTACATATAGTACTGACAATGATGTCACTGAATTGATTGACAATAATGGGAA  
 TTCCCTGAAGATCCGTCGGGACAGCAGTGGCATGCCCGTCACCTGCTCATGCCTGACAACCAGATCATCACCTCACCG  
 15 TGGGCACCAATGGAGGCCTCAAAGTCGTGTCCACACAGAACCTGGAGCTTGGTCTCATGACCTATGATGGCAACACTGGG  
 CTCCTGGCCACCAAGAGCGATGAAACAGGATGGACGACTTTCTATGACTATGACCACGAAGGCCGCTGACCAACGTGAC  
 GCGCCCCACGGGGGTGGTAACAGTCTGCACCGGGAAATGGAGAAATCTATTACCATTGACATTGAGAACTCCAACCGTG  
 ATGATGACGTCACTGTATCATCAACCAACCTCTCTTCAGTAGAGGCCTCTACACAGTGGTACAAGATCAAGTTCGGAACAGC  
 TACCAGCTCTGTAATAATGGTACCCTGAGGGTGATGTATGCTAATGGGATGGGTATCAGCTTCCACAGCGAGCCCCATGT  
 20 CCTAGCGGGCACCATCACCCCCACCATGGACGCTGCAACATCTCCCTGCCTATGGAGAATGGCTTAACTCCATTGAGT  
 GCGCCTAAGAAAGGAACAGATTAAAGGCAAAGTCACCATCTTGGCAGGAAGCTCCGGGTCCATGGAAGAAATCTCTTG  
 TCCATTGACTATGATCGAAATATTTCGGACTGAAAAGATCTATGATGACCACCGGAAGTTCACCCTGAGGATCATTTATGA  
 CCAGGTGGGCGGCCCTTCTCTGGCTGCCAGCAGCGGGCTGGCAGCTGTCAACGTGTCTACTTCTTCAATGGGCGCC  
 TGGCTGGGCTTCAGCGTGGGGCCATGAGCGAGAGGACAGACATCGACAAGCAAGGCCGCATCGTGTCCCGCATGTTTCGCT  
 25 GACGGGAAAGTGTGGAGCTACTCCTACCTTGACAAGTCCATGGTCTCTCTGCTTCAGAGCCAACGTGAGTATATATTTGA  
 GTATGACTCCTCTGACCGCCTCCTTGCCGTACCATGCCAGCGTGGCCCGGCACAGCATGTCCACACACACCTCCATCG  
 GCTACATCCGTAATATTTACAACCCGCTGAAAGCAATGCTTCGGTCACTTTTACTACAGTGATGACGGCCGCATCCTG  
 AAGACCTCCTTTTTGGGCACCGGACGCCAGGTGTTCTACAAGTATGGGAACTCTCCAAGTTATCAGAGATTGTCTACGA  
 CAGTACCGCCGTACCTTCGGGTATGACGAGACCACTGGTGTCTTGAAGATGGTCAACCTCCAAAGTGGGGGCTTCTCCT  
 30 GCACCATCAGGTACCGGAAGATTGGCCCCCTGGTGGACAAGCAGATCTACAGGTTCTCCGAGGAAGGCATGGTCAATGCC  
 AGGTTTGACTACACCTATCATGACAACAGCTTCGCGATCGCAAGCATCAAGCCCGTCATAAGTGAGACTCCCCTCCCCGT  
 TGACCTCTACCGCTATGATGAGATTTCTGGCAAGGTGGAACACTTTGGTAAGTTTGGAGTCATCTATTATGACATCAACC  
 AGATCATCACCCTGCCGTGATGACCTCAGCAAACACTTCGACACCCATGGGCGGATCAAGGAGGTCCAGTATGAGATG  
 TTCCGGTCCCTCATGTACTGGATGACGGTGCAATATGACAGCATGGGCAGGGTGATCAAGAGGGAGCTAAAACCTGGGGCC  
 35 CTATGCCAATACCACGAAGTACACCTATGACTACGATGGGGACGGGCAGCTCCAGAGCGTGGCCGTCAATGACCGCCCGA  
 CCTGGCGCTACAGCTATGACCTTAATGGGAATCTCCACTTACTGAACCCAGGCAACAGTGTGCGCCTCATGCCCTTGCGC  
 TATGACCTCCGGGATCGGATAACCAGACTCGGGGATGTGCAGTACAAAATTGACGACGATGGCTATCTGTGCCAGAGAGG  
 GTCTGACATCTTCGAATACAATTCCAAGGGCCTCCTAACAAGAGCCTACAACAAGGCCAGCGGGTGGAGTGTCCAGTACC  
 GCTATGATGGCGTAGGACGGCGGGCTTCTACAAGACCAACCTGGGCCACCACCTGCAGTACTTCTACTCTGACCTCCAC  
 40 AACCCGACGCGCATCACCCATGTCTACAATCACTCCAACCTCGGAGATTACCTCACTGTACTACGACCTCCAGGGCCACCT  
 CTTTGCCATGGAGAGCAGCAGTGGGGAGGAGTACTATGTTGCCTCTGATAACACAGGGACTCCTCTGGCTGTGTTGAGCA  
 TCAACGGCCTCATGATCAAACAGCTGCAGTACACGGCCTATGGGGAGATTTATTATGACTCCAACCCCGACTTCCAGATG  
 GTCATTGGCTTCCATGGGGGACTCTATGACCCCCCTGACCAAGCTGGTCCACTTCACTCAGCGTGATTATGATGTGCTGGC  
 AGGACGATGGACCTCCCCAGACTATACCATGTGGAAAAACGTGGGCAAGGAGCCGGCCCCCTTTAACCTGTATATGTTCA  
 45 AGAGCAACAATCCTCTCAGCAGTGAGCTAGATTTGAAGAACTACGTGACAGATGTGAAAAGCTGGCTTGTGATGTTTGGA  
 TTTGAGCTTAGCAACATCATTCCTGGCTTCCCGAGAGCCAAAATGTATTTCTGTCCTCCTCCCTATGAATTGTGAGAGAG  
 TCAAGCAAGTGAGAATGGACAGCTCATTACAGGTGTCCAACAGACAACAGAGAGACATAACCAGGCCTTCATGGCTCTGG  
 AAGGACAGGTCACTACTAAAAAGCTCCACGCCAGCATCCGAGAGAAAGCAGGTCACTGGTTTGCCACCACCACGCCCATC  
 ATTGGCAAAGGCATCATGTTTGCCATCAAAGAAGGGCGGGTGACCACGGGCGTGTCCAGCATCGCCAGCGAAGATAGCCG  
 50 CAAGGTGGCATCTGTGCTGAACAACGCCCTACTACCTGGACAAGATGCACTACAGCATCGAGGGCAAGGACACCCACTACT  
 TTGTGAAGATTGGCTCAGCCGATGGCGACCTGGTCACACTAGGCACCACCATCGGCCGCAAGGTGCTAGAGAGCGGGTG  
 AACGTGACCGTGTCCCAGCCCACGCTGCTGGTCAACGGCAGGACTCGAAGGTTACGAACATTGAGTTCAGTACTCCAC  
 GCTGCTGCTCAGCATCCGCTATGGCCTCACCCCCGACACCTGGACGAAGAGAAGGCCCGCTCCTGGACCAGGCGAGAC  
 AGAGGGCCCTGGGCACGGCCTGGGCCAAGGAGCAGCAGAAAGCCAGGGACGGGAGAGAGGGGAGCCGCTGTGGACTGAG  
 55 GGCGAGAAGCAGCAGCTTCTGAGCACCGGGCGCGTGAAGGGTACGAGGGATATTACGTGCTTCCCCTGGAGCAATACCC  
 AGAGCTTGACAGACAGTAGCAGCAACATCCAGTTTTTAAGACAGAATGAGATGGGAAAGAGGTAACAAAATAATCTGCTGC  
 CATTCTTGTCTGAATGGCTCAGCAGGAGTAACTGTTATCTCCTCTCCTAAGGAGATGAAGACCTAACAGGGGCACTGCG  
 GCTGGGCTGCTTTAGGAGACCAAGTGGCAAGAAAGCTCACATTTTTTTGAGTTCAAATGCTACTGTCCAAGCGAGAAGTCC  
 CTCATCCTGAAGTAGACTAAAGCCCGGCTGAAAATTCGAGGAAAACAAAACAAACGAATGAATGAACAGACACACACAA  
 60 TGTTCCAAGTTCCCCTAAAATATGACCCACTTGTCTGGGTCTACGCAGAAAAGAGACGCAAGTGTCCAAAAGGAACAA  
 AAGAACAAAACGAATAAGCAAAGAAGAAACAAACAAAACAAAACAAAACACACGGACCGATAAACAAAGAAGC  
 GAAGATAAGAAAGAAGGCCTCATATCCAATTACCTCACTCATTCACATGTGAGCGACACGCAGACATCCGCGAGGGCCAG  
 CGTCACCAGACCAGCTGCGGGACAAACCACTCAGACTGCTGTAGGACAAATACTTCTGACATTTTCGTTAAGCAAATA  
 CAGGTGCATTTAAAACACGACTTTGGGGGTGATTTGTGTGTAGCGCTGGGGAGGGGGGATAAAAGAGGAGGAGTGAGCA  
 65 CTGGAAATACTTTTTAAAGAAAAAAAACATGAGGGAATAAAAGAAATTCCTATCAAAAATCAAAGTGAAATAATACCAT  
 CCAGCACTTAACTCTCAGGTCCCAACTAAGTCTGGCCTGAGCTAATTTATTTGAGCGCAGAGTGTAATAATTTAATTCAA  
 ATGGTGGCTATAATCACTACAGATAAATTTCTACTCTTTTGTCTTTGGAGATTCCATTGTGGACAGTAATACGCAGTTA  
 CAGGTGTAGTCTGTTTAGATTCCGTAGTTTCGTGGGTATCAGTTTCGGTAGAGGTGACGATCGTGACACTTTTGCTAAC  
 AGGTACCACTTCTGATCACCTGTACATACATGAGCCGAAAGGCACAATCACTGTTTCAGATTTAAATTTATTAGTGTGT  
 70 TTGTTTGGTCCAGAACTGAGACAATCACATGACAGTCAACACGAGGAGAGAAAATTTAAAAAATAAAAAACAAA

AAAAATTTTAAAAATTAAAAAACAAAAATAAAGTCTAATAAGAACTTTGGTACAGGAACTTTTTGTAAATATACATGTA  
TGAATTGTTTCATCGAGTTTTTATATTAATTTTAATTTGCTGCTAAGCAAAGACTAGGGACAGGCAAAGATAATTTATGGC  
AAAGTGTTTAAATTGTTTATACATAAATAAAGTCTCTAAAACTCCTGTG

- 5 The FCTR3f polypeptide (SEQ ID NO:13) encoded by SEQ ID NO:12 is 2724 amino acid residues long and is presented using the one-letter code in Table 3I. This sequence differs from FCTR3b in that it is missing amino acids 758-766 from that polypeptide.

**Table 3I. Encoded FCTR3f protein sequence (SEQ ID NO:13)**

10 MDVKDRRHRSLTRGRCGKECRYTSSSLDSEDCRVPTQKSYSSSETLKAYDHDSDRMHYGNRVTDLIHRESDEFPRQGTNFTLAEL  
 GICEPSPHRSGYCSMDGILHQGYSLSTGSDADSDTEGGMSPEHAIRLWGRGIKSRRSSGLSSRENSALTLTDSNENKSDDENG  
 RPIPTSSPSLLPSAQLPSSHNPFPVSCQMPLLDSNTSHQIMDTNPDEEFSPNSYLLRACSGPQQASSSGPPNHHSQSTLRPPL  
 PPPHNHTLSHHHSSANS LNRS LNRS QI HAPAPAPNDLATTPESVQLQDSWVLNSNVPLETRHFLFKTSSGSTPLESSSSPG  
 YPLTSGTVYTPPPRLLPRNTFSRKAFLKPKSKYCSWKCAALSAIAAALLAILLAYFIVPWSLKNSSIDSGEAEVGRRTQEV  
 PPGVFWRSQIHISQPPQLKFNISLQKDALFGVYIRGLPPSHAQYDFMERLDGKEKWSVVEPRERRSIQTLVQNEAVEFVQYLD  
 15 VGLWHLAFYNDGKDKEMVSFNTVVLDSDVQDCPRNCHGNCECVSGVCHCFPGFLGADCAKAACPVLCSGNGQYSKGTCCQCYSGWK  
 GAECDVPMNQCIDPSCGGHSGCIDGNCVCSAGYKGEHCEEVDCLDPTCSSHGVCVNGECLCSPGWGGLNCELARVQCPDQCSGH  
 GTYLPDTGLCSCDPNWMGPDSCVEVCSVDCGTHGVCIGGACRCEEGWTGAACDQRVCHPRCIEHGTCKDGKCECREGWNGEHCT  
 IDGCPDLGNGRCTLGQNSWQCVCQTGWRGPGCNVAMETSCADNKDNEGDGLVDCLDPCCLQSACQNSLLCRGSRDPLDIQ  
 QGQTDWPAVKSFYDRIKLLAGKDSHTIIPGENPFNSLVSILRGQVVTDTGTPLVGVNVSVFKYKPYGYTITRODGTFDLIANG  
 20 GASLTLHFERAPFMSQERTVWLPWNSEFYAMDTLVMKTEENSIPSCDLSGFVRPDPIIISPLSTFFSAAPGQNPVIVPETQVLHE  
 EIELPGSNVKLRYLSSRTAGYKSLKITMTQSTVPLNLRVHLMVAVEGHLFQKSFQASPNLASTFIWDKTDAYGQRVYGLSDA  
 VVSVGFYETCPSLILWEKRTALLQGFELDPNLSGWSLDKHHILNVKSGILHKGKTGENQFLTQQPAIITSIMGNRRRSISCP  
 SCNGLAEGNKLLAPVALAVGIDGSLYVGDFNYIRRIFFSRNVTSSILELRNKEFKHSNNPAHKYYLAVDPVSGSLYVSDTNSRRI  
 YRVKSLSGTKDLAGNSEVVAGTGEQCLPFDEARCGDGGKAIDATLMSPRGIAVDKNGLMYFVDATMIRKVDQNGIISTLLGSND  
 25 LTAVRPLSCDSSMDVAQVRLEWPTDLAVNPMDNSLYVLENNVILRITENHQVSIAGRPMMCQVPGIDYSLSKLAHSALESAS  
 AIAISHTGVLYITETDEKKINRLRQVTTNGEICLLAGAASDCDCNDVNCNCYSGDDAYATDAILNSPSSSLAVAPDGTIYIADL  
 GNIRIRAVSKNKPVLNAFNQYEAASPGEQELYVFNADGIHQYTVSLVTGEYLYNFTYSTDNDVTELDNNGNSLKRIRDSGMP  
 RHLMPDNQIITLTVGTNGGLKVVSTQNLGLMTYDGNTGLLATKSDETGWTTFYDYDHEGRLTNVTRPTGVVTSLHREMEKS  
 ITIDIENSNRDDVTITNLSSVEASYTVVQDQVRNSYQLCNGTLRVMYANGMGISFHSEPHVLAGTITPTIGRCNISLPMEN  
 30 GLNSIEWRLRKEQIKGKVTIFGRKLRVHGRNLLSIDYDRNIRTEKIYDDHRKFTRLRIYDQVGRPFLLWLPSSGLAANNVSYFFN  
 GRLAGLQRGAMSERTDIDKQGRIVSRMFADGKVWSYSYLDKSMVLLQLSQSQRYIFEYDSSDRLLAVTMPSPVARHSMSTHTSIGY  
 IRNIYNPPESNASVIFDYSDDGRIKLSFLGTGRQVFYKYGKLSKLSEIYVDSTAVTFGYDETGTGLKMNVLQSGGFSCITIRYR  
 KIGPLVDKQIYRFSEEGMVNARFDYTYHDNSFRIASIKPVISETPLPVDLYRYDEISGKVEHFGKFGVIYYDINQIITTAVMTL  
 SKHFDTHGRIKEVQYEMFRSLMYWMTVQYDSMGRVIKRELKLGYPYANTTKYTYDYDGDGQLQSVAVNDRPTWRYSYDLNGLHL  
 35 LNPNSVRLMPLRYDLRDRITRLGDVQYKIDDDGYLCQRGSDIFEYNSKGLLTRAYNKASGWSVQYRYDGVGRRASYKTNLGH  
 LQYFYSDLHNPTRITHVYNHNSSEITSLYDLOQHFLFAMESSSGEEYYVASDNTGTPLAVFSINGLMIKQLQYTAYGEIYYDSN  
 PDFQMVIGFHHGLYDPLTKLVHFTQRDYDVLGRWTSPTYTMWKNVKGEPAPFNLYMFKSNNPLSSELDLKNYVTDVKSXLVME  
 GFQLSNII PGFPRAKMYFVPPPYELSESQASENGQLITGVQQTTERHNQAFMALEGQVITKKLHASIREKAGHWFATTTPIIGK  
 40 GIMFAIKEGRVTTGVSSIASSEDSRKVASVLNNAYYLDKMHYSIEGKDTHYFVKIGSADGDLVTLGTTIGRKVLESQVNVTVSQP  
 TLLVNGRTRRFTNIEFQYSTLLLSIRYGLTPDTLDEEKARVLDQARQALGTAWAKEQQKARDGREGSRLWTEGEKQQLLSTGR  
 VQGYEGYYVLPVEQYPELADSSSNIQFLRQNMGR

- 45 In a BLASTN search it was found that the FCTR3a nucleic acid has homology to three fragments of *Mus musculus* odd Oz/ten-m homolog 2. It has 634 of 685 bases (92%) identical to bases 614-1298, 365 of 406 bases (89%) identical to bases 1420-1825, and 93 of 103 bases (90%) identical to bases 1823-1925 of *Mus musculus* odd Oz/ten-m homolog 2 (GenBank Acc: NM\_011856.2) (Table 3J).

**Table 3J. BLASTN of FCTR3a against *Mus musculus* odd Oz/ten-m homolog 2 (SEQ ID NO:62)**

50 >GI|7657414|REF|NM\_011856.2| MUS MUSCULUS ODD OZ/TEN-M HOMOLOG 2 (DROSOPHILA)  
 (ODZ2), mRNA  
 LENGTH = 8797  
 SCORE = 954 BITS (481), EXPECT = 0.0  
 55 IDENTITIES = 634/685 (92%)

STRAND = PLUS / PLUS

5 QUERY: 114 GGTCGTCCCATTCACCTACATCCTCGCCTAGTCTCCTCCCATCTGCTCAGCTGCCTAGC 173  
|||||  
SBJCT: 614 GGTCGTCCCATTCACCTACATCCTCGTCTAGCCTCCTCCCATCTGCTCAGCTGCCTAGC 673

10 QUERY: 174 TCCCATAAATCCTCCACCAGTTAGCTGCCAGATGCCATTGCTAGACAGCAACACCTCCCAT 233  
|||||  
SBJCT: 674 TCCCATAAATCCTCCACCAGTTAGCTGCCAGATGCCATTGCTAGACAGCAACACCTCCCAT 733

15 QUERY: 234 CAAATCATGGACACCAACCCTGATGAGGAATTCTCCCCAATTCATACCTGCTCAGAGCA 293  
|| |||||  
SBJCT: 734 CAGATCATGGACACCAACCCTGATGAGGAATTCTCCCCAATTCATACCTGCTCAGAGCA 793

20 QUERY: 294 TGCTCAGGGCCCCAGCAAGCCTCCAGCAGTGGCCCTCCGAACCACCACAGCCAGTCGACT 353  
|||||  
SBJCT: 794 TGCTCAGGGCCCCAGCAAGCCTCCAGCAGTGGCCCTCCAAACCACCACAGCCAGTCAACA 853

25 QUERY: 354 CTGAGGCCCCCTCTCCACCCCCCTCACAACCACACGCTGTCCCATCACCACCTCGTCCGCC 413  
|||||  
SBJCT: 854 CTGAGGCCCCCTCTGCCACCCCCCTCATAACCACACCCTGTCCACACCACCTCCTCGGCC 913

30 QUERY: 414 AACTCCCTCAACAGGAACCTCACTGACCAATCGGCGGAGTCAGATCCACGCCCCGGCCCCA 473  
|||||  
SBJCT: 914 AACTCCCTCAACAGGAACCTCACTGACCAATCGGCGGAGTCAAATCCACGCCCCAGCTCCT 973

35 QUERY: 474 GCGCCCAATGACCTGGCCACCACACCAGAGTCCGTTTCTCAGCTTCAGGACAGCTGGGTGCTA 533  
|||||  
SBJCT: 974 GCGCCCAACGACCTGGCCACCACCCAGAGTCTGTTTCTCAGCTCCAGGATAGCTGGGTGCTG 1033

40 QUERY: 534 AACAGCAACGTGCCACTGGAGACCCGGCACTTCCTCTTCAAGACCTCCTCGGGGAGCACA 593  
|||||  
SBJCT: 1034 AACAGTAACGTCCCACTGGAGACTCGGCACTTCCTTTTCAAACGTCGTCTGGAAGCACA 1093

45 QUERY: 594 CCCTTGTTTCAGCAGCTCTTCCCCGGGATAACCTTTGACCTCAGGAACGGTTTACACGCCC 653  
||| |||||  
SBJCT: 1094 CCCCTGTTTCAGCAGCTCTTCTCCGGGATAACCTTTGACCTCAGGGACCGTTTATACACCA 1153

50 QUERY: 654 CCGCCCCGCCTGCTGCCCAGGAATACTTTCTCCAGGAAGGCTTTCAAGCTGAAGAAGCCC 713  
|| |||||  
SBJCT: 1154 CCACCCCGCCTGCTGCCACGGAATACATTCTCCAGGAAGGCCTTCAAGCTGAAGAAACCC 1213

55 QUERY: 714 TCCAAATACTGCAGCTGGAAATGTGCTGCCCTCTCCGCCATTGCCGCGGCCCTCCTCTTG 773  
|||||  
SBJCT: 1214 TCCAAATACTGCAGTTGGAAATGTGCTGCCCTGTCTGCCATCGCCGCGGCCCTCCTCTTG 1273

60 QUERY: 774 GCTATTTTGCTGGCGTATTTTCATAG 798  
|| |||||  
SBJCT: 1274 GCCATTTTGCTGGCATATTTTCATAG 1298

65 SCORE = 480 BITS (242), EXPECT = E-132  
IDENTITIES = 365/406 (89%)  
STRAND = PLUS / PLUS

70 QUERY: 797 AGTGCCCTGGTCGTTGAAAAACAGCAGCATAGACAGTGGTGAAGCAGAAGTTGGTCGGCG 856  
|||||  
SBJCT: 1420 AGTGCCCTGGTCATTGAAAAACAGCAGCATAGACAGTGGCGAAGCAGAAGTTGGTCGGCG 1479

75 QUERY: 857 GGTAACACAAGAAGTCCCACCAGGGGTGTTTGGAGGTCAAAATTCACATCAGTCAGCC 916  
||| |||||  
SBJCT: 1480 GGTGACACAGGAAGTCCCACCAGGGGTGTTTGGAGGTCCCAGATTCACATCAGTCAGCC 1539

80 QUERY: 917 CCAGTTCTTAAAGTTCAACATCTCCCTCGGGAAGGACGCTCTCTTTGGTGTTCACATAAG 976  
|| |||||  
SBJCT: 1540 TCAATTCTTAAAGTTCAACATCTCCCTGGGCAAGGATGCCCTCTTCGGTGTCTATATAAG 1599

85 QUERY: 977 AAGAGGACTTCCACCATCTCATGCCAGTATGACTTCATGGAACGTCTGGACGGGAAGGA 1036  
|||||  
SBJCT: 1600 GAGAGGACTACCACCGTCTCATGCCAGTATGACTTCATGGAACGCCTGGATGGAAAGGA 1659

In another BLASTN search it was found that the FCTR3a nucleic acid has homology to three fragments of *Gallus gallus* mRNA for teneurin-2. It has 541 of 629 bases (86%) identical to bases 502-1130, 302 of 367 bases (82%) identical to bases 1330-1696, and 87 of 103 bases (84%) identical to bases 1711-1813 of *Gallus gallus* mRNA for teneurin-2 (EMBL Acc: AJ245711.1) (Table 3K).

**Table 3K. BLASTN of FCTR3a against *Gallus gallus* mRNA for teneurin-2 (SEQ ID NO:63)**

QUERY: 414 AACTCCCTCAACAGGAAGTCACTGACCAATCGGCGGAGTCAGATCCACGCCCCGGCCCCA 473

5  
10  
15  
20  
25  
30  
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SBJCT: 802 AACTCCCTCAACAGGAACCTCGCTCACCAACCGCCGCAACCAGATCCACGCGCCTGCTCCC 861  
QUERY: 474 GCGCCCAATGACCTGGCCACCACACCAGAGTCCGTTTCAAGACCTCCTCGGGGAGCACA 533  
SBJCT: 862 GCTCCCAATGACCTGGCGACCACGCCTGAGTCTGTGCAGCTGCAGGACAGCTGGGTGCTC 921  
QUERY: 534 AACAGCAACGTGCCACTGGAGACCCGGCACTTCCTCTTCAAGACCTCCTCGGGGAGCACA 593  
SBJCT: 922 AACAGCAACGTGCCGCTGGAGACCAGGCATTCTTGTTTAAGACATCTTCTGGAACGACT 981  
QUERY: 594 CCCTTGTTTCAAGACCTCCTCGGGGAGCACA 653  
SBJCT: 982 CCGCTGTTTCAAGACCTCCTCGGGGAGCACA 1041  
QUERY: 654 CCGCCCCGCTGCTGCCCAGGAATACTTTCTCCAGGAAGGCTTTCAAGCTGAAGAAGCCC 713  
SBJCT: 1042 CCTCCCAGGCTGTTACCTAGAAATACATTTTCCAGGAATGCATTCAAGCTGAAAAAGCCC 1101  
QUERY: 714 TCCAAATACTGCAGCTGGAAATGTGCTGC 742  
SBJCT: 1102 TCCAAGTATTGTAGCTGGAAATGTGCTGC 1130  
SCORE = 212 BITS (107), EXPECT = 4E-52  
IDENTITIES = 302/367 (82%)  
STRAND = PLUS / PLUS  
QUERY: 819 AGCAGCATAGACAGTGGTGAAGCAGAAGTTGGTCGGCGGGTAACACAAGAAGTCCCACCA 878  
SBJCT: 1330 AGCAGCATAGATAGTGGAGAAACAGAAGTTGGCCGCAAGGTACCCAAGAGGTGCCCCCT 1389  
QUERY: 879 GGGGTGTTTGGAGGTCACAAATTCACATCAGTCAGCCCCAGTTCTTAAAGTTCAACATC 938  
SBJCT: 1390 GGAGTGTTCTGGCGGTCTCAGATCCATATCAGCCAGCCACAGTTCCTGAAGTTCAACATA 1449  
QUERY: 939 TCCCTCGGGAAGGACGCTCTCTTTGGTGTTCATAAGAAGAGGACTTCCACCATCTCAT 998  
SBJCT: 1450 TCCCTAGGGAAGGATGCTCTTTTCGGTGTTCATAAGAAGAGGACTCCCACCATCACAT 1509  
QUERY: 999 GCCCAGTATGACTTCATGGAACGCTCTGGACGGGAAGGAGAAGTGGAGTGTGGTTGAGTCT 1058  
SBJCT: 1510 GCACAGTATGATTTTCATGGAACGCTTGGATGGGAAAGAGAAATGGAGTGTGGTGGAAATCC 1569  
QUERY: 1059 CCCAGGGAACGCCGGAGCATAACAGACCTTGGTTCAGAATGAAGCCGTGTTTGTGCAGTAC 1118  
SBJCT: 1570 CCACGGGAACGGCGAAGTATTTCAGACTCTTGTTCAGAATGAGGCTGTGTTTGTTCAGTAC 1629  
QUERY: 1119 CTGGATGTGGGCTGTGGCCTTCTACAATGATGGAAAAGACAAAGAGATGGTT 1178  
SBJCT: 1630 TTGGATGTGGGTTTGTGGCACCTGGCGTTTACAATGATGGCAAGGACAAAGAAGTGGTC 1689  
QUERY: 1179 TCCTTCA 1185  
SBJCT: 1690 TCCTTCA 1696  
SCORE = 77.8 BITS (39), EXPECT = 1E-11  
IDENTITIES = 87/103 (84%)  
STRAND = PLUS / PLUS  
QUERY: 1258 GATTCAGTGCAGGACTGTCCACGTAACCTGCCATGGGAATGGTGAATGTGTGTCGGGGTG 1317  
SBJCT: 1711 GATTCAGTGCAGGACTGTCCACGTAATTCATGGCAATGGCGAGTGTGTTTCTGGTGTC 1770  
QUERY: 1318 TGTCAGTGTTCAGGATTTCTAGGAGCAGACTGTGCTAAAG 1360  
SBJCT: 1771 TGCCACTGTTTCCCGGATTTTCATGGAGCAGATTGTGCTAAAG 1813

In this search it was also found that the fragments of FCTR3bcd and e nucleic acids had homology to three fragments of *Homo sapiens* mRNA for KIAA1127 protein. It has 5537 of 5538 bases (99%) identical to bases 1-5538, 705 of 714 bases (98%) identical to bases 5609-6322, and 176 of 176 bases (100%) identical to bases 6385-6560 of *Homo sapiens* mRNA for KIAA1127 protein (GenBank Acc: AB032953) (Table 3L).

**Table 3L. BLASTN of FCTR3b, c, d, and e against *Homo sapiens* KIAA1127 mRNA (SEQ ID NO:64)**

>GI|6329762|DBJ|AB032953.1|AB032953 HOMO SAPIENS MRNA FOR KIAA1127 PROTEIN, PARTIAL CDS

10 LENGTH = 6560

SCORE = 1.097E+04 BITS (5534), EXPECT = 0.0

IDENTITIES = 5537/5538 (99%)

STRAND = PLUS / PLUS

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QUERY: 3267 CACCTTCTTTAGTGCTGCCCCCTGGGCAGAATCCCATCGTGCCTGAGACCCAGGTTCTTCA 3326

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SBJCT: 1 CACCTTCTTTAGTGCTGCCCCCTGGGCAGAATCCCATCGTGCCTGAGACCCAGGTTCTTCA 60

20

QUERY: 3327 TGAAGAAATCGAGCTCCCTGGTTCCAATGTGAAACTTCGCTATCTGAGCTCTAGAACTGC 3386

|||||  
SBJCT: 61 TGAAGAAATCGAGCTCCCTGGTTCCAATGTGAAACTTCGCTATCTGAGCTCTAGAACTGC 120

25

QUERY: 3387 AGGGTACAAGTCACTGCTGAAGATCACCATGACCCAGTCCACAGTGCCCCTGAACCTCAT 3446

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SBJCT: 121 AGGGTACAAGTCACTGCTGAAGATCACCATGACCCAGTCCACAGTGCCCCTGAACCTCAT 180

30

QUERY: 3447 TAGGGTTCACCTGATGGTGGCTGTCGAGGGGCATCTCTCCAGAAGTCATTCCAGGCTTC 3506

|||||  
SBJCT: 181 TAGGGTTCACCTGATGGTGGCTGTCGAGGGGCATCTCTCCAGAAGTCATTCCAGGCTTC 240

35

QUERY: 3507 TCCCAACCTGGCCTCCACCTTCATCTGGGACAAGACAGATGCGTATGGCCAAAGGGTGTA 3566

|||||  
SBJCT: 241 TCCCAACCTGGCCTCCACCTTCATCTGGGACAAGACAGATGCGTATGGCCAAAGGGTGTA 300

QUERY: 3567 TGGACTCTCAGATGCTGTTGTGTCTGTGCGGGTTTGAATATGAGACCTGTCCCAGTCTAAT 3626

|||||  
SBJCT: 301 TGGACTCTCAGATGCTGTTGTGTCTGTGCGGGTTTGAATATGAGACCTGTCCCAGTCTAAT 360

40

QUERY: 3627 TCTCTGGGAGAAAAGGACAGCCCTCCTTCAGGGATTCGAGCTGGACCCCTCCAACCTCGG 3686

|||||  
SBJCT: 361 TCTCTGGGAGAAAAGGACAGCCCTCCTTCAGGGATTCGAGCTGGACCCCTCCAACCTCGG 420

45

QUERY: 3687 TGGCTGGTCCCTAGACAAACACCACATCCTCAATGTTAAAAGTGGAATCCTACACAAAGG 3746

|||||  
SBJCT: 421 TGGCTGGTCCCTAGACAAACACCACATCCTCAATGTTAAAAGTGGAATCCTACACAAAGG 480

QUERY: 3747 CACTGGGGAAAACAGTTCCTGACCCAGCAGCCTGCCATCATCACCAGCATCATGGGCAA 3806

50

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SBJCT: 481 CACTGGGGAAAACAGTTCCTGACCCAGCAGCCTGCCATCATCACCAGCATCATGGGCAA 540

QUERY: 3807 TGGTCGCCGCCGGAGCATTTCTGTCCCAGCTGCAACGGCCTTGCTGAAGGCAACAAGCT 3866

55

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SBJCT: 541 TGGTCGCCGCCGGAGCATTTCTGTCCCAGCTGCAACGGCCTTGCTGAAGGCAACAAGCT 600

QUERY: 3867 GCTGGCCCCAGTGGCTCTGGCTGTTGGAATCGATGGGAGCCTCTATGTGGGTGACTTCAA 3926

|||||  
SBJCT: 601 GCTGGCCCCAGTGGCTCTGGCTGTTGGAATCGATGGGAGCCTCTATGTGGGTGACTTCAA 660

60

QUERY: 3927 TTACATCCGACGCATCTTCCCTCTCGAAATGTGACCAGCATCTTGGAGTTACGAAATAA 3986

|||||  
SBJCT: 661 TTACATCCGACGCATCTTCCCTCTCGAAATGTGACCAGCATCTTGGAGTTACGAAATAA 720

5  
 QUERY: 3987 AGAGTTTAAACATAGCAACAACCCAGCACACAAGTACTACTTGGCAGTGGACCCCGTGTC 4046  
 |||||  
 SBJCT: 721 AGAGTTTAAACATAGCAACAACCCAGCACACAAGTACTACTTGGCAGTGGACCCCGTGTC 780  
  
 QUERY: 4047 CGGCTCGCTCTACGTGTCCGACACCAACAGCAGGAGAATCTACCGCGTCAAGTCTCTGAG 4106  
 |||||  
 SBJCT: 781 CGGCTCGCTCTACGTGTCCGACACCAACAGCAGGAGAATCTACCGCGTCAAGTCTCTGAG 840  
  
 10  
 QUERY: 4107 TGGAACCAAAGACCTGGCTGGGAATTGCGAAGTTGTGGCAGGGACGGGAGAGCAGTGTCT 4166  
 |||||  
 SBJCT: 841 TGGAACCAAAGACCTGGCTGGGAATTGCGAAGTTGTGGCAGGGACGGGAGAGCAGTGTCT 900  
  
 15  
 QUERY: 4167 ACCCTTTGATGAAGCCCGCTGCGGGGATGGAGGGAAGGCCATAGATGCAACCCTGATGAG 4226  
 |||||  
 SBJCT: 901 ACCCTTTGATGAAGCCCGCTGCGGGGATGGAGGGAAGGCCATAGATGCAACCCTGATGAG 960  
  
 20  
 QUERY: 4227 CCCGAGAGGTATTGCAGTAGACAAGAATGGGCTCATGTACTTTGTCTGATGCCACCATGAT 4286  
 |||||  
 SBJCT: 961 CCCGAGAGGTATTGCAGTAGACAAGAATGGGCTCATGTACTTTGTCTGATGCCACCATGAT 1020  
  
 25  
 QUERY: 4287 CCGGAAGGTTGACCAGAATGGAATCATCTCCACCCTGCTGGGCTCCAATGACCTCACTGC 4346  
 |||||  
 SBJCT: 1021 CCGGAAGGTTGACCAGAATGGAATCATCTCCACCCTGCTGGGCTCCAATGACCTCACTGC 1080  
  
 30  
 QUERY: 4347 CGTCCGGCCGCTGAGCTGTGATTCCAGCATGGATGTAGCCCAGGTCGTCTGGAGTGGCC 4406  
 |||||  
 SBJCT: 1081 CGTCCGGCCGCTGAGCTGTGATTCCAGCATGGATGTAGCCCAGGTCGTCTGGAGTGGCC 1140  
  
 35  
 QUERY: 4407 AACAGACCTTGCTGTCAATCCCATGGATAACTCCTTGATGTTCTAGAGAACAATGTCAT 4466  
 |||||  
 SBJCT: 1141 AACAGACCTTGCTGTCAATCCCATGGATAACTCCTTGATGTTCTAGAGAACAATGTCAT 1200  
  
 40  
 QUERY: 4467 CCTTCGAATCACCGAGAACCACCAAGTCAGCATCATTGCGGGACGCCCCATGCACTGCCA 4526  
 |||||  
 SBJCT: 1201 CCTTCGAATCACCGAGAACCACCAAGTCAGCATCATTGCGGGACGCCCCATGCACTGCCA 1260  
  
 45  
 QUERY: 4527 AGTTCCTGGCATTGACTACTCACTCAGCAAAGTACCCATTCACTCTGCCCTGGAGTCAGC 4586  
 |||||  
 SBJCT: 1261 AGTTCCTGGCATTGACTACTCACTCAGCAAAGTACCCATTCACTCTGCCCTGGAGTCAGC 1320  
  
 50  
 QUERY: 4587 CAGTGCCATTGCCATTTCTCACACTGGGGTCCTCTACATCACTGAGACAGATGAGAAGAA 4646  
 |||||  
 SBJCT: 1321 CAGTGCCATTGCCATTTCTCACACTGGGGTCCTCTACATCACTGAGACAGATGAGAAGAA 1380  
  
 55  
 QUERY: 4647 GATTAACCGTCTACGCCAGGTAACAACCAACGGGGAGATCTGCCTTTTAGCTGGGGCAGC 4706  
 |||||  
 SBJCT: 1381 GATTAACCGTCTACGCCAGGTAACAACCAACGGGGAGATCTGCCTTTTAGCTGGGGCAGC 1440  
  
 60  
 QUERY: 4707 CTCGGACTGCGACTGCAAAAACGATGTCAATTGCAACTGCTATTCAGGAGATGATGCCTA 4766  
 |||||  
 SBJCT: 1441 CTCGGACTGCGACTGCAAAAACGATGTCAATTGCAACTGCTATTCAGGAGATGATGCCTA 1500  
  
 65  
 QUERY: 4767 CGCGACTGATGCCATCTTGAATTCCCCATCATCCTTAGCTGTAGCTCCAGATGGTACCAT 4826  
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 SBJCT: 1501 CGCGACTGATGCCATCTTGAATTCCCCATCATCCTTAGCTGTAGCTCCAGATGGTACCAT 1560  
  
 70  
 QUERY: 4827 TTACATTGCAGACCTTGGAATATTCGGATCAGGGCGGTGAGCAAGAACAAGCCTGTTCT 4886  
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 SBJCT: 1561 TTACATTGCAGACCTTGGAATATTCGGATCAGGGCGGTGAGCAAGAACAAGCCTGTTCT 1620  
  
 QUERY: 4887 TAATGCCTTCAACCAGTATGAGGCTGCATCCCCCGGAGAGCAGGAGTTATATGTTTTCAA 4946  
 |||||  
 SBJCT: 1621 TAATGCCTTCAACCAGTATGAGGCTGCATCCCCCGGAGAGCAGGAGTTATATGTTTTCAA 1680  
  
 QUERY: 4947 CGCTGATGGCATCCACCAATACACTGTGAGCCTGGTGACAGGGGAGTACTTGTACAATTT 5006  
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 SBJCT: 1681 CGCTGATGGCATCCACCAATACACTGTGAGCCTGGTGACAGGGGAGTACTTGTACAATTT 1740  
  
 QUERY: 5007 CACATATAGTACTGACAATGATGTCACTGAATTGATTGACAATAATGGGAATTCCTGAA 5066

SBJCT: 1741 CACATATAGTACTGACAATGATGTCACTGAATTGATTGACAATAATGGGAATTCCTGAA 1800  
 5 QUERY: 5067 GATCCGTCGGGACAGCAGTGGCATGCCCCGTACCTGCTCATGCCTGACAACCAGATCAT 5126  
 SBJCT: 1801 GATCCGTCGGGACAGCAGTGGCATGCCCCGTACCTGCTCATGCCTGACAACCAGATCAT 1860  
 10 QUERY: 5127 CACCCTCACCGTGGGCACCAATGGAGGCCTCAAAGTCGTGTCCACACAGAACCTGGAGCT 5186  
 SBJCT: 1861 CACCCTCACCGTGGGCACCAATGGAGGCCTCAAAGTCGTGTCCACACAGAACCTGGAGCT 1920  
 15 QUERY: 5187 TGGTCTCATGACCTATGATGGCAACACTGGGCTCCTGGCCACCAAGAGCGATGAAACAGG 5246  
 SBJCT: 1921 TGGTCTCATGACCTATGATGGCAACACTGGGCTCCTGGCCACCAAGAGCGATGAAACAGG 1980  
 20 QUERY: 5247 ATGGACGACTTTCTATGACTATGACCACGAAGGCCGCCTGACCAACGTGACGCGCCCCAC 5306  
 SBJCT: 1981 ATGGACGACTTTCTATGACTATGACCACGAAGGCCGCCTGACCAACGTGACGCGCCCCAC 2040  
 25 QUERY: 5307 GGGGGTGGTAACCAGTCTGCACCGGGAAATGGAGAAATCTATTACCATTGACATTGAGAA 5366  
 SBJCT: 2041 GGGGGTGGTAACCAGTCTGCACCGGGAAATGGAGAAATCTATTACCATTGACATTGAGAA 2100  
 30 QUERY: 5367 CTCCAACCGTGATGATGACGTCACCTGTCTCATCACCACCTCTCTTCAGTAGAGGCCTCCTA 5426  
 SBJCT: 2101 CTCCAACCGTGATGATGACGTCACCTGTCTCATCACCACCTCTCTTCAGTAGAGGCCTCCTA 2160  
 35 QUERY: 5427 CACAGTGGTACAAGATCAAGTTCGGAACAGCTACCAGCTCTGTAATAATGGTACCCTGAG 5486  
 SBJCT: 2161 CACAGTGGTACAAGATCAAGTTCGGAACAGCTACCAGCTCTGTAATAATGGTACCCTGAG 2220  
 40 QUERY: 5487 GGTGATGTATGCTAATGGGATGGGTATCAGCTTCCACAGCGAGCCCCATGTCCTAGCGGG 5546  
 SBJCT: 2221 GGTGATGTATGCTAATGGGATGGGTATCAGCTTCCACAGCGAGCCCCATGTCCTAGCGGG 2280  
 45 QUERY: 5547 CACCATCACCCCCACCATTTGGACGCTGCAACATCTCCCTGCCTATGGAGAATGGCTTAAA 5606  
 SBJCT: 2281 CACCATCACCCCCACCATTTGGACGCTGCAACATCTCCCTGCCTATGGAGAATGGCTTAAA 2340  
 50 QUERY: 5607 CTCCATTGAGTGGCGCCTAAGAAAGGAACAGATTAAAGGCAAAGTCACCATCTTTGGCAG 5666  
 SBJCT: 2341 CTCCATTGAGTGGCGCCTAAGAAAGGAACAGATTAAAGGCAAAGTCACCATCTTTGGCAG 2400  
 55 QUERY: 5667 GAAGCTCCGGGTCCATGGAAGAAATCTCTTGTCCATTGACTATGATCGAAATATTTCGGAC 5726  
 SBJCT: 2401 GAAGCTCCGGGTCCATGGAAGAAATCTCTTGTCCATTGACTATGATCGAAATATTTCGGAC 2460  
 60 QUERY: 5727 TGAAAAGATCTATGATGACCACCGGAAGTTCACCCTGAGGATCATTTATGACCAGGTGGG 5786  
 SBJCT: 2461 TGAAAAGATCTATGATGACCACCGGAAGTTCACCCTGAGGATCATTTATGACCAGGTGGG 2520  
 65 QUERY: 5787 CCGCCCCCTCCTCTGGCTGCCCAGCAGCGGGCTGGCAGCTGTCAACGTGTCATACTTCTT 5846  
 SBJCT: 2521 CCGCCCCCTCCTCTGGCTGCCCAGCAGCGGGCTGGCAGCTGTCAACGTGTCATACTTCTT 2580  
 70 QUERY: 5847 CAATGGGCGCCTGGCTGGGCTTCAGCGTGGGGCCATGAGCGAGAGGACAGACATCGACAA 5906  
 SBJCT: 2581 CAATGGGCGCCTGGCTGGGCTTCAGCGTGGGGCCATGAGCGAGAGGACAGACATCGACAA 2640  
 75 QUERY: 5907 GCAAGGCCGCATCGTGTCCCGCATGTTTCGCTGACGGGAAAGTGTGGAGCTACTCCTACCT 5966  
 SBJCT: 2641 GCAAGGCCGCATCGTGTCCCGCATGTTTCGCTGACGGGAAAGTGTGGAGCTACTCCTACCT 2700  
 80 QUERY: 5967 TGACAAGTCCATGGTCCTCCTGCTTCAGAGCCAACGTCAGTATATATTTGAGTATGACTC 6026  
 SBJCT: 2701 TGACAAGTCCATGGTCCTCCTGCTTCAGAGCCAACGTCAGTATATATTTGAGTATGACTC 2760  
 85 QUERY: 6027 CTCTGACCGCCTCCTTGCCGTCACCATGCCAGCGTGGCCCGGCACAGCATGTCCACACA 6086  
 SBJCT: 2761 CTCTGACCGCCTCCTTGCCGTCACCATGCCAGCGTGGCCCGGCACAGCATGTCCACACA 2820

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QUERY: 6087 CACCTCCATCGGCTACATCCGTAATATTTACAACCCGCCTGAAAGCAATGCTTCGGTCAT 6146  
|||||  
SBJCT: 2821 CACCTCCATCGGCTACATCCGTAATATTTACAACCCGCCTGAAAGCAATGCTTCGGTCAT 2880  
QUERY: 6147 CTTTGACTACAGTGATGACGGCCGCATCCTGAAGACCTCCTTTTTGGGCACCGGACGCCA 6206  
|||||  
SBJCT: 2881 CTTTGACTACAGTGATGACGGCCGCATCCTGAAGACCTCCTTTTTGGGCACCGGACGCCA 2940  
QUERY: 6207 GGTGTTCTACAAGTATGGGAAACTCTCCAAGTTATCAGAGATTGTCTACGACAGTACCGC 6266  
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SBJCT: 2941 GGTGTTCTACAAGTATGGGAAACTCTCCAAGTTATCAGAGATTGTCTACGACAGTACCGC 3000  
QUERY: 6267 CGTCACCTTCGGGTATGACGAGACCACTGGTGTCTTGAAGATGGTCAACCTCCAAAGTGG 6326  
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SBJCT: 3001 CGTCACCTTCGGGTATGACGAGACCACTGGTGTCTTGAAGATGGTCAACCTCCAAAGTGG 3060  
QUERY: 6327 GGGCTTCTCCTGCACCATCAGGTACCGGAAGATTGGCCCCCTGGTGGACAAGCAGATCTA 6386  
|||||  
SBJCT: 3061 GGGCTTCTCCTGCACCATCAGGTACCGGAAGATTGGCCCCCTGGTGGACAAGCAGATCTA 3120  
QUERY: 6387 CAGGTTCTCCGAGGAAGGCATGGTCAATGCCAGGTTTGACTACACCTATCATGACAACAG 6446  
|||||  
SBJCT: 3121 CAGGTTCTCCGAGGAAGGCATGGTCAATGCCAGGTTTGACTACACCTATCATGACAACAG 3180  
QUERY: 6447 CTTCCGCATCGCAAGCATCAAGCCCGTCATAAGTGAGACTCCCCTCCCCGTTGACCTCTA 6506  
|||||  
SBJCT: 3181 CTTCCGCATCGCAAGCATCAAGCCCGTCATAAGTGAGACTCCCCTCCCCGTTGACCTCTA 3240  
QUERY: 6507 CCGCTATGATGAGATTTCTGGCAAGGTGGAACACTTTGGTAAGTTTGGAGTCATCTATTA 6566  
|||||  
SBJCT: 3241 CCGCTATGATGAGATTTCTGGCAAGGTGGAACACTTTGGTAAGTTTGGAGTCATCTATTA 3300  
QUERY: 6567 TGACATCAACCAGATCATCACCCTGCCGTGATGACCCTCAGCAAACACTTCGACACCCA 6626  
|||||  
SBJCT: 3301 TGACATCAACCAGATCATCACCCTGCCGTGATGACCCTCAGCAAACACTTCGACACCCA 3360  
QUERY: 6627 TGGGCGGATCAAGGAGGTCCAGTATGAGATGTTCCGGTCCCTCATGTACTGGATGACGGT 6686  
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SBJCT: 3361 TGGGCGGATCAAGGAGGTCCAGTATGAGATGTTCCGGTCCCTCATGTACTGGATGACGGT 3420  
QUERY: 6687 GCAATATGACAGCATGGGCAGGGTGATCAAGAGGGAGCTAAAACTGGGGCCCTATGCCAA 6746  
|||||  
SBJCT: 3421 GCAATATGACAGCATGGGCAGGGTGATCAAGAGGGAGCTAAAACTGGGGCCCTATGCCAA 3480  
QUERY: 6747 TACCACGAAGTACACCTATGACTACGATGGGGACGGGCAGCTCCAGAGCGTGGCCGTCAA 6806  
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SBJCT: 3481 TACCACGAAGTACACCTATGACTACGATGGGGACGGGCAGCTCCAGAGCGTGGCCGTCAA 3540  
QUERY: 6807 TGACCGCCCGACCTGGCGCTACAGCTATGACCTTAATGGGAATCTCCACTTACTGAACCC 6866  
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SBJCT: 3541 TGACCGCCCGACCTGGCGCTACAGCTATGACCTTAATGGGAATCTCCACTTACTGAACCC 3600  
QUERY: 6867 AGGCAACAGTGTGCGCCTCATGCCCTTGCGCTATGACCTCCGGGATCGGATAACCAGACT 6926  
|||||  
SBJCT: 3601 AGGCAACAGTGTGCGCCTCATGCCCTTGCGCTATGACCTCCGGGATCGGATAACCAGACT 3660  
QUERY: 6927 CGGGGATGTGCAGTACAAAATTGACGACGATGGCTATCTGTGCCAGAGAGGGTCTGACAT 6986  
|||||  
SBJCT: 3661 CGGGGATGTGCAGTACAAAATTGACGACGATGGCTATCTGTGCCAGAGAGGGTCTGACAT 3720  
QUERY: 6987 CTTTGAATACAATTCCAAGGGCCTCCTAACAAGAGCCTACAACAAGGCCAGCGGGTGGAG 7046  
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SBJCT: 3721 CTTTGAATACAATTCCAAGGGCCTCCTAACAAGAGCCTACAACAAGGCCAGCGGGTGGAG 3780  
QUERY: 7047 TGTCCAGTACCGCTATGATGGCGTAGGACGGCGGGCTTCTACAAGACCAACCTGGGCCA 7106  
|||||  
SBJCT: 3781 TGTCCAGTACCGCTATGATGGCGTAGGACGGCGGGCTTCTACAAGACCAACCTGGGCCA 3840  
QUERY: 7107 CCACCTGCAGTACTTCTACTCTGACCTCCACAACCCGACGCGCATCACCCATGTCTACAA 7166

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5 SBJCT: 3841 CCACCTGCAGTACTTCTACTCTGACCTCCACAACCCGACGCGCATCACCCATGTCTACAA 3900  
QUERY: 7167 TCACTCCAACCTCGGAGATTACCTCACTGTACTACGACCTCCAGGGCCACCTCTTTGCCAT 7226  
|||||  
10 SBJCT: 3901 TCACTCCAACCTCGGAGATTACCTCACTGTACTACGACCTCCAGGGCCACCTCTTTGCCAT 3960  
QUERY: 7227 GGAGAGCAGCAGTGGGGAGGAGTACTATGTTGCCTCTGATAACACAGGGACTCCTCTGGC 7286  
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15 SBJCT: 3961 GGAGAGCAGCAGTGGGGAGGAGTACTATGTTGCCTCTGATAACACAGGGACTCCTCTGGC 4020  
QUERY: 7287 TGTGTTTCAAGCATCAACGGCCTCATGATCAAACAGCTGCAGTACACGGCCTATGGGGAGAT 7346  
|||||  
20 SBJCT: 4021 TGTGTTTCAAGCATCAACGGCCTCATGATCAAACAGCTGCAGTACACGGCCTATGGGGAGAT 4080  
QUERY: 7347 TTATTATGACTCCAACCCCGACTTCCAGATGGTCATTGGCTTCCATGGGGGACTCTATGA 7406  
|||||  
25 SBJCT: 4081 TTATTATGACTCCAACCCCGACTTCCAGATGGTCATTGGCTTCCATGGGGGACTCTATGA 4140  
QUERY: 7407 CCCCCTGACCAAGCTGGTCCACTTCACTCAGCGTGATTATGATGTGCTGGCAGGACGATG 7466  
|||||  
30 SBJCT: 4141 CCCCCTGACCAAGCTGGTCCACTTCACTCAGCGTGATTATGATGTGCTGGCAGGACGATG 4200  
QUERY: 7467 GACCTCCCCAGACTATACCATGTGGAAAAACGTGGGCAAGGAGCCGGCCCCCTTTAACCT 7526  
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35 SBJCT: 4201 GACCTCCCCAGACTATACCATGTGGAAAAACGTGGGCAAGGAGCCGGCCCCCTTTAACCT 4260  
QUERY: 7527 GTATATGTTCAAGAGCAACAATCCTCTCAGCAGTGAGCTAGATTTGAAGAACTACGTGAC 7586  
|||||  
40 SBJCT: 4261 GTATATGTTCAAGAGCAACAATCCTCTCAGCAGTGAGCTAGATTTGAAGAACTACGTGAC 4320  
QUERY: 7587 AGATGTGAAAAGCTGGCTTGTGATGTTTGGATTTTCACTTAGCAACATCATTCCTGGCTT 7646  
|||||  
45 SBJCT: 4321 AGATGTGAAAAGCTGGCTTGTGATGTTTGGATTTTCACTTAGCAACATCATTCCTGGCTT 4380  
QUERY: 7647 CCCGAGAGCCAAAATGTATTTTCGTGCCTCCTCCCTATGAATTGTCAGAGAGTCAAGCAAG 7706  
|||||  
50 SBJCT: 4381 CCCGAGAGCCAAAATGTATTTTCGTGCCTCCTCCCTATGAATTGTCAGAGAGTCAAGCAAG 4440  
QUERY: 7707 TGAGAATGGACAGCTCATTACAGGTGTCCAACAGACAACAGAGAGACATAACCAGGCCTT 7766  
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55 SBJCT: 4441 TGAGAATGGACAGCTCATTACAGGTGTCCAACAGACAACAGAGAGACATAACCAGGCCTT 4500  
QUERY: 7767 CATGGCTCTGGAAGGACAGGTCACTACTAAAAAGCTCCACGCCAGCATCCGAGAGAAAGC 7826  
|||||  
60 SBJCT: 4501 CATGGCTCTGGAAGGACAGGTCACTACTAAAAAGCTCCACGCCAGCATCCGAGAGAAAGC 4560  
QUERY: 7827 AGGTCACTGGTTTGGCCACCACCACGCCCATCATTTGGCAAAGGCATCATGTTGGCCATCAA 7886  
|||||  
65 SBJCT: 4561 AGGTCACTGGTTTGGCCACCACCACGCCCATCATTTGGCAAAGGCATCATGTTGGCCATCAA 4620  
QUERY: 7887 AGAAGGGCGGGTGACCACGGGCGTGTCCAGCATCGCCAGCGAAGATAGCCGCAAGGTGGC 7946  
|||||  
70 SBJCT: 4621 AGAAGGGCGGGTGACCACGGGCGTGTCCAGCATCGCCAGCGAAGATAGCCGCAAGGTGGC 4680  
QUERY: 7947 ATCTGTGCTGAACAACGCCTACTACCTGGACAAGATGCACTACAGCATCGAGGGCAAGGA 8006  
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75 SBJCT: 4681 ATCTGTGCTGAACAACGCCTACTACCTGGACAAGATGCACTACAGCATCGAGGGCAAGGA 4740  
QUERY: 8007 CACCCACTACTTTGTGAAGATTGGCTCAGCCGATGGCGACCTGGTCACACTAGGCACCAC 8066  
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80 SBJCT: 4741 CACCCACTACTTTGTGAAGATTGGCTCAGCCGATGGCGACCTGGTCACACTAGGCACCAC 4800  
QUERY: 8067 CATCGGCCGCAAGGTGCTAGAGAGCGGGGTGAACGTGACCGTGTCCCAGCCCACGCTGCT 8126  
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85 SBJCT: 4801 CATCGGCCGCAAGGTGCTAGAGAGCGGGGTGAACGTGACCGTGTCCCAGCCCACGCTGCT 4860  
QUERY: 8127 GGTCAACGGCAGGACTCGAAGGTTTACGAACATTGAGTTCCAGTACTCCACGCTGCTGCT 8186  
|||||  
90 SBJCT: 4861 GGTCAACGGCAGGACTCGAAGGTTTACGAACATTGAGTTCCAGTACTCCACGCTGCTGCT 4920

5  
QUERY: 8187 CAGCATCCGCTATGGCCTCACCCCCGACACCCTGGACGAAGAGAAGGCCCGCGTCCTGGA 8246  
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SBJCT: 4921 CAGCATCCGCTATGGCCTCACCCCCGACACCCTGGACGAAGAGAAGGCCCGCGTCCTGGA 4980

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QUERY: 8247 CCAGGCGAGACAGAGGGCCCTGGGCACGGCCTGGGCCAAGGAGCAGCAGAAAGCCAGGGA 8306  
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SBJCT: 4981 CCAGGCGAGACAGAGGGCCCTGGGCACGGCCTGGGCCAAGGAGCAGCAGAAAGCCAGGGA 5040

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QUERY: 8307 CGGGAGAGAGGGGAGCCGCCTGTGGACTGAGGGCGAGAAGCAGCAGCTTCTGAGCACCGG 8366  
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SBJCT: 5041 CGGGAGAGAGGGGAGCCGCCTGTGGACTGAGGGCGAGAAGCAGCAGCTTCTGAGCACCGG 5100

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QUERY: 8367 GCGCGTGCAAGGGTACGAGGGATATTACGTGCTTCCCGTGGAGCAATACCCAGAGCTTGC 8426  
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SBJCT: 5101 GCGCGTGCAAGGGTACGAGGGATATTACGTGCTTCCCGTGGAGCAATACCCAGAGCTTGC 5160

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QUERY: 8427 AGACAGTAGCAGCAACATCCAGTTTTTAAGACAGAATGAGATGGGAAAGAGGTAACAAAA 8486  
|||||  
SBJCT: 5161 AGACAGTAGCAGCAACATCCAGTTTTTAAGACAGAATGAGATGGGAAAGAGGTAACAAAA 5220

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QUERY: 8487 TAATCTGCTGCCATTCCCTTGTCTGAATGGCTCAGCAGGAGTAAGTGTATCTCCTCTCCT 8546  
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SBJCT: 5221 TAATCTGCTGCCATTCCCTTGTCTGAATGGCTCAGCAGGAGTAAGTGTATCTCCTCTCCT 5280

35  
QUERY: 8547 AAGGAGATGAAGACCTAACAGGGGCACTGCGGCTGGGCTGCTTTAGGAGACCAAGTGGCA 8606  
|||||  
SBJCT: 5281 AAGGAGATGAAGACCTAACAGGGGCACTGCGGCTGGGCTGCTTTAGGAGACCAAGTGGCA 5340

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QUERY: 8607 AGAAAGCTCACATTTTTTGAGTTCAAATGCTACTGTCCAAGCGAGAAGTCCCTCATCCTG 8666  
|||||  
SBJCT: 5341 AGAAAGCTCACATTTTTTGAGTTCAAATGCTACTGTCCAAGCGAGAAGTCCCTCATCCTG 5400

45  
QUERY: 8667 AAGTAGACTAAAGCCCGCTGAAAATTCCGAGGAAAACAAAACAAACGAATGAATGAACA 8726  
|||||  
SBJCT: 5401 AAGTAGACTAAAGCCCGCTGAAAATTCCGAGGAAAACAAAACAAACGAATGAATGAACA 5460

50  
QUERY: 8727 GACACACACAATGTTCCAAGTTCCCCTAAAATATGACCCACTTGTTCTGGGTCTACGCAG 8786  
|||||  
SBJCT: 5461 GACACACACAATGTTCCAAGTTCCCCTAAAATATGACCCACTTGTTCTGGGTCTACGCAG 5520

55  
QUERY: 8787 AAAAGAGACGCAAAGTGT 8804  
|||||  
SBJCT: 5521 AAAAGAGACGCAAAGTGT 5538

60  
SCORE = 1362 BITS (687), EXPECT = 0.0  
IDENTITIES = 705/714 (98%)  
STRAND = PLUS / PLUS

65  
QUERY: 8875 CACGGACCGATAAAACAAAGAAGCGAAGATAAGAAAGAAGGCCTCATATCCAATTACCTCA 8934  
|||||  
SBJCT: 5609 CACGGACCGATAAAACAAAGAAGCGAAGATAAGAAAGAAGGCCTCATATCCAATTACCTCA 5668

70  
QUERY: 8935 CTCATTACATGTGAGCGACACGCGAGACATCCGCGAGGGCCAGCGTCACCAGACCAGCTG 8994  
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SBJCT: 5669 CTCATTACATGTGAGCGACACGCGAGACATCCGCGAGGGCCAGCGTCACCAGACCAGCTG 5728

75  
QUERY: 8995 CGGGACAAACCACTCAGACTGCTTGTAGGACAAATACTTCTGACATTTTCGTTTAAGCAA 9054  
|||||  
SBJCT: 5729 CGGGACAAACCACTCAGACTGCTTGTAGGACAAATACTTCTGACATTTTCGTTTAAGCAA 5788

80  
QUERY: 9055 ATACAGGTGCATTTAAACACGACTTTGGGGGTGATTTGTGTGTAGCGCCTGGGGAGGGG 9114  
|||||  
SBJCT: 5789 ATACAGGTGCATTTAAACACGACTTTGGGGGTGATTTGTGTGTAGCGCCTGGGGAGGGG 5848

85  
QUERY: 9115 GGATAAAAGAGGAGGAGTGAGCACTGGAAATACTTTTAAAGNNNNNNNNNCATGAGGGA 9174  
|||||  
SBJCT: 5849 GGATAAAAGAGGAGGAGTGAGCACTGGAAATACTTTTAAAGAAAAAAACATGAGGGA 5908

90  
QUERY: 9175 ATAAAAGAAATTCCTATCAAAAATCAAAGTGAAATAATACCATCCAGCACTTAAGTCTCA 9234

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SBJCT: 5909 ATAAAAGAAATTCCTATCAAAAATCAAAGTGAAATAATACCATCCAGCACTTAACTCTCA 5968
          |||
5  QUERY: 9235 GGTCCCAACTAAGTCTGGCCTGAGCTAATTTATTTGAGCGCAGAGTGTAATAATTTAATTC 9294
          |||
SBJCT: 5969 GGTCCCAACTAAGTCTGGCCTGAGCTAATTTATTTGAGCGCAGAGTGTAATAATTTAATTC 6028
          |||
10  QUERY: 9295 AAAATGGTGGCTATAATCACTACAGATAAATTTTCATACTCTTTTGTCTTTGGAGATTCCA 9354
          |||
SBJCT: 6029 AAAATGGTGGCTATAATCACTACAGATAAATTTTCATACTCTTTTGTCTTTGGAGATTCCA 6088
          |||
15  QUERY: 9355 TTGTGGACAGTAATACGCAGTTACAGGGTGTAGTCTGTTTAGATTCCGTAGTTCGTGGGT 9414
          |||
SBJCT: 6089 TTGTGGACAGTAATACGCAGTTACAGGGTGTAGTCTGTTTAGATTCCGTAGTTCGTGGGT 6148
          |||
20  QUERY: 9415 ATCAGTTTCGGTAGAGGTGCAGCATCGTGACACTTTTGCTAACAGGTACCACTTCTGATC 9474
          |||
SBJCT: 6149 ATCAGTTTCGGTAGAGGTGCAGCATCGTGACACTTTTGCTAACAGGTACCACTTCTGATC 6208
          |||
25  QUERY: 9475 ACCCTGTACATACATGAGCCGAAAGGCACAATCACTGTTTCAGATTTAAAATTATTAGTG 9534
          |||
SBJCT: 6209 ACCCTGTACATACATGAGCCGAAAGGCACAATCACTGTTTCAGATTTAAAATTATTAGTG 6268
          |||
30  QUERY: 9535 TGT'TTGT'TTGGTCCAGAAACTGAGACAATCACATGACAGTCACCACGAGGAGAG 9588
          |||
SBJCT: 6269 TGT'TTGT'TTGGTCCAGAAACTGAGACAATCACATGACAGTCACCACGAGGAGAG 6322
          |||
SCORE = 349 BITS (176), EXPECT = 2E-92
IDENTITIES = 176/176 (100%)
STRAND = PLUS / PLUS
          |||
35  QUERY: 9651 GTCTAATAAGAACTTTGGTACAGGAAC'TTTTTGTAATATACATGTATGAATTGTTTCATC 9710
          |||
SBJCT: 6385 GTCTAATAAGAACTTTGGTACAGGAAC'TTTTTGTAATATACATGTATGAATTGTTTCATC 6444
          |||
40  QUERY: 9711 GAGTTTTTATATTAATTTTAATTTGCTGCTAAGCAAAGACTAGGGACAGGCAAAGATAAT 9770
          |||
SBJCT: 6445 GAGTTTTTATATTAATTTTAATTTGCTGCTAAGCAAAGACTAGGGACAGGCAAAGATAAT 6504
          |||
40  QUERY: 9771 TTATGGCAAAGTGTTTAAATTGTTTATACATAAATAAAGTCTCTAAACTCCTGTG 9826
          |||
SBJCT: 6505 TTATGGCAAAGTGTTTAAATTGTTTATACATAAATAAAGTCTCTAAACTCCTGTG 6560
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In this search it was also found that the FCTR3bcd and e nucleic acids had homology to five fragments of *Mus musculus* mRNA for Ten-m2. It has 5498 of 6108 bases (90%) identical to bases 2504-8610, 1095 of 1196 bases (91%) identical to bases 103-1298, 1000 of 1088 bases (91%) identical to bases 1420-2540, 81 of 89 bases (91%) identical to bases 8655-8743, and 30 of 32 bases (93%) identical to bases 7-38 of *Mus musculus* mRNA for Ten-m2 (Table 3M).

### Table 3M. BLASTN of FCTR3b, c, d, and e against *Mus musculus* mRNA for Ten-m2

#### Mrna (SEQ ID NO:65)

>GI|4760777|DBJ|AB025411.1|AB025411 MUS MUSCULUS MRNA FOR TEN-M2, COMPLETE CDS  
LENGTH = 8797

SCORE = 7263 BITS (3664), EXPECT = 0.0  
IDENTITIES = 5498/6108 (90%), GAPS = 1/6108 (0%)  
STRAND = PLUS / PLUS

QUERY: 2578 GATGGCTGCCCTGACTTGTGCAACGGTAACGGGAGATGCACACTGGGTGAGAAGAGCTGG 2637  
|||||

5 SBJCT: 2504 GATGGCTGCCCTGATTGTGTGCAACGGTAACGGGAGATGCACACTGGGTCAGAACAGCTGG 2563

QUERY: 2638 CAGTGTGTCTGCCAGACCGGCTGGAGAGGGCCCGGATGCAACGTTGCCATGGAAACTTCC 2697  
|||||

10 SBJCT: 2564 CAGTGTGTCTGCCAGACCGGCTGGAGAGGGCCTGGATGCAACGTTGCCATGGAAACCTCC 2623

QUERY: 2698 TGTGCTGATAACAAGGATAATGAGGGAGATGGCCTGGTGGATTGTTTGGACCCTGACTGC 2757  
|| |||

SBJCT: 2624 TGCCTGATAACAAGGATAATGAGGGAGATGGCCTGGTGGACTGCCTGGACCCTGACTGC 2683

QUERY: 2758 TGCCTGCAGTCAGCCTGTGAGAACAGCCTGCTCTGCCGGGGGTCCCGGGACCCACTGGAC 2817  
|||||

15 SBJCT: 2684 TGCCTACAGTCAGCCTGTGAGAACAGCCTGCTCTGCCGGGGGTCTCGGGACCCCTTGGAC 2743

QUERY: 2818 ATCATTGAGCAGGGCCAGACGGATTGGCCCGCAGTGAAGTCCTTCTATGACCGTATCAAG 2877  
|||||

20 SBJCT: 2744 ATCATTGAGCAAGGTCAGACAGACTGGCCTGCAGTGAAGTCCTTCTATGACCGCATCAAG 2803

QUERY: 2878 CTCTTGGCAGGCAAGGATAGCACCCACATCATTCTGGAGAGAACCCTTTCAACAGCAGC 2937  
|||||

25 SBJCT: 2804 CTCTTGGCAGGCAAGGACAGCACCCACATCATTCTGGAGACAACCCTTCAATAGCAGC 2863

QUERY: 2938 TTGGTTTCTCTCATCCGAGGCCAAGTAGTAACCTACAGATGGAACCTCCCTGGTCGGTGTG 2997  
|||||

30 SBJCT: 2864 CTGGTGTCTCTGATCCGAGGCCAAGTAGTAACCATGGATGGGACTCCCTTGGTGGGTGTG 2923

QUERY: 2998 AACGTGTCTTTTGTCAAGTACCCAAAATACGGCTACACCATCACCCGCCAGGATGGCACG 3057  
|| |||

35 SBJCT: 2924 AATGTGTCTTTTGTCAAGTACCCAAAATATGGCTACACCATCACTCGCCAGGATGGCACG 2983

QUERY: 3058 TTCGACCTGATCGCAAATGGAGGTGCTTCTTACTCTACACTTTGAGCGAGCCCCGTTT 3117  
|| |||

40 SBJCT: 2984 TTTGACCTGATTGCCAATGGGGTTCTGCCTTACTCTTCACTTTGAGCGAGCCCCCTTC 3043

QUERY: 3118 ATGAGCCAGGAGCGCACTGTGTGGCTGCCGTGGAACAGCTTTTACGCCATGGACACCCTG 3177  
|||||

45 SBJCT: 3044 ATGAGCCAGGAGCGCACAGTGTGGCTGCCATGGAACAGCTTCTATGCCATGGACACCCTG 3103

QUERY: 3178 GTGATGAAGACCGAGGAGAACTCCATCCCCAGCTGTGACCTCAGTGGCTTTGTCCGGCCT 3237  
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50 SBJCT: 3104 GTAATGAAGACCGAGGAAACTCCATCCCCAGCTGTGACCTCAGTGGCTTTGTCCGGCCA 3163

QUERY: 3238 GATCCAATCATCATCTCCTCCCCACTGTCCACCTTCTTTAGTGCTGCCCCCTGGGCAGAAAT 3297  
|||||

55 SBJCT: 3164 GATCCAATCATCATCTCCTCTCCTCTGTCCACCTTCTTCAGCGCTTCCCCTGCCTCGAAC 3223

QUERY: 3298 CCCATCGTGCCTGAGACCCAGGTTCTTCATGAAGAAATCGAGCTCCCTGGTTCCAATGTG 3357  
|||||

60 SBJCT: 3224 CCCATTGTGCCTGAGACCCAGGTTCTTCATGAAGAAATTGAGCTCCCTGGTACCAATGTG 3283

QUERY: 3358 AACTTCGCTATCTGAGCTCTAGAAGTGCAGGGTACAAGTCACTGCTGAAGATCACCATG 3417  
|| |||

65 SBJCT: 3284 AAGCTCCGTTATCTCAGCTCTAGAAGTGCAGGGTATAAGTCGCTGCTGAAGATCACCATG 3343

QUERY: 3418 ACCCAGTCCACAGTGCCCCCTGAACCTCATTAGGGTTACCTGATGGTGGCTGTGAGGGG 3477  
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70 SBJCT: 3344 ACGCAGTCCACAGTGCCCTTGAACCTCATCAGGGTCACTTGATGGTTGCTGTAGAGGGG 3403

QUERY: 3478 CATCTCTTCCAGAAGTCATTCCAGGCTTCTCCCAACCTGGCCTCCACCTTCATCTGGGAC 3537  
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SBJCT: 3404 CATCTCTTCCAGAAGTCATTCCAGGCTTCTCCCAACCTAGCCTACACATTCATCTGGGAC 3463

QUERY: 3538 AAGACAGATGCGTATGGCCAAAGGGTGTATGGACTCTCAGATGCTGTTGTGTCTGTGCGG 3597  
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75 SBJCT: 3464 AAGACAGATGCTTATGGCCAAAGGGTTATGGCCTATCGGATGCTGTTGTGTCTGTGCGG 3523

QUERY: 3598 TTTGAATATGAGACCTGTCCCAGTCTAATTCTCTGGGAGAAAAGGACAGCCCTCCTTCAG 3657  
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80 SBJCT: 3524 TTTGAATATGAGACCTGCCCCAGTCTCATCCTGTGGGAGAAAAGGACAGCCCTGCTTCAG 3583

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QUERY: 3658 GGATTCGAGCTGGACCCCTCCAACCTCGGTGGCTGGTCCCTAGACAAACACCACATCCTC 3717  
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SBJCT: 3584 GGATTCGAGCTGGACCCCTCCAACCTTGGAGGCTGGTCCCTGGACAAACACCACACCCTC 3643

QUERY: 3718 AATGTTAAAAGTGGAACTCTACACAAAGGCACTGGGGAAAACCAGTTCCTGACCCAGCAG 3777  
|||||  
SBJCT: 3644 AATGTGAAAAGCGGAATACTACACAAAGGGACAGGGGAGAACCAGTTCCTGACCCAGCAG 3703

QUERY: 3778 CCTGCCATCATCACCAGCATCATGGGCAATGGTCGCCGCCGAGCATTTCCTGTCCCAGC 3837  
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SBJCT: 3704 CCTGCCATCATCACGAGCATCATGGGCAACGGTCGCCGCAGAAGCATCTCCTGTCCCAGC 3763

QUERY: 3838 TGCAACGGCCTTGCTGAAGGCAACAAGCTGCTGGCCCCAGTGGCTCTGGCTGTTGGAATC 3897  
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SBJCT: 3764 TGCAATGGCCTTGCTGAAGGCAACAACCTGTTAGCCCCTGTGGCCCTGGCTGTGGGGATC 3823

QUERY: 3898 GATGGGAGCCTCTATGTGGGTGACTTCAATTACATCCGACGCATCTTCCCTCTCGAAAT 3957  
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SBJCT: 3824 GATGGGAGCCTCTTTGTTGGTGACTTCAACTATATCCGGCGCATCTTCCCTCTCGAAAT 3883

QUERY: 3958 GTGACCAGCATCTTGGAGTTACGAAATAAAGAGTTTAAACATAGCAACAACCCAGCACAC 4017  
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SBJCT: 3884 GTGACCAGTATCTTGGAGTTACGAAATAAAGAGTTTAAACATAGCAACAGCCCAGGACAC 3943

QUERY: 4018 AAGTACTACTTGGCAGTGGACCCCGTGTCCGGCTCGCTCTACGTGTCCGACACCAACAGC 4077  
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SBJCT: 3944 AAGTACTACTTGGCTGTGGACCCCGTGACTGGCTCACTCTACGTCTCTGACACCAACAGT 4003

QUERY: 4078 AGGAGAATCTACCGCGTCAAGTCTCTGAGTGGAACCAAAGACCTGGCTGGGAATTTCGGAA 4137  
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SBJCT: 4004 CGCCGAATCTACCGAGTCAAGTCTCTGAGCGGAGCCAAAGACCTGGCTGGGAATTTCGGAA 4063

QUERY: 4138 GTTGTGGCAGGGACGGGAGAGCAGTGTCTACCCTTTGATGAAGCCCGCTGCGGGGATGGA 4197  
|||||  
SBJCT: 4064 GTTGTGGCAGGGACTGGCGAACAATGTCTACCCTTTGATGAAGCCCGCTGTGGGGATGGA 4123

QUERY: 4198 GGGAAGGCCATAGATGCAACCCTGATGAGCCCGAGAGGTATTGCAGTAGACAAGAATGGG 4257  
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SBJCT: 4124 GGGAAGGCTGTGGACGCCACCCTGATGAGCCCGAGAGGTATTGCAGTAGACAAGAATGGG 4183

QUERY: 4258 CTCATGTACTTTGTCTGATGCCACCATGATCCGGAAGGTTGACCAGAATGGAATCATCTCC 4317  
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SBJCT: 4184 CTTATGTACTTTGTTGATGCCACCATGATCCGGAAGGTGGACCAAACCGGAATCATCTCC 4243

QUERY: 4318 ACCCTGCTGGGCTCCAATGACCTCACTGCCGTCGGCCGCTGAGCTGTGATTCCAGCATG 4377  
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SBJCT: 4244 ACCCTGCTGGGCTCCAATGACCTCACAGCTGTCCGACCACTGAGCTGTGACTCGAGCATG 4303

QUERY: 4378 GATGTAGCCCAGGTTCTGCTGGAGTGGCCAACAGACCTTGCTGTCAATCCCATGGATAAC 4437  
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SBJCT: 4304 GACGTGGCCCAGGTCCGTCTAGAATGGCCGACAGACCTCGCCGTCAACCCCATGGACAAC 4363

QUERY: 4438 TCCTTGTATGTTCTAGAGAACAATGTCATCCTTCGAATCACCGAGAACCACCAAGTCAGC 4497  
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SBJCT: 4364 TCCCTGTACGTTCTGGAGAACAACGTCATCCTGCGGATCACGGAGAACCACCAGGTCAGC 4423

QUERY: 4498 ATCATTGCGGGACGCCCCATGCACTGCCAAGTTCTGGCATTGACTACTCACTCAGCAAA 4557  
|||||  
SBJCT: 4424 ATCATCGCGGGACGGCCTATGCACTGCCAGGTTCCCGGCATCGACTACTCGCTCAGCAAA 4483

QUERY: 4558 CTAGCCATTCACTCTGCCCTGGAGTCAGCCAGTGCCATTGCCATTTCTCACACTGGGGTC 4617  
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SBJCT: 4484 CTCGCCATCCACTCTGCGCTGGAATCAGCCAGCGCCATTGCCATTTCTCACACTGGGGTG 4543

QUERY: 4618 CTCTACATCACTGAGACAGATGAGAAGAAGATTAACCGTCTACGCCAGGTAACAACCAAC 4677  
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SBJCT: 4544 CTCTACATCACTGAGACGGACGAGAAGAAGATCAACCGCCTACGCCAAGTCACCACCAAT 4603

QUERY: 4678 GGGGAGATCTGCCTTTTAGCTGGGGCAGCCTCGGACTGCGACTGCAAAAACGATGTCAAT 4737  
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SBJCT: 4604 GGAGAGATCTGCCTCTTAGCCGGGGCGGCCTCAGACTGTGACTGCAAAAACGATGTCAAC 4663

QUERY: 4738 TGCAACTGCTATTTCAGGAGATGATGCCTACGCGACTGATGCCATCTTGAATCCCCATCA 4797  
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SBJCT: 4664 TGCATCTGCTACTCGGGAGATGACGCTTACGCCACGGACGCCATCCTGAACTCGCCGTCC 4723

QUERY: 4798 TCCTTAGCTGTAGCTCCAGATGGTACCATTACATTGCAGACCTTGGAATATTCGGATC 4857  
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SBJCT: 4724 TCCTTAGCCGTGGCTCCGGATGGCACCATCTACATTGCAGACCTTGGAATATTCGGATC 4783

QUERY: 4858 AGGGCGGTCAGCAAGAACAAGCCTGTTCTTAATGCCTTCAACCAGTATGAGGCTGCATCC 4917  
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SBJCT: 4784 AGGGCGGTCAGCAAAAATAAACCCGTTCTTAACGCATTCACCAGTATGAGGCTGCATCT 4843

QUERY: 4918 CCCGGAGAGCAGGAGTTATATGTTTTCAACGCTGATGGCATCCACCAATACACTGTGAGC 4977  
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SBJCT: 4844 CCGGGAGAACAGGAATTGTACGTGTTCAACGCTGATGGTATCCATCAGTACACTGTGAGT 4903

QUERY: 4978 CTGGTGACAGGGGAGTACTTGTACAATTTACATATAGTACTGACAATGATGTCACTGAA 5037  
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SBJCT: 4904 CTGGTGACTGGGGAGTACTTGTACAATTTACATACAGCGCTGACAATGACGTCACCGAG 4963

QUERY: 5038 TTGATTGACAATAATGGGAATTCCTGAAGATCCGTCGGGACAGCAGTGGCATGCCCCGT 5097  
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SBJCT: 4964 TTGATTGACAACAACGGGAATTCCTAAAGATCCGCCGGGACAGCAGTGGCATGCCCCGC 5023

QUERY: 5098 CACCTGCTCATGCCTGACAACCAGATCATCACCTCACCGTGGGCACCAATGGAGGCCTC 5157  
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SBJCT: 5024 CACCTGCTCATGCCGGATAATCAGATTATCACCTTACTGTGGGCACCAATGGAGGCCTC 5083

QUERY: 5158 AAAGTCGTGTCCACACAGAACCTGGAGCTTGGTCTCATGACCTATGATGGCAACACTGGG 5217  
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SBJCT: 5084 AAAGCCGTGTCCACTCAGAACCTGGAGCTGGGCCTCATGACTTATGATGGGAACACTGGA 5143

QUERY: 5218 CTCCTGGCCACCAAGAGCGATGAAACAGGATGGACGACTTTCTATGACTATGACCACGAA 5277  
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SBJCT: 5144 CTCCTAGCCACCAAGAGTGATGAAACCGGATGGACAACCTTTTATGACTATGACCACGAG 5203

QUERY: 5278 GGCCGCCTGACCAACGTGACGCGCCCCACGGGGTGGTAACCAGTCTGCACCGGGAAATG 5337  
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SBJCT: 5204 GGCCGTCTGACCAATGTGACCCGCCCCACGGGCGTGGTGACCAGTCTGCACCGGGAAATG 5263

QUERY: 5338 GAGAAATCTATTACCATTGACATTGAGAACTCCAACCGTGATGATGACGTCCTGTCATC 5397  
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SBJCT: 5264 GAGAAATCTATCACCATTGACATTGAGAACTCCAACCGGGATGATGACGTCCTGTCATC 5323

QUERY: 5398 ACCAACCTCTCTTCAGTAGAGGCCTCCTACACAGTGGTACAAGATCAAGTTCGGAACAGC 5457  
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SBJCT: 5324 ACCAACCTCTCTCCGTGGAGGCCTCCTATACAGTGGTACAAGATCAAGTGCGAAACAGC 5383

QUERY: 5458 TACCAGCTCTGTAATAATGGTACCCTGAGGGTGATGTATGCTAATGGGATGGGTATCAGC 5517  
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SBJCT: 5384 TACCAGCTCTGCAATAATGGAACCCTGCGGGTGATGTACGCCAACGGCATGGCTGTCAGC 5443

QUERY: 5518 TTCCACAGCGAGCCCCATGTCCTAGCGGGCACCATCACCCCCACCATTGGACGCTGCAAC 5577  
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SBJCT: 5444 TTCCACAGTGAGCCCCACGTCCTCGCAGGCACCATCACCCCCACCATCGGGCGCTGCAAC 5503

QUERY: 5578 ATCTCCCTGCCTATGGAGAATGGCTTAAACTCCATTGAGTGGCGCCTAAGAAAGGAACAG 5637  
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SBJCT: 5504 ATCTCTCTGCCCATGGAGAATGGCCTGAACTCCATCGAGTGGCGCCTGAGGAAGGAACAG 5563

QUERY: 5638 ATTAAAGGCAAAGTCACCATCTTTGGCAGGAAGCTCCGGGTCCATGGAAGAAATCTCTTG 5697  
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SBJCT: 5564 ATCAAAGGCAAAGTCACCATCTTTGGGAGGAAGCTTCGGGTCCACGGAAGGAATCTCCTG 5623

QUERY: 5698 TCCATTGACTATGATCGAAATATTCGGACTGAAAAGATCTATGATGACCACCGGAAGTTC 5757  
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SBJCT: 5624 TCCATTGATTATGACCGAAATATCCGTACGGAGAAGATCTACGATGACCACCGGAATTC 5683

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QUERY: 5758 ACCCTGAGGATCATTTATGACCAGGTGGGCCGCCCTTCCTCTGGCTGCCCAGCAGCGGG 5817  
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SBJCT: 5684 ACCCTGAGGATCATCTATGACCAGGTGGGCCGCCCTTCCTGTGGCTCCCGAGCAGTGGG 5743

QUERY: 5818 CTGGCAGCTGTCAACGTGTCATACTTCTTCAATGGGCGCCTGGCTGGGCTTCAGCGTGGG 5877  
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SBJCT: 5744 CTGGCAGCCGTCAATGTCTCCTACTTCTTCAATGGGCGCTTGGCCGGCCTCCAGCGAGGG 5803

QUERY: 5878 GCCATGAGCGAGAGGACAGACATCGACAAGCAAGGCCGCATCGTGTCCCGCATGTTTCGCT 5937  
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SBJCT: 5804 GCCATGAGCGAGAGGACAGACATTGACAAGCAAGGCCGGATCGTGTCCCGCATGTTTCGCC 5863

QUERY: 5938 GACGGGAAAGTGTGGAGCTACTCCTACCTTGACAAGTCCATGGTCTCCTGCTTCAGAGC 5997  
|||||  
SBJCT: 5864 GACGGGAAAGTCTGGAGTTATTCCTATCTTGACAAGTCCATGGTCTTCTGCTACAGAGC 5923

QUERY: 5998 CAACGTCAGTATATATTTGAGTATGACTCCTCTGACCGCCTCCTTGCCGTCACCATGCCC 6057  
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SBJCT: 5924 CAACGTCAGTACATATTTGAATATGACTCCTCCGATCGCCTCCACGCAGTCACTATGCCC 5983

QUERY: 6058 AGCGTGGCCCGGCACAGCATGTCCACACACACCTCCATCGGCTACATCCGTAATATTTAC 6117  
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SBJCT: 5984 AGTGTGCCCCGGCACAGCATGTCCACGCACACCTCCATTGGTTACATCCGAAACATTTAC 6043

QUERY: 6118 AACCCGCCTGAAAGCAATGCTTCGGTCATCTTTGACTACAGTGATGACGGCCGCATCCTG 6177  
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SBJCT: 6044 AACCCACCCGAAAGCAATGCATCGGTCATCTTTGACTACAGTGATGACGGCCGCATCCTA 6103

QUERY: 6178 AAGACCTCCTTTTTTGGGCACCGGACGCCAGGTGTTCTACAAGTATGGGAAACTCTCCAAG 6237  
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SBJCT: 6104 AAGACATCTTTCTTGGGCACTGGGCGCCAGGTGTTCTACAAGTATGGGAAACTCTCCAAG 6163

QUERY: 6238 TTATCAGAGATTGTCTACGACAGTACCGCCGTCACCTTCGGGTATGACGAGACCACTGGT 6297  
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SBJCT: 6164 TTATCAGAGATAGTCTACGACAGCACAGCCGTCACCTTTGGGTATGACGAGACCACCGGT 6223

QUERY: 6298 GTCTTGAAGATGGTCAACCTCCAAAGTGGGGGCTTCTCCTGCACCATCAGGTACCGGAAG 6357  
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SBJCT: 6224 GTCCTGAAGATGGTCAATCTCCAAAGTGGGGGCTTCTCCTGTACCATCAGGTACCGAAAG 6283

QUERY: 6358 ATTGGCCCCCTGGTGGACAAGCAGATCTACAGGTTCTCCGAGGAAGGCATGGTCAATGCC 6417  
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SBJCT: 6284 GTTGGGCCCTTGTGGACAAGCAGATTTACAGGTTCTCTGAGGAAGGAATGATCAACGCC 6343

QUERY: 6418 AGGTTTGACTACACCTATCATGACAACAGCTTCCGCATCGCAAGCATCAAGCCCGTCATA 6477  
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SBJCT: 6344 AGGTTTGATTATACCTATCACGACAATAGCTTCCGCATTGCCAGCATCAAACCCGTCATT 6403

QUERY: 6478 AGTGAGACTCCCCTCCCCGTTGACCTCTACCGCTATGATGAGATTTCTGGCAAGGTGGAA 6537  
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SBJCT: 6404 AGCGAGACTCCCCTTCCTGTTGACCTCTACCGCTATGACGAGATTTCCGGCAAGGTGGAA 6463

QUERY: 6538 CACTTTGGTAAGTTTGGAGTCATCTATTATGACATCAACCAGATCATCACCCTGCCGTG 6597  
|||||  
SBJCT: 6464 CACTTCGGCAAGTTTGGGGTCATCTACTACGACATCAACCAGATCATCACCCTGCCGTC 6523

QUERY: 6598 ATGACCCTCAGCAAACACTTCGACACCCATGGGCGGATCAAGGAGGTCCAGTATGAGATG 6657  
|||||  
SBJCT: 6524 ATGACGCTTAGCAAGCACTTTGACACCCATGGGCGCATCAAGGAAGTGCAATATGAGATG 6583

QUERY: 6658 TTCCGGTCCCTCATGTACTGGATGACGGTGCAATATGACAGCATGGGCAGGGTGATCAAG 6717  
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SBJCT: 6584 TTCCGGTCCCTCATGTACTGGATGACTGTGCAATATGACAGTATGGGTAGGGTCATCAAG 6643

QUERY: 6718 AGGGAGCTAAAACTGGGGCCCTATGCCAATACCACGAAGTACACCTATGACTACGATGGG 6777  
|||||  
SBJCT: 6644 AGGGAAGTGAAGTAGGGCCCTATGCCAACACCACAAAGTACACCTATGACTATGACGGG 6703

QUERY: 6778 GACGGGCAGCTCCAGAGCGTGGCCGTCAATGACCGCCCGACCTGGCGCTACAGCTATGAC 6837  
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5 SBJCT: 223 GAAGTCCTACAGTTCCAGTGAGACCTTGAAGGCTTATGACCATGACAGCAGAATGCACTA 282  
QUERY: 450 TGGAAACCGAGTCACAGACCTCATCCACCGGGAGTCAGATGAGTTTCTAGACAAGGAAC 509  
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10 SBJCT: 283 TGGAAACCGAGTCACAGACCTGGTGCACCGGGAGTCCGATGAGTTTCTAGACAAGGGAC 342  
QUERY: 510 CAACTTCACCTTGCCGAACCTGGGCATCTGTGAGCCCTCCCCACACCGAAGCGGCTACTG 569  
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10 SBJCT: 343 AAATTCACCTGGCAGAATTGGGAATCTGCGAGCCCTCCCCACACCGAAGTGGTACTG 402  
QUERY: 570 CTCCGACATGGGGATCCTTCACCAGGGCTACTCCCTTAGCACAGGGTCTGACGCCGACTC 629  
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15 SBJCT: 403 TTCCGACATGGGTATCCTCCACCAGGGCTACTCCCTGAGCACTGGGTCTGATGCAGACTC 462  
QUERY: 630 CGACACCGAGGGAGGGATGTCTCCAGAACACGCCATCAGACTGTGGGGCAGAGGGATAAA 689  
|||||  
15 SBJCT: 463 GGACACCGAGGGAGGGATGTCTCCAGAACATGCCATCAGACTGTGGGGACGAGGGATAAA 522  
QUERY: 690 ATCCAGGCGCAGTTCCGGCCTGTCCAGTCGTGAAAACCTCGGCCCTTACCCTGACTGACTC 749  
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20 SBJCT: 523 ATCCAGGCGCAGCTCTGGCTTGTCCAGCCGCGAGAACTCGGCCCTTACTCTGACTGACTC 582  
QUERY: 750 TGACAACGAAAACAAATCAGATGATGAGAACGGTCGTCCCATTCCACCTACATCCTCGCC 809  
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25 SBJCT: 583 TGACAATGAAAATAAATCGGATGACGACAATGGTCGTCCCATTCCACCTACATCCTCGTC 642  
QUERY: 810 TAGTCTCCTCCCATCTGCTCAGCTGCCTAGCTCCCATAATCCTCCACCAGTTAGCTGCCA 869  
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30 SBJCT: 643 TAGCCTCCTCCCATCTGCTCAGCTGCCTAGCTCCCATAATCCTCCACCAGTTAGCTGCCA 702  
QUERY: 870 GATGCCATTGCTAGACAGCAACACCTCCCATCAAATCATGGACACCAACCCTGATGAGGA 929  
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30 SBJCT: 703 GATGCCATTGCTAGACAGCAACACCTCCCATCAGATCATGGACACCAACCCTGATGAGGA 762  
QUERY: 930 ATTCTCCCCAATTCATACCTGCTCAGAGCATGCTCAGGGCCCCAGCAAGCCTCCAGCAG 989  
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35 SBJCT: 763 ATTCTCCCCAATTCATACCTGCTCAGAGCATGCTCAGGGCCCCAGCAAGCCTCCAGCAG 822  
QUERY: 990 TGGCCCTCCGAACCACCACAGCCAGTCGACTCTGAGGCCCCCTCTCCACCCCCTCACAA 1049  
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40 SBJCT: 823 TGGCCCTCCAAACCACCACAGCCAGTCAACACTGAGGCCCCCTCTGCCACCCCCTCATAA 882  
QUERY: 1050 CCACACGCTGTCCCATCACCACCTCGTCCGCCAACTCCCTCAACAGGAACTCACTGACCAA 1109  
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45 SBJCT: 883 CCACACCCTGTCCCACCACCACCTCCTCGGCCAACTCCCTCAACAGGAACTCACTGACCAA 942  
QUERY: 1110 TCGGCGGAGTCAGATCCACGCCCCGGCCCCAGCGCCCCAATGACCTGGCCACCACACCAGA 1169  
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50 SBJCT: 943 TCGGCGGAGTCAAATCCACGCCCCAGCTCCTGCGCCCAACGACCTGGCCACCACCCCAGA 1002  
QUERY: 1170 GTCCGTTTACGCTTACAGGACAGCTGGGTGCTAAACAGCAACGTGCCACTGGAGACCCGGCA 1229  
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50 SBJCT: 1003 GTCTGTTTACGCTCCAGGATAGCTGGGTGCTGAACAGTAACGTCCCACTGGAGACTCGGCA 1062  
QUERY: 1230 CTTCTCTTCAAGACCTCCTCGGGGAGCACACCCTTGTTTACGAGCTCTTCCCCGGGATA 1289  
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55 SBJCT: 1063 CTTCTTTTCAAACGTCGTCTGGAAGCACACCCCTGTTTACGAGCTCTTCTCCGGGATA 1122  
QUERY: 1290 CCCTTTGACCTCAGGAACGGTTTACACGCCCCCGCCCCGCTGCTGCCACGGAATACTTT 1349  
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60 SBJCT: 1123 CCCTTTGACCTCAGGACCGTTTATACACCACCACCCCGCCTGCTGCCACGGAATACTTT 1182  
QUERY: 1350 CTCCAGGAAGGCTTTCAAGCTGAAGAAGCCCTCCAAATACTGCAGCTGGAAATGTGCTGC 1409  
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65 SBJCT: 1183 CTCCAGGAAGGCTTTCAAGCTGAAGAAACCCTCCAAATACTGCAGTTGGAAATGTGCTGC 1242  
QUERY: 1410 CCTCTCCGCCATTGCCGCGGCCCTCCTCTTGCTATTTTGCTGGCGTATTTTCATAG 1465  
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70 SBJCT: 1243 CCTGTCTGCCATCGCCGCGGCCCTCCTCTTGCCATTTTGCTGGCATATTTTCATAG 1298

SCORE = 1455 BITS (734), EXPECT = 0.0  
IDENTITIES = 1000/1088 (91%), GAPS = 3/1088 (0%)  
STRAND = PLUS / PLUS

5 QUERY: 1464 AGTGCCCTGGTCGTTGAAAAACAGCAGCATAGACAGTGGTGAAGCAGAAGTTGGTCGGCG 1523  
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SBJCT: 1420 AGTGCCCTGGTCATTGAAAAACAGCAGCATAGACAGTGGCGAAGCAGAAGTTGGTCGGCG 1479

10 QUERY: 1524 GGTAACACAAGAAGTCCCACCAGGGGTGTTTGGAGGTCACAAATTCACATCAGTCAGCC 1583  
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SBJCT: 1480 GGTGACACAGGAAGTCCCACCAGGGGTGTTTGGAGGTCACAGATTCACATCAGTCAGCC 1539

15 QUERY: 1584 CCAGTTCTTAAAGTTCAACATCTCCCTCGGGAAGGACGCTCTCTTGGTGTTTACATAAG 1643  
|| |||||  
SBJCT: 1540 TCAATTCTTAAAGTTCAACATCTCCCTGGGCAAGGATGCCCTCTTCGGTGTCTATATAAG 1599

20 QUERY: 1644 AAGAGGACTTCCACCATCTCATGCCAGTATGACTTCATGGAACGTCTGGACGGGAAGGA 1703  
||||| |||||  
SBJCT: 1600 GAGAGGACTACCACCGTCTCATGCCAGTATGACTTCATGGAACGCCTGGATGGAAAGGA 1659

25 QUERY: 1704 GAAGTGGAGTGTGGTTGAGTCTCCAGGGAACGCCGGAGCATAACAGACCTTGGTTCAGAA 1763  
||| |||||  
SBJCT: 1660 GAAATGGAGCGTGGTTCGAGTCGCCCAGGGAACGCCGGAGCATCCAGACTCTGGTGCAGAA 1719

30 QUERY: 1764 TGAAGCCGTGTTTGTGCAGTACCTGGATGTGGGCCTGTGGCATCTGGCCTTCTACAATGA 1823  
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SBJCT: 1720 CGAGGCTGTGTTTGTGCAGTACTGGATGTGGGCCTGTGGCACCTGGCCTTCTACAATGA 1779

35 QUERY: 1824 TGGAAAAGACAAAGAGATGGTTTCCTTCAATACTGTTGTCCTAGATTTCAGTGCAGGACTG 1883  
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SBJCT: 1780 CGGCAAGGACAAGGAGATGGTCTCCTTCAACACTGTTGTCTTAGATTTCAGTGCAGGACTG 1839

40 QUERY: 1884 TCCACGTAAGTCCCATGGGAATGGTGAATGTGTGTCCGGGGTGTGTCACTGTTTCCCAGG 1943  
||||| |||||  
SBJCT: 1840 TCCACGGAAGTGTACGGGAACGGTGAATGCGTGTCTGGACTGTGTCACTGTTTCCCAGG 1899

45 QUERY: 1944 ATTTCTAGGAGCAGACTGTGCTAAAGCTGCCTGCCCTGTCTGTGCAGTGGGAATGGACA 2003  
||| |||||  
SBJCT: 1900 ATTCCTAGGTGCAGACTGTGCTAAAGCTGCCTGCCCTGTACTGTGCAGCGGAAATGGACA 1959

50 QUERY: 2004 ATATTCTAAAGGGACGTGCCAGTGCTACAGCGGCTGGAAAGGTGCAGAGTGCGACGTGCC 2063  
||||| |||||  
SBJCT: 1960 GTATTCTAAAGGAACGTGCCAGTGCTACAGCGGCTGGAAAGGTGCAGAGTGATGTGCC 2019

55 QUERY: 2064 CATGAATCAGTGCATCGATCCTTCCTGCGGGGGCCACGGCTCCTGCATTGATGGGAACTG 2123  
||||| || || |||||  
SBJCT: 2020 TATGAACCAATGTATCGATCCTTCCTGTGGGGGCCATGGCTCCTGCATTGATGGGAACTG 2079

60 QUERY: 2124 TGTCTGCTCTGCTGGCTACAAAGGCGAGCACTGTGAGGAAGTTGATTGCTTGGATCCAC 2183  
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SBJCT: 2080 CGTGTGTGCTGCTGGCTACAAAGGCGAGCACTGTGAGGAAGTTGATTGCTTGGATCCTAC 2139

65 QUERY: 2184 CTGCTCCAGCCACGGAGTCTGTGTGAATGGAGAATGCCTGTGCAGCCCTGGCTGGGGTGG 2243  
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SBJCT: 2140 CTGCTCCAGCCATGGTGTCTGTGTGAATGGAGAGTGTCTATGCAGCCCCGGCTGGGGTGG 2199

70 QUERY: 2244 TCTGAACTGTGAGCTGGCGAGGGTCCAGTGCCCAGACCAAGTGCAGTGGGCATGGCACGTA 2303  
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SBJCT: 2200 TCTCAACTGTGAGCTGGCGAGGGTCCAGTGCCCAGACCAAGTGTAGTGGGCATGGCACTTA 2259

QUERY: 2304 CCTGCCTGACACGGGCCTCTGCAGCTGCGATCCCAACTGGATGGGTCCCGACTGCTCTGT 2363  
||| |||||  
SBJCT: 2260 CCTCCCTGACTCCGGCCTCTGCAGCTGTGATCCGAACCTGGATGGGTCCCGACTGCTCTGT 2319

QUERY: 2364 TGAAGTGTGCTCAGTAGACTGTGGCACTCACGGCGTCTGCATCGGGGGAGCCTGCCGCTG 2423  
| |||||  
SBJCT: 2320 T---GTGTGCTCAGTAGACTGTGGCACTCACGGCGTCTGCATCGGGGGAGCCTGCCGCTG 2376

QUERY: 2424 TGAAGAGGGCTGGACAGGCGCAGCGTGTGACCAGCGCGTGTGCCACCCCGCTGCATTGA 2483  
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SBJCT: 2377 TGAAGAGGGCTGGACAGGCGCAGCTTGTGACCAGCGCGTGTGCCACCCCGCTGCATTGA 2436

QUERY: 2484 GCACGGGACCTGTAAAGATGGCAAATGTGAATGCCGAGAGGGCTGGAATGGTGAACACTG 2543

5 SBJCT: 2437 GCACGGGACCTGTAAAGATGGCAAATGTGAATGCCGAGAGGGCTGGAATGGTGAACACTG 2496

QUERY: 2544 CACCATTG 2551

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10 SBJCT: 2497 CACCATTG 2504

SCORE = 105 BITS (53), EXPECT = 5E-19

IDENTITIES = 81/89 (91%), GAPS = 1/89 (1%)

STRAND = PLUS / PLUS

15 QUERY: 8711 AACGAATGAATGAACAGACACACACAATGTTCCAAGTTCCCCTAAAATATGACCCACTTG 8770

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SBJCT: 8655 AACGAACGAATGAAACACACACAAAATGTTTCAAGTTCCCCTAAAATATGACCCACTTG 8714

QUERY: 8771 TTCTGGGTCT-ACGCAGAAAAGAGACGCA 8798

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20 SBJCT: 8715 TTCCGGGTCTAAGGCAGAAAAGAGACGCA 8743

SCORE = 48.1 BITS (24), EXPECT = 0.093

IDENTITIES = 30/32 (93%)

STRAND = PLUS / PLUS

25 QUERY: 475 CACCGGGAGTCAGATGAGTTTCCTAGACAAGG 506

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SBJCT: 7 CACCGGGAGTCCGATGAGTTTCTAGACAAGG 38

30 In this search it was also found that the FCTR3bcd and e nucleic acids had homology to three fragments of *Rattus norvegicus* neurestin alpha. It has 5498 of 6132 bases (89%) identical to bases 2527-8658, 1081 of 1196 bases (90%) identical to bases 123-1318, 996 of 1088 bases (91%) identical to bases 1440-2527 of *Rattus norvegicus* neurestin alpha (GenBank Acc:NM\_020088.1) (Table 3N).

35 **Table 3N. BLASTN of FCTR3b, c, d, and e against *Rattus norvegicus* Neurestin alpha mRNA (SEQ ID NO:66)**

>GI|9910319|REF|NM\_020088.1| RATTUS NORVEGICUS NEURESTIN ALPHA (LOC56762), MRNA  
LENGTH = 8689

40 SCORE = 7129 BITS (3596), EXPECT = 0.0  
IDENTITIES = 5498/6132 (89%)  
STRAND = PLUS / PLUS

45 QUERY: 2578 GATGGCTGCCCTGACTTGTGCAACGGTAACGGGAGATGCACACTGGGTGAGAACAGCTGG 2637

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SBJCT: 2527 GATGGCTGCCCTGATTGTGCAACGGTAACGGGAGATGCACACTGGGTGAGAACAGCTGG 2586

QUERY: 2638 CAGTGTGTCTGCCAGACCGGCTGGAGAGGGCCCGGATGCAACGTTGCCATGGAACTTCC 2697

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50 SBJCT: 2587 CAGTGTGTCTGCCAGACCGGCTGGAGAGGGCCCGGATGCAACGTTGCCATGGAACTTCC 2646

QUERY: 2698 TGTGCTGATAACAAGGATAATGAGGGAGATGGCCTGGTGGATTGTTGGACCTGACTGC 2757

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55 SBJCT: 2647 TCGCTGATAACAAGGATAATGAGGGAGATGGCCTGGTGGACTGCCTGGACCTGACTGC 2706

QUERY: 2758 TGCCTGCAGTCAGCCTGTGAGAACAGCCTGCTCTGCCGGGGTCCCGGGACCCACTGGAC 2817

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SBJCT: 2707 TGCCTCCAGTCAGCCTGTGAGAACAGCCTGCTCTGTGCGGGGTCTCGGGACCCCTTGGAC 2766

60 QUERY: 2818 ATCATTCAGCAGGGCCAGACGGATTGGCCCGCAGTGAAGTCCTTCTATGACCGTATCAAG 2877

||||| ||||||| ||||||| || ||||| || ||||||| ||||||| ||||||| |||||||

SBJCT: 2767 ATCATTCAGCAAGGCCAGACAGACTGGCCTGCGGTGAAGTCCTTCTATGATCGTATCAAG 2826

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QUERY: 2878 CTCTTGGCAGGCAAGGATAGCACCCACATCATTCCTGGAGAGAACCCTTTCAACAGCAGC 2937  
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SBJCT: 2827 CTCTTGGCAGGCAAGGACAGCACCCACATCATTCCTGGAGACAACCCCTTCAATAGCAGC 2886

QUERY: 2938 TTGGTTTCTCTCATCCGAGGCCAAGTAGTAACACAGATGGAACCTCCCCTGGTGGGTGTG 2997  
|||||  
SBJCT: 2887 CTGGTGTCTCTGATCCGAGGCCAAGTAGTAACCACGGATGGGACCCCCCTGGTGGGTGTG 2946

QUERY: 2998 AACGTGTCTTTTGTCAAGTACCCAAAATACGGCTACACCATCACCCGCCAGGATGGCAGC 3057  
||  
SBJCT: 2947 AATGTGTCTTTTGTCAAGTACCCAAAATATGGCTACACCATCACTCGCCAGGACGGCAGC 3006

QUERY: 3058 TTCGACCTGATCGCAAATGGAGGTGCTTCCTTGACTCTACACTTTGAGCGAGCCCCGTTT 3117  
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SBJCT: 3007 TTTGACCTGATTGCCAATGGGGGCTCTGCCTTGACTCTTCACTTTGAGCGAGCCCCCTTTC 3066

QUERY: 3118 ATGAGCCAGGAGCGCACTGTGTGGCTGCCGTGGAACAGCTTTTACGCCATGGACACCCTG 3177  
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SBJCT: 3067 ATGAGCCGGGAGCGCACAGTATGGCCGCCGTGGAACAGCTTCTATGCCATGGACACCCTG 3126

QUERY: 3178 GTGATGAAGACCGAGGAGAACTCCATCCCCAGCTGTGACCTCAGTGGCTTTGTCCGGCCT 3237  
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SBJCT: 3127 GTAATGAAGACGGAGGAGAACTCCATCCCCAGCTGTGACCTCAGTGGCTTTGTCCGGCCT 3186

QUERY: 3238 GATCCAATCATCATCTCCTCCCCACTGTCCACCTTCTTTAGTGCTGCCCCCTGGGCAGAAAT 3297  
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SBJCT: 3187 GATCCGATCATCATCTCCTCTCCTCTGTCCACCTTCTTCAGCGCTTCCCCTGCGGCGAAC 3246

QUERY: 3298 CCCATCGTGCCTGAGACCCAGGTTCTTCATGAAGAAATCGAGCTCCCTGGTTCCAATGTG 3357  
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SBJCT: 3247 CCCATTGTGCCTGAGACCCAGGTTCTTCATGAGGAGATCGAGCTCCCTGGCACCAACGTG 3306

QUERY: 3358 AAATTTCGCTATCTGAGCTCTAGAACTGCAGGGTACAAGTCACTGCTGAAGATCACCATG 3417  
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SBJCT: 3307 AAGCTCCGTTACCTCAGCTCCAGAACAGCAGGGTACAAGTCACTGCTGAAGATCACCATG 3366

QUERY: 3418 ACCCAGTCCACAGTGCCCCTGAACCTCATTAGGGTTACCTGATGGTGGCTGTCGAGGGG 3477  
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SBJCT: 3367 ACCCAGTCCACGGTGCCCTTGAACCTCATCCGGGTTCACTTGATGGTTGCCGTGGAGGGG 3426

QUERY: 3478 CATCTCTTCCAGAAGTCATTCCAGGCTTCTCCCAACCTGGCCTCCACCTTCATCTGGGAC 3537  
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SBJCT: 3427 CATCTCTTCCAGAAGTCGTTCCAGGCTTCTCCCAACCTGGCCTACACATTCATCTGGGAC 3486

QUERY: 3538 AAGACAGATGCGTATGGCCAAAGGGTGTATGGACTCTCAGATGCTGTTGTGTCTGTCTGGG 3597  
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SBJCT: 3487 AAGACAGACGCTTATGGCCAAAGGGTTTATGGCCTATCGGATGCTGTTGTGTCTGTTGGA 3546

QUERY: 3598 TTTGAATATGAGACCTGTCCCAGTCTAATTCTCTGGGAGAAAAGGACAGCCCTCCTTCAG 3657  
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SBJCT: 3547 TTTGAATATGAGACCTGCCCCAGTCTCATCTGTGGGAAAAAAGGACAGCCCTACTTCAA 3606

QUERY: 3658 GGATTTCGAGCTGGACCCCTCCAACCTCGGTGGCTGGTCCCTAGACAAACACCACATCCTC 3717  
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SBJCT: 3607 GGATTTCGAGCTGGACCCCTCCAACCTTGGTGGCTGGTCCCTGGATAAGCACACACCTC 3666

QUERY: 3718 AATGTTAAAAGTGGAATCCTACACAAAGGCACTGGGGAAAACCAGTTCCTGACCCAGCAG 3777  
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SBJCT: 3667 AATGTGAAAAGCGGAATACTACTCAAAGGCACAGGGGAGAACCAGTTCCTGACCCAGCAG 3726

QUERY: 3778 CCTGCCATCATCACCAGCATCATGGGCAATGGTCCGCCCGGAGCATTTCTGTCCCAGC 3837  
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SBJCT: 3727 CCCGCCATCATCACCAGCATCATGGGTAAACGGTCGCCGCAGAAGCATCTCCTGTCCCAGC 3786

QUERY: 3838 TGCAACGGCCTTGCTGAAGGCAACAAGCTGCTGGCCCCAGTGGCTCTGGCTGTTGGAATC 3897  
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SBJCT: 3787 TGCAATGGCCTTGCTGAAGGCAACAACCTGTTGGCCCCCGTGGCCCTGGCTGTGGGGATC 3846

QUERY: 3898 GATGGGAGCCTCTATGTGGGTGACTTCAATTACATCCGACGCATCTTTCCTCTCGAAAT 3957

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5 SBJCT: 3847 GATGGGAGCCTCTTTGTCTGGTGACTTCAATTATATCCGGCGCATCTTCCCTTCTCGAAAC 3906  
QUERY: 3958 GTGACCAGCATCTTGGAGTTACGAAATAAAGAGTTTAAACATAGCAACAACCCAGCACAC 4017  
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SBJCT: 3907 GTGACCAGTATCTTGGAGTTACGAAATAAAGAGTTTAAACATAGCAACAGCCCAGGACAC 3966  
10 QUERY: 4018 AAGTACTACTTGGCAGTGGACCCCGTGTCCGGCTCGCTCTACGTGTCCGACACCAACAGC 4077  
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SBJCT: 3967 AAGTACTACTTGGCTGTGGACCCTGTGACTGGCTCGCTCTATGTCTCTGACACCAACAGT 4026  
QUERY: 4078 AGGAGAATCTACCGCGTCAAGTCTCTGAGTGGAAACAAAGACCTGGCTGGGAATTCGGAA 4137  
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15 SBJCT: 4027 CGCCGGATCTACCGAGTCAAGTCTCTAAGCGGAGCCAAAGACCTGGCTGGGAATTCGGAA 4086  
QUERY: 4138 GTTGTGGCAGGGACGGGAGAGCAGTGTCTACCCCTTTGATGAAGCCCGCTGCGGGGATGGA 4197  
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SBJCT: 4087 GTTGTGGCCGGGACTGGCGAACAATGTCTACCCCTTTGATGAAGCCCGCTGTGGGGATGGC 4146  
20 QUERY: 4198 GGGAAAGGCCATAGATGCAACCCTGATGAGCCCGAGAGGTATTGCAGTAGACAAGAATGGG 4257  
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SBJCT: 4147 GGGAAAGGCTGTGGATGCCACCCTGATGAGCCCTAGAGGTATTGCAGTAGACAAGAACGGG 4206  
25 QUERY: 4258 CTCATGTACTTTGTCTGATGCCACCATGATCCGGAAGGTTGACCAGAATGGAATCATCTCC 4317  
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SBJCT: 4207 CTTATGTATTTTGTGATGCCACCATGATCCGGAAGGTCGACCAAAATGGAATCATCTCC 4266  
QUERY: 4318 ACCCTGCTGGGCTCCAATGACCTCACTGCCGTCCGGCCGCTGAGCTGTGATTCCAGCATG 4377  
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30 SBJCT: 4267 ACCCTGCTGGGCTCCAATGACCTCACAGCTGTCCGACCACTGAGCTGTGACTCTAGCATG 4326  
QUERY: 4378 GATGTAGCCCAGGTTCTGCTGGAGTGGCCAACAGACCTTGCTGTCAATCCCATGGATAAC 4437  
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35 SBJCT: 4327 GACGTGGCCCAGGTCCGTCTAGAATGGCCGACAGACCTTGCGGTCAACCCCATGGACAAT 4386  
QUERY: 4438 TCCTTGTATGTTCTAGAGAACAATGTCTCCTTCGAATCACCGAGAACCACCAAGTCAGC 4497  
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SBJCT: 4387 TCCCTGTACGTCCTGGAGAACAACGTCATCCTGCGGATCACCGAGAATCACCGAGTCAGC 4446  
40 QUERY: 4498 ATCATTGCGGGACGCCCCATGCACTGCCAAGTTCCTGGCATTGACTACTCACTCAGCAAA 4557  
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SBJCT: 4447 ATCATCGCGGGACGCCCCATGCACTGCCAGGTTCCCGGCATCGACTACTCGCTCAGCAAG 4506  
45 QUERY: 4558 CTAGCCATTCACTCTGCCCTGGAGTCAGCCAGTGCCATTGCCATTTCTCACACTGGGGTC 4617  
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SBJCT: 4507 CTCGCCATCCACTCTGCTCTGGAGTCAGCCAGCGCCATCGCCATTTCTCACACCGGGGTG 4566  
QUERY: 4618 CTCTACATCACTGAGACAGATGAGAAGAAGATTAACCGTCTACGCCAGGTAACAACCAAC 4677  
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50 SBJCT: 4567 CTCTACATCACCGAGACGGACGAGAAGAAGATCAACCGCCTACGCCAGGTCAACCAAC 4626  
QUERY: 4678 GGGGAGATCTGCCTTTTAGCTGGGGCAGCCTCGGACTGCGACTGCAAAAACGATGTCAAT 4737  
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55 SBJCT: 4627 GGAGAGATCTGCCTCTTAGCCGGGGCAGCCTCAGACTGTGACTGCAAAAATGACGTCAAC 4686  
QUERY: 4738 TGCAACTGCTATTTCAGGAGATGATGCCTACGCGACTGATGCCATCTTGAATTCCTCATCA 4797  
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SBJCT: 4687 TGCATCTGCTATTTCGGGAGATGACGCATACGCCACGGATGCCATCTTGAATTCCTCATCA 4746  
60 QUERY: 4798 TCCTTAGCTGTAGCTCCAGATGGTACCATTACATTGCAGACCTTGGAATATTCGGATC 4857  
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SBJCT: 4747 TCCTTAGCTGTGGCTCCGGATGGCACCATCTACATCGCAGACCTCGGGAATATCCGGATC 4806  
65 QUERY: 4858 AGGGCGGTCAGCAAGAACAAGCCTGTTCTTAATGCCTTCAACCAGTATGAGGCTGCATCC 4917  
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SBJCT: 4807 AGGGCGGTCAGCAAAAACAACCTGTTCTTAACGCGTTCAACCAGTATGAGGCTGCGTCT 4866  
QUERY: 4918 CCCGGAGAGCAGGAGTTATATGTTTCAACGCTGATGGCATCCACCAATACACTGTGAGC 4977  
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70 SBJCT: 4867 CCGGGAGAACAGGAACGTACGTGTTCAACGCCGATGGTATCCATCAGTACACCGTGAGC 4926

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QUERY: 4978 CTGGTGACAGGGGAGTACTTGTACAATTTACATATAGTACTGACAATGATGTCACCTGAA 5037  
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SBJCT: 4927 CTGGTGACCGGGGAGTACTTATACAATTTACCTACAGCGCTGACAATGATGTCACCGAG 4986  
QUERY: 5038 TTGATTGACAATAATGGGAATTCCTGAAGATCCGTCGGGACAGCAGTGGCATGCCCCGT 5097  
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SBJCT: 4987 TTGATTGACAACAACGGGAATTCCTAAAGATCCGCCGGGACAGCAGTGGCATGCCCCGA 5046  
QUERY: 5098 CACCTGCTCATGCCTGACAACCAGATCATCACCTCACCGTGGGCACCAATGGAGGCCTC 5157  
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SBJCT: 5047 CACCTGCTCATGCCTGATAATCAGATCATCACCTTACGGTGGGCACCAACGGAGGCCTC 5106  
QUERY: 5158 AAAGTCGTGTCCACACAGAACCTGGAGCTTGGTCTCATGACCTATGATGGCAACACTGGG 5217  
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SBJCT: 5107 AAAGCCGTGTCAACGCAGAACCTGGAGCTGGGCCTCATGACTTATGATGGGAACACTGGA 5166  
QUERY: 5218 CTCCTGGCCACCAAGAGCGATGAAACAGGATGGACGACTTTCTATGACTATGACCACGAA 5277  
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SBJCT: 5167 CTCCTAGCCACCAAGAGCGATGAAACCGGATGGACAACTTTTATGACTATGACCACGAG 5226  
QUERY: 5278 GGCCGCCTGACCAACGTGACGCGCCCCACGGGGGTGGTAACCAGTCTGCACCGGGAAATG 5337  
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SBJCT: 5227 GGCCGTCTGACCAATGTGACTCGCCCCACGGGGGTGGTGACCAGCCTGCACCGGGAAATG 5286  
QUERY: 5338 GAGAAATCTATTACCATTGACATTGAGAACTCCAACCGTGATGATGACGTCACTGTCATC 5397  
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SBJCT: 5287 GAGAAATCCATCACCGTTGACATTGAGAACTCCAACCGTGATAACGATGTCACTGTGATT 5346  
QUERY: 5398 ACCAACCTCTCTTCAGTAGAGGCCTCCTACACAGTGGTACAAGATCAAGTTCGGAACAGC 5457  
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SBJCT: 5347 ACCAACCTCTCTTCAGTGGAGGCCTCCTACACCGTGGTACAAGATCAAGTGCAGAACAGC 5406  
QUERY: 5458 TACCAGCTCTGTAATAATGGTACCCTGAGGGTGATGTATGCTAATGGGATGGGTATCAGC 5517  
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SBJCT: 5407 TACCAGCTCTGCAGCAACGGGACCCTGCGCGTCATGTACGCCAACGGCATGGGCGTCAGC 5466  
QUERY: 5518 TTCCACAGCGAGCCCCATGTCTAGCGGGCACCATCACCCCCACCATTGGACGCTGCAAC 5577  
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SBJCT: 5467 TTCCACAGCGAGCCCCACGTCTCGCAGGCACCCTCACCCCCACCATCGGGCGCTGTAAC 5526  
QUERY: 5578 ATCTCCCTGCCTATGGAGAATGGCTTAACTCCATTGAGTGGCGCCTAAGAAAGGAACAG 5637  
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SBJCT: 5527 ATCTCCCTGCCCATGGAGAACGGCCTGAACTCCATCGAGTGGCGCCTGAGGAAGGAACAG 5586  
QUERY: 5638 ATTAAAGGCAAAGTCACCATCTTTGGCAGGAAGCTCCGGGTCCATGGAAGAAATCTCTTG 5697  
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SBJCT: 5587 ATTAAAGGCAAAGTCACCATCTTTGGGAGGAAGCTTCGGGTCCACGGAAGGAACCTCCTG 5646  
QUERY: 5698 TCCATTGACTATGATCGAAATATTCGGACTGAAAAGATCTATGATGACCACCGGAAGTTC 5757  
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SBJCT: 5647 TCCATTGATTATGACCGAAATATCCGCACTGAGAAGATCTATGACGACCACCGGAAGTTC 5706  
QUERY: 5758 ACCCTGAGGATCATTTATGACCAGGTGGGCCGCCCTTCTCTGGCTGCCAGCAGCGGG 5817  
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SBJCT: 5707 ACCCTGAGGATCATTTATGACCAGGTGGGCCGCCCTTCTGTGGCTCCCCAGCAGTGA 5766  
QUERY: 5818 CTGGCAGCTGTCAACGTGTCATACTTCTTCAATGGGCGCCTGGCTGGGCTTCAGCGTGGG 5877  
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SBJCT: 5767 CTGGCGGCCGTCAATGTCTCCTACTTCTTCAACGGGCGCCTGGCCGGCCTCCAGCGCGGG 5826  
QUERY: 5878 GCCATGAGCGAGAGGACAGACATCGACAAGCAAGGCCGCATCGTGTCCCGCATGTTTCGCT 5937  
||||| ||||||| ||||||| || || || || || || || || || ||  
SBJCT: 5827 GCCATGAGCGAGAGGACAGACATTGACAAGCAAGGCCGGATTGTGTCCCGAATGTTTCGCC 5886  
QUERY: 5938 GACGGGAAAGTGTGGAGCTACTCCTACCTTGACAAGTCCATGGTCCTCCTGCTTCAGAGC 5997  
||||| || || || || || || || || || || || || || || ||  
SBJCT: 5887 GACGGGAAAGTCTGGAGCTATTCCTACCTTGACAAGTCCATGGTCCTCCTGCTGCAGAGC 5946

62

SBJCT: 6967 AGAGCGTACAACAAGGCCAGCGGGTGGAGTGTGCAGTACCGCTATGATGGCGTGAGCCGC 7026

5 QUERY: 7078 CGGGCTTCCTACAAGACCAACCTGGGGCCACCACCTGCAGTACTTCTACTCTGACCTCCAC 7137  
 SBJCT: 7027 CGGGCTTCCTACAAGACCAACCTGGGGCCACCACCTACAGTACTTCTATTCCGACCTCCAC 7086

10 QUERY: 7138 AACCCGACGCGCATCACCCATGTCTACAATCACTCCAACCTCGGAGATTACCTCACTGTAC 7197  
 SBJCT: 7087 CACCCACACGTATCACCCATGTTTACAACCACCTCCAACCTCTGAGATCACCTCACTCTAC 7146

15 QUERY: 7198 TACGACCTCCAGGGCCACCTCTTTGCCATGGAGAGCAGCAGTGGGGAGGAGTACTATGTT 7257  
 SBJCT: 7147 TATGACCTCCAGGGCCACCTCTTTGCCATGGAGAGCAGTAGTGGGGAAGAGTACTATGTT 7206

20 QUERY: 7258 GCCTCTGATAACACAGGGACTCCTCTGGCTGTGTTTCAAGCATCAACGGCCTCATGATCAAA 7317  
 SBJCT: 7207 GCCTCAGATAACACCGGGACTCCTCTGGCTGTTTTTAGTATCAATGGCCTCATGATCAAG 7266

25 QUERY: 7318 CAGCTGCAGTACACGGCCTATGGGGAGATTTATTATGACTCCAACCCGACTTCCAGATG 7377  
 SBJCT: 7267 CAACTCCAATACACAGCCTATGGGGAGATTTACTATGACTCCAATCCAGACTTTCAGATG 7326

30 QUERY: 7378 GTCATTGGCTTCCATGGGGGACTCTATGACCCCTGACCAAGCTGGTCCACTTCACTCAG 7437  
 SBJCT: 7327 GTCATCGGCTTCCACGGAGGCCTCTACGACCCCTCACCAAGCTCGTTCACTTTACGCAG 7386

35 QUERY: 7438 CGTGATTATGATGTGCTGGCAGGACGATGGACCTCCCCAGACTATACCATGTGGAAAAAC 7497  
 SBJCT: 7387 CGTGATTATGACGTGCTGGCAGGACGGTGGACGTCCCCGACTACACCATGTGGAGGAAT 7446

40 QUERY: 7498 GTGGGCAAGGAGCCGCCCCCTTTAACCTGTATATGTTCAAGAGCAACAATCCTCTCAGC 7557  
 SBJCT: 7447 GTGGGCAAGGAGCCAGCCCCCTTCAACCTGTACATGTTCAAGAACAACAATCCACTCAGT 7506

45 QUERY: 7558 AGTGAGCTAGATTTGAAGAACTACGTGACAGATGTGAAAAGCTGGCTTGTGATGTTTGGA 7617  
 SBJCT: 7507 AATGAGCTGGATTTAAAGAACTACGTGACAGACGTGAAGAGCTGGCTCGTGATGTTTGGA 7566

50 QUERY: 7618 TTTCAGCTTAGCAACATCATTCCTGGCTTCCCGAGAGCCAAAATGTATTTCTGCCTCCT 7677  
 SBJCT: 7567 TTTCAGCTCAGCAACATCATTCCTGGATTCCCAAGAGCCAAAATGTATTTTGTGCCTCCC 7626

55 QUERY: 7678 CCCTATGAATTGTCAGAGAGTCAAGCAAGTGAGAATGGACAGCTCATTACAGGTGTCCAA 7737  
 SBJCT: 7627 CCCTATGAAGTGTGAGAGAGCCAAGCAAGTGAGAATGGACAGCTCATTACAGGTGTCCAG 7686

60 QUERY: 7738 CAGACAACAGAGAGACATAACCAGGCCTTCATGGCTCTGGAAGGACAGGTCACTACTAAA 7797  
 SBJCT: 7687 CAGACAACAGAGAGGCATAACCAGGCCTTTCTGGCTCTAGAAGGACAGGTCACTCTAAA 7746

65 QUERY: 7798 AAGCTCCACGCCAGCATCCGAGAGAAAGCAGGTCACTGGTTTGCCACCACCACGCCCATC 7857  
 SBJCT: 7747 AAGCTCCATGCAGGCATCCGAGAGAAAGCAGGCCACTGGTTTGCTACGACCACGCCCATC 7806

70 QUERY: 7858 ATTGGCAAAGGCATCATGTTTGCCATCAAAGAAGGGCGGGTGACCACGGGCGTGTCCAGC 7917  
 SBJCT: 7807 ATCGGCAAAGGCATCATGTTGCGCATCAAAGAAGGGCGGGTGACCACAGGCGTGTCTAGC 7866

QUERY: 7918 ATCGCCAGCGAAGATAGCCGCAAGGTGGCATCTGTGCTGAACAACGCCTACTACTTGGAC 7977  
 SBJCT: 7867 ATCGCCAGTGAGGACAGCCGCAAGGTAGCATCCGTGTTGAACAACGCCTACTACTTGGAC 7926

QUERY: 7978 AAGATGCACTACAGCATCGAGGGCAAGGACACCCACTACTTTGTGAAGATTGGCTCAGCC 8037  
 SBJCT: 7927 AAGATGCACTACAGCATCGAGGGCAAGGACACACACTACTTCGTGAAGATCGGTGCAGCG 7986

QUERY: 8038 GATGGCGACCTGGTCACACTAGGCACCACCATCGGCCGCAAGGTGCTAGAGAGCGGGGTG 8097  
 SBJCT: 8038 GATGGCGACCTGGTCACACTAGGCACCACCATCGGCCGCAAGGTGCTAGAGAGCGGGGTG 8097

5 SBJCT: 7987 GACGGTGACCTGGTTACGCTGGGGACCACCATTGGGCGCAAGGTGCTGGAGAGCGGGGTG 8046

QUERY: 8098 AACGTGACCGTGTCCCAGCCCACGCTGCTGGTCAACGGCAGGACTCGAAGGTTACGAAC 8157  
|||||

10 SBJCT: 8047 AACGTGACCGTGTACAGCCCACGCTGCTGGTGAACGGCAGGACTCGAAGGTTACCAAC 8106

QUERY: 8158 ATTGAGTTCCAGTACTCCACGCTGCTGCTCAGCATCCGCTATGGCCTCACCCCCGACACC 8217  
|||||

15 SBJCT: 8107 ATTGAATTCCAGTACTCCACGCTGCTGCTCAGCATACGCTACGGCCTCACCCCCGACACA 8166

QUERY: 8218 CTGGACGAAGAGAAGGCCCGCGTCTGGACCAGGCGAGACAGAGGGCCCTGGGCACGGCC 8277  
|||||

20 SBJCT: 8167 CTGGATGAAGAGAAGGCCCGCGTCTGGACCAAGCGCGACAGAGGGCCCTGGGTACTGCC 8226

QUERY: 8278 TGGGCCAAGGAGCAGCAGAAAGCCAGGGACGGGAGAGAGGGGAGCCGCCTGTGGACTGAG 8337  
|||||

25 SBJCT: 8227 TGGGCCAAGGAGCAGCAGAAAGCCAGGGACGGGAGAGAGGGCAGCCGTCTGTGGACGGAG 8286

QUERY: 8338 GGCGAGAAGCAGCAGCTTCTGAGCACCGGGCGCGTGCAAGGGTACGAGGGATATTACGTG 8397  
|||||

30 SBJCT: 8287 GGCGAGAAGCAGCAACTCCTGAGCACGGGACGGGTGCAAGGTTATGAGGGCTATTACGTG 8346

QUERY: 8398 CTTCCCGTGGAGCAATACCCAGAGCTTGACAGACAGTAGCAGCAACATCCAGTTTAAAGA 8457  
|||||

35 SBJCT: 8347 CTTCCCGTGGAGCAATACCCAGAGCTGGCAGACAGTAGCAGCAACATCCAGTTCTTAAGA 8406

QUERY: 8458 CAGAATGAGATGGGAAAGAGGTAACAAAATAATCTGCTGCCATTCTTGTCTGAATGGCT 8517  
|||||

40 SBJCT: 8407 CAGAATGAGATGGGAAAGAGGTAACAAAATAACCTGCTGCCACCTCTTCTCTGGGTGGCT 8466

QUERY: 8518 CAGCAGGAGTAAGTGTATCTCCTCTCCTAAGGAGATGAAGACCTAACAGGGGCACTGCG 8577  
|||||

45 SBJCT: 8467 CAGCAGGAGCAACTGTGACCTCCTCTCCTAAGGAGACGAAGACCTAACAGGGGCACTGAG 8526

QUERY: 8578 GCTGGGCTGCTTTAGGAGACCAAGTGGCAAGAAAGCTCACATTTTTTGAGTTCAAATGCT 8637  
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50 SBJCT: 8527 GCCGGGCTGCTTTAGGACCCCAAGTGGCAAGAAAGCTCACATTTTTTGAGTTCAAATGCT 8586

QUERY: 8638 ACTGTCCAAGCGAGAAGTCCCTCATCCTGAAGTAGACTAAAGCCCGGCTGAAAATTCCGA 8697  
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55 SBJCT: 8587 ACTGTCCAAGCGCAAAGTCCCTCATCCTGAAGTAGACTAGAGCTCGGCCACAAATTCTGA 8646

QUERY: 8698 GGAAAACAAAAC 8709  
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60 SBJCT: 8647 GGAAAACAAAAC 8658

SCORE = 1459 BITS (736), EXPECT = 0.0  
IDENTITIES = 1081/1196 (90%)  
STRAND = PLUS / PLUS

65 QUERY: 270 ATCTGGAATAATGGATGTAAAGGACCGGCGACACCGCTCTTTGACCAGAGGACGCTGTGG 329  
|||||

70 SBJCT: 123 ATCTGCAATAATGGATGTGAAGGATCGGCGACATCGCTCTTTGACCAGGGGACGGTGTGG 182

QUERY: 330 CAAAGAGTGTGCTACACAAGCTCCTCTCTGGACAGTGAGGACTGCCGGGTGCCACACA 389  
|||

75 SBJCT: 183 CAAGGAGTGTGCTACACCAGCTCCTCTCTGGACAGTGAGGACTGCCGTGTGCCACGCA 242

QUERY: 390 GAAATCCTACAGCTCCAGTGAGACTCTGAAGGCCTATGACCATGACAGCAGGATGCACTA 449  
|||

80 SBJCT: 243 GAAGTCCTACAGTTCCAGTGAGACCCTGAAGGCTTATGACCATGACAGCAGAATGCACTA 302

QUERY: 450 TGGAACCGAGTCACAGACCTCATCCACCGGAGTCAGATGAGTTTCCTAGACAAGGAAC 509  
|||||

85 SBJCT: 303 TGGAACCGAGTCACAGACCTGGTGCACCGGGAGTCCGATGAGTTTCTAGACAAGGGGC 362

QUERY: 510 CAACTTCACCCTTGCCGAAGTGGGCATCTGTGAGCCCTCCCCACACCGAAGCGGCTACTG 569  
||

90 SBJCT: 363 TAATTTACCCCTGGCAGAATTGGGAATCTGCGAGCCCTCCCCACACCGAAGTGGTTACTG 422

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QUERY: 570 CTCCGACATGGGGATCCTTCACCAGGGCTACTCCCTTAGCACAGGGTCTGACGCCGACTC 629  
|||||  
SBJCT: 423 TTCCGACATGGGGATCCTTCACCAGGGCTACTCCCTGAGCACTGGGTCTGATGCGGACTC 482

QUERY: 630 CGACACCGAGGGAGGGATGTCTCCAGAACACGCCATCAGACTGTGGGGCAGAGGGATAAA 689  
|||||  
SBJCT: 483 GGACACCGAGGGAGGGATGTCTCCAGAACATGCCATCAGACTGTGGGGACGAGGGATAAA 542

QUERY: 690 ATCCAGGCGCAGTTCCGGCCTGTCCAGTCGTGAAAACCTCGGCCCTTACCCTGACTGACTC 749  
||| |||||  
SBJCT: 543 ATCGAGGCGCAGCTCTGGCTTGTCCAGCCGCGAGAACTCAGCCCTTACTCTGACTGATTC 602

QUERY: 750 TGACAACGAAAACAAATCAGATGATGAGAACGGTTCGTCCCATTCCACCTACATCCTCGCC 809  
|||||  
SBJCT: 603 TGACAATGAAAATAAATCGGATGACGACAATGGTCGACCCATTCCACCTACATCCTCGTC 662

QUERY: 810 TAGTCTCCTCCCATCTGCTCAGCTGCCTAGCTCCCATAATCCTCCACCAGTTAGCTGCCA 869  
||| |||||  
SBJCT: 663 TAGCCTCCTCCCATCTGCTCAGCTGCCTAGCTCCCATAATCCTCCACCAGTTAGCTGCCA 722

QUERY: 870 GATGCCATTGCTAGACAGCAACACCTCCCATCAAATCATGGACACCAACCCTGATGAGGA 929  
|||||  
SBJCT: 723 GATGCCATTGCTAGACAGCAACACCTCCCATCAGATCATGGACACCAACCCGATGAGGA 782

QUERY: 930 ATTCTCCCCCAATTTCATACCTGCTCAGAGCATGCTCAGGGCCCCAGCAAGCCTCCAGCAG 989  
||| |||||  
SBJCT: 783 ATTCTCCCCTAATTTCATACCTGCTCAGAGCATGCTCAGGGCCCCAGCAAGCCTCCAGTAG 842

QUERY: 990 TGGCCCTCCGAACCACCACAGCCAGTCGACTCTGAGGCCCCCTCTCCCACCCCTCACAA 1049  
||| |||||  
SBJCT: 843 TGGCCCTCCGAACCACCACAGCCAGTCAACGCTGAGGCCCCCTCTGCCACCTCCTCATAA 902

QUERY: 1050 CCACACGCTGTCCCATCACCCTCGTCCGCCAACTCCCTCAACAGGAACTCACTGACCAA 1109  
|||||  
SBJCT: 903 CCACACCCTGTCCCACCACCCTCCTCTGCCAACTCCCTCAACAGAACTCACTGACCAA 962

QUERY: 1110 TCGGCGGAGTCAGATCCACGCCCCGGCCCCAGCGCCCAATGACCTGGCCACCACACCAGA 1169  
|||||  
SBJCT: 963 TCGGCGGAGTCAAATCCACGCCCCAGCTCCTGCACCCAATGACCTGGCCACCACGCCGGA 1022

QUERY: 1170 GTCCGTTTCAGCTTCAGGACAGCTGGGTGCTAAACAGCAACGTGCCACTGGAGACCCGGCA 1229  
|||||  
SBJCT: 1023 GTCCGTTTCAGCTCCAGGACAGCTGGGTGCTGAACAGTAACGTGCCGCTGGAGACGCGGCA 1082

QUERY: 1230 CTTCTCTTCAAGACCTCCTCGGGAGCACACCCTTGTTCAGCAGCTCTTCCCCGGGATA 1289  
|||||  
SBJCT: 1083 CTTCTCTTCAAGACGTCCTCCGGAAGCACACCCTGTTCAGCAGCTCTTCTCCAGGATA 1142

QUERY: 1290 CCCTTTGACCTCAGGAACGGTTTACACGCCCCCGCCCCGCCTGCTGCCCAGGAATACTTT 1349  
||| |||||  
SBJCT: 1143 CCCCTTGACCTCAGGGACCGTTTATACACCACCACCCCGCCTGCTGCCACGGAATACATT 1202

QUERY: 1350 CTCCAGGAAGGCTTTCAAGCTGAAGAAGCCCTCCAAATACTGCAGCTGGAAATGTGCTGC 1409  
||| |||||  
SBJCT: 1203 CTCTAGGAAGGCCTTCAAGCTGAAGAAACCCTCCAAATACTGCAGTTGGAATGCGCCGC 1262

QUERY: 1410 CCTCTCCGCCATTGCCGCGGCCCTCCTCTTGCTATTTTGCTGGCGTATTTTCATAG 1465  
||| ||| |||||  
SBJCT: 1263 CCTGTCTGCCATTGCCGCTGCCCTCCTTCTGGCCATTTTGCTGGCCTATTTTCATAG 1318

SCORE = 1427 BITS (720), EXPECT = 0.0  
IDENTITIES = 996/1088 (91%)  
STRAND = PLUS / PLUS

QUERY: 1464 AGTGCCCTGGTCGTTGAAAAACAGCAGCATAGACAGTGGTGAAGCAGAAGTTGGTCGGCG 1523  
|||||  
SBJCT: 1440 AGTGCCCTGGTCGTTGAAAAACAGCAGCATAGACAGCGGCGAGGCAGAAGTCGGTCGACG 1499

QUERY: 1524 GGTAACACAAGAAGTCCCACCAGGGGTGTTTTGGAGGTCACAAATTCACATCAGTCAGCC 1583  
||| |||||

5 SBJCT: 1500 GGTGACACAGGAAGTCCCACCAGGGGTGTTTTGGAGGTCCCAGATTCACATCAGTCAGCC 1559  
QUERY: 1584 CCAGTTCTTAAAGTTCAACATCTCCCTCGGGAAGGACGCTCTTTGGTGTTCACATAAG 1643  
|||||  
10 SBJCT: 1560 TCAGTTCTTAAAGTTCAACATCTCCCTGGGGAAGGATGCCCTCTTCGGCGTCTACATAAG 1619  
QUERY: 1644 AAGAGGACTTCCACCATCTCATGCCAGTATGACTTCATGGAACGTCTGGACGGGAAGGA 1703  
|||||  
15 SBJCT: 1620 AAGAGGACTGCCACCATCTCATGCACAGTATGACTTCATGGAACGCCTGGACGGAAAGGA 1679  
QUERY: 1704 GAAGTGGAGTGTGGTTGAGTCTCCAGGGAACGCCGGAGCATAACAGACCTTGGTTCAGAA 1763  
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20 SBJCT: 1680 GAAGTGGAGTGTGGTCGAGTCACCCAGGGAACGCCGGAGCATCCAGACCCTGGTGCAGAA 1739  
QUERY: 1764 TGAAGCCGTGTTTGTGCAGTACCTGGATGTGGGCCTGTGGCATCTGGCCTTCTACAATGA 1823  
|| || |||||  
25 SBJCT: 1740 CGAGGCTGTGTTTCGTGCAGTACTTGGATGTGGGCCTGTGGCACCTCGCCTTCTACAATGA 1799  
QUERY: 1824 TGGAAAAGACAAAGAGATGGTTTCCTTCAATACTGTTGTCCTAGATTCAGTGCAGGACTG 1883  
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30 SBJCT: 1800 CGGCAAGGACAAGGAGATGGTCTCCTTCAATACGGTTGTCTTAGATTCAGTGCAGGACTG 1859  
QUERY: 1884 TCCACGTAAGTCCCATGGGAATGGTGAATGTGTGTCCGGGGTGTGTCACTGTTTCCCAGG 1943  
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35 SBJCT: 1860 TCCACGAAACTGCCACGGGAACGGCGAATGCGTGTCTGACTGTGTCACTGTTTCCCAGG 1919  
QUERY: 1944 ATTTCTAGGAGCAGACTGTGCTAAAGCTGCCTGCCCTGTCTGTGCAGTGGGAATGGACA 2003  
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40 SBJCT: 1920 ATTCCTAGGTGCAGACTGCGCTAAAGCTGCCTGCCCTGTTCTGTGCAGTGGGAATGGACA 1979  
QUERY: 2004 ATATTCTAAAGGGACGTGCCAGTGCTACAGCGGCTGGAAAGGTGCAGAGTGCAGACGTGCC 2063  
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45 SBJCT: 1980 GTATTCCAAAGGGACATGCCAGTGCTACAGTGGCTGGAAAGGAGCAGAATGCGATGTGCC 2039  
QUERY: 2064 CATGAATCAGTGCATCGATCCTTCCTGCGGGGGCCACGGCTCCTGCATTGATGGGAACTG 2123  
|||||  
50 SBJCT: 2040 CATGAACCAGTGCATCGATCCTTCCTGTGGGGGGCCACGGCTCCTGCATTGATGGGAACTG 2099  
QUERY: 2124 TGTCTGCTCTGCTGGCTACAAAGGCGAGCACTGTGAGGAAGTTGATTGCTTGGATCCAC 2183  
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55 SBJCT: 2100 CGTGTGTGCAGCTGGCTACAAGGGCGAGCACTGCGAAGAAGTGGATTGCTTGGATCCAAC 2159  
QUERY: 2184 CTGCTCCAGCCACGGAGTCTGTGTGAATGGAGAATGCCTGTGCAGCCCTGGCTGGGGTGG 2243  
|||||  
60 SBJCT: 2160 CTGCTCCAGCCATGGTGTCTGTGTGAACGGAGAGTGTCTATGCAGCCCCGGCTGGGGCGG 2219  
QUERY: 2244 TCTGAACTGTGAGCTGGCGAGGGTCCAGTGCCCAGACCAGTGCAGTGGGCATGGCACGTA 2303  
|| |||||  
65 SBJCT: 2220 GCTCAACTGCGAGCTGGCGAGGGTCCAGTGCCCAGACCAGTGTAGTGGGCATGGCACTTA 2279  
QUERY: 2304 CCTGCCTGACACGGGCCTCTGCAGCTGCGATCCCAACTGGATGGGTCCCGACTGCTCTGT 2363  
||| |||||  
70 SBJCT: 2280 CCTCCCTGACTCTGGCCTCTGCAACTGTGATCCGAATTGGATGGGTCCCGACTGCTCTGT 2339  
QUERY: 2364 TGAAGTGTGCTCAGTAGACTGTGGCACTCACGGCGTCTGCATCGGGGGAGCCTGCCGCTG 2423  
|||||  
75 SBJCT: 2340 TGAAGTGTGCTCAGTAGACTGTGGCACTCACGGCGTCTGCATCGGGGGAGCCTGCCGCTG 2399  
QUERY: 2424 TGAAGAGGGCTGGACAGGCGCAGCGTGTGACCAGCGCGTGTGCCACCCCCGCTGCATTGA 2483  
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80 SBJCT: 2400 TGAAGAGGGCTGGACAGGCGCGGCTTGTGACCAGCGCGTGTGCCACCCCCGCTGCATTGA 2459  
QUERY: 2484 GCACGGGACCTGTAAAGATGGCAAATGTGAATGCCGAGAGGGCTGGAATGGTGAACACTG 2543  
|||||  
85 SBJCT: 2460 GCACGGGACCTGTAAAGATGGCAAATGTGAATGCCGAGAGGGCTGGAATGGTGAACACTG 2519  
QUERY: 2544 CACCATTG 2551  
|||||  
90 SBJCT: 2520 CACCATTG 2527

In this search it was also found that the FCTR3bcd and e nucleic acid had homology to six fragments of *Gallus gallus* partial mRNA for teneurin-2. It has 2780 of 3449 bases (80%) identical to bases 3386-6834, 1553 of 1862 bases (83%) identical to bases 1414-3275, 540 of 628 bases (85%) identical to bases 587-1214, 593 of 725 bases (81%) identical to bases 7084-7808, 429 of 515 bases (83%) identical to bases 7895-8409, and 397 of 475 bases (83%) identical to bases 20-494 of *Gallus gallus* partial mRNA for teneurin-2. (EMBL Acc: GGA278031) (Table 3O).

**Table 3O. BLASTN of FCTR3b, c, d, and e against *Gallus gallus* Teneurin-2 mRNA**  
(SEQ ID NO:67)

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>GI|10241573|EMBL|AJ279031.1|GGA279031 GALLUS GALLUS PARTIAL MRNA FOR TENEURIN-2
(TEN2 GENE), LONG SPLICE
VARIANT
LENGTH = 8409

SCORE = 1532 BITS (773), EXPECT = 0.0
IDENTITIES = 2780/3449 (80%)
STRAND = PLUS / PLUS

QUERY: 3458 TGATGGTGGCTGTGCGAGGGGCATCTCTCCAGAAGTCATTCCAGGCTTCTCCCAACCTGG 3517
      |||||  ||  ||  ||  |||||  ||  ||  ||  |||||  ||  ||  |||||  |||
SBJCT: 3386 TGATGGTAGCAGTAGAAGGGGCATCTATTTCAAAAATCATTTCTGGCATCTCCCAACTTGG 3445

QUERY: 3518 CCTCCACCTTCATCTGGGACAAGACAGATGCGTATGGCCAAAGGGTGTATGGACTCTCAG 3577
      ||  ||  |||||  |||||  |||||  |||||  ||  ||  |||||  ||  |||||
SBJCT: 3446 CTTATACATTCATCTGGGACAAAACAGATGCATATGGTCAGAAGGTTTATGGGTGTGTCAG 3505

QUERY: 3578 ATGCTGTTGTGTCTGTCTCGGGTTTGAATATGAGACCTGTCCCAGTCTAATTCTCTGGGAGA 3637
      |||||  ||  |||||  ||  |||||  |||||  |||||  ||  |||||  |||||
SBJCT: 3506 ATGCTGTAGTTTCTGTGGGTTTGAATATGAGACTTGTCCCAGTTTGATTCTGTGGGAGA 3565

QUERY: 3638 AAAGGACAGCCCTCCTTCAGGGATTTCGAGCTGGACCCCTCCAACCTCGGTGGCTGGTCCC 3697
      |||||  ||  ||  ||  ||  |||||  |||||  ||  ||  |||||  ||  ||  |||||
SBJCT: 3566 AAAGGACTGCGCTGCTGCAAGGATTTGAGCTAGATCCTTCCAATCTAGGAGGATGGTCTT 3625

QUERY: 3698 TAGACAAACACCACATCCTCAATGTTAAAAGTGGAATCCTACACAAAGGCACTGGGGAAA 3757
      ||  |||||  ||  ||  |||||  ||  |||||  ||  ||  |||||  |||||  |||||
SBJCT: 3626 TGGATAAACATCATGTACTGAATGTCAAGAGTGGTATATTGCACAAAGGCAATGGAGAAA 3685

QUERY: 3758 ACCAGTTCCTGACCCAGCAGCCTGCCATCATCACCAGCATCATGGGCAATGGTCGCCGCC 3817
      |||||  ||  ||  |||||  ||  ||  |||||  |||||  |||||  |||||
SBJCT: 3686 ATCAGTTTCTAACTCAGCAGCCAGCTGTGATAACCAGCATTATGGGGAATGGGCGCCGAA 3745

QUERY: 3818 GGAGCATTTCTGTCCCAGCTGCAACGGCCTTGCTGAAGGCAACAAGCTGCTGGCCCCAG 3877
      |||||  |||||  |||||  |||||  ||  |||||  |||||  ||  |||||  |||||
SBJCT: 3746 GAAGCATATCCTGTCTAGCTGCAATGGTCTTGCAAGGAAATAAGCTTTTGGCCCCCTG 3805

QUERY: 3878 TGGCTCTGGCTGTTGGAATCGATGGGAGCCTCTATGTGGGTGACTTCAATTACATCCGAC 3937
      ||  |||||  ||  |||||  |||||  |||||  |||||  ||  ||  ||  |||||  ||  ||
SBJCT: 3806 TAGCACTGGCAGTGGGAATTGATGGAAGCCTCTTGTGGAGATTTTAATTACATTCCGC 3865

QUERY: 3938 GCATCTTTCCCTCTCGAAATGTGACCAGCATCTTGAGTTACGAAATAAAGAGTTTAAAC 3997
      |||||  ||  ||  |||||  |||||  |||||  |||||  ||  |||||  |||||
SBJCT: 3866 GTATCTTCCCATCCAGGAATGTGACTAGCATATTGGAGCTGAGAAATAAAGAGTTTAAAC 3925

QUERY: 3998 ATAGCAACAACCCAGCACACAAGTACTACTTGGCAGTGGACCCCGTGTCCGGCTCGCTCT 4057
      |||||  ||  ||  |||||  |||||  |||||  |||||  ||  |||||  ||  ||
SBJCT: 3926 ATAGCAACAATCCTGCTCACAATACTATCTGGCCGTGGACCCCGTTTCGGGCTCCCTGT 3985
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QUERY: 4058 ACGTGTCCGACACCAACAGCAGGAGAATCTACCGCGTCAAGTCTCTGAGTGGAACCAAAG 4117  
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 SBJCT: 3986 ACGTATCAGACACCAACAGCCGACGGATATACAAAGTCAAATCTCTTACTGGCACGAAAG 4045  
 5 QUERY: 4118 ACCTGGCTGGGAATTTCGGAAGTTGTGGCAGGGACGGGAGAGCAGTGTCTACCCTTTGATG 4177  
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 SBJCT: 4046 ACCTGGCTGGTAATTCTGAAGTGGTAGCGGGGACTGGAGAGCAATGCCTGCCCTTTGATG 4105  
 10 QUERY: 4178 AAGCCCGCTGCGGGGATGGAGGGAAGGCCATAGATGCAACCCTGATGAGCCCGAGAGGTA 4237  
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 SBJCT: 4106 AAGCCAGATGTGGAGATGGAGGGAAGCAGTGGACGCAACCCTAATGAGTCCTCGAGGAA 4165  
 QUERY: 4238 TTGCAGTAGACAAGAATGGGCTCATGTACTTTGTTCGATGCCACCATGATCCGGAAGGTTG 4297  
 ||||| | | | | | | | | | | | | | | | | | | | | |  
 15 SBJCT: 4166 TTGCAGTGGATAAGTATGGACTCATGTATTTTGTGATGCCACTATGATTGAAAAGTGG 4225  
 QUERY: 4298 ACCAGAATGGAATCATCTCCACCCTGCTGGGCTCCAATGACCTCACTGCCGTCCGGCCGC 4357  
 | ||||| | | | | | | | | | | | | | | | | | | | | |  
 20 SBJCT: 4226 ATCAGAATGGAATTATATCAACTCTGCTGGGCTCCAATGACCTAACTGCCGTCCGACCTC 4285  
 QUERY: 4358 TGAGCTGTGATTCCAGCATGGATGTAGCCCAGGTTCTGCTGGAGTGGCCAACAGACCTTG 4417  
 | ||||| | | | | | | | | | | | | | | | | | | | | |  
 SBJCT: 4286 TAAGCTGTGATTCCAGCATGGATGTCAGCCAGGTACGGCTGGAGTGGCCTACTGATCTCG 4345  
 25 QUERY: 4418 CTGTCAATCCCATGGATAACTCCTTGTATGTTCTAGAGAACAATGTCATCCTTCGAATCA 4477  
 |||| | | | | | | | | | | | | | | | | | | | | | |  
 SBJCT: 4346 CTGTCGATCCCATGGACAACTCACTTTATGCTCTAGAGAACAATGTTATTTTACGGATCA 4405  
 QUERY: 4478 CCGAGAACCACCAAGTCAGCATCATTCGCGGACGCCCCATGCACTGCCAAGTTCCTGGCA 4537  
 | | | | | | | | | | | | | | | | | | | | | | | | | |  
 30 SBJCT: 4406 CAGAAAACCATCAAGTTAGCATTATTGCTGGACGCCCCATGCACTGCCAGGTTCTGGTA 4465  
 QUERY: 4538 TTGACTACTCACTCAGCAAAGTAGCCATTCACTCTGCCCTGGAGTCAGCCAGTGCCATTG 4597  
 | ||||| | | | | | | | | | | | | | | | | | | | | |  
 35 SBJCT: 4466 TAGACTACTCTCTTAGCAAAGTGGCTATTTCATTCGCACTTGAATCAGCCAGTGCCATTG 4525  
 QUERY: 4598 CCATTTCTCACACTGGGGTCTCTACATCACTGAGACAGATGAGAAGAAGATTAACCGTC 4657  
 |||| | | | | | | | | | | | | | | | | | | | | | |  
 40 SBJCT: 4526 CCATCTCACACACAGGAGTTCTTTACATCAGTGAGACAGATGAAAAAAAAAATTAATCGGC 4585  
 QUERY: 4658 TACGCCAGGTAACAACCAACGGGGAGATCTGCCTTTTAGCTGGGGCAGCCTCGGACTGCG 4717  
 ||||| | | | | | | | | | | | | | | | | | | | | |  
 SBJCT: 4586 TACGCCAGGTAACCAATGGAGAAATATGCCTTCTTGACGGGGCAGCTTCAGACTGTG 4645  
 45 QUERY: 4718 ACTGCAAAAACGATGTCAATTGCAACTGCTATTCAGGAGATGATGCCTACGCGACTGATG 4777  
 | ||||| | | | | | | | | | | | | | | | | | | | | |  
 SBJCT: 4646 ATTGCAAAAATGATGTCAACTGTAATTGCTATTCCTGGGGATGATGGGTATGCCACTGATG 4705  
 QUERY: 4778 CCATCTTGAATTCCTCATCATCCTTAGCTGTAGCTCCAGATGGTACCATTACATTGCAG 4837  
 ||||| | | | | | | | | | | | | | | | | | | | | |  
 50 SBJCT: 4706 CCATCTTAAATTCACCATCTTCCTTAGCTGTGGCCCAGATGGTACCATCTACATAGCTG 4765  
 QUERY: 4838 ACCTTGAAATATTCGGATCAGGGCGGTGAGCAAGAACAAGCCTGTTCTTAATGCCTTCA 4897  
 | | | | | | | | | | | | | | | | | | | | | | | | | |  
 55 SBJCT: 4766 ATCTCGGAAATATCCGCATTAGGGCTGTGAGTAAAAACAGGCCCATCTTAATCTTTTA 4825  
 QUERY: 4898 ACCAGTATGAGGCTGCATCCCCCGAGAGCAGGAGTTATATGTTTTCAACGCTGATGGCA 4957  
 |||| | | | | | | | | | | | | | | | | | | | | | |  
 60 SBJCT: 4826 ACCAATATGAAGCTGCATCTCCAGGAGAACAGGAGCTGTATGTCTTCAATGCTGATGGGA 4885  
 QUERY: 4958 TCCACCAATACACTGTGAGCCTGGTGACAGGGGAGTACTTGTACAATTTACATATAGTA 5017  
 | |||| | | | | | | | | | | | | | | | | | | | | | |  
 SBJCT: 4886 TTCACCAGTACACTCTCAGCCTTGTTACCGGGGAGTACTTGTACAATTTACCTATAGCA 4945  
 65 QUERY: 5018 CTGACAATGATGTCACTGAATTGATTGACAATAATGGGAATTCCTGAAGATCCGTCGGG 5077  
 || | | | | | | | | | | | | | | | | | | | | | | | |  
 SBJCT: 4946 GTGATAACGATGTACCGAGGTGATGGACAGCAATGGCAACTCCTTGAAGGTCCGTCGGG 5005  
 QUERY: 5078 ACAGCAGTGGCATGCCCCGTCACCTGCTCATGCCTGACAACCAGATCATCACCTCACCG 5137  
 | | | | | | | | | | | | | | | | | | | | | | | | | |  
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5 SBJCT: 1594 GCACAGTATGATTTTCATGGAACGCTTGGATGGGAAAGAGAAATGGAGTGTGGTGAATCC 1653  
QUERY: 1726 CCCAGGGAACGCCGGAGCATAACAGACCTTGGTTCAGAAATGAAGCCGTGTTTGTGCAGTAC 1785  
|| ||||| || || ||||| | ||||| || ||||| |||||  
10 SBJCT: 1654 CCACGGGAACGGCGAAGTATTCAGACTCTTGTTCAGAAATGAGGCTGTGTTTGTTCAGTAC 1713  
QUERY: 1786 CTGGATGTGGGCTGTGGCATCTGGCCTTCTACAATGATGGAAAAGACAAAGAGATGGTT 1845  
||||||| ||||| ||||| || ||||| || ||||| |||||  
10 SBJCT: 1714 TTGGATGTGGGTTTGTGGCACCTGGCGTTTACAATGATGGCAAGGACAAAGAAGTGGTC 1773  
QUERY: 1846 TCCTTCAATACTGTTGTCCTAGATTTCAGTGCAGGACTGTCCACGTAACCTGCCATGGGAAT 1905  
||||||| || ||||| | | ||||| ||||| ||||| ||||| |||||  
15 SBJCT: 1774 TCCTTCAGTACAGTTATTTGGATTTCAGTGCAGGACTGTCCACGTAATTGTCATGGCAAT 1833  
QUERY: 1906 GGTGAATGTGTGTCCGGGGTGTGTCACTGTTTCCCAGGATTTCTAGGAGCAGACTGTGCT 1965  
|| || ||||| || || || || ||||| || ||||| ||||| |||||  
15 SBJCT: 1834 GGCGAGTGTGTTTCTGGTGTCTGCCACTGTTTCCCAGGATTTTCATGGAGCAGATTGTGCT 1893  
QUERY: 1966 AAAGCTGCCTGCCCTGTCTGTGCAGTGGGAATGGACAATATTCTAAAGGGACGTGCCAG 2025  
||||||| ||||| || ||||| ||||| || || || ||||| || |||||  
20 SBJCT: 1894 AAAGCTGCCTGCCCGGTGCTGTGCAGTGGCAATGGTTCAGTACTCCAAAGGAACCTGCTTG 1953  
QUERY: 2026 TGCTACAGCGGCTGGAAAGGTGCAGAGTGGGACGTGCCCATGAATCAGTGCATCGATCCT 2085  
||||||| ||||| ||||| || || || || ||||| | ||||| || |||||  
25 SBJCT: 1954 TGCTACAGTGGCTGGAAAGGTCCGGAATGTGATGTACCCATCAGCCAGTGTATTGATCCC 2013  
QUERY: 2086 TCCTGCGGGGGCCACGGCTCCTGCATTGATGGGAACTGTGTCTGCTCTGCTGGCTACAAA 2145  
|| || || || || || ||||| || ||||| ||||| ||||| |||||  
30 SBJCT: 2014 TCGTGTGGAGGTTCATGTTTCTGCATCGAAGGGAACGTGTGTCTGTTCCATTGGCTATAAA 2073  
QUERY: 2146 GGCGAGCACTGTGAGGAAGTTGATTGCTTGGATCCACCTGCTCCAGCCACGGAGTCTGT 2205  
|| || ||||| ||||| ||||| ||||| ||||| ||||| |||||  
30 SBJCT: 2074 GGAGAAAACGTGTGAGGAAGTTGATTGCTTAGATCCAACATGCTCCAATCACGGGGTCTGT 2133  
QUERY: 2206 GTGAATGGAGAATGCCTGTGCAGCCCTGGCTGGGGTGGTCTGAACGTGTGAGCTGGCGAGG 2265  
||||| ||||| || ||||| ||||| ||||| | ||||| ||||| |||||  
35 SBJCT: 2134 GTGAACGGAGAATGTCTCTGCAGCCAGGCTGGGGTGGAAATAAATGTGAGCTTCCCAGA 2193  
QUERY: 2266 GTCCAGTGGCCAGACCAGTGCAGTGGGCATGGCACGTACCTGCCTGACACGGGCCTCTGC 2325  
| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||  
40 SBJCT: 2194 GCCCAGTGGCCAGACCAGTGCAGTGGGCATGGCACATACCTGTCTGACACCGGTCTCTGT 2253  
QUERY: 2326 AGCTGCGATCCCAACTGGATGGGTCCCGACTGCTCTGTTGAAGTGTGCTCAGTAGACTGT 2385  
||||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||  
45 SBJCT: 2254 AGCTGCGATCCCAACTGGATGGGTCCCGACTGCTCCGTTGAAGTGTGCTCTGTAGACTGT 2313  
QUERY: 2386 GGCACCTCACGGCGTCTGCATCGGGGGAGCCTGCCGCTGTGAAGAGGGCTGGACAGGCGCA 2445  
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50 SBJCT: 2314 GGCACCCATGGGGTGTGCATTGGCGGAGCGTGTGCTGTGAAGAAGGGTGGACAGGAGTG 2373  
QUERY: 2446 GCGTGTGACCAGCGCGTGTGCCACCCCGCTGCATTGAGCACGGGACCTGTAAAGATGGC 2505  
||||||| ||||| || ||||| || || ||||| || ||||| |||||  
50 SBJCT: 2374 GCGTGTGACCAGCGTGTGTGCATCCCGGTGTACAGAGCACGGAACCTGTAAAGATGGG 2433  
QUERY: 2506 AAATGTGAATGCCGAGAGGGCTGGAATGGTGAACACTGCACCATTTGGTAGGCAAACGGCA 2565  
||||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||  
55 SBJCT: 2434 AAATGTGAATGCAGAGAGGGCTGGAATGGGAGCACTGCACCATTTGGTAGGCAAACGACA 2493  
QUERY: 2566 GGCACCGAAACAGATGGCTGCCCTGACTTGTGCAACGGTAACGGGAGATGCACACTGGGT 2625  
||||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||  
60 SBJCT: 2494 GGCACCGAAACAGATGGCTGCCCTGACTTGTGCAATGGCAACGGGAGGTGCACGCTGGGC 2553  
QUERY: 2626 CAGAACAGCTGGCAGTGTGTCTGCCAGACCGGCTGGAGAGGGCCCGGATGCAACGTTGCC 2685  
||||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||  
65 SBJCT: 2554 CAGAACAGCTGGCAGTGTGTCTGCCAGACCGGCTGGAGAGGGCCTGGATGCAACGTTGCC 2613  
QUERY: 2686 ATGGAAACTTCTGTGCTGATAACAAGGATAATGAGGGAGATGGCCTGGTGGATTGTTTG 2745  
||||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||  
70 SBJCT: 2614 ATGGAAACCTCCTGTGCCGATAACAAGGATAACGAGGGAGATGGCTTGGTTGACTGCCTA 2673

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SBJCT: 887 ACTCCCTCAACAGGAACTCGCTCACCAACCGCCGCAACCAGATCCACGCGCCTGCTCCCG 946  
 5 QUERY: 1142 CGCCCAATGACCTGGCCACCACACCAGAGTCCGTTTCAGCTTCAGGACAGCTGGGTGCTAA 1201  
 SBJCT: 947 CTCCCAATGACCTGGCGACCACGCCTGAGTCTGTGCAGCTGCAGGACAGCTGGGTGCTCA 1006  
 10 QUERY: 1202 ACAGCAACGTGCCACTGGAGACCCGGCACTTCCTCTTCAAGACCTCCTCGGGGAGCACAC 1261  
 SBJCT: 1007 ACAGCAACGTGCCGCTGGAGACCAGGCATTTCTTGTTTAAGACATCTTCTGGAACGACTC 1066  
 15 QUERY: 1262 CCTTGTTTCAGCAGCTCTTCCCCGGGATACCCCTTTGACCTCAGGAACGGTTTACACGCCCC 1321  
 SBJCT: 1067 CGCTGTTTCAGTAGCTCTTCCCCTGGCTACCCACTGACCTCAGGAACAGTTTATACTCCAC 1126  
 20 QUERY: 1322 CGCCCCGCTGCTGCCCAGGAATACTTTCTCCAGGAAGGCTTTCAAGCTGAAGAAGCCCT 1381  
 SBJCT: 1127 CTCCCAGGCTGTTACCTAGAAATACATTTTCCAGGAATGCATTCAAGCTGAAAAAGCCCT 1186  
 25 SCORE = 391 BITS (197), EXPECT = E-105  
 IDENTITIES = 593/725 (81%)  
 STRAND = PLUS / PLUS  
 30 QUERY: 7156 CATGTCTACAATCACTCCAACTCGGAGATTACCTCACTGTACTACGACCTCCAGGGCCAC 7215  
 SBJCT: 7084 CATGTCTACAATCATTCCAATTGAGAAATTACCTCTCTGTATTATGATCTGCAAGGCCAC 7143  
 35 QUERY: 7216 CTCTTTGCCATGGAGAGCAGCAGTGGGGAGGAGTACTATGTTGCCTCTGATAACACAGGG 7275  
 SBJCT: 7144 CTCTTTGCAATGGAGAGTAGCAGTGGGGAAGAATATTATGTGCTCTCCGATAACACGGGC 7203  
 40 QUERY: 7276 ACTCCTCTGGCTGTGTTTCAGCATCAACGGCCTCATGATCAAACAGCTGCAGTACACGGCC 7335  
 SBJCT: 7204 ACTCCGCTAGCCGTATTCAGCATCAATGGCCTCATGATCAAACAGCTTCAGTACACTGCA 7263  
 45 QUERY: 7336 TATGGGGAGATTTATTATGACTCCAACCCCGACTTCCAGATGGTCATTGGCTTCCATGGG 7395  
 SBJCT: 7264 TACGGAGAGATTTATTATGACTCAAACCCCTGATTTCCAGCTGGTTATTGGGTTCATGGA 7323  
 50 QUERY: 7396 GGACTCTATGACCCCTGACCAAGCTGGTCCACTTCACTCAGCGTGATTATGATGTGCTG 7455  
 SBJCT: 7324 GGGCTGTATGATCCTTTAACCAAACTCGTCCATTTTACCCAAAGGGACTACGATGTCTT 7383  
 55 QUERY: 7456 GCAGGACGATGGACCTCCCCAGACTATACCATGTGGAAAAACGTGGGCAAGGAGCCGGCC 7515  
 SBJCT: 7384 GCTGGACGCTGGACATCTCCTGATTACACAATGTGGAAAAACATTGGTAGAGAACCTGCT 7443  
 60 QUERY: 7516 CCCTTTAACCTGTATATGTTCAAGAGCAACAATCCTCTCAGCAGTGAGCTAGATTTGAAG 7575  
 SBJCT: 7444 CCCTTCAATCTGTACATGTTCAAGAGTAACAACCTCTCAGCAATGAACTGGATCTAAAG 7503  
 65 QUERY: 7576 AACTACGTGACAGATGTGAAAAGCTGGCTTGTGATGTTTGGATTTAGCAACATC 7635  
 SBJCT: 7504 AATTATGTAACAGATGTCAAAAGCTGGCTGGTGATGTTTCGGATTTAGCAACATT 7563  
 70 QUERY: 7636 ATTCCTGGCTTCCCGAGAGCCAAAATGTATTTTCGTGCCTCCTCCCTATGAATTGTCAGAG 7695  
 SBJCT: 7564 ATTCCTGGCTTCCCTAGAGCAAAAATGTACTTTGTGTACCTCCATACGAGCTGACTGAG 7623  
 75 QUERY: 7696 AGTCAAGCAAGTGAGAATGGACAGCTCATTACAGGTGTCCAACAGACAACAGAGAGACAT 7755  
 SBJCT: 7624 AGTCAAGCGTGTGAAAATGGACAGCTAATTACAGGAGTCCAGCAGACAACAGAAAGACAC 7683  
 80 QUERY: 7756 AACCAGGCCTTCATGGCTCTGGAAGGACAGGTCACTTAAAGCTCCACGCCAGCATC 7815  
 SBJCT: 7684 AATCAAGCTTTCATGGCTCTTGAGGGACAGGTCAATCTAAAAGATTACATGCCAGTATT 7743

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SBJCT: 260 GTGAGCCCTCTCCCCATCGAAGTGGCTACTGCTCGGACATAGGAATACTCCATCAAGGCT 319  
 5 QUERY: 599 ACTCCCTTAGCACAGGGTCTGACGCCGACTCCGACACCGAGGGAGGGATGTCTCCAGAAC 658  
 SBJCT: 320 ATTCCTTGAGCACTGGCTCTGATGCTGACTCAGACACGGAGGGCGGGATGTCTCCAGAGC 379  
 10 QUERY: 659 ACGCCATCAGACTGTGGGGCAGAGGGATAAAATCCAGGCGCAGTTCCGGCCTGTCCAGTC 718  
 SBJCT: 380 ACGCGATCAGGCTGTGGGGAAGAGGGATCAAATCCAGCCGAAGTTCTGGCCTGTCAAGTC 439  
 QUERY: 719 GTGAAAACTCGGCCCTTACCCTGACTGACTCTGACAACGAAAACAAATCAGATGA 773  
 15 SBJCT: 440 GTGAAAACTCGGCTCTCACGCTCACTGACTCCGACAATGAGAACAAGTCAGATGA 494

The full FCTR3a amino acid sequence also has 342 of 383 amino acid residues (89%) identical to, and 342 of 383 residues (89%) positive with, the 276 amino acid residue Odd Oz/ten-m homolog 2 (*Drosophila*) (GenBank Acc: NP\_035986.2) (SEQ ID NO:68) (Table 3P).

## 20 Table 3P. BLASTP of FCTR3a against Odd Oz/ten-m homolog 2 - (SEQ ID NO:68)

>GI|7657415|REF|NP\_035986.2| ODD OZ/TEN-M HOMOLOG 2 (DROSOPHILA); ODD OZ/TEN-M  
 HOMOLOG 3  
 (DROSOPHILA) [MUS MUSCULUS]  
 25 GI|4760778|DBJ|BAA77397.1| (AB025411) TEN-M2 [MUS MUSCULUS]  
 LENGTH = 2764  
 SCORE = 495 BITS (1274), EXPECT = E-139  
 IDENTITIES = 342/383 (89%), POSITIVES = 342/383 (89%), GAPS = 41/383 (10%)  
 30 QUERY: 37 HNPPPVSCQMPLLDSNTSHQIMDTNPDEEFSPNSYLLRACSGPQQASSSGPPNHHSQSTL 96  
 SBJCT: 189 HNPPPVSCQMPLLDSNTSHQIMDTNPDEEFSPNSYLLRACSGPQQASSSGPPNHHSQSTL 248  
 35 QUERY: 97 RPPLPPPHNHTLSHHHSSANSLNRNSLTNRRSQIHAPAPAPNDLATTPESVQLQDSWVLN 156  
 SBJCT: 249 RPPLPPPHNHTLSHHHSSANSLNRNSLTNRRSQIHAPAPAPNDLATTPESVQLQDSWVLN 308  
 40 QUERY: 157 SNVPLETRHFLFKTSSGSTPLFSSSSPGYPLTSGTVYTPPRLLPRNTFSRKAFLKKPS 216  
 SBJCT: 309 SNVPLETRHFLFKTSSGSTPLFSSSSPGYPLTSGTVYTPPRLLPRNTFSRKAFLKKPS 368  
 45 QUERY: 217 KYCSWKCAALSAIAAALLLAILLAYFI----- 243  
 SBJCT: 369 KYCSWKCAALSAIAAALLLAILLAYFIAMHLLGLNWQLQPADGHTFNNGVRTGLPGNDDV 428  
 QUERY: 244 -----VPWSLKNSSIDSGEAEVGRRVTQEVPPGVFWRSQIHISQPQFLKFNISLGKD 295  
 SBJCT: 429 ATVPSSGGKVPWSLKNSSIDSGEAEVGRRVTQEVPPGVFWRSQIHISQPQFLKFNISLGKD 488  
 50 QUERY: 296 ALFGVYIRRGLPSSHAQYDFMERLDGKEKWSVVESPRERRSIQTLVQNEAVFVQYLDVGL 355  
 SBJCT: 489 ALFGVYIRRGLPSSHAQYDFMERLDGKEKWSVVESPRERRSIQTLVQNEAVFVQYLDVGL 548  
 55 QUERY: 356 WHLAFYNDGKDKEMVSEFNTTVLD 378  
 SBJCT: 549 WHLAFYNDGKDKEMVSEFNTTVLD 571

The full FCTR3b amino acid sequence has 2442 of 2802 amino acid residues (87%) identical to, and 2532 of 2802 residues (90%) positive with, the 2802 amino acid residue teneurin-2 [*Gallus gallus*] (GenBank Acc: AJ279031) (SEQ ID NO:69) (Table 3Q).

**Table 3Q. BLASTP of FCTR3a against Teneurin-2 - (SEQ ID NO:69)**

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5  >GI|10241574|EMBL|CAC09416.1| (AJ279031) TENEURIN-2 [GALLUS GALLUS]
    LENGTH = 2802

    SCORE = 4853 BITS (12589), EXPECT = 0.0
    IDENTITIES = 2510/2802 (87%), POSITIVES = 2600/2802 (90%), GAPS = 69/2802 (2%)

10  QUERY: 1   MDVKDRRHRSLTRGRCGKECRYTSSSLDSEDCRVPTQKSYSSSETLKAYDHDSRMHYGNR 60
    SBJCT: 1   MDIKDRRHRSLTRGRCGKECRYTSSSLDSEDCRVPAQKSYSSSETLKAYGHDTRMHYGNR 60

15  QUERY: 61  VTDLIHRESDEFPRQGTNFTLAE LGICEPSPHRSGYCSDMGILHQGYSLSTGSDADSDTE 120
    SBJCT: 61  VSDLVHRESDEFPRQGTNFTLAE LGICEPSPHRSGYCDIGILHQGYSLSTGSDADSDTE 120

20  QUERY: 121 GGMSPEHAIRLWGRGIKSSRSSLSSRENSALTLTDS DNENKSDDENG----- 168
    SBJCT: 121 GGMSPEHAIRLWGRGIKSSRSSLSSRENSALTLTDS DNENKSDEENDFHTLSEKLDKDR 180

    QUERY: 169 -----RPIPTSSPSLLPSAQLPSSHNPFPVSCQMPLLDSNTSHQIMDT 212
    SBJCT: 181 QTSWQQLAETKNSLIRRP IPTSSPSLLPSAQLPSSHNPFPVSCQMPLLDSNTSHQIMDT 240

25  QUERY: 213 NPDEEFSPNSYLLRACSGPQQASSSGPPNHHSQSTLRPPLPPPHNHTLSHHHSSANSINR 272
    SBJCT: 241 NPDEEFSPNSYLLRACSGPQQASSSGPPNHHSQSTLRPPLPPPHNHTLSHHHSSANSINR 300

30  QUERY: 273 XXXXXXXXQIHAPAPAPNDLATTPESVQLQDSWVLNSNVPLETRHFLFKXXXXXXXXXXXXX 332
    SBJCT: 301 NSLTNRRNQIHAPAPAPNDLATTPESVQLQDSWVLNSNVPLETRHFLFKTSSGTTPLESS 360

35  QUERY: 333 XXXXYPLTSGTVYTPPRLLP RNTFSRKAFLKKPSKYCSWKCXKXXXXXXXXXXXXXXXXX 392
    SBJCT: 361 SSPGYPLTSGTVYTPPRLLP RNTFSRNAFLKKPSKYCSWKCAALSAIAAAVLLAILLA 420

40  QUERY: 393 YFIV-----PWSLKNSSIDSGEAE 411
    SBJCT: 421 YFIAMHLLGLNWQLQPADGHTFSNGLRPGAAGAEDGAAAPPAGRGFWVTRNSSIDSGETE 480

    QUERY: 412 VGRRTVQEVP PGVFWRSQIHISQPQFLKENISLGKDALFGVYIRRG LPPSHAQYDFMERL 471
    SBJCT: 481 VGRKVTQEVP PGVFWRSQIHISQPQFLKENISLGKDALFGVYIRRG LPPSHAQYDFMERL 540

45  QUERY: 472 DGKEKWSVVESPRERRSIQTLVQNEAVFVQYLDVGLWHLAFYNDGKD KEMVSENTVVLD S 531
    SBJCT: 541 DGKEKWSVVESPRERRSIQTLVQNEAVFVQYLDVGLWHLAFYNDGKD KEVVSEFSTVILDS 600

50  QUERY: 532 VQDCPRNCHGN GECVSGVCHCFPGFLGADCAKAACPVLC SGNGQYSKGTCCQYSGWKGA E 591
    SBJCT: 601 VQDCPRNCHGN GECVSGVCHCFPGFHGADCAKAACPVLC SGNGQYSKGTCLCYSGWKGP E 660

55  QUERY: 592 CDVPMNQCIDPSCGGHGSCIDGNCVCSAGYKGEHCEEVDCLDPTCSSHGVCVNGECLCSP 651
    SBJCT: 661 CDVPISQCIDPSCGGHGSCIEGNCVCSIGYKGENCEEVDCLDPTCSNHGVCVNGECLCSP 720

60  QUERY: 652 GWGGLNCELARVQCPDQCSGHGTYLPDTGLCSCDPNWMGPDCSVEVCSVDCGTHGVCIGG 711
    SBJCT: 721 GWGGINCELPR AQCPDQCSGHGTYLSDTGLCSCDPNWMGPDCSVEVCSVDCGTHGVCIGG 780

    QUERY: 712 ACRCEEGWTGAACDQRVCHPRCIEHGTCCKDGKCECREGWNGEHCTIGRQTAGTETDGC PD 771
    SBJCT: 781 ACRCEEGWTGVACDQRVCHPRCTEHGTCCKDGKCECREGWNGEHCTIGRQTTGTETDGC PD 840

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5  
 QUERY: 772 LCNGNGRCTLGQNSWQCVCQTGWRGPGCNVAMETSCADNKDNEGDGLVDCLDPDCCLQSA 831  
 SBJCT: 841 LCNGNGRCTLGQNSWQCVCQTGWRGPGCNVAMETSCADNKDNEGDGLVDCLVPDCCLQST 900  
 QUERY: 832 CQNSLLCRGSRDPLDIIQQGQTDWPAVKSFYDRIKLLAGKDSTHIIPGENPFNSSLVSLI 891  
 SBJCT: 901 CQNSLLCRGSRDPLDIIQQSHSGSPAVKSFYDRIKLLVGKDSTHIIPGENPFNSSLVSLI 960  
 10  
 QUERY: 892 RGQVVTTDGTPLVGVNVSVFKYPKYGYTITRQDGTFDLIANGGASLTLHFERAPFMSQER 951  
 SBJCT: 961 RGQVVTTDGTPLVGVNVSVFKYPKYGYTITRQDGMFDLVANGGSSLTLHFERAPFMSQER 1020  
 15  
 QUERY: 952 TVWLPWNSEFYAMDTLVMKTEENSIPSCDLSGFVRPDPPIISSPLSTFFSAAPGQNPPIVPE 1011  
 SBJCT: 1021 TVWLPWNSEFYAMDTLVMKTEENSIPSCDLSGFVRPDPVPIISSPLSTFFSDAPGRNPPIVPE 1080  
 20  
 QUERY: 1012 TQVLHEEIELPGSNVKLRYLSSRTAGYKSLKITMTQSTVPLNLIHVHLMVAVEGHLFQK 1071  
 SBJCT: 1081 TQVLHEEIEVPGSSIKLIYLSSRTAGYKSLKIIMTQSLVPLNLIKVHLMVAVEGHLFQK 1140  
 25  
 QUERY: 1072 SFQASPNLASTFIWDKTDAYGQRVYGLSDAVVSVGFYETCPSLILWEKRTALLQGFELD 1131  
 SBJCT: 1141 SFLASPNLAYTFIWDKTDAYGQKVYGLSDAVVSVGFYETCPSLILWEKRTALLQGFELD 1200  
 30  
 QUERY: 1132 PSNLGGWSLDKHHILNVKSGILHKGKTGENQFLTQQPAIITSIMGNRRRSISCPSCNGLA 1191  
 SBJCT: 1201 PSNLGGWSLDKHHVILNVKSGILHKGNGENQFLTQQPAVITSIMGNRRRSISCPSCNGLA 1260  
 35  
 QUERY: 1192 EGNKLLAPVALAVGIDGSLYVGDFNYIRRIFFPSRNVTSILELRNKEFKHSNNPAHKYYLA 1251  
 SBJCT: 1261 EGNKLLAPVALAVGIDGSLFVGDFNYIRRIFFPSRNVTSILELRNKEFKHSNNPAHKYYLA 1320  
 40  
 QUERY: 1252 VDPVSGSLYVSDTNSRRIYRVKSLSGTKDLAGNSEVVAGTGEQCLPFDEARCGDGGKAID 1311  
 SBJCT: 1321 VDPVSGSLYVSDTNSRRIYKVSLTGTDLAGNSEVVAGTGEQCLPFDEARCGDGGKAVD 1380  
 45  
 QUERY: 1312 ATLMSPRGIAVDKNGLMYFVDATMIRKVDQNGIISTLLGSNDLTAVRPLSCDSSMDVAQV 1371  
 SBJCT: 1381 ATLMSPRGIAVDKYGLMYFVDATMIRKVDQNGIISTLLGSNDLTAVRPLSCDSSMDVSVQV 1440  
 50  
 QUERY: 1372 RLEWPTDLAVNPMDNSLYVLENNVILRITENHQVSIAGRPMHCQVPGIDYSLSKXXXXX 1431  
 SBJCT: 1441 RLEWPTDLAVDPMMDNSLYVLENNVILRITENHQVSIAGRPMHCQVPGIDYSLSKLAIHS 1500  
 55  
 QUERY: 1432 XXXXXXXXXXXXXTGVLITETDEKKINRLRQVTTNGEICLLAGAASXXXXXXXXXXXXYS 1491  
 SBJCT: 1501 ALESASAIASHTGVLITSETDEKKINRLRQVTTNGEICLLAGAASDCDCKNDVNCNCYS 1560  
 60  
 QUERY: 1492 GDDAYATDAILNSPSSLAVAPDGTIYIADLGNIRIRAVSKNKPVLNAFNQYEAASPGEQE 1551  
 SBJCT: 1561 GDDGYATDAILNSPSSLAVAPDGTIYIADLGNIRIRAVSKNRPILNSFNQYEAASPGEQE 1620  
 65  
 QUERY: 1552 LYVFNADGIHQYTVSLVTGEYLYNFTYSTDNDVTELDNNGNSLKIIRRDSSGMPRHLLMP 1611  
 SBJCT: 1621 LYVFNADGIHQYTLVSLVTGEYLYNFTYSSDNDVTEVMDNSNGNSLKVRRDASGMPRHLLMP 1680  
 70  
 QUERY: 1612 DNQIITLTVGTNGGLKVVSTQNLGLMTYDGNLGLLTKSDETGWTTFYDYDHEGRLTN 1671  
 SBJCT: 1681 DNQIVTLAVGTNGGLKLVSTQTLGLMTYNGNSGLLTKSDETGWTTFYDYDHEGRLTN 1740  
 QUERY: 1672 VTRPTGVVTS LHREMEKSITIDIENSNRDDVTITNLSSVEASYTVVQDQVRNSYQLCN 1731  
 SBJCT: 1741 VTRPTGVVTS LHREMEKSITIDIENSNRDDVTITNLSSVEASYTVVQDQVRNSYQLCN 1800  
 QUERY: 1732 NGTLRVMYANGMGISFHSEPHVLAGTITPTIGRCNISLPMENGLNSIEWRLRKEQIKGKV 1791  
 SBJCT: 1801 NGTLRVMYANGMSISFHSEPHVLAGTVTPTIGRCNISLPMENGLNSIEWRLRKEQIKGKV 1860  
 QUERY: 1792 TIFGRKLRVHGRNLLSIDYDRNIRTEKIYDDHRKFTLRRIYDQVGRPFLWLPSSGLAAVN 1851

SBJCT: 1861 TVEGRKLRVHGRNLLSIDYDRNIRTEKIYDDHRKFTLRRIYDQLGRPFLLWLPSSGLAAVN 1920  
 5 QUERY: 1852 VSYFFNGRLAGLQRGAMSERTDIDKQGRIVSRMFADGKVWSYSYLDKSMVLLQLSQSQRYI 1911  
 SBJCT: 1921 VSYFFNGRLAGLQRGAMSERTDIDKQGRISRMFADGKVWSYTYLEKSMVLLQLSQSQRYI 1980  
 10 QUERY: 1912 FEYDSSDRLLAVTMPVARHSMSTHTSIGYIRNIYNPPESNASVIFDYSDDGRIKTSFL 1971  
 SBJCT: 1981 FEYDSSDRLLHAVTMPVARHSMSTHTSVGYIRNIYNPPESNASVIFDYSDDGRIKTSFL 2040  
 15 QUERY: 1972 GTGRQVFYKYGKLSKLSEIVYDSTAVTFGYDETTGVLKMNQLSGGFSCITIRYRKIGPLV 2031  
 SBJCT: 2041 GTGRQVFYKYGKLSKLSEIVYDSTAVTFGYDETTGVLKMNQLSGGFSCITIRYRKIGPLV 2100  
 20 QUERY: 2032 DKQIYRFSEEGMVNARFDYTYHDNSFRIASIKPVISETPLPVDLYRYDEISGKVEHFGKF 2091  
 SBJCT: 2101 DKQIYRFSEEGMVNARFDYTYHDNSFRIASIKPIISETPLPVDLYRYDEISGKVEHFGKF 2160  
 25 QUERY: 2092 GVIYYDINQIITTAVMTLSKHFDTHGRIKEVQYEMFRSLMYWMTVQYDSMGRVIKRELKL 2151  
 SBJCT: 2161 GVIYYDINQIITTAVMTLSKHFDTHGRIKEVQYEMFRSLMYWMTVQYDSMGRVTKRELKL 2220  
 30 QUERY: 2152 GPYANTTKYTYDYDGDGQLQSVAVNDRPTWRYSDXXXXXXXXXXXXXSVRLMPLRYDLRD 2211  
 SBJCT: 2221 GPYANTTKYTYDYDGDGQLQSVAVNDRPTWRYSDNLGNLHLLNPGNSVRLMPLRYDLRD 2280  
 35 QUERY: 2212 RITRLGDVQYKIDDDGYLCQSGSDIFEYNSKGLLTRAYNKASGWSVQYRYDGVGRRASYK 2271  
 SBJCT: 2281 RITRLGDIPYKIDDDGFLCQSGSDVFEYNSKGLLTRAYNKANGWNVQYRYDGLGRRASCK 2340  
 40 QUERY: 2272 TNLGHHLLQYFYSDLHNPTRITHVYNHNSSEITSLYYDLQGHLFAMESSSGEEYYVASDNT 2331  
 SBJCT: 2341 TNLGHHLLQYFYADLHNPTRVTHVYNHNSSEITSLYYDLQGHLFAMESSSGEEYYVASDNT 2400  
 45 QUERY: 2332 GTPLAVFSINGLMIKQLQYTAYGEIYYDSNPDFQMVIGFHGGLYDPLTKLVHFTQRDYDV 2391  
 SBJCT: 2401 GTPLAVFSINGLMIKQLQYTAYGEIYYDSNPDFQLVIGFHGGLYDPLTKLVHFTQRDYDV 2460  
 50 QUERY: 2392 LAGRWTSPDYTMWKNVGKEPAPFNLYMFKSNNPLSSELDLKNYVTDVKSWLVMFGFQLSN 2451  
 SBJCT: 2461 LAGRWTSPDYTMWKNIGREPAPFNLYMFKSNNPLSNELDLKNYVTDVKSWLVMFGFQLSN 2520  
 55 QUERY: 2452 IIPGFPRAKMYFVPPPYELSESQASENGQLITGVQQTTERHNQAFMALEGQVITKKLHAS 2511  
 SBJCT: 2521 IIPGFPRAKMYFVSPPPYELTESQACENGQLITGVQQTTERHNQAFMALEGQVISKRLHAS 2580  
 60 QUERY: 2512 IREKAGHWFATTTPIIGKGIMFAIKEGRVTTGVSSIASSEDSRKVASVLNNAYYLDKMHYS 2571  
 SBJCT: 2581 IREKAGHWFATSTPIIGKGIMFAVKKGRVTTGISSIATDDSRKIASVLNSAHYLEKMHYS 2640  
 65 QUERY: 2572 IEGKDTHYFVKIGSADGDLVTLGTTIGRKVLESGVNVTVSQPTLLVNGRTRRFTNIEFQY 2631  
 SBJCT: 2641 IEGKDTHYFVKIGSADSDLVTLAMTSGRKVLD SGVNVTVSQPTLLINGRTRRFTNIEFQY 2700  
 70 QUERY: 2632 STLLLSIRYGLTPDTLDEEKARVLDQARQALGTAWAKEQQKARDGREGSRLWTEGEKQQ 2691  
 SBJCT: 2701 STLLINIRYGLTADTLDEEKARVLDQARQALGSAWAKEQQKARDGREGSRVWTDGEKQQ 2760  
 75 QUERY: 2692 LLSTGRVQGYEGYYVLPVEQYPELADSSSNIQFLRQNMKGKR 2733  
 SBJCT: 2761 LLNTGRVQGYEGYYVLPVEQYPELADSSSNIQFLRQNMKGKR 2802

The FCTR3bcde and f amino acid sequences have 1524 of 2352 amino acid residues  
 (64%) identical to, and 1881 of 2532 residues (79%) positive with, the amino acid residues  
 429-2771, 93 of 157 residues (59%) identical to and 118 of 157 residues (74%) positive with

amino acid residues 1-155, and 59 of 152 residues (38%) identical to and 68 of 152 residues (43%) positive with amino acid residues 211-361 of Ten-m4 [*Mus musculus*] (ptnr: GenBank Acc: BAA77399.1) (SEQ ID NO:70) (Table 3R).

**Table 3R. BLASTP of FCTR3b, c, d, e, and f against *Mus musculus* Ten-m4 - (SEQ ID NO:70)**

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>GI|4760782|DBJ|BAA77399.1| (AB025413) TEN-M4 [MUS MUSCULUS]
  LENGTH = 2771

SCORE = 3089 BITS (8008), EXPECT = 0.0
IDENTITIES = 1524/2352 (64%), POSITIVES = 1881/2352 (79%), GAPS = 28/2352 (1%)

QUERY: 401  KNSSIDSGEAEVGRRTQEVPPGVFWRISOIHISQPOFLKFNISLGKDALFGVYIRRLPP 460
          ++| ||||| +||| +|+||| ||||| + | | ||||+||| | | +| | +|||
SBJCT: 429  EDSFIDSGEIDVGRRASQKIPPGTFWRSQVFIDHPVHLKFNVS LGKAALVGIYGRKGLPP 488

QUERY: 461  SHAQYDFMERLDGK-----EKWSVVESPRERRSIQTLVQNEAVFVQYLDVGLWHLAFYND 515
          || |++|+| |||+ | | + | | + | | +||| | +||| |||
SBJCT: 489  SHTQFDFVELLDGRRLTQEARSLGEPQRQSRGPVPPSSHETGFIQYLDSGIWHLAFYND 548

QUERY: 516  GKDKEMVSFNTTVVLDSVQDCPRNCHNGECVSGVCHCFPGFLGADCAKAACPVLCSGNGQ 575
          ||+ |++| | | ++| | +| ||+|||+|+| ||| ||| | | +|+||| |||
SBJCT: 549  GKESEVVSFLTTAIESVDNCPSPNCYGNDCISGTCHCFLGFLGPDCCRASCVPVLCSGNGQ 608

QUERY: 576  YSKGTCQCYSGWKGAECDVPMNQCIDPSCGGHSGCIDGNCVCSAGYKGEHCEEVDCLDPT 635
          | | | | +| ||| ||| ||| ||| +| ||+| | | +| + | ||| ||| ||| +|||
SBJCT: 609  YMKGRCLCHSGWKGAECDVPTNQCIDVACSSHGTCIMGTICNPGYKGESCEEVD CMDPT 668

QUERY: 636  CSSHGVCVNGECLCSPGWGGLNCELARVQCPDQCSGHGTYLPDTGLCSCDPNWMGPDCSV 695
          ||| ||| ||| ||| ||| ||| | | ||| ||| +||| ||| +||| +| | ||| +
SBJCT: 669  CSSRGVCVRGECHCSVGWGGTNCETPRATCLDQCSGHGTFLPDTGLCNCDPSTGHDCSI 728

QUERY: 696  EVCSVDCGTHGVCIGGACRCEE GWTGAACDQRVCHPRCIEHGTCKDGKCECREGWNGEHC 755
          |++| ||| ||| +|| ||| +|| ||| ||| ||| ||| +||| ||| ||| |||
SBJCT: 729  EICAADCGGHGVCVGGTCRCEDGWMGAACDQACHPRCAEHGTCTRDGKCECSPGWNGEHC 788
          *****

QUERY: 756  TIGRQTAGTETDGCPLCNGNGRCTLGQNSWQCVCQTGWRGPGCNVAMETSCADNKDNEG 815
          || | | +||| ||| ||| ||| ||| ||| ||| ||| +||| | | ||| +|
SBJCT: 789  TIAHYLDRVVKEGCPGLCNGNGRCTLDLNGWHVCVQLGWRGTGCDTSMETGCGDGKDNDG 848

QUERY: 816  DGLVDCLDPDCCLQSACQNSLLCRGSRDPLDIIQOGQT--DWPVAVKSFYDRIKLLAGKDS 873
          ||| ||| +||| ||| | + || || ||| ||| + | | + ||| || | +||
SBJCT: 849  DGLVDCMDPDCCLQPLCHVNPLCLGSPDPLDIIQETQAPVSQQNLNPFYDRIKFLVGRDS 908

QUERY: 874  THIIPGENPFNSSLVSLIRGQVVTDTGTPLVGVNVSEFVKYPKYGYTITRQDGTDFDLIANG 933
          || ||| ||| + | | ||| +|+||| ||| +|| + | +||| +||| +|| + ||
SBJCT: 909  THSIPGENPFDGGHACVIRGQVMTSDGTPLVGVNISFINNPLFGYTISRQDGSFDLVTNG 968

QUERY: 934  GASLTLHFERAPFMSQERTVWLPWNSFYAMDTLVMKTEENSIPSCDLSGFVRPDPIIIS 993
          | | + | ||| ||| +|| | +||| + | +| +|| + || ||| || | ||| +|| +
SBJCT: 969  GISIILRFERAPFITQEHTLWLPWDRFFVMETIVMRHEENEIPSCDLSNFARPNPVVSPS 1028

QUERY: 994  PLSTFFSAAPGQNPIVPETQVLHEEIELPGSNVKRLRYLSSRTAGYKSLKITMTQSTVPL 1053
          ||++| | + | ||| | | ||| + | ++| ||| ||| ||| +||++| | +|
SBJCT: 1029 PLTSFASSCAEKGPVPEIQALQEEI VIAGCKMRLSYLSSRTPGYKSVLRISLTHPTIPF 1088

QUERY: 1054 NLIRVHLMVAVEGHLEFQKSFQASPNLASTFIWDKTDAYGQRVYGLSDAVSVGFYETCP 1113
          ||++||| ||| ||| | | +|| + ||| ||| | | +|| | +| ||| +|| +||
SBJCT: 1089 NLMKVHLMVAVEGRLEFRKWFAAAPDLSYYFIWDKTDVYNQKVFGFSEAFVSVGYEYESCP 1148

QUERY: 1114 SLILWEKRTALLOGFELDPSNLGGWSLDKHHILNVKSGILHKGTGENQFLTQQPAIITSI 1173
          ||| ||| ||| +||| +|| | ||| ||| ||| +||| ||| ||| +|| +||
SBJCT: 1149 DLILWEKRTAVLQGYEIDASKLGGWSLDKHHALNIQSGILHKNGENQFVSQQPPVIGSI 1208

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WO 01/66747

PCT/US01/07160

5 SBJCT: 2227 LLSPGNSARLTPLRYDLRDRITRLGVDQYKMDDEGFLRQGGDVFEYNSAGLLIKAYNRA 2286

QUERY: 2253 SGWSVQYRYDGVGRRASYKTNLGHHLQYFYSDLHNPTRITHVYNHSNSEITSLYYDLQGH 2312  
 |||||+|||||+||| | |++ |||||+||+|| |||++||+||||+||||| |||||

10 SBJCT: 2287 SGWSVRYRYDGLGRRVSSKSSSHHLQFFYADLTNP TKVTHLYNHSSEITSLYYDLQGH 2346

QUERY: 2313 LFAMESSSGEEYYVASDNTGTPLAVFSINGLMIKQLQYTAYGEIYYDSNPDFQMVIGFHG 2372  
 ||||| |||+||+|| | | ||||| |||||+ ||||| |||+||+||+||+||

10 SBJCT: 2347 LFAMELSSGDEFYIACDNIGTPLAVFSGTGLMIKQILYTAYGEIYMDTNP NFQIIIGYHG 2406

QUERY: 2373 GLYDPLTKLVHFTQRDYDVLAGRWTSPDYTMWKNVGKEP-APFNLYMFKSNNPLSSELDL 2431  
 ||||| ||||| +||||| |||||+ +|| + ||+|||||+|||+|| +

15 SBJCT: 2407 GLYDPLTKLVHMGRRDYDVLAGRWTSPDHELWKRLSSNSIVPFHLYMFKNNNPISNSQDI 2466

QUERY: 2432 KNYVTDVKS WLVMFGFQLSNIIPGFPRAKMYFVPPPYELSESQAS----ENGQLITGVQQ 2487  
 | ++||| |||+ ||||| |++||+ + | ||| +| +| + | |||

15 SBJCT: 2467 KCFMTDVNSWLLTFGEFQLHNVIPGYPKPDTDAMEPSYELVHTQMKTOEWDNSKSILGVQC 2526

20 QUERY: 2488 TTERHNQAFMALE-----GQVITKKLHASIREKAGHWFATTTPIIGKGIMFAIKEGRVT 2541  
 ++ +||+ || | || | +| ||++ | |||+ |||+|||

20 SBJCT: 2527 EVQKQLKAFVTLERFDQLYGSTITSCQAPETKK----FASSGSIFGKGVKFALKDGRVT 2582

25 QUERY: 2542 TGVSSIASEDSRKVASVLNNAYYLDKMHYSIEGKDTHYFVKIGSADGDLVTLGTTIGRKV 2601  
 | + |++|| |++||+|||+||+ +||+|| | ||||| | ++||| || + ||+

25 SBJCT: 2583 TDIISVANEDGRRIAAILNNAHYLENLHFTIDGVDTHYFVKPGPSEGLAILGLSGGRRT 2642

30 QUERY: 2602 LESGVNVTVSQPTLLVNGRTRRETNI EFQYSTLLLSIRYGLTPDTLDEEKARVLDQARQR 2661  
 ||+||||||| ++|||+||+|| | | | + ||| |++||| |||+ |||

30 SBJCT: 2643 LENGVNVTVSQINTMLSGRTRRYTDIQLQYRALCLNTRYG---TTVDEEKVRVLELARQR 2699

35 QUERY: 2662 ALGTAWAKEQQKARDGREGSRLWTEGEKQQLLSTGRVQGYEGYYVLPVEQYPELADSSSN 2721  
 |+ |||+|||+ |+| || | ||+|||+||+|||+||+|| | |||||+||+||

35 SBJCT: 2700 AVRQAWAREQQRLREGEEGLRAWTDGEKQQVLNTGRVQGYDGFVTSVEQYPELSDSANN 2759

35 QUERY: 2722 IQFLRQNE MGKR 2733  
 | |++|||+||+|

35 SBJCT: 2760 IHFMRQSEMGRR 2771

40 SCORE = 161 BITS (407), EXPECT = 2E-37  
 IDENTITIES = 93/157 (59%), POSITIVES = 118/157 (74%), GAPS = 4/157 (2%)

45 QUERY: 1 MDVKDRR-HRSLTRGRCGKECRYTSSSLDSEDCRVPTQKSYSSSETLKAYDHDSRMHYGN 59  
 |||||+| +||||| | | ||||| |||+ + | ||||| ||||| |||+ ||+

45 SBJCT: 1 MDVKERKPYRSLTRRR-DAERRY TSSSADSEEGKGP-QKSYSSSETLKAYDQDARLAYGS 58

50 QUERY: 60 RVTDLIHRESDEFPRQGTNFTLAE LGICEPS-PHRSGYCSDMGILHQGYSLSTGSDADSD 118  
 || |++ +|++|| | ||||| |||+ | + || + | +||+ | |||+ ||| +

50 SBJCT: 59 RVKDMVPQEAEEFCRTGTNFTLRELGLGEMTPPHGTLYRTDIGLPHCGYSMGASSDADLE 118

55 QUERY: 119 TEGGMSPEHAIRLWGRGIKSRSSSGLSSRENSALTTLT 155  
 + +|||| +|||| +| ||| |||| || ||||

55 SBJCT: 119 ADTVLSPEHPVRLWGRSTRSGRSSCLSSRANSNLTLT 155

60 SCORE = 72.1 BITS (176), EXPECT = 8E-11  
 IDENTITIES = 59/152 (38%), POSITIVES = 68/152 (43%), GAPS = 42/152 (27%)

60 QUERY: 285 PAPAPND--LATTP-----ESVQLQDSWVLNSNVPLETR----- 316  
 |+||| | | + | | |||+|||+|||

60 SBJCT: 211 PSPAPTDHSLSGEPPAGSAQEPTHAQDNWLLNSNIPLETRNLGKQPFGLTLQDNLIEMDI 270

65 QUERY: 317 -----HFLFKXXXXXXXXXXXXXXXXXYPLTSGTVYTPPPRLLPRNTFSRKAFK 363  
 ||||| ||||| |||+||| |||+||| ||

65 SBJCT: 271 LSASRHDGAYS DGHFLFK-PGCTSPLFCTTSPGYPLTSSTVYSPPPRPLPRSTFSRPAFN 329

65 QUERY: 364 LKKPSKYCSWKXXXXXXXXXXXXXXXXXYFI 395  
 |||||+||| ||+

65 SBJCT: 330 LKKPSKYCNWKCAALSAILISATLVILLAYFV 361

\*FCTR3F DOES NOT CONTAIN THESE AMINO ACIDS

The 997-2733 amino acid fragment of the FCTR3bcde and f protein was also found to have 1695 of 1737 amino acid residues (97%) identical to, and 1695 of 1737 residues (97%) positive with the amino a 1737 amino acid residue protein KIAA1127 protein [*Homo sapiens*] (GenBank Acc:(AB032953) (SEQ ID NO:71), (Table 3S).

5      **Table 3S. BLASTP of FCTR3b, c, d, e, and f against *Homo sapiens* KIAA1127 protein (SEQ ID NO:71)**

>GI|6329763|DBJ|BAA86441.1| (AB032953) KIAA1127 PROTEIN [HOMO SAPIENS]  
LENGTH = 1737

10      SCORE = 3295 BITS (8545), EXPECT = 0.0  
IDENTITIES = 1695/1737 (97%), POSITIVES = 1695/1737 (97%)

15      QUERY: 997    TFFSAAPGQNPIVPETQVLHEEEIELPGSNVKLRYLSSRTAGYKSLKITMTQSTVPLNLI 1056  
                 |||  
                 SBJCT: 1    TFFSAAPGQNPIVPETQVLHEEEIELPGSNVKLRYLSSRTAGYKSLKITMTQSTVPLNLI 60

20      QUERY: 1057   RVHLMVAVEGHLFQKSFQASPNLASTFIWDKTDAYGQRVYGLSDAVSVGFYETCPSLI 1116  
                 |||  
                 SBJCT: 61    RVHLMVAVEGHLFQKSFQASPNLAYTFIWDKTDAYGQRVYGLSDAVSVGFYETCPSLI 120

25      QUERY: 1117   LWEKRTALLQGFELDPNLSGGWSLDKHHILNVKSGILHKGTGENQFLTQQPAITSIMGN 1176  
                 |||  
                 SBJCT: 121   LWEKRTALLQGFELDPNLSGGWSLDKHHILNVKSGILHKGTGENQFLTQQPAITSIMGN 180

30      QUERY: 1177   GRRRSISCPSCNGLAEGNKLLAPVALAVGIDGSLYVGDFNYIRRIFFSRNVTSTILELRNK 1236  
                 |||  
                 SBJCT: 181   GRRRSISCPSCNGLAEGNKLLAPVALAVGIDGSLYVGDFNYIRRIFFSRNVTSTILELRNK 240

35      QUERY: 1237   EFKHSNNPAHKYYLAVDPVSGSLYVSDTNSRRIYRVKSLSGTKDLAGNSEVVAGTGEQCL 1296  
                 |||  
                 SBJCT: 241   EFKHSNNPAHKYYLAVDPVSGSLYVSDTNSRRIYRVKSLSGTKDLAGNSEVVAGTGEQCL 300

40      QUERY: 1297   PFDEARCGDGGKAIDATLMSPRGIAVDKNGLMYFVDATMIRKVDQNGIISTLLGSNDLTA 1356  
                 |||  
                 SBJCT: 301   PFDEARCGDGGKAIDATLMSPRGIAVDKNGLMYFVDATMIRKVDQNGIISTLLGSNDLTA 360

45      QUERY: 1357   VRPLSCDSSMDVAQVRLEWPTDLAVNPMDNSLYVLENNVILRITENHQVSIIAGRPMHCQ 1416  
                 |||  
                 SBJCT: 361   VRPLSCDSSMDVAQVRLEWPTDLAVNPMDNSLYVLENNVILRITENHQVSIIAGRPMHCQ 420

50      QUERY: 1417   VPGIDYSLSKXXXXXXXXXXXXXXXXXXTGVLYITETDEKKINRLRQVTTNGEICLLAGAA 1476  
                 |||  
                 SBJCT: 421   VPGIDYSLSKLAIHSALESASAIASHTGVLYITETDEKKINRLRQVTTNGEICLLAGAA 480

55      QUERY: 1477   SXXXXXXXXXXXXXSGDDAYATDAILNSPSSLAVAPDGTIYIADLGNIRIRAVSKNKPVL 1536  
                 |  
                 SBJCT: 481   SDCDCCKNDVNCNCYSGDDAYATDAILNSPSSLAVAPDGTIYIADLGNIRIRAVSKNKPVL 540

60      QUERY: 1537   NAFNQYEAASPGEQELYVFNADGIHQYTVSLVTGEYLYNFTYSTDNDVTELIDNNGNSLK 1596  
                 |||  
                 SBJCT: 541   NAFNQYEAASPGEQELYVFNADGIHQYTVSLVTGEYLYNFTYSTDNDVTELIDNNGNSLK 600

65      QUERY: 1597   IRRDSSGMPRHLLMPDNQIITLTVGTNGGLKVSTQNLELGLMTYDGNTGLLATKSDETG 1656  
                 |||  
                 SBJCT: 601   IRRDSSGMPRHLLMPDNQIITLTVGTNGGLKVSTQNLELGLMTYDGNTGLLATKSDETG 660

70      QUERY: 1657   WTTYDYDHEGRLTNVTRPTGVVTSLHREMEKSITIDIENSNRDDVTVITNLSSVEASY 1716  
                 |||  
                 SBJCT: 661   WTTYDYDHEGRLTNVTRPTGVVTSLHREMEKSITIDIENSNRDDVTVITNLSSVEASY 720

75      QUERY: 1717   TVVQDQVRNSYQLCNGTLRVMYANGMGISFHSSEPHVLAGTITPTIGRCNISLPMENGLN 1776  
                 |||  
                 SBJCT: 721   TVVQDQVRNSYQLCNGTLRVMYANGMGISFHSSEPHVLAGTITPTIGRCNISLPMENGLN 780

5  
 QUERY: 1777 SIEWRLRKEQIKGKVTIFGRKLRVHGRNLLSIDYDRNIRTEKIYDDHRKFTLRRIYDQVG 1836  
 SBJCT: 781 SIEWRLRKEQIKGKVTIFGRKLRVHGRNLLSIDYDRNIRTEKIYDDHRKFTLRRIYDQVG 840  
 10  
 QUERY: 1837 RPFLWLPSSGLAAVNVSYFFNGRLAGLQRGAMSERTDIDKQGRIVSRMFADGKVWSYSYL 1896  
 SBJCT: 841 RPFLWLPSSGLAAVNVSYFFNGRLAGLQRGAMSERTDIDKQGRIVSRMFADGKVWSYSYL 900  
 15  
 QUERY: 1897 DKSMVLLQLSQSQRYIFEYDSSDRLLAVTMPVARHSMSTHTSIGYIRNIYNPPESNASVI 1956  
 SBJCT: 901 DKSMVLLQLSQSQRYIFEYDSSDRLLAVTMPVARHSMSTHTSIGYIRNIYNPPESNASVI 960  
 20  
 QUERY: 1957 FDYSDDGRILKTSFLGTGRQVFYKYGKLSKLSEIVYDSTAVTFGYDETTGVLKMNVLQSG 2016  
 SBJCT: 961 FDYSDDGRILKTSFLGTGRQVFYKYGKLSKLSEIVYDSTAVTFGYDETTGVLKMNVLQSG 1020  
 25  
 QUERY: 2017 GFSCITIRYRKIGPLVDKQIYRFSEEGMVNARFDYTYHDNSFRIASIKPVISETPLPVDLY 2076  
 SBJCT: 1021 GFSCITIRYRKIGPLVDKQIYRFSEEGMVNARFDYTYHDNSFRIASIKPVISETPLPVDLY 1080  
 30  
 QUERY: 2077 RYDEISGKVEHFGKFGVIYYDINQIITTAVMTLSKHFDTHGRIKEVQYEMFSLMYWMTV 2136  
 SBJCT: 1081 RYDEISGKVEHFGKFGVIYYDINQIITTAVMTLSKHFDTHGRIKEVQYEMFSLMYWMTV 1140  
 35  
 QUERY: 2137 QYDSMGRVIKRELKLGPIYANTTKYTYDYDGDGQLQSVAVNDRPTWRYSYDXXXXXXXXXX 2196  
 SBJCT: 1141 QYDSMGRVIKRELKLGPIYANTTKYTYDYDGDGQLQSVAVNDRPTWRYSYDLNGLHLLNP 1200  
 40  
 QUERY: 2197 XXSVRLMPLRYDLRDRITRLGDVQYKIDDDGYLCQRGSDIFEYNSKGLLTRAYNKASGWS 2256  
 SBJCT: 1201 GNSVRLMPLRYDLRDRITRLGDVQYKIDDDGYLCQRGSDIFEYNSKGLLTRAYNKASGWS 1260  
 45  
 QUERY: 2257 VQYRYDGVGRRASYKTNLGHHLQYFYSDLHNPTRITHVYNHSNSEITSLYYDLQGHLEFAM 2316  
 SBJCT: 1261 VQYRYDGVGRRASYKTNLGHHLQYFYSDLHNPTRITHVYNHSNSEITSLYYDLQGHLEFAM 1320  
 50  
 QUERY: 2317 ESSSGEEYYVASDNTGTPLAVFSINGLMIKQLQYTAYGEIYYDSNPDFQMVIGFHGGLYD 2376  
 SBJCT: 1321 ESSSGEEYYVASDNTGTPLAVFSINGLMIKQLQYTAYGEIYYDSNPDFQMVIGFHGGLYD 1380  
 55  
 QUERY: 2377 PLTKLVHFTQRDYDVLAGRWTSPDYTMWKNVGKEPAPFNLYMFKSNNPLSSELDLKNYVT 2436  
 SBJCT: 1381 PLTKLVHFTQRDYDVLAGRWTSPDYTMWKNVGKEPAPFNLYMFKSNNPLSSELDLKNYVT 1440  
 60  
 QUERY: 2437 DVKSWLVMFGFQLSNIIPGFPRAKMYFVPPPYELSESQASENGQLITGVQQTTERHNQAF 2496  
 SBJCT: 1441 DVKSWLVMFGFQLSNIIPGFPRAKMYFVPPPYELSESQASENGQLITGVQQTTERHNQAF 1500  
 65  
 QUERY: 2497 MALEGQVITKKLHASIREKAGHWFATTTPIIGKGIMFAIKEGRVTTGVSSIASEDSRKVA 2556  
 SBJCT: 1501 MALEGQVITKKLHASIREKAGHWFATTTPIIGKGIMFAIKEGRVTTGVSSIASEDSRKVA 1560  
 QUERY: 2557 SVLNNAYYLDKMHSIEGKDTYFVKIGSADGDLVTLGTTIGRKVLESGVNVTVSQPTLL 2616  
 SBJCT: 1561 SVLNNAYYLDKMHSIEGKDTYFVKIGSADGDLVTLGTTIGRKVLESGVNVTVSQPTLL 1620  
 QUERY: 2617 VNGRTRRETNIIEFYSTLLLSIRYGLTPDTLDEEKARVLDQARQALGTAWAKEQQKARD 2676  
 SBJCT: 1621 VNGRTRRETNIIEFYSTLLLSIRYGLTPDTLDEEKARVLDQARQALGTAWAKEQQKARD 1680  
 QUERY: 2677 GREGSRLWTEGEKQQLLSTGRVQGYEGYYVLPVEQYPELADSSSNIQFLRQNEGMGR 2733  
 SBJCT: 1681 GREGSRLWTEGEKQQLLSTGRVQGYEGYYVLPVEQYPELADSSSNIQFLRQNEGMGR 1737

The amino acid sequences of the FCTR3bcde and f proteins were also found to have 2528 of 2774 amino acid residues (91%) identical to, and 2557 of 2774 residues (92%)

positive with, the 2765 amino acid residue protein neurestin alpha [*Rattus norvegicus*]  
(GenBank Acc:AF086607) (SEQ ID NO:72), shown in Table 3T.

**Table 3T. BLASTP of FCTR3bcd and f against *Rattus norvegicus* Neurestin alpha (SEQ ID NO:72)**

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5  >GI|9910320|REF|NP_064473.1| NEURESTIN ALPHA [RATTUS NORVEGICUS]
   GI|5712201|GB|AAD47383.1|AF086607.1 (AF086607) NEURESTIN ALPHA [RATTUS NORVEGICUS]
   LENGTH = 2765

10  SCORE = 4988 BITS (12938), EXPECT = 0.0
   IDENTITIES = 2528/2774 (91%), POSITIVES = 2557/2774 (92%), GAPS = 50/2774 (1%)

15  QUERY: 1 MDVKDRRHRSLTRGRCGKECRYTSSSLDSEDCRVPTQKSYSSSETLKAYDHDSRMHYGNR 60
   SBJCT: 1 MDVKDRRHRSLTRGRCGKECRYTSSSLDSEDCRVPTQKSYSSSETLKAYDHDSRMHYGNR 60

20  QUERY: 61 VTDLIHRESDEFPRQGTNFTLAELGICEPSPHRSGYCSDMGILHQGYSLSTGSDADSDTE 120
   SBJCT: 61 VTDLVHRESDEFPSRQGANFTLAELGICEPSPHRSGYCSDMGILHQGYSLSTGSDADSDTE 120

25  QUERY: 121 GGMSPEHAIRLWGRGIKSRSSGLSSRENSALTLTXXXXXXXXXXXXXXXXXGRXXXXXXXXXXXX 180
   SBJCT: 121 GGMSPEHAIRLWGRGIKSRSSGLSSRENSALTLTDSNENKSDDDNGRPIPTSSSSLL 180

30  QUERY: 181 XXXXXXXXHNPPPVSCQMPLLDSNTSHQIMDTNPDEEFSPNSYLLRACXXXXXXXXXXXX 240
   SBJCT: 181 PSAQLPSSHNPFPVSCQMPLLDSNTSHQIMDTNPDEEFSPNSYLLRACSGPQQASSSGPP 240

35  QUERY: 241 NHHSQXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXQIHAPAPAPNDLATTPEVQ 300
   SBJCT: 241 NHHSQSTLRPPLPPPHNHTLSHHSSANSNLNRSLTNRRSQIHAPAPAPNDLATTPEVQ 300

40  QUERY: 301 LQDSWVLNSNVPLETRHFLEKXXXXXXXXXXXXXXXXXYPLTSGTVYTPPPRLLPRNTFSRK 360
   SBJCT: 301 LQDSWVLNSNVPLETRHFLEKTSSGSTPLESSSSPGYPLTSGTVYTPPPRLLPRNTFSRK 360

45  QUERY: 361 AFKLKKPSKYCSWKXXXXXXXXXXXXXXXXXXXXFYI----- 395
   SBJCT: 361 AFKLKKPSKYCSWKCAALSAIAAALLAILLAYFIAMHLLGLNWQLQPADGHTFNNGVRT 420

50  QUERY: 396 -----VPWSLKNSSIDSGEAEVGRRVTQEVPPGVFWRSQIHISQPFQFLK 439
   SBJCT: 421 GLPGNDDVATVPSPGGKVPWSLKNSSIDSGEAEVGRRVTQEVPPGVFWRSQIHISQPFQFLK 480

55  QUERY: 440 FNISLGKDALFGVYIRRLPPSHAQYDEMERLDGKEKWSVVEsprerrsiQTLVQNEAVF 499
   SBJCT: 481 FNISLGKDALFGVYIRRLPPSHAQYDEMERLDGKEKWSVVEsprerrsiQTLVQNEAVF 540

60  QUERY: 500 VQYLDVGLWHLAFYNDGKDKEMVSFNTVVLDVQDCPRNCHGNGECVSGVCHCFPGFLGA 559
   SBJCT: 541 VQYLDVGLWHLAFYNDGKDKEMVSFNTVVLDVQDCPRNCHGNGECVSGVCHCFPGFLGA 600

65  QUERY: 560 DCAKAACPVLCSGNGQYSKGTCCQYSGWKGAECDVPMNQCIDPSCGGHGSCIDGNCVCSA 619
   SBJCT: 601 DCAKAACPVLCSGNGQYSKGTCCQYSGWKGAECDVPMNQCIDPSCGGHGSCIDGNCVCAA 660

70  QUERY: 620 GYKGEHCEEVDCLDPTCSSHGVCVNGECLCSPGWGGLNCELARVQCPDQCSGHGTYLPDT 679
   SBJCT: 661 GYKGEHCEEVDCLDPTCSSHGVCVNGECLCSPGWGGLNCELARVQCPDQCSGHGTYLPDS 720

75  QUERY: 680 GLCSCDPNWMGPDCSVEVCSVDCGTHGVCIGGACRCEEGWTGAACDQRVCHPRCIEHGTC 739
   SBJCT: 721 GLCNCDPNWMGPDCSVEVCSVDCGTHGVCIGGACRCEEGWTGAACDQRVCHPRCIEHGTC 780
   *****

80  QUERY: 740 KDGKCECREGWNGEHCTIGRQTAGTETDGCPLCNGNGRCTLGQNSWQCVCQTGWRGPGC 799
   SBJCT: 740 KDGKCECREGWNGEHCTIGRQTAGTETDGCPLCNGNGRCTLGQNSWQCVCQTGWRGPGC 799

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85

QUERY: 1820 YDDHRKFTLRRIYDQVGRPFLWLPSSGLAAVNVSYFFNGRLAGLQRGAMSERTDIDKQGR 1879  
 |||||  
 SBJCT: 1852 YDDHRKFTLRRIYDQVGRPFLWLPSSGLAAVNVSYFFNGRLAGLQRGAMSERTDIDKQGR 1911  
  
 5 QUERY: 1880 IVSRMFADGKVWSYSYLDKSMVLLQLSQQRQYIFEYDSSDRLLAVTMPVARHSMSTHTSI 1939  
 |||||  
 SBJCT: 1912 IVSRMFADGKVWSYSYLDKSMVLLQLSQQRQYIFEYDSSDRLLAVTMPVARHSMSTHTSI 1971  
  
 10 QUERY: 1940 GYIRNIYNPPESNASVIFDYSDGRILKTSFLGTGRQVFYKYGKLSKLSEIVYDSTAVTF 1999  
 |||||  
 SBJCT: 1972 GYIRNIYNPPESNASVIFDYSDGRILKTSFLGTGRQVFYKYGKLSKLSEIVYDSTAVTF 2031  
  
 15 QUERY: 2000 GYDETTGVLKMNVLQSGGFSCITIRYRKIGPLVDKQIYRFSEEGMVNARFDYTYHDNSFRI 2059  
 |||||+|||  
 SBJCT: 2032 GYDETTGVLKMNVLQSGGFSCITIRYRKIGPLVDKQIYRFSEEGMINARFDYTYHDNSFRI 2091  
  
 20 QUERY: 2060 ASIKPVISETPLPVDLYRYDEISGKVEHFGKFGVIYYDINQIITTAVMTLSKHFDTHGRI 2119  
 |||||  
 SBJCT: 2092 ASIKPVISETPLPVDLYRYDEISGKVEHFGKFGVIYYDINQIITTAVMTLSKHFDTHGRI 2151  
  
 25 QUERY: 2120 KEVQYEMFRSLMYWMTVQYDSMGRVIKRELKLGPIYANTTKYTYDYDGDGQLQSVAVNDRP 2179  
 |||||  
 SBJCT: 2152 KEVQYEMFRSLMYWMTVQYDSMGRVIKRELKLGPIYANTTKYTYDYDGDGQLQSVAVNDRP 2211  
  
 30 QUERY: 2180 TWRYSDYXXXXXXXXXXXXSVRLMPLRYDLRDRITRLGDVQYKIDDDGYLCQRGSDIFEY 2239  
 |||||  
 SBJCT: 2212 TWRYSDYDLNGNLHLNPGNSARLMPLRYDLRDRITRLGDVQYKIDDDGYLCQRGSDIFEY 2271  
  
 35 QUERY: 2240 NSKGLLTRAYNKASGWSVQYRYDGVRRASYKTNLGHHLQYFYSDLHNPTRITHVYNHSN 2299  
 |||||+|||  
 SBJCT: 2272 NSKGLLTRAYNKASGWSVQYRYDGVRRASYKTNLGHHLQYFYSDLHNPTRITHVYNHSN 2331  
  
 40 QUERY: 2300 SEITSLYYDLQGHLFAMESSSGEEYYVASDNTGTPLAVFSINGLMIKQLQYTAYGEIYYD 2359  
 |||||  
 SBJCT: 2332 SEITSLYYDLQGHLFAMESSSGEEYYVASDNTGTPLAVFSINGLMIKQLQYTAYGEIYYD 2391  
  
 45 QUERY: 2360 SNPDMQMVIGFHGGLYDPLTKLVHFTQRDYDVLAGRWTSPDYTMWKNVGKEPAPFNLYMF 2419  
 |||||+|||  
 SBJCT: 2392 SNPDMQMVIGFHGGLYDPLTKLVHFTQRDYDVLAGRWTSPDYTMWKNVGKEPAPFNLYMF 2451  
  
 50 QUERY: 2420 KSNPLSSELDLKNYVTDVKSVMFGFQLSNIIPGFPRAKMYFVPPPYELSESQASENG 2479  
 |+|||+|||  
 SBJCT: 2452 KSNPLSSELDLKNYVTDVKSVMFGFQLSNIIPGFPRAKMYFVPPPYELSESQASENG 2511  
  
 55 QUERY: 2480 QLITGVQQTTERHNQAFMALEGQVITKKLHASIREKAGHWFATTTPIIGKIMFAIKEGR 2539  
 |||||+|||+|||  
 SBJCT: 2512 QLITGVQQTTERHNQAFMALEGQVITKKLHASIREKAGHWFATTTPIIGKIMFAIKEGR 2571  
  
 60 QUERY: 2540 VTTGVSSIASEDSRKVASVLNNAYYLDKMHYSIEGKDTYFVKIGSADGDLVTLGTTIGR 2599  
 |||||+|||  
 SBJCT: 2572 VTTGVSSIASEDSRKVASVLNNAYYLDKMHYSIEGKDTYFVKIGSADGDLVTLGTTIGR 2631  
  
 65 QUERY: 2600 KVLESGVNVTVSQPTLLVNGRTRRFTNIEFYSTLLLSIRYGLTPDTLDEEKARVLDQAR 2659  
 |||||  
 SBJCT: 2632 KVLESGVNVTVSQPTLLVNGRTRRFTNIEFYSTLLLSIRYGLTPDTLDEEKARVLDQAR 2691  
  
 QUERY: 2660 QRALGTAWAKEQOKARDGREGSRLWTEGEKQQLSTGRVQGYEGYYVLPVEQYPELADSS 2719  
 |||||  
 SBJCT: 2692 QRALGTAWAKEQOKARDGREGSRLWTEGEKQQLSTGRVQGYEGYYVLPVEQYPELADSS 2751  
  
 60 QUERY: 2720 SNIQFLRQNEGKR 2733  
 |||||  
 SBJCT: 2752 SNIQFLRQNEGKR 2765  
  
 65 \* = FCTR3F DOES NOT CONTAIN THESE AMINO ACIDS

The amino acid sequences of the FCTR3bcde and f proteins were also found to have 2536 of 2774 amino acid residues (91%) identical to, and 2558 of 2774 residues (91%) positive with, the 2764 amino acid residue protein Odd Oz/ten-m homolog 2 (*Drosophila*) (GenBank Acc:NP\_035986.2) (SEQ ID NO:65), shown in Table 3U.

5      **Table 3U. BLASTP of FCTR3bcde and f against Odd Oz/ten-m homolog 2 (SEQ ID NO:65)**

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>GI|7657415|REF|NP_035986.2| ODD OZ/TEN-M HOMOLOG 2 (DROSOPHILA); ODD OZ/TEN-M
HOMOLOG 3
      (DROSOPHILA) [MUS MUSCULUS]
10      GI|4760778|DBJ|BAA77397.1| (AB025411) TEN-M2 [MUS MUSCULUS]
      LENGTH = 2764

      SCORE = 4996 BITS (12961), EXPECT = 0.0
      IDENTITIES = 2536/2774 (91%), POSITIVES = 2558/2774 (91%), GAPS = 51/2774 (1%)
15      QUERY: 1      MDVKDRRHRSLTRGRCGKECRYTSSSLDSEDCRVPTQKSYSSSETLKAYDHDSRMHYGNR 60
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
      SBJCT: 1      MDVKDRRHRSLTRGRCGKECRYTSSSLDSEDCRVPTQKSYSSSETLKAYDHDSRMHYGNR 60

20      QUERY: 61      VTDLIHRESDEFPRQGTNFTLAE LGICEPSPHRSGYCSDMGILHQGYSLSTGSDADSDTE 120
      ||||+||||||| ||||||||||||||||||||||||||||||||||||||||||||
      SBJCT: 61      VTDLVHRESDEFPSRQGTNFTLAE LGICEPSPHRSGYCSDMGILHQGYSLSTGSDADSDTE 120

25      QUERY: 121      GGMSPEHAIRLWGRGIKSRSSGLSSRENSALTLTXXXXXXXXXXXXXXXXXGRXXXXXXXXXXXX 180
      |||||||||||||||||||||||||||||||||||||||| ||
      SBJCT: 121      GGMSPEHAIRLWGRGIKSRSSGLSSRENSALTLTSDNENKSDDDNGRPIPTSSSSLL 180

30      QUERY: 181      XXXXXXXXHNPPPVSCQMPLLDSNTSHQIMDTNPDEEFSPNSYLLRACXXXXXXXXXXXXX 240
      ||||||||||||||||||||||||||||||||||||||||
      SBJCT: 181      PSAQLPSSHNPFPVSCQMPLLDSNTSHQIMDTNPDEEFSPNSYLLRACSGPQQASSSGPP 240

35      QUERY: 241      NHHSQXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXQIHAPAPAPNDLATTPEVSVQ 300
      ||||| ||||||||||||||||||||||||||||||
      SBJCT: 241      NHHSQSTLRPPLPPPHNHTLSHHSSANSLSNRSLTNRRSQIHAPAPAPNDLATTPEVSVQ 300

40      QUERY: 301      LQDSWVLNSNVPLETRHFLFKXXXXXXXXXXXXXXXXXYP LTSGTVYTPPPRLLPRNTFSRK 360
      ||||||||||||||||||||| |||||||||||||||||||||
      SBJCT: 301      LQDSWVLNSNVPLETRHFLFKTSSGSTPLESSSPGYPLTSGTVYTPPPRLLPRNTFSRK 360

45      QUERY: 361      AFKLLKPSKYCSWKXXXXXXXXXXXXXXXXXXXXXYFI----- 395
      |||||||||||||||| |||
      SBJCT: 361      AFKLLKPSKYCSWKCAALSAIAAALLLAILLAYFIAMHLLGLNWQLQPADGHTFNNGVRT 420

50      QUERY: 396      -----VPWSLKNSSIDSGEAEVGRRVTQEVPPGVFWRSQIHISQPQFLK 439
      ||||||||||||||||||||||||||||||||||||||||
      SBJCT: 421      GLPGNDDVATVPSSGKVPWSLKNSSIDSGEAEVGRRVTQEVPPGVFWRSQIHISQPQFLK 480

55      QUERY: 440      FNISLGKDALFGVYIRRLPSSHAQYDFMERLDGKEKWSVVE SPRERRSIQTLVQNEAVF 499
      ||||||||||||||||||||||||||||||||||||||||
      SBJCT: 481      FNISLGKDALFGVYIRRLPSSHAQYDFMERLDGKEKWSVVE SPRERRSIQTLVQNEAVF 540

60      QUERY: 500      VQYLDVGLWHLAFYNDGKDKEMVSFNTVVLDSDVQDCPRNCHGNGECVSGVCHCFPGFLGA 559
      ||||||||||||||||||||||||||||||||||||||||+|||||||
      SBJCT: 541      VQYLDVGLWHLAFYNDGKDKEMVSFNTVVLDSDVQDCPRNCHGNGECVSGVCHCFPGFLGA 600

65      QUERY: 560      DCAKAACPVLCSGNGQYSKGTCQCYSGWKGAECDVPMNQCIDPSCGGHGS CIDGNCVCSA 619
      ||||||||||||||||||||||||||||||||||||||||+|
      SBJCT: 601      DCAKAACPVLCSGNGQYSKGTCQCYSGWKGAECDVPMNQCIDPSCGGHGS CIDGNCVCAA 660

70      QUERY: 620      GYKGEHCEEVDCLDPTCSSHGVCVNGECLCSPGWGGLNCELARVQCPDQCSGHGTYLPDT 679
      ||||||||||||||||||||||||||||||||||||||||+
      SBJCT: 661      GYKGEHCEEVDCLDPTCSSHGVCVNGECLCSPGWGGLNCELARVQCPDQCSGHGTYLPDS 720

```

QUERY: 680 GLCSCDPNWMGPDCSVEVCSVDCGTHGVCIGGACRCEEGWTGAACDQRVCHPRCIEHGTC 739  
|||||  
SBJCT: 721 GLCSCDPNWMGPDCSV-VCSVDCGTHGVCIGGACRCEEGWTGAACDQRVCHPRCIEHGTC 779  
\*\*\*\*\*

5 QUERY: 740 KDGKCECREGWNGEHCTIGRQTAGTETDGCPLCNGNGRCTLGQNSWQCVCQTGWRGPGC 799  
|||||  
SBJCT: 780 KDGKCECREGWNGEHCTI-----DGCPLCNGNGRCTLGQNSWQCVCQTGWRGPGC 830

10 QUERY: 800 NVAMETSCADNKDNEGDGLVDCLDPDCCLQSACQNSLLCRGSRDPLDIIQQGQTDWPAVK 859  
|||||  
SBJCT: 831 NVAMETSCADNKDNEGDGLVDCLDPDCCLQSACQNSLLCRGSRDPLDIIQQGQTDWPAVK 890

15 QUERY: 860 SFYDRIKLLAGKDSSTHIIPGENPFNSSLSLIRGQVVTTDGTPLVGVNVSEFVKYPKYGYT 919  
|||||+|||||  
SBJCT: 891 SFYDRIKLLAGKDSSTHIIPGDNPFNSSLSLIRGQVVTTDGTPLVGVNVSEFVKYPKYGYT 950

20 QUERY: 920 ITRQDGTFDLIANGGASLTLLHFERAPFMSQERTVWLPWNSFYAMDTLVMKTEENSIPSCD 979  
|||||++|||||  
SBJCT: 951 ITRQDGTFDLIANGGASLTLLHFERAPFMSQERTVWLPWNSFYAMDTLVMKTEENSIPSCD 1010

25 QUERY: 980 LSGFVRPDPIIISSPLSTFFSAAFGQNPPIVETQVLHHEIELPGSNVKLRYLSSRTAGYK 1039  
|||||+|||||+|||||  
SBJCT: 1011 LSGFVRPDPIIISSPLSTFFSASPASNPIVETQVLHHEIELPGTNVKLRYLSSRTAGYK 1070

30 QUERY: 1040 SLLKITMTQSTVPLNLIRVHLMVAVEGHLFQKSFQASPNLASTFIWDKTDAYGQRVYGLS 1099  
|||||  
SBJCT: 1071 SLLKITMTQSTVPLNLIRVHLMVAVEGHLFQKSFQASPNLAYTFIWDKTDAYGQRVYGLS 1130

35 QUERY: 1100 DAVVSVGFYETCPSLILWEKRTALLOGFELDPSNLGGWSLDKHHILNVKSGILHKGTE 1159  
|||||  
SBJCT: 1131 DAVVSVGFYETCPSLILWEKRTALLOGFELDPSNLGGWSLDKHHILNVKSGILHKGTE 1190

40 QUERY: 1160 NQFLTQQPAIITSIMGNRRRSISCPSCNGLAEGNKLLAPVALAVGIDGSLYVGDFNYIR 1219  
|||||+|||||  
SBJCT: 1191 NQFLTQQPAIITSIMGNRRRSISCPSCNGLAEGNKLLAPVALAVGIDGSLYVGDFNYIR 1250

45 QUERY: 1220 RIFPSRNVTSILELRNKEFKHSNNPAHKYYLAVDPVSGSLYVSDTNSRRIYRVKSLSGTK 1279  
|||||+|||||+|||||  
SBJCT: 1251 RIFPSRNVTSILELRNKEFKHSNSPGHKYYLAVDPVTGSLYVSDTNSRRIYRVKSLSGAK 1310

50 QUERY: 1280 DLAGNSEVVAGTGEQCLPFDEARCGDGGKAIDATLMSPRGIAVDKNGLMYFVDATMIRKV 1339  
|||||+|||||  
SBJCT: 1311 DLAGNSEVVAGTGEQCLPFDEARCGDGGKAIDATLMSPRGIAVDKNGLMYFVDATMIRKV 1370

55 QUERY: 1340 DQNGIISTLLGSNDLTAVRPLSCDSSMDVAQVRLEWPTDLAVNPMDNSLYVLENNVILRI 1399  
|||||  
SBJCT: 1371 DQNGIISTLLGSNDLTAVRPLSCDSSMDVAQVRLEWPTDLAVNPMDNSLYVLENNVILRI 1430

60 QUERY: 1400 TENHQVSIIAGRPMHCQVPGIDYLSKXXXXXXXXXXXXXXXXXSGVLYITETDEKKINR 1459  
|||||  
SBJCT: 1431 TENHQVSIIAGRPMHCQVPGIDYLSKSLAIHSALESASAIASHTGVLYITETDEKKINR 1490

65 QUERY: 1460 LRQVTTNGEICLLAGAASXXXXXXXXXXXXXSGDDAYATDAILNSPSSLAVAPDGTIYIA 1519  
|||||  
SBJCT: 1491 LRQVTTNGEICLLAGAASDCDCKNDVNCICYSGDDAYATDAILNSPSSLAVAPDGTIYIA 1550

70 QUERY: 1520 DLGNIRIRAVSKNKPVLNAFNQYEAASPGEQELYVFENADGIHQYTVSLVTGEYLYNFTYS 1579  
|||||  
SBJCT: 1551 DLGNIRIRAVSKNKPVLNAFNQYEAASPGEQELYVFENADGIHQYTVSLVTGEYLYNFTYS 1610

75 QUERY: 1580 TDNDVTELDIDNNGNSLKIIRDSSGMPRHLLMPDNQIITLTVTGNGGLKVVSTQNLGLM 1639  
|||||  
SBJCT: 1611 ADNDVTELDIDNNGNSLKIIRDSSGMPRHLLMPDNQIITLTVTGNGGLKAVSTQNLGLM 1670

80 QUERY: 1640 TYDGNTGLLATKSDETGWTTFYDYDHEGRLTNVTRPTGVVTSLHREMEKSITIDIENSNR 1699  
|||||  
SBJCT: 1671 TYDGNTGLLATKSDETGWTTFYDYDHEGRLTNVTRPTGVVTSLHREMEKSITIDIENSNR 1730

85 QUERY: 1700 DDDVTVITNLSSVEASYTVVQDQVRNSYQLCNGTLRVMYANGMGISFHSEPHVLAGTIT 1759  
|||||+|||||

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\* = FCTR3F DOES NOT CONTAIN THESE AMINO ACIDS

FCTR3 is related to rat neurestin, a gene implicated in neuronal development (Otaki JM, Firestein S Dev Biol 1999 Aug 1;212(1):165-81) Neurestin shows homology to human gamma-heregulin, a *Drosophila* receptor-type pair-rule gene product, Odd Oz (Odz) / Ten(m), and Ten(a). Neurestin has putative roles in synapse formation and brain morphogenesis. A mouse neurestin homolog, DOC4, has independently been isolated from the NIH-3T3 fibroblasts. DOC4 is also known as tenascin M (TNM), a *Drosophila* pair-rule gene homolog containing extracellular EGF-like repeats. The significant homology to these molecules and in particular,  $\gamma$ -heregulin, have important implications regarding the potential contribution of FCTR3 to disease progression. Heregulin is the ligand for HER-2/ErbB2/NEU, a proto-oncogene receptor tyrosine kinase implicated in breast and prostate cancer progression that was originally identified in rat neuro/glioblastoma cell lines. Extopic expression of HER-2/ErbB2/NEU in MDA-MB-435 breast adenocarcinoma cells confers chemoresistance to Taxol-induced apoptosis relative to vector transfected control cells (Yu et al. Overexpression of ErbB2 blocks Taxol-induced apoptosis by up-regulation of p21Cip1, which inhibits p34Cdc2 kinase. Molec. Cell 2: 581-591, 1998).

#### **FCTR3 related tenascins and cancer biology**

As mentioned, FCTR3 also has significant homology to DOC4, (AKA tenascin M), a *Drosophila* pair-rule gene homolog containing extracellular EGF-like repeats. The tenascins are a growing family of extracellular matrix proteins that play prominent roles in tissue interactions critical to embryogenesis. Overexpression of tenascins has been described in multiple human solid malignancies.

The role of the tenascin family of related proteins is to regulate epithelial-stromal interactions, participate in fibronectin-dependent cell attachment and interaction. Indeed, tenascin-C (TN) is overexpressed in the stroma of malignant ovarian tumours particularly at the interface between epithelia and stroma leading to suggestions that it may be involved in the process of invasion (Wilson et al (1996) Br J Cancer 74: 999-1004). Tenascin-C is considered a therapeutic target for certain malignant brain tumors (Gladson CL : J Neuropathol Exp Neurol 1999 Oct;58(10):1029-40). Stromal or moderate to strong periductal Tenascin-C expression in DCIS (ductal carcinoma in situ) correlates with tumor cell invasion. (Jahkola et al. Eur J Cancer 1998 Oct;34(11):1687-92. Tenascin-C expression at the invasion border of early breast cancer is a useful predictor of local and distant recurrence. Jahkola T, et al. Br J Cancer. 1998 Dec;78(11):1507-13). Tenascin (TN) is an extracellular matrix protein found in areas of cell migration during development and expressed at high levels in migratory glioma

cells. Treasurywala S, Berens ME *Glia* 1998 Oct;24(2):236-43 Migration arrest in glioma cells is dependent on the alphaV integrin subunit. Phillips GR, Krushel LA, Crossin KL *J Cell Sci* 1998 Apr;111 ( Pt 8):1095-104 Domains of tenascin involved in glioma migration. Finally, tenascin expression in hormone-dependent tissues of breast and endometrium indicate that

5 Tenascin expression reflects malignant progression and is down-regulated by antiprogesterins during terminal differentiation of rat mammary tumors (Vollmer et al. *Cancer Res* 1992 Sep 1;52(17):4642-8 )

#### **Potential role of FCTR3 in oncologic disease progression:**

10 Based on the bioactivity described in the medical literature for related molecules, FCTR3 may play a role in one or more aspects of tumor cell biology that alter the interactions of tumor epithelial cells with stromal components. In consideration, FCTR3 may play a role in the following malignant properties:

Autocrine/paracrine stimulation of tumor cell proliferation

15 Autocrine/paracrine stimulation of tumor cell survival and tumor cell resistance to cytotoxic therapy

Local tissue remodeling, paranechmal and basement membrane invasion and motility of tumor cells thereby contributing to metastasis.

20 Tumor-mediated immunosuppression of T-cell mediated immune effector cells and pathways resulting in tumor escape from immune surveillance.

#### **Therapeutic intervention targeting FCTR3 in oncologic and central nervous system indications:**

25 Predicted disease indications from expression profiling in 41 normal human tissues and 55 human cancer cell lines (see Example 2) include a subset of human gliomas, astrocytomas, mixed glioma/astrocytomas, renal cells carcinoma, breast adenocarcinoma, ovarian cancer, melanomas. Targeting of FCTR3 by human or humanized monoclonal antibodies designed to disrupt predicted interactions of FCTR3 with its cognate ligand may result in significant anti-tumor/anti-metastatic activity and the amelioration of associated symptomatology.

30 Identification of small molecules that specifically/selectively interfere with downstream signaling components engaged by FCTR3/ligand interactions would also be expected to result in significant anti-tumor/anti-metastatic activity and the amelioration of associated symptomatology. Likewise, modified antisense ribonucleotides or antisense gene expression constructs (plasmids, adenovirus, adeno-associated viruses, "naked" DNA approaches)

designed to diminish the expression of FCTR3 transcripts/messenger RNA (mRNA) would be anticipated based on predicted properties of FCTR3 to have anti-tumor impact.

Based on the relatedness to neurestin and heregulins, as well as its high level expression in brain tissue, FCTR3 may also be used for remyelination in order to promote regeneration/repair/remyleination of injured central nervous system cells resulting from ischemia, brain trauma and various neurodegenerative diseases.. This postulate is based on reports indicating that neuregulin, glial growth factor 2, diminishes autoimmune demyelination and enhances remyelination in a chronic relapsing model for multiple sclerosis (Cannella et al. . Proc. Nat. Acad. Sci. 95: 10100-10105, 1998). The expression of the related molecule neurestin can be induced in external tufted cells during regeneration of olfactory sensory neurons.

#### FCTR4

FCTR4 is a plasma membrane protein related to NF-Kappa-B P65delta3 protein. The clone is expressed in fetal liver tissues.

The novel FCTR4 nucleic acid of 609 nucleotides (also referred to as 29692275.0.1) is shown in Table 4A. An ORF begins with an ATG initiation codon at nucleotides 99-101 and ends with a TAA codon at nucleotides 522-524. A putative untranslated region upstream from the initiation codon and downstream from the termination codon is underlined in Table 4A, and the start and stop codons are in bold letters.

**Table 4A. FCTR4 Nucleotide Sequence (SEQ ID NO:14)**

CTGACATACTATATTAGTTGTTTGTTCACCTGTCTCCACTCCAGCTAGAAATATAAGTTCATAGGGCAGAGTTTTTGTTCATGCTATATTTTATAAGCATGAATGAATGCATGAACGAATGGACTGATAACCCACAAGCCAAAGACCTCCATGACCTGCCACTGCCCTCCTTTCATTTTATTCTCACCTCTACCAATACTAAATCACCTAGTTATGTAAATACGATATGCACTTTTCATGGCCCCTTGCTTTGTCATATGCTGTTCCCTTTGCCTGGAATATAAACTCTCAAATACCATCCACATTTTAAATCTTCTCCAGAAAGCTTCCTCTGTCCACCCCCACCCTCCACCCCCATATAGAGTAAGTCAGTCTTTCCTTTGTGCTACATTTGTACCTGTATCTACAGTGGCTCTAATCAAACCTGCACTGTGTCTCTCACTTCCTAGATTGTGAACTCTTTGAGGCTGAAGACTACTTATTCATCTCTTTACCTCCAATGCCTAGGACAGGACCTTCATAAAGCAACTACTCTATAAATGTTGAAACATATGCATGACTATCTGTAAACAGGAATGAAAATATGGCATTTCAGGAAGTCACTACTC

The FCTR4 protein encoded by SEQ ID NO:14 has 141 amino acid residues and is presented using the one-letter code in Table 4B. The Psort profile for FCTR4 predicts that this sequence has no N-terminal signal peptide and is likely to be localized at the plasma membrane with a certainty of 0.6000. The most likely cleavage site for a peptide is between amino acids 39 and 40, *i.e.*, at the dash in the amino acid sequence ACT-CCA, based on the SignalP result. The predicted molecular weight of this protein is 16051.5 Daltons.

**Table 4B. Encoded FCTR4 protein sequence (SEQ ID NO:15).**

MNECMNEWTDPQAKDLHDLPLPSFHFILTSTNTKSPSYVNTICTFMAPCFVICCSLCLEYKLSKYHPHFKIFSRKLPSTPTLPPPYRVSQSLFCATFVPVSTVALIKLHCVSHFLDCELFEAEDYLFISLPPMPRTGPS

The predicted amino acid sequence was searched in the publicly available GenBank database FCTR4 protein showed 30 % identities (22 over 72 amino acids) and 43% homologies (31 over 72 amino acids) with hypothetical 10 kD protein of *Trypanosoma cruzi* (86 aa; ACC:Q99233) shown in Table 4C. The best homologies with a human protein were 54 % identities (114 over 343 amino acids) with NF-Kappa-B P65delta3 protein (71 aa fragment; ACC:Q13313) (SEQ ID NO:77).

**Table 4C. BLASTP of FCTR4 against protein sequences**

BLAST X search results are shown below:

ptnr:SPTREMBL-ACC:Q99233 HYPOTHETICAL 10 KD PROTEIN +3, 68, 0.60, 1, (SEQ ID NO:73)

ptnr:SPTREMBL-ACC:Q16896 GABA RECEPTOR SUBUNIT - AEDES +3, 66, 0.81, 4 (SEQ ID NO:74)

ptnr:SPTREMBL-ACC:O76473 GABA RECEPTOR SUBUNIT - LEPTI... +3, 66, 0.99, 2 (SEQ ID NO:75)

ptnr:TREMBLNEW-ACC:AAD28317 F13J11.13 PROTEIN - Arabid... +3, 62, 0.99, 1 (SEQ ID NO:76)

Based upon homology, FCTR4 proteins and each homologous protein or peptide may share at least some activity.

## FCTR5

FCTR5 is a protein bearing sequence homology to human complement C1R component precursor. The clone is expressed in breast, heart, lung, fetal lung, salivary gland, adrenal gland, spleen, kidney, and fetal kidney.

The novel FCTR5 nucleic acid of 1667 nucleotides (also referred to as 32125243.0.21) is shown in Table 5A. An ORF begins with an ATG initiation codon at nucleotides 34-36 and ends with a TGA codon at nucleotides 1495-1497. A putative untranslated region upstream from the initiation codon and downstream from the termination codon is underlined in Table 5A, and the start and stop codons are in bold letters.

**Table 5A. FCTR5a Nucleotide Sequence (SEQ ID NO:16)**

GTTCTCTCGCAGGTCCAGATGTCCAGTTCAGATGCCTGGACCCAGAGTGTGGGGGAAATATCTCTGGAGAAGCCCTCA  
 CTCCAAAGGCTGTCCAGGCGCAATGTGGTGGCTGCTTCTCTGGGGAGTCCTCCAGGCTTGCCCAACCCGGGGCTCCGTCC  
 TCTTGGCCCAAGAGCTACCCAGCAGCTGACATCCCCGGGTACCCAGAGCCGTATGGCAAAGGCCAAGAGAGCAGCACG  
 GACATCAAGGCTCCAGAGGGCTTTGCTGTGAGGCTCGTCTTCCAGGACTTCGACCTGGAGCCGTCCAGGACTGTGCAGG  
 GGACTCTGTCAATCTCATTCGTCGGTTCGGATCCAAGCCAGTTCTGTGGTCAGCAAGGCTCCCCTCTGGGCAGGCCCC  
 CTGGTCAGAGGGAGTTTGTATCCTCAGGGAGGAGTTTGC GGCTGACCTTCCGCACACAGCCTTCCTCGGAGAACAAGACT

5 GCCCACCTCCACAAGGGCTTCCTGGCCCTCTACCAAACCGTGGCTGTGAACTATAGTCAGCCCATCAGCGAGGCCAGCAG  
 GGGCTCTGAGGCCATCAACGCACCTGGAGACAACCCTGCCAAGGTCCAGAACCCTGCCAGGAGCCCTATTATCAGGCCG  
 CGGCAGCAGGGGCACTCACCTGTGCAACCCAGGGACCTGGAAAGACAGACAGGATGGGGAGGAGGTTCTTCAGTGTATG  
 CCTGTCTGCGGACGGCCAGTCACCCCATTTGCCAGAATCAGACGACCCTCGGTTCTTCCAGAGCCAAGCTGGGCAACTT  
 10 CCCCTGGCAAGCCTTCACCAGTATCCACGGCCGTGGGGGCGGGGCCCTGCTGGGGGACAGATGGATCCTCACTGCTGCCC  
 ACACCATCTACCCCAAGGACAGTGTCTCTCAGGAAGAACCAGAGTGTGAATGTGTTCTTGGGCCACACAGCCATAGAT  
 GAGATGCTGAAACTGGGGAACCACCTGTCCACCGTGTCTGTTGTGCACCCCGACTACCGTCAGAATGAGTCCCATAACTT  
 TAGCGGGGACATCGCCCTCCTGGAGCTGCAGCACAGCATCCCCCTGGGCCCCAACGTCTCCCGGTCTGTCTGCCCGATA  
 ATGAGACCCTCTACCGCAGCGGCTTGTGGGCTACGTGAGTGGGTTTGGCATGGAGATGGGCTGGCTAACTACTGAGCTG  
 15 AAGTACTCGAGGCTGCCTGTAGCTCCAGGGAGGCCTGCAACGCCTGGCTCCAAAAGAGACAGAGACCCGAGGTGTTTTC  
 TGACAATATGTTCTGTGTTGGGGATGAGACGCAAGGCACAGTGTCTGCCAGGGGACAGTGGCAGCCTCTATGTGGTAT  
 GGGACAATCATGCCCATCACTGGGTGGCCACGGGCATTGTGTCTGGGGCATAGGGTGTGGCGAAGGGTATGACTTCTAC  
 ACCAAGGTGCTCAGCTATGTGGACTGGATCAAGGGAGTGATGAATGGCAAGAATGACCCCTGGGGGCTTGAACAGGGACT  
 GACCAGCACAGTGGAGGCCCCAGGCAACAGAGGGCCTGGAGTGAAGTGAACACTGGGGTAGGGGTGGGGGTTTCTCT  
 20 TGCAGTGGCTTGGTGCAACAGTGATGTGAATAGGATTCCCTTTTTTTTTTTTTTTTTTAAAAAAA

The FCTR5 protein encoded by SEQ ID NO:16 has 487 amino acid residues, and is  
 presented using the one-letter code in Table 5B. FCTR5 was searched against other databases  
 using SignalPep and PSort search protocols. The FCTR5 protein is most likely microbody  
 20 (peroxisome) (Certainty=0.6406) and seems to have no N-terminal signal sequence. The  
 predicted molecular weight of FCTR5 protein is 53511.9 daltons.

**Table 5B. Encoded FCTR5a protein sequence (SEQ ID NO:17).**

25 MPGPRVWGKYLWRSPLSKGCPGAMWWLLWGLVQACPTRGSVLLAQELPQQLTSPGYPEPYGKGQESSTDIKAPEGFAVRLVFQ  
 DFDLEPSQDCAGDSVTISFVGSQPSQFCGQGSPLGRPPGQREFVSSGRSLRLTFRTPQPSSENKTAHLHKGFALYQTVAVNYS  
 QPISEASRGSEAINAPGDNPAKVQNHQEPYQAAAAGALTCATPGTWKDRQDGEVLQCMFVGRPVTPIAQNQTTLGSSRAK  
 LGNFPWQAFSTIHGRGGGALLGDRWILTAAHTIYPKDSVSLRKNQSVNVFLGHTAIDEMKLGNHPVHRVVVHPDYRQNESHNF  
 30 SGDIALLELQHSIPLGPNVLPVCLPDNETLYRSGLLGYVSGFGMEMGWLTELKYSRLPVAPREACNAWLQKRQRPVEFSDNMF  
 CVGDETQRHSVCQGDGSLYVVDNHAHHWVATGIVSWGIGCGEGYDFYTKVLSYVDWIKGVMNGKN

An alternative embodiment, FCTR5b, is a 1691 base sequence shown in Table 5C.

**Table 5C. FCTR5b Nucleotide Sequence (SEQ ID NO:18)**

35 TTTTTTTTTTAAAAAAAAAAAAAAAAAGGGAAATCCTATTCACATCACTGTTGCACCAAGCCACTGCAAGAGAAACCCCCACCCC  
 CTACCCCAGTGTTCAGTCCCTCACTCCAGGCCCTCTGTTGCCTGGGGCCTCCACTGTGCTGGTCACTCCCTGTCAAGCCCCCAG  
 GGTCAATCTTGCCATTCATCACTCCCTTGATCCAGTCCACATAGCTGAGCACCTTGGTGTAGAAGTCATACCCTTCGCCACAC  
 CCTATGCCCCAGGACACAATGCCCGTGGCCACCCAGTGATGGGCATGATTGTCCCATACCACATAGAGGCTGCCACTGTCCCC  
 TGGCAGACACTGTGCCTTTGCGTCTCATCCCCAACACAGAACATATTGTGAGAAACACCTCGGGTCTCTGTCTCTTTTGGAGC  
 40 CAGGCGTTGCAGGCCTCCCTGGGAGCTACAGGCAGCCTCGAGTACTTCAGCTCAGTAGTTAGCCAGCCCATCTCCATGCCAAAC  
 CCACTGACGTAGCCCAACAAGCCGCTGCGGTAGAGGGTCTCATTATCGGGCAGACAGACCGGGAGGACGTTGGGGCCAGGGGG  
 ATGCTGTGCTGCAGCTCCAGGAGGGCGATGTCCCCGCTAAAGTTATGGGACTCATTCTGACGGTAGTCGGGGTGCACAACGACA  
 CGGTGGACAGGGTGGTTCCCCAGTTTCAGCATCTCATCTATGGCTGTGTGGCCCAAGAACACATTCACTCTGGTTCTTCCTG  
 AGAGAAACACTGTCCTTGGGGTAGATGGTGTGGGCAGCAGTGAGGATCCATCTGTCCCCCAGCAGGGCCCCGCCCCACGGCCG  
 45 TGGATACTGGTGAAGGCTTGCCAGGGGAAGTTGCCAGCTTGGCTCTGGAAGAACCAGAGGGTCTGTGATTCTGGGCAATGGGG  
 GTGACTGGCCGTCCGACAGACAGGCATACACTGAAGAACCTCCTCCCCATCCTGTCTGTCTTTCCAGGTCCCTGGGGTTGCACAG  
 GTGAGTGGCCCTGCTGCCGCGGCCTGATAATAGGGCTCCTGGCAGTGGTCTGGACCTTGGCAGGGTGTCTCCAGGTGCGTTG  
 ATGGCCTCAGAGCCCCCTGCTGGCCTCGCTGATGGGCTGACTATAGTTACAGCCACGGTTTGGTAGAGGGCCAGGAAGCCCTTG  
 TGGAGGTGGGCAGTCTTGTCTCCGAGGAAGGCTGTGTGCGGAAGGTGAGCCGCAAACTCCTCCCTGAGGATACAACTCCCTC  
 50 TGACCAGGGGGCCTGCCAGAGGGGAGCCTTGTGACCACAGAACTGGCTTGGATCCGAACCGACGAATGAGATTGTGACAGAG  
 TCCCCTGCACAGTCTTGGGACGGCTCCAGGTGGAAGTCTGGAAGACGAGCCTCACAGCAAAGCCCTCTGGAGCCTTGATGTCC  
 GTGCTGCTCTCTTGGCCTTTGCCATACGGCTCTGGGTACCCGGGGGATGTCAGCTGCTGGGGTAGCTCTTGGGCCAAGAGGACG  
 GAGCCCCGGGTGGGCAAGCCTGGAGGACTCCCCAGAGAAGCAGCCACCACATTGCGCCTGGACAGCCTTTGGAGTGAGGGCTT  
 CTCCAGAGATATTTCCCCCACACTCTGGGTCCAGGCATCTGGAAGTGGACATCTGGGACCTGCGAGAGAACTGGCCAGGATAG  
 55 GGAACAAAAGG

The FCTR5b protein encoded by SEQ ID NO:18 has 487 amino acid residues, and is presented using the one-letter code in Table 5D. FCTR5 was searched against other databases using SignalPep and PSort search protocols. The FCTR5b protein is most likely microbody (peroxisome) (Certainty=0.6406) and seems to have no N-terminal signal sequence. The predicted molecular weight of FCTR5 protein is 53511.9 daltons.

**Table 5D. Encoded FCTR5b protein sequence (SEQ ID NO:19).**

MPGPRVWGKYLWRSPPHSGKCPGAMWWLLWGVLLQACPTRGSVLLAQQLPQQLTSPGYPEFYGKGQESSTDIKAPEGFAVRLVFQ  
DFDLEPSQDCAGDSVTISFVGSDPSQFCGQQGSPLGRPPGQREFVSSGRSLRLTFRTPQPSSENKTAHLHKGFLALYQTVAVNYS  
QPISEASRGSEAINAPGDNPAKVQNHCOEPYQAAAAGALTCATPGTWKDRQDGEEVLQCMFVCGRPVTPIAQNQTTLGSSRAK  
LGNFPWQAFTSIHGRGGGALLGDRWILTAAHTIYPKDSVSLRKNQSVNVFLGHTAIDEMKLGNHPVHRVVVHPDYRQNESHNF  
SGDIALLELQHSIPLGPNVLPVCLPDNETLYRSGLLGYVSGFGMEMGWLTTTELKYSRLPVAPREACNAWLQKRQREVEFSDNMF  
CVGDETQRHSVCQGDSSGLYVVDNHAHHWVATGIVSWGIGCGEGYDFYTKVLSYVDWIKGVMNGKN

The predicted amino acid sequence was searched in the publicly available GenBank database FCTR5a protein showed 58 % identities (177 over 302 amino acids) and 74 % homologies (226 over 302 amino acids) with human complement C1R component precursor (EC 3.4.21.41) (705 aa.; ACC:P00736). Based upon homology, FCTR5 proteins and each homologous protein or peptide may share at least some activity.

In a search of sequence databases, it was found, for example, that the nucleic acid sequence the nucleotides 17-1594 of FCTR5a have 1575 of 1578 bases (99 %) identical to *Homo sapiens* complement C1r-like proteinase precursor (GENBANK-ID: XM\_007061.1) (SEQ ID NO:78) (Table 5E).

**Table 5E. BLASTN of FCTR5a against *Homo sapiens* complement C1r-like proteinase precursor (SEQ ID NO:78)**

>GI|11436767|REF|XM\_007061.1| HOMO SAPIENS COMPLEMENT C1R-LIKE PROTEINASE PRECURSOR,  
(LOC51279),  
MRNA  
LENGTH = 3318

SCORE = 3104 BITS (1566), EXPECT = 0.0  
IDENTITIES = 1575/1578 (99%)  
STRAND = PLUS / PLUS

QUERY: 17 CAGATGTCCAGTTCCAGATGCCTGGACCCAGAGTGTGGGGGAAATATCTCTGGAGAAGCC 76  
|||||  
SBJCT: 1 CAGATGTCCAGTTCCAGATGCCTGGACCCAGAGTGTGGGGGAAATATCTCTGGAGAAGCC 60

QUERY: 77 CTCACCTCCAAAGGCTGTCCAGGCGCAATGTGGTGGCTGCTTCTCTGGGGAGTCCTCCAGG 136  
|||||  
SBJCT: 61 CTCACCTCCAAAGGCTGTCCAGGCGCAATGTGGTGGCTGCTTCTCTGGGGAGTCCTCCAGG 120

QUERY: 137 CTTGCCCCAACC CGGGGCTCCGTCCTCTTGGCCCCAAGAGCTACCCAGCAGCTGACATCCC 196  
|||||  
SBJCT: 121 CTTGCCCCAACC CGGGGCTCCGTCCTCTTGGCCCCAAGAGCTACCCAGCAGCTGACATCCC 180

QUERY: 197 CCGGGTACCCAGAGCCGTATGGCAAAGGCCAAGAGAGCAGCACGGACATCAAGGCTCCAG 256  
|||||  
SBJCT: 181 CCGGGTACCCAGAGCCGTATGGCAAAGGCCAAGAGAGCAGCACGGACATCAAGGCTCCAG 240

QUERY: 257 AGGGCTTTGCTGTGAGGCTCGTCTTCCAGGACTTCGACCTGGAGCCGTCCCAGGACTGTG 316

|||||  
5 SBJCT: 241 AGGGCTTTGCTGTGAGGCTCGTCTTCCAGGACTTCGACCTGGAGCCGTCCCAGGACTGTG 300  
QUERY: 317 CAGGGGACTCTGT CACAATCTCATTCGT CGGTTCGGATCCAAGCCAGTTCTGTGGTCAGC 376  
|||||  
SBJCT: 301 CAGGGGACTCTGT CACAATCTCATTCGT CGGTTCGGATCCAAGCCAGTTCTGTGGTCAGC 360  
10 QUERY: 377 AAGGCTCCCCCTCTGGGCAGGCCCCCTGGTCAGAGGGAGTTTGTATCCTCAGGGAGGAGTT 436  
|||||  
SBJCT: 361 AAGGCTCCCCCTCTGGGCAGGCCCCCTGGTCAGAGGGAGTTTGTATCCTCAGGGAGGAGTT 420  
15 QUERY: 437 TCGGGCTGACCTTCCGCACACAGCCTTCCTCGGAGAACAAGACTGCCCACCTCCACAAGG 496  
|||||  
SBJCT: 421 TCGGGCTGACCTTCCGCACACAGCCTTCCTCGGAGAACAAGACTGCCCACCTCCACAAGG 480  
20 QUERY: 497 GCTTCCTGGCCCTCTACCAAACCGTGGCTGTGAACTATAGTCAGCCCATCAGCGAGGCCA 556  
|||||  
SBJCT: 481 GCTTCCTGGCCCTCTACCAAACCGTGGCTGTGAACTATAGTCAGCCCATCAGCGAGGCCA 540  
25 QUERY: 557 GCAGGGGCTCTGAGGCCATCAACGCACCTGGAGACAACCCTGCCAAGGTCCAGAACCCT 616  
|||||  
SBJCT: 541 GCAGGGGCTCTGAGGCCATCAACGCACCTGGAGACAACCCTGCCAAGGTCCAGAACCCT 600  
30 QUERY: 617 GCCAGGAGCCCTATTATCAGGCCGCGGCAGCAGGGGCACTCACCTGTGCAACCCAGGGA 676  
|||||  
SBJCT: 601 GCCAGGAGCCCTATTATCAGGCCGCGGCAGCAGGGGCACTCACCTGTGCAACCCAGGGA 660  
35 QUERY: 677 CCTGGAAAGACAGACAGGATGGGGAGGAGGTTCTTCAGTGTATGCCTGTCTGCGGACGGC 736  
|||||  
SBJCT: 661 CCTGGAAAGACAGACAGGATGGGGAGGAGGTTCTTCAGTGTATGCCTGTCTGCGGACGGC 720  
40 QUERY: 737 CAGTCACCCCCATTGCCCAGAATCAGACGACCCTCGGTTCCTCCAGAGCCAAGCTGGGCA 796  
|||||  
SBJCT: 721 CAGTCACCCCCATTGCCCAGAATCAGACGACCCTCGGTTCCTCCAGAGCCAAGCTGGGCA 780  
45 QUERY: 797 ACTTCCCCTGGCAAGCCTTCACCAGTATCCACGGCCGTGGGGGCGGGGCCCTGCTGGGGG 856  
|||||  
SBJCT: 781 ACTTCCCCTGGCAAGCCTTCACCAGTATCCACGGCCGTGGGGGCGGGGCCCTGCTGGGGG 840  
50 QUERY: 857 ACAGATGGATCCTCACTGCTGCCACACCATCTACCCCAAGGACAGTGTCTCTCAGGA 916  
|||||  
SBJCT: 841 ACAGATGGATCCTCACTGCTGCCACACCATCTACCCCAAGGACAGTGTCTCTCAGGA 900  
55 QUERY: 917 AGAACCAGAGTGTGAATGTGTCTTGGGCCACACAGCCATAGATGAGATGCTGAAACTGG 976  
|||||  
SBJCT: 901 AGAACCAGAGTGTGAATGTGTCTTGGGCCACACAGCCATAGATGAGATGCTGAAACTGG 960  
60 QUERY: 977 GGAACCACCCTGTCCACCGTGTGTTGTGCACCCCGACTACCGTCAGAATGAGTCCCAT 1036  
|||||  
SBJCT: 961 GGAACCACCCTGTCCACCGTGTGTTGTGCACCCCGACTACCGTCAGAATGAGTCCCAT 1020  
65 QUERY: 1037 ACTTTAGCGGGGACATCGCCCTCCTGGAGCTGCAGCACAGCATCCCCCTGGGCCCCAACG 1096  
|||||  
SBJCT: 1021 ACTTTAGCGGGGACATCGCCCTCCTGGAGCTGCAGCACAGCATCCCCCTGGGCCCCAACG 1080  
70 QUERY: 1097 TCCTCCCGGTCTGTCTGCCCGATAATGAGACCCTCTACCGCAGCGGCTTGTGGGCTACG 1156  
|||||  
SBJCT: 1081 TCCTCCCGGTCTGTCTGCCCGATAATGAGACCCTCTACCGCAGCGGCTTGTGGGCTACG 1140  
75 QUERY: 1157 TCAGTGGGTTTGGCATGGAGATGGGCTGGCTAACTACTGAGCTGAAGTACTCGAGGCTGC 1216  
|||||  
SBJCT: 1141 TCAGTGGGTTTGGCATGGAGATGGGCTGGCTAACTACTGAGCTGAAGTACTCGAGGCTGC 1200  
80 QUERY: 1217 CTGTAGCTCCCAGGGAGGCCTGCAACGCCTGGCTCCAAAAGAGACAGAGACCCGAGGTGT 1276  
|||||  
SBJCT: 1201 CTGTAGCTCCCAGGGAGGCCTGCAACGCCTGGCTCCAAAAGAGACAGAGACCCGAGGTGT 1260  
85 QUERY: 1277 TTTCTGACAATATGTTCTGTGTTGGGGATGAGACGCAAAGGCACAGTGTCTGCCAGGGGG 1336  
|||||  
SBJCT: 1261 TTTCTGACAATATGTTCTGTGTTGGGGATGAGACGCAAAGGCACAGTGTCTGCCAGGGGG 1320

5  
 QUERY: 1337 ACAGTGGCAGCCTCTATGTGGTATGGGACAATCATGCCCATCACTGGGTGGCCACGGGCA 1396  
 |||||  
 SBJCT: 1321 ACAGTGGCAGCGTCTATGTGGTATGGGACAATCATGCCCATCACTGGGTGGCCACGGGCA 1380  
 10  
 QUERY: 1397 TTGTGTCCTGGGGCATAGGGTGTGGCGAAGGGTATGACTTCTACACCAAGGTGCTCAGCT 1456  
 |||||  
 SBJCT: 1381 TTGTGTCCTGGGGCATAGGGTGTGGCGAAGGGTATGACTTCTACACCAAGGTGCTCAGCT 1440  
 15  
 QUERY: 1457 ATGTGGACTGGATCAAGGGAGTGATGAATGGCAAGAATTGACCCTGGGGGCTTGAACAGG 1516  
 |||||  
 SBJCT: 1441 ATGTGGACTGGATCAAGGGAGTGATGAATGGCAAGAATTGACCCTGGGGGCTTGAACAGG 1500  
 20  
 QUERY: 1517 GACTGACCAGCACAGTGGAGGCCCCAGGCAACAGAGGGCCTGGAGTGAGGACTGAACACT 1576  
 |||||  
 SBJCT: 1501 GACTGACCAGCACAGTGGAGGCCCCAGGCAACAGAGGGCCTGGAGTGAGGACTGAACACT 1560  
 QUERY: 1577 GGGGTAGGGGGTGGGGGT 1594  
 |||||  
 SBJCT: 1561 GGGGTAGGGGTGGGGGT 1578

In this search it was also found that the FCTR5a nucleic acid had homology to three  
 fragments of *Homo sapiens* complement component 1, r subcomponent. It has 102 of 117  
 bases (87%) identical to 1458-1574, 82 of 94 bases (87%) identical to 2052-2145, and 54 of  
 63 bases (85%) identical to 1678-1740 all fragments of *Homo sapiens* complement component  
 1, r subcomponent (GenBank Acc: NM\_001733.1) (Table 5F).

**Table 5F. BLASTN of FCTR5a against *Homo sapiens* complement component 1, r subcomponent (SEQ ID NO:79)**

30 >GI|4502492|REF|NM\_001733.1| HOMO SAPIENS COMPLEMENT COMPONENT 1, R SUBCOMPONENT  
 (C1R), MRNA  
 LENGTH = 2386  
 SCORE = 113 BITS (57), EXPECT = 3E-22  
 IDENTITIES = 102/117 (87%)  
 35 STRAND = PLUS / PLUS  
 40  
 QUERY: 783 AGCCAAGCTGGGCAACTTCCCCTGGCAAGCCTTCACCAGTATCCACGGCCGTGGGGGCGG 842  
 |||||  
 SBJCT: 1458 AGCCAAGATGGGCAACTTCCCCTGGCAGGTGTTACCAACATCCACGGGCGCGGGGCGG 1517  
 45  
 QUERY: 843 GGCCCTGCTGGGGGACAGATGGATCCTCACTGCTGCCACACCATCTACCCCAAGGA 899  
 |||||  
 SBJCT: 1518 GGCCCTGCTGGGCGACCGCTGGATCCTCACAGCTGCCACACCCTGTATCCCAAGGA 1574  
 50  
 QUERY: 1380 CTGGGTGGCCACGGGCATTGTGTCCTGGGGCATAGGGTGTGGCGAAGGGTATGACTTCTA 1439  
 |||||  
 SBJCT: 2052 CTGGGTGGCCACGGGCATCGTGTCTGGGGCATCGGGTGACAGAGGGCTATGGCTTCTA 2111  
 55  
 QUERY: 1440 CACCAAGGTGCTCAGCTATGTGGACTGGATCAAG 1473  
 |||||  
 SBJCT: 2112 CACCAAGTGCTCAACTACGTGGACTGGATCAAG 2145  
 60  
 SCORE = 54.0 BITS (27), EXPECT = 2E-04  
 IDENTITIES = 54/63 (85%)  
 STRAND = PLUS / PLUS

```

5      QUERY: 1066 CTG 1068
           |||
      SBJCT: 1738 CTG 1740

```

**Table 5G. BLASTP of FCTR5a and b against Complement C1R-like proteinase precursor (SEQ ID NO:80)**

SCORE = 972 BITS (2513), EXPECT = 0.0  
IDENTITIES = 485/487 (99%), POSITIVES = 487/487 (100%)

60 SBJCT: 481 GVMNGKN 487

5 The full amino acid sequence of the protein of FCTR5a has 175 of 303 amino acid  
residues (58%) identical to, and 226 of 303 residues (74%) positive with the 400-701 amino  
acid segment, 72 of 157 residues (45%) identical and 94 of 157 residues (59%) positive with  
amino acids 1-155, and 36 of 139 residues (25%) identical and 58 of 139 residues (40%)  
positive with amino acids 188-312 of the 705 amino acid Complement C1R Component  
10 Precursor from *Homo sapiens* (GenBank-ACC: AAA51851.1) (SEQ ID NO:43) (Table 5H).

SCORE = 36.3 BITS (83), EXPECT = 0.93

IDENTITIES = 36/139 (25%), POSITIVES = 58/139 (40%), GAPS = 17/139 (12%)

R

5 QUERY: 35 ACPTRGSVLLAQELPQQLTSPGYPEFYGKGQESSTDIDKAPEGFAVRLVF-QDFDLEPSQD 93  
 +| | | | ++| || | + |+ | + | | + ||++ |  
 SBJCT: 188 SCQAECSSSELYTEASGYISSLEYPRSYPPDLRCNYSIRVERGLTLHLKFLEPFDDIDHQQ 247

10 QUERY: 94 --CAGDSVTISFVGSQDPSQFCGQOGSPLGRPPGQREFVSSGRSLRLTFRTQPSSENKTAH 151  
 | | + | | + +|||+| ||| + +| ++ | | | | ++  
 SBJCT: 248 VHCPYDQLQIYANGKNIGEFCKQ-----RPP---DLDTSSNAVDLLFFTDSESGDS---- 295

QUERY: 152 LHKGFLALYQTVAVNYSQP 170  
 ++ | | + ||  
 15 SBJCT: 296 --RGWKLRYTTEIIKCPQP 312

R = AT RESIDUE 46, FCTR5B DIFFERS FROM FCTR5A IN THAT Q46R. THE REST OF THE HOMOLOGY IS THE SAME.

20 Based upon homology, FCTR5 proteins and each homologous protein or peptide may share at least some activity.

## FCTR6

The novel nucleic acid of 1078 nucleotides FCTR6a (also designated 27455183.0.19) encoding a novel human blood coagulation factor XI-like protein is shown in Table 6A. An ORF was identified beginning with an ATG initiation codon at nucleotides 243-245 and ending with a TAA codon at nucleotides 1044-1046. A putative untranslated region upstream from the initiation codon and downstream from the termination codon is underlined in Table 6A, and the start and stop codons are in bold letters.

**Table 6A FCTR6a Nucleotide Sequence (SEQ ID NO:20)**

30 TTGATCCGTGCCAAGTGGCTTTTTGTGGGCTCTGTAGAGTGCTCTAAACCCAGCTCGGCCTTTGCTGTATTAGACAGAAGCACC  
TCATTCATATCCCTGGGGCCCCTGATGGTGCAGTGGTCTGGCTGTGGTCTGCACACCAGCTATTCTGTTTTGTTTTGTTTGT  
TTTTCTACCTTTTCCAATCCTCACACCTTCTGATCAACAGCCCCAGTAGGGTTTAAAGGTCTAGAGCTACATGGGATTTA  
 GGTTTCTGGGCACAGCCAATTCTGCCACTTTTGAGACTTCCCTTCCCCTTCCACTTGCCCCTCTCTGGTTCTCTGCCACCAAGTC

35 CAGAAGAAGTGAAGTGTGCTGCTGGGGACCAACGACTTAAGTAGCCCATCCATGGAAATAAAGGAGGTGCGCCAGCATCATTCTTC  
 ACAAGAGCTTTAAGAGAGCCAACATGGACAATGACATTGCCTTGCTGCTGCTGGCTTCGCCCATCAAGCTCGATGACCTGAAGG  
 TGCCCATCTGCCTCCCCACGCAGCCCCGCCCTGCCACATGGCGCGAATGCTGGGTGGCAGGTGTTGGGGCCAGACCAATGCTGCTG  
 ACAAAAAGTCTGTGAAAACGGATCTGATGAAAGTGCCAATGGTCATCATGGACTGGGAGGAGTGTCAAAGATGTTTCCAAAAC  
 TTACCAAAAATATGCTGTGTGCCGGATACAAGAATGAGAGCTATGATGCCTGCAAGGGTGACAGTGGGGGGCCTCTGGTCTGCA  
 CCCCAGAGCCTGGTGAGAAGTGGTACCAGGTGGGCATCATCAGCTGGGGAAAGAGCTGTGGAGATAAGAACACCCAGGGATAT

40 ACACCTCGTTGGTGAAGTACAACCTCTGGATCGAGAAAGTGACCCAGCTAGGAGGCAGGCCCTTCAATGCAGAGAAAAGGAGGA  
 CTTCTGTCAAACAGAAACCTATGGGCTCCCCAGTCTCGGGAGTCCAGAGCCAGGCAGCCCCAGATCCTGGCTCCTGCTCTGTC  
 CCCTGTCCCATGTGTTGTTTCAGAGCTATTTTGTACTGATAATAAAATAGAGGCTATTCTTTCAACCGAAA

The FCTR6a protein encoded by SEQ ID NO:20 has 267 amino acid residues and is presented using the one-letter code in Table 6B. FCTR6a was searched against other databases using SignalPep and PSort search protocols. The FCTR6a protein is most likely mitochondrial matrix space (Certainty= 0.4372) and seems to have no N-terminal signal sequence. The predicted molecular weight of FCTR6a protein is 29412.8 daltons.

MGFRFLGTANSATFETSLPLPLAPLWFSATSPEELSVVLGTNDLTSPSMEIKEVASIILHKDFKRANMDNDIALLLLASPIKLD  
DLKVPICLPTQPGPATWRECWVAGWGQTNAADKNSVKTDLMKVPVMIMDWEESKMFPKLTKNMLCAGYKNESYDACKGDSGGP  
LVCTPEPGEKWYQVGII SWGKSCGDKNTPGIYTSLVNYNLWIEKVTQLGGRPFNAEKRRTSVKQKPMGSPVSGVPEPGSPRSWL  
LLCPLSHVLFRAILY

GATTTTAGAAGGTTAATCAAAAACCCGGGGACAGTTTCTTCATGGCATAACCCACAGACCTTTGTGGCACCCGCTGT  
CGTGGGATATCAAATATCCTCTGGGGTTCGGAATGTGGGCTTATTACTGAAGATCCTGTCTGCTTGGTCAGTGGCAGGTC  
TAGACTAACTTCTGGTCCTGAGTTTCTAAAGTGCTGGTAGACCAGTTGATACAAAACAGATATAATAATGAATGCCTTAT  
CTATCTGAAGGTCAGTTTGATCCGTGCCAAGTGGCTTTTTGTGGGCTGTGTAGAGTGCTCTAAACCCAGCTCGGCCTTG  
CTGTATTAGACAGAAGCACCTCATTATCATATCCCTGGGGCCCCCTGATGGTGCAGTGGTCTGGCTGTGGTCTGCACACCAGC  
TATTCTGTTTTGTTTTGTTTTGTTTTGTTTTTCTACCTTTTTTCCAATCCTCACACCTTCTGATCAACAGCCCCAGTAG  
GGTTTAAAGGTCCTAGAGCTACATGGGATTTAGGTTTCTGGGCACAGCCAATTCTGCCACTTTTGAGACTTCCCTTCCCC  
TTCCACTTGCCCCCTCTCTGGTTCTCTGCCACCAGTCCAGAAGAACTGAGTGTCTGTGCTGGGGACCAACGACTTAACTAGC  
CCATCCATGGAATAAAGGAGGTGCGCAGCATCATTCCTCACAAAGACTTTAAGAGAGCCAACATGGACAATGACATTGC  
CTTGCTGCTGCTGGCTTCGCCCATCAAGCTCGATGACCTGAAGGTGCCCATCTGCCTCCCCACGCAGCCCCGGCCCTGCCA  
CATGGCGCGAATGCTGGGTGGCAGGTTGGGGCCAGACCAATGCTGCTGACAAAAACTCTGTGAAAACGGATCTGATGAAA  
GTGCCAATGGTCATCATGGACTGGGAGGAGTGTTCAAAGATGTTTCCAAAACCTTACCAAAAATATGCTGTGTGCCGGATA  
CAAGAATGAGAGCTATGATGCCTGCAAGGGTGACAGTGGGGGGCCTCTGGTCTGCACCCCAGAGCCTGGTGAGAAGTGGT  
ACCAGGTGGGCATCATCAGCTGGGGAAAGAGCTGTGGAGAGAAGAACACCCCAGGGATATACACCTCGTTGGTGAACCTAC  
AACCTCTGGATCGAGAAAGTGACCCAGCTAGAGGGCAGGCCCTTCAATGCAGAGAAAAGGAGGACTTCTGTCAAACAGAA  
ACCTATGGGCTCCCCAGTCTCGGGAGTCCAGAGCCAGGCAGCCCCAGATCCTGGCTCCTGCTCTGTCCCCTGTCCCATG  
TGTTGTTTCAGAGCTATTTTGTACTGATAATAAAATAGAGGCTATTCTTTCAACCGAAA

MGFREFLG TANSATFETSLPLPLAPLWFSATSPEELSVVLGTNDLTSPSMEIKEVASIIILHKDFKRANMDNDIALLLLSPKLD  
DLKVPICLPTQPGPATWRECWVAGWGQTNAADKNSVKTDLMKVMVIMDWEESCKMFPKLTKNMLCAGYKNESYDACKGDSGGP  
LVCTPEPEGKQYQVGIIISWGKSCGEKNTPGIYTSLVNYNLWIEKVTQLEGRPFNAEKRRTSVKQKPMGSPVSGVPEPGSPRSWL  
LLCPLSHVLFRAILY

**Table 6E. BLASTN of FCTR6a against *Macaca fascicularis* brain cDNA, clone QccE-17034 (SEQ ID NO:82)**

>GI|9651112|DBJ|AB046651.1|AB046651 MACACA FASCICULARIS BRAIN CDNA, CLONE QCCE-17034  
LENGTH = 1746

5  
SCORE = 1429 BITS (721), EXPECT = 0.0  
IDENTITIES = 853/897 (95%)  
STRAND = PLUS / PLUS

10  
QUERY: 434 CCTTTTCCAATCCTCACACCTTCTGATCAACAGCCCCAGTAGGGTTTAAAGGTCCTAGA 493  
|||||  
SBJCT: 551 CCTTTTCCAATCCTCACACCTTCTGAGCTACAGCCCCAGTAGGGTCTAAATGTCCTAGA 610

15  
QUERY: 494 GCTACATGGGATTTAGGTTTCTGGGCACAGCCAATTCTGCCACTTTTGAGACTTCCCTTC 553  
|||||  
SBJCT: 611 GCTATATGAGATTTAGGTTTCTGAGCACAGCCAATTCTCCCACTTTTGAGGCTTCCCTTC 670

20  
QUERY: 554 CCCTTCCACTTGCCCCCTCTCTGGTTCTCTGCCACCAGTCCAGAAGAACTGAGTGTGCTGC 613  
|||||  
SBJCT: 671 CCCTTTCACCTCGCCCCCTCTCTGGTTCTCTGCCACCAGTCCAGAAGAACTGAATGTGCTGC 730

25  
QUERY: 614 TGGGGACCAACGACTTAACTAGCCCATCCATGGAAATAAAGGAGGTCGCCAGCATCATTC 673  
|||||  
SBJCT: 731 TGGGGACCAACGACTTAACTAGCTCATCCATGGAAATAAAGGAGGTCGCCAGCATCATTC 790

30  
QUERY: 674 TTCACAAAGACTTTAAGAGAGCCAACATGGACAATGACATTGCCTTGCTGCTGCTGGCTT 733  
|||||  
SBJCT: 791 TTCACAAGGACTTTAAGAGAGCCAACATGGACAATGACATTGCCTTGCTGCTGCTGGCCT 850

35  
QUERY: 734 CGCCCATCAAGCTCGATGACCTGAAGGTGCCCATCTGCCTCCCCACGCAGCCCGGCCCTG 793  
|||||  
SBJCT: 851 CGCCCATCACACTCGATGACCTGAAGGTGCCCATCTGCCTCCCTACGCAGCACGGCCCCG 910

40  
QUERY: 794 CCACATGGCGCGAATGCTGGGTGGCAGGTGGGGCCAGACCAATGCTGCTGACAAAAACT 853  
|||||  
SBJCT: 911 CCACATGGCAGCAATGCTGGGTGGCAGGTGGGGCCAGACCAATGCTGCTGACAAAAACT 970

45  
QUERY: 854 CTGTGAAAACGGATCTGATGAAAGTGCCAATGGTCATCATGGACTGGGAGGAGTGTTCAA 913  
|||||  
SBJCT: 971 CTGTGAAAACGGATCTGATGAAAGCGCCGATGGTCATCATGGACTGGGAGGAGTGTTCAA 1030

50  
QUERY: 914 AGATGTTTCCAAAACCTACCAAAAATATGCTGTGTGTCGGGATACAAGAATGAGAGCTATG 973  
||  
SBJCT: 1031 AGGCGTTTCCAAAACCTACCAAAAATATGCTGTGTGCTGGATACAATAATGAGAGCTATG 1090

55  
QUERY: 974 ATGCCTGCAAGGGTGACAGTGGGGGGCCTCTGGTCTGCACCCAGAGCCTGGTGAGAAGT 1033  
|  
SBJCT: 1091 ACGCCTGCCAGGGTGACAGCGGGGACCTCTGGTCTGCACCCAGAGCCTGGTGAGAAGT 1150

60  
QUERY: 1034 GGTACCAGGTGGGCATCATCAGCTGGGGAAAGAGCTGTGGAGAGAAGAACACCCAGGGA 1093  
|||||  
SBJCT: 1151 GGTACCAGGTGGGTATCATCAGCTGGGGAAAGAGCTGTGGAGAGAAGAACACCCAGGGA 1210

65  
QUERY: 1094 TATACACCTCGTTGGTGAACCTACAACCTCTGGATCGAGAAAGTGACCCAGCTAGAGGGCA 1153  
|||||  
SBJCT: 1211 TATACACCTCGTTGGTGAACCTACAACCTCTGGATCGAGAAGGTGACCCAGCTAGAGGGCA 1270  
QUERY: 1154 GGCCCTTCAATGCAGAGAAAAGGAGGACTTCTGTCAAACAGAAACCTATGGGCTCCCCAG 1213  
|||||  
SBJCT: 1271 GGCCCTTCAGTGCAGAGAAAATGAGGACCTCTGTCAAACAGAAACCTATGGGCTCCCGAG 1330

65  
QUERY: 1214 TCTCGGGAGTCCCAGAGCCAGGCAGCCCCAGATCCTGGCTCCTGCTCTGTCCCCTGTCCC 1273  
|||||  
SBJCT: 1331 TCTCGGGGTCCCAGAGCCAGGCGGCCTCAGATCCTGGCTCCTGCTCTGTCCCCTGTCCC 1390

65  
QUERY: 1274 ATGTGTTGTTTCAGAGCTATTTTGTACTGATAATAAAATAGAGGCTATTCTTTCAACC 1330  
|||||  
SBJCT: 1391 ATGTGTTGTTTCAGAGCTATTTTGTACTGATAATAAAATAGAGGCTATTTTCTTTAACC 1447

SCORE = 428 BITS (216), EXPECT = E-117  
 IDENTITIES = 346/388 (89%), GAPS = 1/388 (0%)  
 STRAND = PLUS / PLUS

5  
 QUERY: 1 GATTTTAGAAGGTTAATCAAAAACCCGGGGACAGTTTCTTCATGGCATAACCACAGACCT 60  
 |||||  
 SBJCT: 127 GATTTTAGAAGGTTAATCAAAAACCCAAGGACAGTTTCTTCATGTCATAACCAAAGACCC 186

10  
 QUERY: 61 TTGTGGCACCCGCTGTCGTGGGATATCAAATATCCTCTGGGGTTCGGAATGTGGGCTTAT 120  
 |||||  
 SBJCT: 187 TTGTGGCACCTGCTGTCATGGGATAACAAATATCTTGTGGGGTTCGAATGTGGACTTAT 246

15  
 QUERY: 121 TACTGAAGATCCTGTCTGCTTGGTCAGTGGCAGGTCTAGACTAACTTCTGGTCCTGAGTT 180  
 |||||  
 SBJCT: 247 TACTGAAGCTCCTGTCTGCTTGGTCAGTGG-TGGTCTAGACTAACTTCTGGTCCTGAGAT 305

20  
 QUERY: 181 TCTAAAGTGCTGGTAGACCAGTTGATACAAAACAGATATAATAATGAATGCCTTATCTAT 240  
 |||||  
 SBJCT: 306 TCTAAAGTGTTGGTAGACCGTTGAGATAAAAGATATATAATAATGAATGCCTTACCTAT 365

25  
 QUERY: 241 CTGAAGGTCAGTTTGATCCGTGCCAAGTGGCTTTTTGTGGGCTGTGTAGAGTGCTCTAAA 300  
 |||||  
 SBJCT: 366 CTGAAAACAGTTTGATCCGTGCCAAGGGGCTTTTTGTGGGCTGTGTAGAGTGCCCTAAA 425

30  
 QUERY: 301 CCCAGCTCGGCCTTTGCTGTATTAGACAGAAGCACCTCATTCATATCCCTGGGGCCCCCTG 360  
 |||||  
 SBJCT: 426 CCCAGCTCTGCCTTTGCTGTGTTAGACAGAAGCACGCCATTCACATCTCTGGGGCCCCCA 485

30  
 QUERY: 361 ATGGTGCAGTGGTCTGGCTGTGGTCTGC 388  
 |||||  
 SBJCT: 486 ATGGTGCCATGGTGTGTTGTGGTCTGC 513

35 In a search of sequence databases, it was found, for example, that the FCTR6a nucleic acid sequence has 295 of 378 bases (78 %) identical to bases 410-779 of *Mus musculus* adult male testis cDNA, RIKEN full-length enriched (GENBANK-ID:AK09660) (Table 6F).

**Table 6F. BLASTN of FCTR6a against *Mus musculus* adult male testis cDNA, RIKEN full-length enriched (SEQ ID NO:83)**

40 >GI|12855429|DBJ|AK016601.1|AK016601 MUS MUSCULUS ADULT MALE TESTIS CDNA, RIKEN  
 FULL-LENGTH ENRICHED  
 LIBRARY, CLONE:4933401F05, FULL INSERT SEQUENCE  
 LENGTH = 1047

45 SCORE = 97.6 BITS (49), EXPECT = 2E-17  
 IDENTITIES = 295/378 (78%), GAPS = 8/378 (2%)  
 STRAND = PLUS / PLUS

50  
 QUERY: 697 AACATGGACAATGACATTGCCTTGCTGCTGCTGGCTTCGCCCATCAAGCTCGATGACCTG 756  
 |||||  
 SBJCT: 410 AACATGGACAACGACATTGCCTTGTTGCTGCTAGCCAAGCCCTTGACGTTCAATGAGCTG 469

55  
 QUERY: 757 AAGGTGCCCATCTGCCTCCCCACGCAGCCCGGCCCTGCCACATGGCGGAATGCTGGGTG 816  
 | |||||  
 SBJCT: 470 ACGGTGCCCATCTGCCTTCCTCTCTGGCCCGCCCTCCAGCTGGCACGAATGCTGGGTG 529

60  
 QUERY: 817 GCAGGTTGGGGCCAGACCAATGCTGCTGACAAAACTCTGTGAAAACGGATCTGATGAAA 876  
 |||||  
 SBJCT: 530 GCAGGATGGGGCGTAACCAACTCAACTGACAAGGAATCTATGTCAACGGATCTGATGAAG 589

60  
 QUERY: 877 GTGCCAATGGTCATCATGGACTGGGAGGAGTGTTCAAAGATGTTTCCAAACTTACCAA 936  
 |||||  
 SBJCT: 590 GTGCCCATGCGTATCATAGAGTGGGAGGAATGCTTACAGATGTTTCCAGCCTCACCACA 649

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GI|125184|SP|P03952|KAL HUMAN PLASMA KALLIKREIN PRECURSOR (PLASMA PREKALLIKREIN)  
(KININOGENIN)

(FLETCHER FACTOR)

GI|67591|PIR||KQHUP PLASMA KALLIKREIN (EC 3.4.21.34) PRECURSOR - HUMAN

GI|190263|GB|AAA60153.1| (M13143) PLASMA PREKALLIKREIN [HOMO SAPIENS]

GI|8809781|GB|AAF79940.1| (AF232742) PLASMA KALLIKREIN PRECURSOR [HOMO SAPIENS]

LENGTH = 638

SCORE = 133 BITS (334), EXPECT = 3E-30

IDENTITIES = 80/201 (39%), POSITIVES = 119/201 (58%), GAPS = 18/201 (8%)

QUERY: 20 LPLAPLWFSATSPEELSVVLGTNDLT--SPSMEIKEVASIILHKDFKRANMDNDIALLLL 77

||| +| | +| +|+| +| +||| ||+|++| + ++|||+ |

SBJCT: 439 LPLQDVW-----RIYSGIILNLSDITKDTPFSSQIKE---IIIHQNYKVSEGNHDIALIKL 489

QUERY: 78 ASPIKLDDDLKVPICLPTQPGPAT-WRECWVAGWGQTNAADKNSVKTDLMKVPMVIMDWEE 136

+|+ + + |||||++ +| + ||| ||| + +| ++ | || + ++ ||

SBJCT: 490 QAPLNYTEFQKPICLPSKGDSTIYTNCWVTGWGFSK--EKGEIQNILQKVNIPLVTNEE 547

K

QUERY: 137 CSKMFP--KLTKNMLCAGYKNESYDACKGDSGGPLVCTPEPGEKWKYQVGIISWGKSCGDK 194

| | + |+|+ |+||| ||||| ||||| ||| + | ||| |||+ | +

SBJCT: 548 CQKRYQDYKITQRMVCAGYKEGGKDAKGDGSGGPLVC--KHNGMWRLVGITSWGEGCARR 605

QUERY: 195 NTPGIYTSLVNYNLWIEKVTD 215

||+|| + | || + ||

SBJCT: 606 EQPGVYTKVAEYMDWILEKTQ 626

K IS A RESIDUE THAT DIFFERS BETWEEN FCTR6A AND B. D193K.

The FCTR6a amino acid has 73 of 183 amino acid residues (39%) identical to, and 110 of 183 residues (59%) positive with, the 643 amino acid kallikrein [*Sus scrofa*] (GENBANK-ID:BAA37147.1) (SEQ ID NO:86) (Table 6I).

**Table 6I. BLASTP of FCTR6a and b against kallikrein [*Sus scrofa*] (SEQ ID NO:86)**

>GI|4165315|DBJ|BAA37147.1| (AB022425) KALLIKREIN [SUS SCROFA]

LENGTH = 643

SCORE = 128 BITS (322), EXPECT = 9E-29

IDENTITIES = 73/183 (39%), POSITIVES = 110/183 (59%), GAPS = 12/183 (6%)

QUERY: 38 VLGTNDLT--SPSMEIKEVASIILHKDFKRANMDNDIALLLLASPIKLDDDLKVPICLPTQ 95

+| +++| +| ++|| ||+|++| +||| | +|+ | + |||||++

SBJCT: 459 ILNISEITKETPFSSQVKE---IIIHQNYKILES GHDIALLKLETPLNVTDFQKPICLPSR 515

QUERY: 96 PGP-ATWRECWVAGWGQTNAADKNSVKTDLMKVPMVIMDWEECSKMFP--KLTKNMLCAG 152

+ ||| ||| | +| ++ | || + ++ ||| | + |++| |++|

SBJCT: 516 DDTNVVYTNCWVTGWGFTE--EKGEIQNILQKVNIPLVSNEECQKSYRDHKISKQMICAG 573

K

QUERY: 153 YKNESYDACKGDSGGPLVCTPEPGEKWKYQVGIISWGKSCGDKNTPGIYTSLVNYNLWIEK 212

|| |||||+||| ||| + |+ || |||+ | + ||+|| ++ | || +

SBJCT: 574 YKEGGKDAKGESGGPLVC--KYNGIWHLVGTTSWGEGCARREQPGVYTKVIEYMDWILE 631

QUERY: 213 VTQ 215

||

SBJCT: 632 KTQ 634

K IS A RESIDUE THAT DIFFERS BETWEEN FCTR6A AND B. D193K.

The FCTR6a amino acid has 81 of 205 amino acid residues (39%) identical to, and 112 of 205 residues (54%) positive with, the 625 amino acid Coagulation factor XI [*Homo sapiens*] (embCAA64368.1) (SEQ ID NO:87) (Table 6J).

**Table 6J. BLASTP of FCTR6a and b against Coagulation factor XI [*Homo sapiens*]  
(SEQ ID NO:87)**

```

>GI|180352|GB|AAA51985.1| (M20218) COAGULATION FACTOR XI [HOMO SAPIENS]
      LENGTH = 625

5  SCORE = 127 BITS (320), EXPECT = 1E-28
   IDENTITIES = 81/205 (39%), POSITIVES = 112/205 (54%), GAPS = 17/205 (8%)

10  QUERY: 20  LPLAPLWFSATSPEELSVVLGTNDLTSPSMEIKE-----VASIILHKDFKRAMDNDIA 73
      | | ++ ||+ | | | + + |||| | ||+| +| | |||
   SBJCT: 427 LTAAHCFYGVESPKILRVYSGILNQS----EIKEDTSFFGVQEIIHDOYKMAESGYDIA 482

      QUERY: 74  LLLLASPIKLDDLKVPICLPTQPG-PATWRECWVAGWGQTNAADKNSVKTDLMKVPVMIM 132
      || | + + | + |||||++ + +||| ||| || ++ | | + ++
15  SBJCT: 483 LLKLETTVNYTDSQRPICLPSKGDNRVIYTDWVTGWGYRKLRLDK--IQNTLQAKIPLV 540

      QUERY: 133 DWEECSKMFP--KLTKNMLCAGYKNESYDACKGDSGGPLVCTPEPGEKQYQVGIISWGKS 190
      ||| | + | + | + |||||+ ||||| |||| | + | | + ||| |||+
20  SBJCT: 541 TNEECQKRYRGHKITHKMICAGYREGGKDACKGDSGGPLSC--KHNEVWHLVIGITSWGEG 598
      K
   QUERY: 191 CGDKNTPGIYTSLVNYNLWIEKVTQ 215
      | + ||+||++| | || + ||
   SBJCT: 599 CAQRETPGVYTNVVEYVDWILEKTQ 623

25  K IS A RESIDUE THAT DIFFERS BETWEEN FCTR6A AND B. D193K.

```

The number of new cases of renal cell carcinoma in the United States in 1996 was projected to be 30,600 with an estimated 12,000 deaths. Tumors with a proposed histogenesis from the proximal tubule (clear-cell and chromophilic tumors) amount to 85% of renal cancers, whereas tumors with a proposed histogenesis from the connecting tubule/collecting duct (chromophobic-, oncocytic-, and duct Bellini-type tumors) amount to only 11%.

Adenocarcinomas may be separated into clear cell and granular cell carcinomas, although the 2 cell types may occur together in some tumors. The distinction between well-differentiated renal carcinomas and renal adenomas can be difficult. The diagnosis is usually made arbitrarily on the basis of size of the mass, but size alone should not influence the treatment approach, since metastases can occur with lesions as small as 0.5 centimeters.

While radical nephrectomy with regional lymphadenectomy, is the accepted, often curative therapy for stage I (localized disease) renal cell cancer, very little therapy is available for advance disease that represent about 70% of the patients. Radiotherapy as a postoperative adjuvant has not been effective, and when used preoperatively, may decrease local recurrence but does not appear to improve 5-yr survival. A chemotherapeutic agent capable of significantly altering the course of metastatic renal cell carcinoma has not been identified. (Renal Cell Cancer (PDQ®) Treatment - Health Professionals, Cancernet, NCI)

There is therefore a need to identify genes that are differentially modulated in renal-cell carcinomas. In addition there is a need for methods to assay candidate therapeutic substances for modulating expression of these genes. These substances might be recombinant

protein expressed by the identified genes or antibodies that bind to the identified proteins. There is yet additionally a need for an effective method of identifying target molecules or related components. These and related needs and defects are addressed in the present invention.

5

### **Novel kallikrein-like/coagulation factor XI-like Proteins and Nucleic Acids Encoding Same**

FCTR6 is surprisingly found to be differentially expressed in clear cell Renal cell carcinoma tissues vs the normal adjacent kidney tissues. The present invention discloses a novel protein encoded by a cDNA and/or by genomic DNA and proteins similar to it, namely, new proteins bearing sequence similarity to kallikrein-like, nucleic acids that encode these proteins or fragments thereof, and antibodies that bind immunospecifically to a protein of the invention. It may have use as a therapeutic agent in the treatment of renal cancer and liver cirrhosis.

15

### **The utility of kallikrein family members in protein therapy of Renal cancer**

The treatment of renal cell carcinoma with recombinant kallikrein could improve disease outcome through several potential mechanisms. The literature suggests that members of this protein family are inhibitory to the process of angiogenesis, a process of vital importance to tumor progression. Renal cell carcinoma is known to be a highly angiogenic cancer. Thus, treatment of renal cell carcinoma with kallikrein may effectively shutdown the active recruitment of a blood supply to a tumor. Members of this protein family are known to play a role in vascular coagulation. Similar to anti-angiogenic therapy, a factor produced by cancer cells that is pro-coagulatory may also act to inhibit cancer growth by effectively “clogging” the tumor vascular supply. In addition, through its proteolytic activity, kallikrein may degrade ECM proteins or growth factors necessary for the progressive growth of cancer cells. Following is a relevant reference underlining the importance of Kallikrein in cancer therapy.

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### **The New Human Kallikrein Gene Family: Implications in Carcinogenesis.**

Diamandis EP; Yousef GM; Luo I; Magklara I; Obiezu CV

Department of Pathology and Laboratory Medicine, Mount Sinai Hospital, Toronto, Ontario, Canada.

Trends Endocrinol Metab 2000 Mar;11(2):54-60.

ABSTRACT: The traditional human kallikrein gene family consists of three genes, namely KLK1 [encoding human kallikrein 1 (hK1) or pancreatic/renal kallikrein], KLK2 (encoding hK2, previously known as human glandular kallikrein 1) and KLK3 [encoding hK3 or prostate-specific antigen (PSA)]. KLK2 and KLK3 have important applications in prostate cancer diagnostics and, more recently, in breast cancer diagnostics. During

the past two to three years, new putative members of the human kallikrein gene family have been identified, including the PRSSL1 gene [encoding normal epithelial cell-specific 1 gene (NES1)], the gene encoding zyme/protease M/neurosin, the gene encoding prostase/KLK-L1, and the genes encoding neuropsin, stratum corneum chymotryptic enzyme and trypsin-like serine protease. Another five putative kallikrein genes, provisionally named KLK-L2, KLK-L3, KLK-L4, KLK-L5 and KLK-L6, have also been identified. Many of the newly identified kallikrein-like genes are regulated by steroid hormones, and a few kallikreins (NES1, protease M, PSA) are known to be downregulated in breast and possibly other cancers. NES1 appears to be a novel breast cancer tumor suppressor protein and PSA a potent inhibitor of angiogenesis. This brief review summarizes recent developments and possible applications of the newly defined and expanded human kallikrein gene locus.

#### **The utility of kallikrein-like/coagulation factor XI-like family members in protein therapy of liver cirrhosis**

Results related to inflammation shown below in Example A, Table CC3, panel 4, indicate over-expression of 27455183.0.19 in the liver cirrhosis sample, as compared to panel 1 data (Table CC1), where there is little or no expression in normal adult liver. Panel 4 was generated from various human cell lines that were untreated or resting as well as the same cells that were treated with a wide variety of immune modulatory molecules. There are several disease tissues represented as well as organ controls.

#### **Potential Role(s) of FCTR6 in Inflammation:**

Liver cirrhosis occurs in patients with hepatitis C and also in alcoholics. This protein is 41% related to coagulation factor XI and its potential role in liver cirrhosis may be related to cleavage of kininogen. A reference for this follows:

*Thromb Haemost* 2000 May;83(5):709-14 High molecular weight kininogen is cleaved by FXIa at three sites: Arg409-Arg410, Lys502-Thr503 and Lys325-Lys326. Mauron T, Lammle B, Wuillemin WA Central Hematology Laboratory, University of Bern, Inselspital,

Switzerland.

Abstract:

We investigated the cleavage of high molecular weight kininogen (HK) by activated coagulation factor XI (FXIa) in vitro. Incubation of HK with FXIa resulted in the generation of cleavage products which were subjected to SDS-Page and analyzed by silverstaining, ligand-blotting and immunoblotting, respectively. Upon incubation with FXIa, bands were generated at 111, 100, 88 kDa on nonreduced and at 76, 62 and 51 kDa on reduced gels. Amino acid sequence analysis of the reaction mixtures revealed three cleavage sites at Arg409-Arg410, at Lys502-Thr503 and at Lys325-Lys326. Analysis of HK-samples incubated with FXIa for 3 min, 10 min and 120 min indicated HK to be cleaved first at Arg409-Arg410, followed by cleavage at Lys502-Thr503 and then at Lys325-Lys326. In conclusion, HK is cleaved by FXIa at three sites. Cleavage of HK by FXIa results in the loss of the surface binding site of HK, which may constitute a mechanism of inactivation of HK and of control of contact system activation.

#### Impact of Therapeutic Targeting of FCTR6 in Inflammation:

Therapeutic targeting of FCTR6 with a monoclonal antibody is anticipated to limit or block the extent of breakdown of kininogen and thereby reduce the degradation of liver that occurs in liver cirrhosis. A pertinent reference is:

*Thromb Haemost* 1999 Nov;82(5):1428-32 Parallel reduction of plasma levels of high and low molecular weight kininogen in patients with cirrhosis.

Cugno M, Scott CF, Salerno F, Lorenzano E, Muller-Esterl W, Agostoni A, Colman RW  
Department of Internal Medicine, IRCCS Maggiore Hospital, University of Milan, Italy.  
massimo.cugno@unimi.it

Abstract:

Little is known about the regulation of high-molecular-weight-kininogen (HK) and low-molecular-weight-kininogen (LK) or the relationship of each to the degree of liver function impairment in patients with cirrhosis. In this study, we evaluated HK and LK quantitatively by a recently described particle concentration fluorescence immunoassay (PCFIA) and qualitatively by SDS PAGE and immunoblotting analyses in plasma from 33 patients with cirrhosis presenting various degrees of impairment of liver function. Thirty-three healthy subjects served as normal controls. Patients with cirrhosis had significantly lower plasma levels of HK (median 49 microg/ml [range 22-99 microg/ml]) and LK (58 microg/ml [15-100 microg/ml]) than normal subjects (HK 83 microg/ml [65-115 microg/ml]; LK 80

microg/ml [45-120 microg/ml]) ( $p < 0.0001$ ). The plasma concentrations of HK and LK were directly related to plasma levels of cholinesterase ( $P < 0.0001$ ) and albumin ( $P < 0.0001$  and  $P < 0.001$ ) and inversely to the Child-Pugh score ( $P < 0.0001$ ) and to prothrombin time ratio ( $P < 0.0001$ ) (reflecting the clinical and laboratory abnormalities in liver disease). Similar to normal individuals, in patients with cirrhosis, plasma HK and LK levels paralleled one another, suggesting that a coordinate regulation of those proteins persists in liver disease. SDS PAGE and immunoblotting analyses of kininogens in cirrhotic plasma showed a pattern similar to that observed in normal controls for LK (a single band at 66 kDa) with some lower molecular weight forms noted in cirrhotic plasma. A slight increase of cleavage of HK (a major band at 130 kDa and a faint but increased band at 107 kDa) was evident. The increased cleavage of HK was confirmed by the lower cleaved kininogen index (CKI), as compared to normal controls. These data suggest a defect in hepatic synthesis as well as increased destructive cleavage of both kininogens in plasma from patients with cirrhosis. The decrease of important regulatory proteins like kininogens may contribute to the imbalance in coagulation and fibrinolytic systems, which frequently occurs in cirrhotic patients.

In summary, the differential expression of FCTR6 (Kallikrein family) in renal cell carcinoma is an important finding that could have immense potential in renal carcinogenesis. In addition, overexpression of the above gene in liver cirrhosis demonstrates its anticipated use as an immunotherapeutic target.

## FCTR7

The novel nucleic acid of 1498 nucleotides FCTR7 (also designated. 32592466.0.64) encoding a novel trypsin inhibitor-like protein is shown in Table 7A. An ORF begins with an ATG initiation codon at nucleotides 470-472 and ends with a TAA codon at nucleotides 1369-1371. Putative untranslated regions, if any, are found upstream from the initiation codon and downstream from the termination codon.

**Table 7A. FCTR7 Nucleotide Sequence (SEQ ID NO:24)**

AGGCGCCTGGTTCTGCGCGTACTGGCTGTACGGAGCAGGAGCAAGAGGTGCGCCGAGCCTCCGCCGCCGAGCCTCGTTCGTGT  
 CCCC GCCCCTCGCTCCTGCAGCTACTGCTCAGAAACGCTGGGGCGCCACCCTGGCAGACTAACGAAGCAGCTCCCTTCCCACC  
 CCAACTGCAGGTCTAATTTTGGACGCTTTGCCTGCCATTTCTTCCAGGTGAGGGAGCCGAGAGGCGGAGGCTCGCGTATTCC  
 TGCAGTCAGCACCCACGTGCCCCCGGACGCTCGGTGCTCAGGCCCTTCGCGAGCGGGGCTCTCCGTCTGCGGTCCCTTGTGAA  
 GGCTCTGGGCGGCTGCAGAGGCCGGCCGTCCGGTTTGGCTCACCTCTCCAGGAACTTCACACTGGAGAGCCAAAAGGAGTGG  
 AAGAGCCTGTCTTGAGATTTTCTGGGAAATCCTGAGGTCATTCAATATGAAGTGTACCGCGCGGGAGTGGCTCAGAGTAAC  
 CACAGTGCTGTTTCATGGCTAGAGCAATTCAGCCATGGTGGTTCCTCAATGCCACTTTATTGGAGAACTTTGGAAAAATACAT  
 GGATGAGGATGGTGAGTGGTGGATAGCCAAACAACGAGGGAAAAGGGCCATCACAGACAATGACATGCAGAGTATTTTGGACCT  
 TCATAATAAATTACGAAGTCAGGTGTATCCAACAGCCTCTAATATGGAGTATATGACATGGGATGTAGAGCTGGAAAGATCTGC  
 AGAATCCAGGGCTGAAATTGCTTGTGGGAACATGGACCTGCAAGCTTGCTTCCATCAATTGGACAGAATTTGGGAGCACACTGG  
 GGAAGATATAGGCCCCGACGTTTCATGTACAATCGTGGTATGATGAAGTGAAAGACTTTAGCTACCCATATGAACATGAATGC

AACCCATATTGTCCATTCAGGTGTTCTGGCCCTGTATGTACACATTATACACAGGTGCTGTGGGCAACTAGTAACAGAATCGGT  
 TGTGCCATTAATTTGTGTGCTAACATGAACATCTGGGGGCAGATATGGCCCAAAGCTGTCTACCTGGTGTGCAATTACTCCCCA  
 AAGGGAACTGGTGGGGCCATGCCCCTTACAAACATGGGCGGCCCTGTTCTGCTTGCCACCTAGTTTTGGAGGGGGCTGTAGA  
 5 GAAAATCTGTGCTACAAAGAAGGGTCAGACAGGTATTATCCCCCTCGAGAAGAGGAAACAAATGAAATAGAACGGCAGCAGTCA  
 CAAGTCCATGACACCCATGTCCGGACAAGATCAGATGATAGTAGCAGAAATGAAGTCATTAGCTTTGGGAAAAGTAATGAAAAT  
 ATAATGGTTTTAGAAATCCTGTGTTAAATATTGCTATATTTTCTTAGCAGTTATTTCTACAGTTAATTACATAGTCATGATTGT  
 TCTACGTTTCATATATTATATGGTGCTTTGTATATGCCCTAATAAAATGAATCTAAACATTGAAAAAA

The FCTR7 protein encoded by SEQ ID NO:24 has 300 amino acid residues and is  
 10 presented using the one-letter code in Table 7B. The FCTR7 gene was found to be expressed  
 in: brain; germ cell tumors. FCTR7 gene maps to Unigene cluster Hs.182364 which is  
 expressed in the following tissues: brain, breast, ear, germ cell, heart, liver, lung, whole  
 embryo, ovary, pancreas, pooled, prostate, stomach, testis, uterus, vascular. Therefore the  
 FCTR7 protein described in this invention is also expressed in the above tissues.

15 The SignalP, Psort and/or Hydropathy profile for FCTR7 predict that this sequence has  
 a signal peptide and is likely to be localized outside of the cell with a certainty of 0.4228. The  
 SignalP shows a cleavage site between amino acids 20 and 21, *i.e.*, at the dash in the sequence  
 amino acid ARA-IP. The predicted molecular weight of FCTR7 is 34739.9 Daltons.  
 Hydropathy profile shows an amino terminal hydrophobic region. This region could function  
 20 as a signal peptide and target the invention to be secreted or plasma membrane localized.

#### Table 7B. Encoded FCTR7 protein sequence (SEQ ID NO:25).

MKCTAREWLRVTTVLFMARAI PAMVVPENATLLEKLLEKYMDDEGEWWIAKQRGKRAITDNDMQSILDLHNLRSQVYPTASNME  
 YMTWDVELERSAESRAESCLWEHGPA SLLPSIGQNLGAHWGRYRPPTFHVQSWYDEVKDFSYPYEHECNPYCPFRCSGPVCTHY  
 25 TQVVWATSNRIGCAINLCHNMNIWQIWP KAVYLV CNYS PKGNWWGHAPYKHGRPC SACPPSFGGGCRENLCYKEGSDRYPPR  
 EETNEIERQQSQVHDTHVRTRSDSSRNEVISFGKSNENIMVLEILC

This gene maps to Unigene cluster Hs.182364 which has been assigned the following  
 mapping information shown in table 7C. Therefore the chromosomal assignment for this gene  
 is the same as that for Unigene cluster 182364.

#### Table 7C. Mapping Information.

30 **Chromosome:** 8  
**Gene Map 98:** Marker SHGC-32056 , Interval D8S279-D8S526  
**Gene Map 98:** Marker SGC32056 , Interval D8S526-D8S275  
**Gene Map 98:** Marker sts-G20223 , Interval D8S526-D8S275  
**Gene Map 98:** Marker stSG30385 , Interval D8S526-D8S275  
**Whitehead map:** EST67946, Chr.8  
**dbSTS entries:** G25853, G29349, G20223

The predicted amino acid sequence was searched in the publicly available GenBank  
 database

FCTR7 protein showed Score = 743 (261.5 bits), Expect = 1.4e-73, P = 1.4e-73, 54 %

**Table 7D. BLAST X search results are shown below:**

ptnr:SWISSNEW-ACC:019010 CYSTEINE-RICH SECRETORY PROTE... +2 258 9.4e-21 1  
(SEQ ID NO:92)

**Table 7E. BLASTN of FCTR7 against Putative secretory protein precursor (SEQ ID NO:93)**

Query: 604 gtggtggatagccaaacaacgagggaaaagggccatcacagacaatgacatgcagagtat 663  
|||||

WO 01/66747

PCT/US01/07160

Sbjct: 241 gtggtggatagccaaacaacgagggaaaagggccatcacagacaatgacatgcagagtat 300  
 Query: 664 tttggaccttcataataaattacgaagtcaggtgtatccaacagcctctaataatggagta 723  
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||  
 5 Sbjct: 301 tttggaccttcataataaattacgaagtcaggtgtatccaacagcctctaataatggagta 360  
 Query: 724 tatgacatgggatgtagagctggaaagatctgcagaatccagggctgaaa-ttgcttggtg 782  
 ||||||||||||||||||||||||||||||||||||||||||||| ||||||||| |||||||||  
 10 Sbjct: 361 tatgacatgggatgtagagctggaaagatctgcagaatcctgggctgaaagttgcttggtg 420  
 Query: 783 ggaacatggacctgcaagcttgcttccatcaattggacagaatttgggagcacactgggg 842  
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||  
 Sbjct: 421 ggaacatggacctgcaagcttgcttccatcaattggacagaatttgggagcacactgggg 480  
 15 Query: 843 aagatataggcccccgacgtttcatgtacaatcgtgggtatgatgaagtgaagacttttag 902  
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||  
 Sbjct: 481 aagatataggcccccgacgtttcatgtacaatcgtgggtatgatgaagtgaagacttttag 540  
 Query: 903 ctacccatatgaacatgaatgcaaccatattgtccattcaggtgttctggccctgtatg 962  
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||  
 20 Sbjct: 541 ctacccatatgaacatgaatgcaaccatattgtccattcaggtgttctggccctgtatg 600  
 Query: 963 tacacattatacacagggtcgtgtgggcaactagtaacagaatcggttggtgccaattaattt 1022  
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||  
 25 Sbjct: 601 tacacattatacacagggtcgtgtgggcaactagtaacagaatcggttggtgccaattaattt 660  
 Query: 1023 gtgtcataacatgaacatctgggggcagatatggcccaaagctgtctacctggtgtgcaa 1082  
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||  
 30 Sbjct: 661 gtgtcataacatgaacatctgggggcagatatggcccaaagctgtctacctggtgtgcaa 720  
 Query: 1083 ttactccccaaggggaaactggtggggccatgcccttacaaacatgggcggccctgttc 1142  
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||  
 35 Sbjct: 721 ttactccccaaggggaaactggtggggccatgcccttacaaacatgggcggccctgttc 780  
 Query: 1143 tgcttgcccacctagtttttgaggggggctgtagagaaaatctgtgctacaaagaagggtc 1202  
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||  
 40 Sbjct: 781 tgcttgcccacctagtttttgaggggggctgtagagaaaatctgtgctacaaagaagggtc 840  
 Query: 1203 agacaggtattatccccctcgagaagaggaaacaaatgaaatagaacggcagcagtcaca 1262  
 ||||||||||||||||||||||||||||||||||||||||||||| |||||||||||  
 45 Sbjct: 841 agacaggtattatccccctcgagaagaggaaacaaatgaaatagaacgacagcagtcaca 900  
 Query: 1263 agtccatgacacccatgtccggacaagatcagatgatagtagcagaaatgaagtcac 1319  
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||  
 50 Sbjct: 901 agtccatgacacccatgtccggacaagatcagatgatagtagcagaaatgaagtcac 957  
 Score = 339 bits (171), Expect = 3e-90  
 Identities = 174/175 (99%)  
 Strand = Plus / Plus  
 55 Query: 1317 cattagctttgggaaaagtaatgaaaatataatggtttttagaaatcctgtgttaaatt 1376  
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||  
 60 Sbjct: 1779 cattagctttgggaaaagtaatgaaaatataatggtttttagaaatcctgtgttaaatt 1838  
 Query: 1377 gctatatattttcttagcagttattttctacagtttaattacatagtcattgttctacgtt 1436

|||||  
Sbjct: 1839 gctatatatttcttagcagttatttctacagttaattacatagtcattgattgttctacgtt  
1898

5 Query: 1437 tcatatattatatggtgctttgtatatgcccctaataaaaatgaatctaaacattg 1491  
|||||  
Sbjct: 1899 tcatatattatatggtgctttgtatatgccactaataaaaatgaatctaaacattg 1953

The FCTR7 amino acid has 284 of 285 amino acid residues (99%) identical to, and 284  
10 of 285 amino acid residues (99%) similar to, the 500 amino acid Putative secretory protein  
precursor [*Homo sapiens*] (GenBank-Acc No.: AF142573) (SEQ ID NO:94) (Table 7F).

**Table 7F. BLASTP alignments of FCTR7 against Putative secretory protein precursor,  
(SEQ ID NO:94)**

15 >gi|12002311|gb|AAG43287.1|AF142573.1 (AF142573) putative secretory protein  
precursor [*Homo sapiens*]  
Length = 500

Score = 581 bits (1499), Expect = e-165  
Identities = 284/285 (99%), Positives = 284/285 (99%)

20 Query: 1 MKCTAREWLRVTTVLFMARAI PAMVVPNATLLEKLLLEKYMDDEDGEWWIAKQRGKRAITDN 60  
|||||  
Sbjct: 1 MKCTAREWLRVTTVLFMARAI PAMVVPNATLLEKLLLEKYMDDEDGEWWIAKQRGKRAITDN 60

25 Query: 61 DMQSILDLHNKLR SQVYPTASNMEYMTWDVELERSAESRAESCLWEHGPASLLPSIGQNL 120  
|||||  
Sbjct: 61 DMQSILDLHNKLR SQVYPTASNMEYMTWDVELERSAESWAESCLWEHGPASLLPSIGQNL 120

30 Query: 121 GAHWGRYRPPTFHVQSWYDEVKDFSYPYEHECNPYCPFRCSGPVCTHYTQVWVWATSNRIG 180  
|||||  
Sbjct: 121 GAHWGRYRPPTFHVQSWYDEVKDFSYPYEHECNPYCPFRCSGPVCTHYTQVWVWATSNRIG 180

35 Query: 181 CAINLCHNMNIWGQIWPKAVYLV CNYS PKGNWWGHAPYKHGRPCSACPPSFGGGCRENL C 240  
|||||  
Sbjct: 181 CAINLCHNMNIWGQIWPKAVYLV CNYS PKGNWWGHAPYKHGRPCSACPPSFGGGCRENL C 240

40 Query: 241 YKEGSDRYYP PREEETNEIERQQSQVHDTHVRTRSDSSRNEVIS 285  
|||||  
Sbjct: 241 YKEGSDRYYP PREEETNEIERQQSQVHDTHVRTRSDSSRNEVIS 285

The FCTR7 amino acid has 137 of 176 amino acid residues (78%) identical to, and 151  
of 176 amino acid residues (86%) similar to, the 188 amino acid Late gestation lung protein 1  
[*Rattus norvegicus*] (GenBank-Acc No.: AF109674) (SEQ ID NO:95) (Table 7G).

**Table 7G. BLASTP alignments of FCTR7 against Late gestation lung protein 1, (SEQ ID  
NO:95)**

45 >gi|4324682|gb|AAD16986.1| (AF109674) late gestation lung protein 1 [*Rattus  
norvegicus*]  
Length = 188

50 Score = 277 bits (709), Expect = 1e-73  
Identities = 137/176 (78%), Positives = 151/176 (86%)

Query: 68 LHNKLR SQVYPTASNMEYMTWDVELERSAESRAESCLWEHGPASLLPSIGQNLGAHWGRY 127

Sbjct: 2     ||||| |||| ||||| |||||     |     ||||| ||||| ||||| |||||  
 LHNKLRGQVYPPASNMEYMTWDEELERSAAAWAQRCLWEHGPASLLVSIQNLAVHWGRY 61  
 Query: 128 RPPTFHVQSWYDEVKDFSYPYEHECNPYCPFRCSGPVCTHYTQVWVWATSNRIGCAINLCH 187  
 5     | | ||||| ||||| ++||| ||||| +|| |||| +||| ||| +||| +||| +||| ++ |  
 Sbjct: 62     RSPGFHVQSWYDEVKDYTFYPHECNPWCPERC SGAMCTHYTQMVWATTNKIGCAVHTCR 121  
 Query: 188 NMNIWGQIWP KAVYLV CNYS PKGNWWGHAPYKHGRPCSACPPSFGGGCRENL CYKE 243  
 +|++|| || ||||| ||||| || ||||| || || +||| |||| +|  
 10 Sbjct: 122 SMSVWGD IWENAVYLV CNYS PKGNWIGEAPYKHGRPCSECPSSYGGGCRNNLCYRE 177

The FCTR7 amino acid has 130 of 237 amino acid residues (55%) identical to, and 165  
 of 237 amino acid residues (70%) similar to, the 258 amino acid R3H domain-containing  
 preproprotein; 25 kDa trypsin inhibitor [*Homo sapiens*] (GenBank-Acc No.: D45027) (SEQ  
 15 ID NO:96) (Table 7H).

**Table 7H. BLASTP alignments of FCTR7 against R3H domain-containing  
 preproprotein, 25 kDa trypsin inhibitor (SEQ ID NO:96)**

>gi|7705676|ref|NP\_056970.1| R3H domain-containing preproprotein; 25 kDa  
 20 trypsin inhibitor; R3H  
       domain (binds single-stranded nucleic acids) containing  
       [*Homo sapiens*]  
       gi|2943716|dbj|BAA25066.1| (D45027) 25 kDa trypsin inhibitor [*Homo sapiens*]  
       Length = 258  
 25  
       Score = 265 bits (678), Expect = 4e-70  
       Identities = 130/237 (55%), Positives = 165/237 (70%), Gaps = 3/237 (1%)  
 Query: 12     TTVLFMARAI PAMVVP NATLLEK LLEKYMD EDEGEWWIAKQ RGRKRAITDNDMQS ILDLH NK 71  
 30     +| | + +     +     | | +|     | + +|     | | | | | + | | | +| | | | +|  
 Sbjct: 20     STVVLLNSTD SSPPTNNFTD IEAALKAQLDSAD---IPKARRKRYISQNDMIAILDYHNQ 76  
 Query: 72     LRSQVYPTASNMEYMTWDVELERSAESRAESCLWEHGPASLLPSIQNLGAHWGRYRPPT 131  
       +| +| +| | +| | | | | | | | | | | | | | | +| +| | | | | | | | | |  
 35 Sbjct: 77     VRGKVFPFAANMEYMWVDENLAKSAEAWAATCIWDHGPSYLLRFLGQNL SVRTGRYRSIL 136  
 Query: 132 FHVQSWYDEVKDFSYPYEHECNPYCPFRCSGPVCTHYTQVWVWATSNRIGCAINLCHNMNI 191  
       | + | | | | | | | + + + | | + | | | | | | | | | | | | | | | | + | | | +  
 40 Sbjct: 137 QLVKFWYDEVKDYAFYPQDCNPRCPMRCFGPMCTHYTQMVWATSNRIGCAIHTCQNMNV 196  
 Query: 192 WGQIWP KAVYLV CNYS PKGNWWGHAPYKHGRPCSACPPSFGGGCRENL CYKEGSDRY 248  
       | | +| +| | | | | | | +| | | | | | | | | | | | | | | +| | | +     +     |  
 Sbjct: 197 WGSVWRRAYLV CNYAPKGNWIGEAPYKVGVP CSSCPPSYGGGCTDNL CFPGVTSNY 253

45     The FCTR7 amino acid has 109 of 233 amino acid residues (47%) identical to, and 146  
 of 233 amino acid residues (63%) similar to, the 253 amino acid Novel protein similar to a  
 trypsin inhibitor [*Homo sapiens*] 25 kDa trypsin inhibitor (EMBL Acc No.: AL117382) (SEQ  
 ID NO:97) (Table 7I).

**Table 7I. BLASTP alignments of FCTR7 against Novel protein similar to a trypsin inhibitor, (SEQ ID NO:97)**

5 >gi|9885193|emb|CAC04190.1| (AL117382) dJ881L22.3 (novel protein similar to  
a trypsin inhibitor) [Homo sapiens]  
Length = 253

10 Score = 225 bits (575), Expect = 4e-58  
Identities = 109/233 (47%), Positives = 146/233 (63%), Gaps = 8/233 (3%)

Query: 10 RVTTVLFMARAIPAMVVPNATLLEKLLLEKYMDEEDGEWWIAKQRGKRAITDNDMQSILDLH 69  
+ | | | | | + | + | + + | | | + | | ++ | |  
15 Sbjct: 19 QAVNALIMP NATPAPAQPESTAMRL-----SGLEVPRYRRKRHISVRDMNALLDYH 70

Query: 70 NKLRSQVYPTASNMEYMTWDVELERSAESRAESCLWEHG PASLLPSIGQNLGAHWGRYRP 129  
| + | + | | | | + | | | | | | | | | | | + | + | + | | | | | + | + | |  
20 Sbjct: 71 NHIRASVYPPAANMEYMVWDKRLARAAEAWATQCIWAHG PSQLMRYVGQNLSIHSGQYRS 130

Query: 130 PTFHVQSWYDEVKDFSYPYEHECNPYCPFRCSGPVCTHYTQV VWATSNRIGCAINLCHNM 189  
++ | | + | + + | + | | + | | + | | + | | + | | + | | + | | + | ++  
Sbjct: 131 VVDLMKSWSEEKWHYLFAPRDCNPHCPWRCDGPTCSHYTQMVWASSNRLGCAIHTCSSI 190

25 Query: 190 NIWGQIWPKAVYLV CNYSPKGNWWGHAPYKHGRPCSACPPSF GGGCRENL CYK 242  
++ | | | + | | | | | + | | | | + | | + | | + | | + | | + | | + | + |  
Sbjct: 191 SVWGNTWHRAAYLV CNYAIKGNWIGESPYKMGKPCSSCPPSYQ GSCNSNMCFK 243

30 The FCTR7 amino acid has 129 of 237 amino acid residues (54%) identical to, and 167  
of 237 amino acid residues (70%) similar to, the 258 amino acid 25 kDa Trypsin Inhibitor  
from *Homo sapiens* (EMBL Acc No.: O43692) (SEQ ID NO:88) (Table 7J).

**Table 7J. BLASTP alignments of FCTR7 against 25 kDa Trypsin Inhibitor, (SEQ ID NO:88)**

35 ptnr: SPTREMBL-ACC:O43692 25 KDA TRYPSIN INHIBITOR - Homo sapiens (Human), 258  
aa.

Score = 743 (261.5 bits), Expect = 1.6e-73, P = 1.6e-73  
40 Identities = 129/237 (54%), Positives = 167/237 (70%)

The FCTR7 amino acid has 79 of 193 amino acid residues (40%) identical to, and 110  
of 193 amino acid residues (56%) similar to, the 266 amino acid Glioma Pathogenesis-Related  
Protein (RTVP-1 Protein) - *Homo sapiens* (SWISSPROT Acc No.: P48060) (SEQ ID NO:90)  
(Table 7K).

**Table 7K. BLASTP alignments of FCTR7 against Glioma Pathogenesis-Related Protein, (SEQ ID NO:90)**

ptnr:SWISSPROT-ACC:P48060 GLIOMA PATHOGENESIS-RELATED PROTEIN (RTVP-1  
 5 PROTEIN) - *Homo sapiens* (Human), 266 aa  
 Score = 314 (110.5 bits), Expect = 4.7e-28, P = 4.7e-28  
 Identities = 79/193 (40%), Positives = 110/193 (56%)

10 The FCTR7 amino acid has 66 of 186 amino acid residues (35%) identical to, and 91  
 of 186 amino acid residues (48%) similar to, the 186 amino acid Neutrophil granules matrix  
 glycoprotein SGP28 precursor from *Homo sapiens* (SWISSPROT Acc No.: S68691) (SEQ ID  
 NO:98) (Table 7L).

**Table 7L. BLASTP alignments of FCTR7 against Neutrophil granules matrix glycoprotein, (SEQ ID NO:98)**

15 ptnr:PIR-ID:S68691 neutrophil granules matrix glycoprotein SGP28 precursor -  
 human  
 Score = 254 (89.4 bits), Expect = 1.1e-21, P = 1.1e-21  
 Identities = 66/186 (35%), Positives = 91/186 (48%)  
 20

A novel developmentally regulated gene with homology to a tumor derived trypsin  
 inhibitor is expressed in lung mesenchyme, as described in Am. J. Physiol. 0:0-0(1999).  
 cDNA cloning of a novel trypsin inhibitor with similarity to pathogenesis-related proteins, and  
 its frequent expression in human brain cancer cells is disclosed in Biochim. Biophys. Acta  
 25 1395:202-208(1998). RTVP-1, a novel human gene with sequence similarity to genes of  
 diverse species, is expressed in tumor cell lines of glial but not neuronal origin, as published in  
 Gene 180:125-130(1996). The human glioma pathogenesis-related protein is structurally  
 related to plant pathogenesis-related proteins and its gene is expressed specifically in brain  
 tumors (Gene 159:131-135(1995)). Structure comparison of human glioma pathogenesis-  
 30 related protein GliPR and the plant pathogenesis-related protein P14a indicates a functional  
 link between the human immune system and a plant defense system (Proc. Natl. Acad. Sci.  
 U.S.A. 95:2262-2266(1998)). GliPR is highly expressed in the human brain tumor,  
 glioblastoma multiform/astrocytoma, but neither in normal fetal or adult brain tissue, nor in  
 other nervous system tumors. GliPR belongs to a family that groups mammalian SCP/TPX1;  
 35 insects AG3/AG5; FUNGI SC7/SC14 and plants PR-1. SGP28, a novel matrix glycoprotein in  
 specific granules of human neutrophils with similarity to a human testis-specific gene product  
 and to a rodent sperm-coating glycoprotein (FEBS Lett. 380, 246-250, 1996). The primary  
 structure and properties of helothermine, a peptide toxin that blocks ryanodine receptors is

described in Biophys. J. 68:2280-2288(1995). As GliPR, Helothermine belongs to a family that groups mammalian SCP/TPX1; insects AG3/AG5; FUNGI SC7/SC14 and plants PR-1.

Based upon homology, FCTR7 protein and each homologous protein or peptide may share at least some activity.

5

#### Therapeutic uses:

FCTR7 protein has homology to trypsin inhibitors, Q91055 helothermine, tumor derived tyrpsin inhibitors, glioma pathogenesis-related protein, Q9Z0U6 LATE GESTATION LUNG PROTEIN 1, and to the Prosite family which groups mammalian SCP/TPX1;INSECTS AG3/AG5; FUNGI SC7/SC14 AND PLANTS PR-1 proteins. Therefore the FCTR7 protein disclosed in this invention could function like the proteins which it has homology to. These functions include tissue development *in vitro* and *in vivo*, and cancer pathogenesis.

Based the tissue expression pattern, the gene is implicated in diseases of tissues in which it is expressed. These diseases include but are not limited to:

- Glioma,
- cancer,
- lung diseases,
- gestation,
- male and female reproductive diseases,
- deafness,
- neurological disorders,
- gastric disorders, and
- pancreatic diseases like diabetes.

25

These materials are further useful in the generation of antibodies that bind immunospecifically to the novel FCTR7 substances for use in therapeutic or diagnostic methods. These antibodies may be generated according to methods known in the art, using prediction from hydrophobicity charts, as described in the "Anti-FCTR7 Antibodies" section below. In one embodiment, a contemplated FCTR7 epitope is from aa 40 to 120. In another embodiment, a FCTR7 epitope is from aa 130 to 170. In additional embodiments, FCTR7 epitopes are from aa 210 to 230, and from aa 240 to 280.

30

**TABLE 8A: Summary Of Nucleic Acids And Proteins Of The Invention**

| Name  | Tables    | Clone; Description of Homolog                                         | Nucleic Acid<br>SEQ ID NO | Amino Acid<br>SEQ ID NO |
|-------|-----------|-----------------------------------------------------------------------|---------------------------|-------------------------|
| FCTR1 | 1A, 1B,   | 58092213.0.36 follistatin-like protein                                | 1                         | 2                       |
| FCTR2 | 2A, 2B    | AC012614_1.0.123; KIAA1061-like protein                               | 3                         | 4                       |
| FCTR3 | 3A, 3B    | 10129612.0.118; neurestin-like protein                                | 5                         | 6                       |
|       | 3C, 3D    | 10129612.0.405; neurestin-like protein                                | 7                         | 8                       |
|       | 3E        | 10129612.0.154; neurestin-like protein                                | 9                         |                         |
|       | 3F        | 10129612.0.67; neurestin-like protein                                 | 10                        |                         |
|       | 3G        | 10129612.0.258; neurestin-like protein                                | 11                        |                         |
|       | 3H, 3I    | 10129612.0.352; neurestin-like protein                                | 12                        | 13                      |
| FCTR4 | 4A, 4B    | 29692275.0.1; NF-Kappa-B P65delta3-like protein                       | 14                        | 15                      |
| FCTR5 | 5A, 5B    | 32125243.0.21; human complement C1R component precursor -like protein | 16                        | 17                      |
|       | 5C, 5D    |                                                                       | 18                        | 19                      |
| FCTR6 | 6A, 6B    | 27455183.0.19; novel human blood coagulation factor XI -like protein  | 20                        | 21                      |
|       | 6C, 6D    | 27455183.0.145; novel human blood coagulation factor XI -like protein | 22                        | 23                      |
| FCTR7 | 7A, 7B    | 32592466.0.64; trypsin inhibitor -like protein                        | 24                        | 25                      |
| FCTR1 | Example 2 | Ag809 Forward                                                         | 26                        |                         |
| FCTR1 | Example 2 | Ag809 Probe                                                           | 27                        |                         |
| FCTR1 | Example 2 | Ag809 Reverse                                                         | 28                        |                         |
| FCTR4 | Example 2 | Ag2773 Forward                                                        | 29                        |                         |
| FCTR4 | Example 2 | Ag2773 Probe                                                          | 30                        |                         |
| FCTR4 | Example 2 | Ag2773 Reverse                                                        | 31                        |                         |
| FCTR5 | Example 2 | Ag427 Forward                                                         | 32                        |                         |
| FCTR5 | Example 2 | Ag427 Probe                                                           | 33                        |                         |
| FCTR5 | Example 2 | Ag427 Reverse                                                         | 34                        |                         |
| FCTR6 | Example 2 | Ag1541 Forward                                                        | 35                        |                         |
| FCTR6 | Example 2 | Ag1541 Probe                                                          | 36                        |                         |
| FCTR6 | Example 2 | Ag1541 Reverse                                                        | 37                        |                         |

**TABLE 8B: Summary of Query Sequences Disclosed**

| Table  | Database  | Acc. No. | Sequence Name                   | Species | SEQ ID NO. |
|--------|-----------|----------|---------------------------------|---------|------------|
| 1C, 1K | remtrEmbl | BAA21725 | IGFBP-like protein              | mouse   | 38         |
| 1D     | sptrEmbl  | Q61581   | Follistatin-like protein-2      | Mouse   | 39         |
| 1E     | SptrEmbl  | Q07822   | Mac25 protein                   | Human   | 40         |
| 1F, 1K | SptrEmbl  | O88812   | Mac25 protein                   | Mouse   | 41         |
| 1G, 1K | SptrEmbl  | Q16270   | Prostacyclin-stimulating factor | Human   | 42         |
| 1H, 1K | PIR       | B40098   | Colorectal cancer suppressor    | Rat     | 43         |
| 1I     | TrEmblnew | AAD9360  | PTP sigma (brain) precursor     | Human   | 44         |
| 1J     | SptrEmbl  | Q13332   | PTP sigma precursor             | Human   | 45         |
| 2C     | GenBank   | AB028984 | KIAA1061 cDNA                   | Human   | 46         |

|               |               |             |                                                         |                           |    |
|---------------|---------------|-------------|---------------------------------------------------------|---------------------------|----|
| 2D            | TrEmblne<br>w | BAA85677    | KIAA1263                                                | Human                     | 47 |
| 2E            | TrEmblne<br>w | BAA83013    | KIAA1061 protein fragment                               | Human                     | 48 |
| 2F            | Embl          | CAB70877.1  | Hypothetical protein<br>DKFzp566D234.1                  | Human                     | 49 |
| 2G            | GenBank       | Q62632      | Follistatin-related protein-1 precursor                 | Rat                       | 50 |
| 2H            | GenBank       | Q62536      | Follistatin-related protein-1 precursor                 | Mouse                     | 51 |
| 2I            | GenBank       | JG0187      | Follistatin related protein                             | African<br>clawed<br>frog | 52 |
| 2J            | GenBank       | Q12841      | Follistatin related protein-1 precursor                 | Human                     | 53 |
| 2K            | Embl          | CAB42968.1  | Flik protein                                            | Chicken                   | 54 |
| 2L            | GenBank       | T13822      | Frazzled gene protein                                   | Fruit fly                 | 55 |
| 2M            | GenBank       | AAC38849.1  | Roundabout 1                                            | Fruit fly                 | 56 |
| 2N            | GenBank       | O60469      | Down Syndrome Cell Adhesion<br>Molecule Precursor       | Human                     | 57 |
| 2O            | SwissProt     | Q13449      | Limbic system-associated membrane<br>protein precursor  | Human                     | 58 |
| 2P            | SptrEmbl      | O70246      | Putative neuronal cell adhesion<br>molecule, short form | Mouse                     | 59 |
| 2Q            | SptrEmbl      | O02869      | CHLAMP, G11-isoform precursor                           | Chicken                   | 60 |
| 2R            | SwissProt     | Q62813      | Limbic system-associated membrane<br>protein precursor  | Rat                       | 61 |
| 3J            | GenBank       | NM_011856.2 | Odd Oz/ten-m homology 2                                 | Fruit fly                 | 62 |
| 3K            | Embl          | AJ245711.1  | Teneurin-2 cDNA, short splice variant                   | Chicken                   | 63 |
| 3L            | GenBank       | AB032953    | KIAA 1127 cDNA                                          | Human                     | 64 |
| 3M,<br>3U     | GenBank       | AB025411    | Ten-m2 cDNA                                             | Mouse                     | 65 |
| 3N            | GenBank       | NM_020088.1 | Neurestin alpha cDNA                                    | Rat                       | 66 |
| 3O            | Embl          | GGA278031   | Teneurin-2                                              | Chicken                   | 67 |
| 3P            | GenBank       | NP_035986.2 | Odd Oz/ten-m homology 2                                 | Fruit fly                 | 68 |
| 3Q            | Embl          | CAC09416.1  | Teneurin-2                                              | Chicken                   | 69 |
| 3R            | GenBank       | BAA77399.1  | Ten-m4                                                  | Mouse                     | 70 |
| 3S            | GenBank       | AB032953    | KIAA1127 protein                                        | Human                     | 71 |
| 3T            | GenBank       | AF086607    | Neurestin alpha                                         | Rat                       | 72 |
| 4C            | SptrEmbl      | Q99233      | Hypothetical 10 kD protein                              | Trypanos<br>ome           | 73 |
| 4C            | SptrEmbl      | Q16896      | GABA receptor subunit                                   |                           | 74 |
| 4C            | SptrEmbl      | O76473      | GABA receptor subunit                                   |                           | 75 |
| 4C            | TrEmblne<br>w | AAD28317    | FI3J11.13 protein                                       |                           | 76 |
| Text p.<br>90 | SptrEmbl      | Q13313      | NF-kappa B P65 delta 3 protein                          | Human                     | 77 |
| 5E            | GenBank       | XM_007061.1 | Complement C1R-like proteinase<br>precursor             | Human                     | 78 |
| 5F            | GenBank       | NM_001733.1 | Complement component 1, R<br>subcomponent cDNA          | Human                     | 79 |

|        |           |             |                                                            |         |    |
|--------|-----------|-------------|------------------------------------------------------------|---------|----|
| 5G     | GenBank   | AAF44349.1  | Complement C1R-like proteinase precursor                   | Human   | 80 |
| 5H     | GenBank   | AAA5185.1   | Complement C1R component precursor                         | Human   | 81 |
| 6E     | GenBank   | AB046651    | Brain cDNA clone Qcc-17034                                 | Macaque | 82 |
| 6F     | GenBank   | AK09660     | Adult testis cDNA, RIKEN full length enriched              | Mouse   | 83 |
| 6G     | GenBank   | AB046651    | Hypothetical protein                                       | Macaque | 84 |
| 6H     | GenBank   | NP_000838.1 | Plasma kallikrein B1 precursor                             | Human   | 85 |
| 6I     | GenBank   | BAA37147.1  | Kallikrein                                                 | Pig     | 86 |
| 6J     | Embl      | CAA64368.1  | Coagulation factor XI                                      | Human   | 87 |
| 7D, 7J | SpPtrEmbl | O43692      | 25 kDa trypsin inhibitor                                   | Human   | 88 |
| 7D     | SpPtrEmbl | O44228      | HRTT-1                                                     |         | 89 |
| 7D, 7K | SpPtrEmbl | P418060     | Glioma pathogenesis-related protein                        | Human   | 90 |
| 7D     | PIR-ID    | JC4131      | Glioma pathogenesis-related protein                        | Human   | 91 |
| 7D     | SwissProt | O19010      | Cysteine-rich secretory protein                            |         | 92 |
| 7E     | GenBank   | AF142573    | Putative secretory protein precursor cDNA                  | Human   | 93 |
| 7F     | GenBank   | AF142573    | Putative secretory protein precursor                       | Human   | 94 |
| 7G     | GenBank   | AF109674    | Late gestation lung protein 1                              | Rat     | 95 |
| 7H     | GenBank   | D45027      | R3H domain containing preprotein, 25 kDa trypsin inhibitor | Human   | 96 |
| 7I     | Embl      | AL117382    | Novel protein similar to a trypsin inhibitor               | Human   | 97 |
| 7L     | PIR-ID    | S68691      | Neutrophil granules matrix glycoprotein SGP28 precursor    | Human   | 98 |

### FCRX Nucleic Acids and Polypeptides

One aspect of the invention pertains to isolated nucleic acid molecules that encode FCRX polypeptides or biologically-active portions thereof. Also included in the invention are nucleic acid fragments sufficient for use as hybridization probes to identify FCRX-encoding nucleic acids (*e.g.*, FCRX mRNAs) and fragments for use as PCR primers for the amplification and/or mutation of FCRX nucleic acid molecules. As used herein, the term “nucleic acid molecule” is intended to include DNA molecules (*e.g.*, cDNA or genomic DNA), RNA molecules (*e.g.*, mRNA), analogs of the DNA or RNA generated using nucleotide analogs, and derivatives, fragments and homologs thereof. The nucleic acid molecule may be single-stranded or double-stranded, but preferably is comprised double-stranded DNA.

An FCRX nucleic acid can encode a mature FCRX polypeptide. As used herein, a “mature” form of a polypeptide or protein disclosed in the present invention is the product of a naturally occurring polypeptide or precursor form or proprotein. The naturally occurring

polypeptide, precursor or proprotein includes, by way of nonlimiting example, the full length gene product, encoded by the corresponding gene. Alternatively, it may be defined as the polypeptide, precursor or proprotein encoded by an ORF described herein. The product “mature” form arises, again by way of nonlimiting example, as a result of one or more naturally occurring processing steps as they may take place within the cell, or host cell, in which the gene product arises. Examples of such processing steps leading to a “mature” form of a polypeptide or protein include the cleavage of the N-terminal methionine residue encoded by the initiation codon of an ORF, or the proteolytic cleavage of a signal peptide or leader sequence. Thus a mature form arising from a precursor polypeptide or protein that has residues 1 to N, where residue 1 is the N-terminal methionine, would have residues 2 through N remaining after removal of the N-terminal methionine. Alternatively, a mature form arising from a precursor polypeptide or protein having residues 1 to N, in which an N-terminal signal sequence from residue 1 to residue M is cleaved, would have the residues from residue M+1 to residue N remaining. Further as used herein, a “mature” form of a polypeptide or protein may arise from a step of post-translational modification other than a proteolytic cleavage event. Such additional processes include, by way of non-limiting example, glycosylation, myristoylation or phosphorylation. In general, a mature polypeptide or protein may result from the operation of only one of these processes, or a combination of any of them.

The term “probes”, as utilized herein, refers to nucleic acid sequences of variable length, preferably between at least about 10 nucleotides (nt), 100 nt, or as many as approximately, *e.g.*, 6,000 nt, depending upon the specific use. Probes are used in the detection of identical, similar, or complementary nucleic acid sequences. Longer length probes are generally obtained from a natural or recombinant source, are highly specific, and much slower to hybridize than shorter-length oligomer probes. Probes may be single- or double-stranded and designed to have specificity in PCR, membrane-based hybridization technologies, or ELISA-like technologies.

The term “isolated” nucleic acid molecule, as utilized herein, is one which is separated from other nucleic acid molecules which are present in the natural source of the nucleic acid. Preferably, an “isolated” nucleic acid is free of sequences which naturally flank the nucleic acid (*i.e.*, sequences located at the 5'- and 3'-termini of the nucleic acid) in the genomic DNA of the organism from which the nucleic acid is derived. For example, in various embodiments, the isolated FCTR<sub>X</sub> nucleic acid molecules can contain less than about 5 kb, 4 kb, 3 kb, 2 kb, 1 kb, 0.5 kb or 0.1 kb of nucleotide sequences which naturally flank the nucleic acid molecule in genomic DNA of the cell/tissue from which the nucleic acid is derived (*e.g.*, brain, heart,

liver, spleen, etc.). Moreover, an "isolated" nucleic acid molecule, such as a cDNA molecule, can be substantially free of other cellular material or culture medium when produced by recombinant techniques, or of chemical precursors or other chemicals when chemically synthesized.

5 A nucleic acid molecule of the invention, *e.g.*, a nucleic acid molecule having the nucleotide sequence of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, or a complement of this aforementioned nucleotide sequence, can be isolated using standard molecular biology techniques and the sequence information provided herein. Using all or a portion of the nucleic acid sequence of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20,  
10 22, and 24 as a hybridization probe, FCTRX molecules can be isolated using standard hybridization and cloning techniques (*e.g.*, as described in Sambrook, *et al.*, (eds.), MOLECULAR CLONING: A LABORATORY MANUAL 2<sup>nd</sup> Ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 1989; and Ausubel, *et al.*, (eds.), CURRENT PROTOCOLS IN MOLECULAR BIOLOGY, John Wiley & Sons, New York, NY, 1993.)

15 A nucleic acid of the invention can be amplified using cDNA, mRNA or alternatively, genomic DNA, as a template and appropriate oligonucleotide primers according to standard PCR amplification techniques. The nucleic acid so amplified can be cloned into an appropriate vector and characterized by DNA sequence analysis. Furthermore, oligonucleotides corresponding to FCTRX nucleotide sequences can be prepared by standard  
20 synthetic techniques, *e.g.*, using an automated DNA synthesizer.

As used herein, the term "oligonucleotide" refers to a series of linked nucleotide residues, which oligonucleotide has a sufficient number of nucleotide bases to be used in a PCR reaction. A short oligonucleotide sequence may be based on, or designed from, a genomic or cDNA sequence and is used to amplify, confirm, or reveal the presence of an  
25 identical, similar or complementary DNA or RNA in a particular cell or tissue.

Oligonucleotides comprise portions of a nucleic acid sequence having about 10 nt, 50 nt, or 100 nt in length, preferably about 15 nt to 30 nt in length. In one embodiment of the invention, an oligonucleotide comprising a nucleic acid molecule less than 100 nt in length would further comprise at least 6 contiguous nucleotides of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11,  
30 12, 14, 16, 18, 20, 22, and 24, or a complement thereof. Oligonucleotides may be chemically synthesized and may also be used as probes.

In another embodiment, an isolated nucleic acid molecule of the invention comprises a nucleic acid molecule that is a complement of the nucleotide sequence shown in SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, or a portion of this nucleotide

sequence (*e.g.*, a fragment that can be used as a probe or primer or a fragment encoding a biologically-active portion of an FCTR<sub>X</sub> polypeptide). A nucleic acid molecule that is complementary to the nucleotide sequence shown in SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, is one that is sufficiently complementary to the nucleotide sequence shown in SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, that it can hydrogen bond with little or no mismatches to the nucleotide sequence shown in SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, thereby forming a stable duplex.

As used herein, the term “complementary” refers to Watson-Crick or Hoogsteen base pairing between nucleotides units of a nucleic acid molecule, and the term “binding” means the physical or chemical interaction between two polypeptides or compounds or associated polypeptides or compounds or combinations thereof. Binding includes ionic, non-ionic, van der Waals, hydrophobic interactions, and the like. A physical interaction can be either direct or indirect. Indirect interactions may be through or due to the effects of another polypeptide or compound. Direct binding refers to interactions that do not take place through, or due to, the effect of another polypeptide or compound, but instead are without other substantial chemical intermediates.

Fragments provided herein are defined as sequences of at least 6 (contiguous) nucleic acids or at least 4 (contiguous) amino acids, a length sufficient to allow for specific hybridization in the case of nucleic acids or for specific recognition of an epitope in the case of amino acids, respectively, and are at most some portion less than a full length sequence. Fragments may be derived from any contiguous portion of a nucleic acid or amino acid sequence of choice. Derivatives are nucleic acid sequences or amino acid sequences formed from the native compounds either directly or by modification or partial substitution. Analogs are nucleic acid sequences or amino acid sequences that have a structure similar to, but not identical to, the native compound but differs from it in respect to certain components or side chains. Analogs may be synthetic or from a different evolutionary origin and may have a similar or opposite metabolic activity compared to wild type. Homologs are nucleic acid sequences or amino acid sequences of a particular gene that are derived from different species.

Derivatives and analogs may be full length or other than full length, if the derivative or analog contains a modified nucleic acid or amino acid, as described below. Derivatives or analogs of the nucleic acids or proteins of the invention include, but are not limited to, molecules comprising regions that are substantially homologous to the nucleic acids or proteins of the invention, in various embodiments, by at least about 70%, 80%, or 95% identity (with a preferred identity of 80-95%) over a nucleic acid or amino acid sequence of

identical size or when compared to an aligned sequence in which the alignment is done by a computer homology program known in the art, or whose encoding nucleic acid is capable of hybridizing to the complement of a sequence encoding the aforementioned proteins under stringent, moderately stringent, or low stringent conditions. See *e.g.* Ausubel, *et al.*, CURRENT  
5 PROTOCOLS IN MOLECULAR BIOLOGY, John Wiley & Sons, New York, NY, 1993, and below.

A "homologous nucleic acid sequence" or "homologous amino acid sequence," or variations thereof, refer to sequences characterized by a homology at the nucleotide level or amino acid level as discussed above. Homologous nucleotide sequences encode those sequences coding for isoforms of FCTR<sub>X</sub> polypeptides. Isoforms can be expressed in  
10 different tissues of the same organism as a result of, for example, alternative splicing of RNA. Alternatively, isoforms can be encoded by different genes. In the invention, homologous nucleotide sequences include nucleotide sequences encoding for an FCTR<sub>X</sub> polypeptide of species other than humans, including, but not limited to: vertebrates, and thus can include, *e.g.*, frog, mouse, rat, rabbit, dog, cat, cow, horse, and other organisms. Homologous nucleotide  
15 sequences also include, but are not limited to, naturally occurring allelic variations and mutations of the nucleotide sequences set forth herein. A homologous nucleotide sequence does not, however, include the exact nucleotide sequence encoding human FCTR<sub>X</sub> protein. Homologous nucleic acid sequences include those nucleic acid sequences that encode conservative amino acid substitutions (see below) in SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19,  
20 21, 23, and 25, as well as a polypeptide possessing FCTR<sub>X</sub> biological activity. Various biological activities of the FCTR<sub>X</sub> proteins are described below.

An FCTR<sub>X</sub> polypeptide is encoded by the open reading frame ("ORF") of an FCTR<sub>X</sub> nucleic acid. An ORF corresponds to a nucleotide sequence that could potentially be translated into a polypeptide. A stretch of nucleic acids comprising an ORF is uninterrupted by a stop  
25 codon. An ORF that represents the coding sequence for a full protein begins with an ATG "start" codon and terminates with one of the three "stop" codons, namely, TAA, TAG, or TGA. For the purposes of this invention, an ORF may be any part of a coding sequence, with or without a start codon, a stop codon, or both. For an ORF to be considered as a good candidate for coding for a *bona fide* cellular protein, a minimum size requirement is often set,  
30 *e.g.*, a stretch of DNA that would encode a protein of 50 amino acids or more.

The nucleotide sequences determined from the cloning of the human FCTR<sub>X</sub> genes allows for the generation of probes and primers designed for use in identifying and/or cloning FCTR<sub>X</sub> homologues in other cell types, *e.g.* from other tissues, as well as FCTR<sub>X</sub> homologues from other vertebrates. The probe/primer typically comprises substantially

purified oligonucleotide. The oligonucleotide typically comprises a region of nucleotide sequence that hybridizes under stringent conditions to at least about 12, 25, 50, 100, 150, 200, 250, 300, 350 or 400 consecutive sense strand nucleotide sequence of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24; or an anti-sense strand nucleotide sequence of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24; or of a naturally occurring mutant of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24.

Probes based on the human FCTR<sub>X</sub> nucleotide sequences can be used to detect transcripts or genomic sequences encoding the same or homologous proteins. In various embodiments, the probe further comprises a label group attached thereto, *e.g.* the label group can be a radioisotope, a fluorescent compound, an enzyme, or an enzyme co-factor. Such probes can be used as a part of a diagnostic test kit for identifying cells or tissues which mis-express an FCTR<sub>X</sub> protein, such as by measuring a level of an FCTR<sub>X</sub>-encoding nucleic acid in a sample of cells from a subject *e.g.*, detecting FCTR<sub>X</sub> mRNA levels or determining whether a genomic FCTR<sub>X</sub> gene has been mutated or deleted.

"A polypeptide having a biologically-active portion of an FCTR<sub>X</sub> polypeptide" refers to polypeptides exhibiting activity similar, but not necessarily identical to, an activity of a polypeptide of the invention, including mature forms, as measured in a particular biological assay, with or without dose dependency. A nucleic acid fragment encoding a "biologically-active portion of FCTR<sub>X</sub>" can be prepared by isolating a portion of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, that encodes a polypeptide having an FCTR<sub>X</sub> biological activity (the biological activities of the FCTR<sub>X</sub> proteins are described below), expressing the encoded portion of FCTR<sub>X</sub> protein (*e.g.*, by recombinant expression *in vitro*) and assessing the activity of the encoded portion of FCTR<sub>X</sub>.

### **FCTR<sub>X</sub> Nucleic Acid and Polypeptide Variants**

The invention further encompasses nucleic acid molecules that differ from the nucleotide sequences shown in SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, due to degeneracy of the genetic code and thus encode the same FCTR<sub>X</sub> proteins as that encoded by the nucleotide sequences shown in SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24. In another embodiment, an isolated nucleic acid molecule of the invention has a nucleotide sequence encoding a protein having an amino acid sequence shown in SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25.

In addition to the human FCTR<sub>X</sub> nucleotide sequences shown in SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, it will be appreciated by those skilled in the art that

DNA sequence polymorphisms that lead to changes in the amino acid sequences of the FCTR<sub>X</sub> polypeptides may exist within a population (*e.g.*, the human population). Such genetic polymorphism in the FCTR<sub>X</sub> genes may exist among individuals within a population due to natural allelic variation. As used herein, the terms "gene" and "recombinant gene" refer to nucleic acid molecules comprising an open reading frame (ORF) encoding an FCTR<sub>X</sub> protein, preferably a vertebrate FCTR<sub>X</sub> protein. Such natural allelic variations can typically result in 1-5% variance in the nucleotide sequence of the FCTR<sub>X</sub> genes. Any and all such nucleotide variations and resulting amino acid polymorphisms in the FCTR<sub>X</sub> polypeptides, which are the result of natural allelic variation and that do not alter the functional activity of the FCTR<sub>X</sub> polypeptides, are intended to be within the scope of the invention.

Moreover, nucleic acid molecules encoding FCTR<sub>X</sub> proteins from other species, and thus that have a nucleotide sequence that differs from the human sequence of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, are intended to be within the scope of the invention. Nucleic acid molecules corresponding to natural allelic variants and homologues of the FCTR<sub>X</sub> cDNAs of the invention can be isolated based on their homology to the human FCTR<sub>X</sub> nucleic acids disclosed herein using the human cDNAs, or a portion thereof, as a hybridization probe according to standard hybridization techniques under stringent hybridization conditions.

Accordingly, in another embodiment, an isolated nucleic acid molecule of the invention is at least 6 nucleotides in length and hybridizes under stringent conditions to the nucleic acid molecule comprising the nucleotide sequence of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24. In another embodiment, the nucleic acid is at least 10, 25, 50, 100, 250, 500, 750, 1000, 1500, or 2000 or more nucleotides in length. In yet another embodiment, an isolated nucleic acid molecule of the invention hybridizes to the coding region. As used herein, the term "hybridizes under stringent conditions" is intended to describe conditions for hybridization and washing under which nucleotide sequences at least 60% homologous to each other typically remain hybridized to each other.

Homologs (*i.e.*, nucleic acids encoding FCTR<sub>X</sub> proteins derived from species other than human) or other related sequences (*e.g.*, paralogs) can be obtained by low, moderate or high stringency hybridization with all or a portion of the particular human sequence as a probe using methods well known in the art for nucleic acid hybridization and cloning.

As used herein, the phrase "stringent hybridization conditions" refers to conditions under which a probe, primer or oligonucleotide will hybridize to its target sequence, but to no other sequences. Stringent conditions are sequence-dependent and will be different in

different circumstances. Longer sequences hybridize specifically at higher temperatures than shorter sequences. Generally, stringent conditions are selected to be about 5°C lower than the thermal melting point ( $T_m$ ) for the specific sequence at a defined ionic strength and pH. The  $T_m$  is the temperature (under defined ionic strength, pH and nucleic acid concentration) at which 50% of the probes complementary to the target sequence hybridize to the target sequence at equilibrium. Since the target sequences are generally present at excess, at  $T_m$ , 50% of the probes are occupied at equilibrium. Typically, stringent conditions will be those in which the salt concentration is less than about 1.0 M sodium ion, typically about 0.01 to 1.0 M sodium ion (or other salts) at pH 7.0 to 8.3 and the temperature is at least about 30°C for short probes, primers or oligonucleotides (*e.g.*, 10 nt to 50 nt) and at least about 60°C for longer probes, primers and oligonucleotides. Stringent conditions may also be achieved with the addition of destabilizing agents, such as formamide.

Stringent conditions are known to those skilled in the art and can be found in Ausubel, *et al.*, (eds.), CURRENT PROTOCOLS IN MOLECULAR BIOLOGY, John Wiley & Sons, N.Y. (1989), 6.3.1-6.3.6. Preferably, the conditions are such that sequences at least about 65%, 70%, 75%, 85%, 90%, 95%, 98%, or 99% homologous to each other typically remain hybridized to each other. A non-limiting example of stringent hybridization conditions are hybridization in a high salt buffer comprising 6X SSC, 50 mM Tris-HCl (pH 7.5), 1 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.02% BSA, and 500 mg/ml denatured salmon sperm DNA at 65°C, followed by one or more washes in 0.2X SSC, 0.01% BSA at 50°C. An isolated nucleic acid molecule of the invention that hybridizes under stringent conditions to the sequences of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, corresponds to a naturally-occurring nucleic acid molecule. As used herein, a "naturally-occurring" nucleic acid molecule refers to an RNA or DNA molecule having a nucleotide sequence that occurs in nature (*e.g.*, encodes a natural protein).

In a second embodiment, a nucleic acid sequence that is hybridizable to the nucleic acid molecule comprising the nucleotide sequence of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, or fragments, analogs or derivatives thereof, under conditions of moderate stringency is provided. A non-limiting example of moderate stringency hybridization conditions are hybridization in 6X SSC, 5X Denhardt's solution, 0.5% SDS and 100 mg/ml denatured salmon sperm DNA at 55°C, followed by one or more washes in 1X SSC, 0.1% SDS at 37°C. Other conditions of moderate stringency that may be used are well-known within the art. See, *e.g.*, Ausubel, *et al.* (eds.), 1993, CURRENT PROTOCOLS IN

MOLECULAR BIOLOGY, John Wiley & Sons, NY, and Kriegler, 1990; GENE TRANSFER AND EXPRESSION, A LABORATORY MANUAL, Stockton Press, NY.

In a third embodiment, a nucleic acid that is hybridizable to the nucleic acid molecule comprising the nucleotide sequences of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, or fragments, analogs or derivatives thereof, under conditions of low stringency, is provided. A non-limiting example of low stringency hybridization conditions are hybridization in 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 mg/ml denatured salmon sperm DNA, 10% (wt/vol) dextran sulfate at 40°C, followed by one or more washes in 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS at 50°C. Other conditions of low stringency that may be used are well known in the art (*e.g.*, as employed for cross-species hybridizations). See, *e.g.*, Ausubel, *et al.* (eds.), 1993, CURRENT PROTOCOLS IN MOLECULAR BIOLOGY, John Wiley & Sons, NY, and Kriegler, 1990, GENE TRANSFER AND EXPRESSION, A LABORATORY MANUAL, Stockton Press, NY; Shilo and Weinberg, 1981. *Proc Natl Acad Sci USA* 78: 6789-6792.

#### Conservative Mutations

In addition to naturally-occurring allelic variants of FCTR<sub>X</sub> sequences that may exist in the population, the skilled artisan will further appreciate that changes can be introduced by mutation into the nucleotide sequences of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, thereby leading to changes in the amino acid sequences of the encoded FCTR<sub>X</sub> proteins, without altering the functional ability of said FCTR<sub>X</sub> proteins. For example, nucleotide substitutions leading to amino acid substitutions at "non-essential" amino acid residues can be made in the sequence of SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25. A "non-essential" amino acid residue is a residue that can be altered from the wild-type sequences of the FCTR<sub>X</sub> proteins without altering their biological activity, whereas an "essential" amino acid residue is required for such biological activity. For example, amino acid residues that are conserved among the FCTR<sub>X</sub> proteins of the invention are predicted to be particularly non-amenable to alteration. Amino acids for which conservative substitutions can be made are well-known within the art.

Another aspect of the invention pertains to nucleic acid molecules encoding FCTR<sub>X</sub> proteins that contain changes in amino acid residues that are not essential for activity. Such FCTR<sub>X</sub> proteins differ in amino acid sequence from SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25, yet retain biological activity. In one embodiment, the isolated nucleic acid molecule comprises a nucleotide sequence encoding a protein, wherein the protein comprises an amino acid sequence at least about 45% homologous to the amino acid sequences of SEQ

ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25. Preferably, the protein encoded by the nucleic acid molecule is at least about 60% homologous to SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25; more preferably at least about 70% homologous to SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25; still more preferably at least about 80% homologous to SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25; even more preferably at least about 90% homologous to SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25; and most preferably at least about 95% homologous to SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25.

An isolated nucleic acid molecule encoding an FCTR<sub>X</sub> protein homologous to the protein of SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25, can be created by introducing one or more nucleotide substitutions, additions or deletions into the nucleotide sequence of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, such that one or more amino acid substitutions, additions or deletions are introduced into the encoded protein.

Mutations can be introduced into SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25, by standard techniques, such as site-directed mutagenesis and PCR-mediated mutagenesis. Preferably, conservative amino acid substitutions are made at one or more predicted, non-essential amino acid residues. A "conservative amino acid substitution" is one in which the amino acid residue is replaced with an amino acid residue having a similar side chain. Families of amino acid residues having similar side chains have been defined within the art. These families include amino acids with basic side chains (*e.g.*, lysine, arginine, histidine), acidic side chains (*e.g.*, aspartic acid, glutamic acid), uncharged polar side chains (*e.g.*, glycine, asparagine, glutamine, serine, threonine, tyrosine, cysteine), nonpolar side chains (*e.g.*, alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan), beta-branched side chains (*e.g.*, threonine, valine, isoleucine) and aromatic side chains (*e.g.*, tyrosine, phenylalanine, tryptophan, histidine). Thus, a predicted non-essential amino acid residue in the FCTR<sub>X</sub> protein is replaced with another amino acid residue from the same side chain family. Alternatively, in another embodiment, mutations can be introduced randomly along all or part of an FCTR<sub>X</sub> coding sequence, such as by saturation mutagenesis, and the resultant mutants can be screened for FCTR<sub>X</sub> biological activity to identify mutants that retain activity. Following mutagenesis of SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25, the encoded protein can be expressed by any recombinant technology known in the art and the activity of the protein can be determined.

The relatedness of amino acid families may also be determined based on side chain interactions. Substituted amino acids may be fully conserved "strong" residues or fully conserved "weak" residues. The "strong" group of conserved amino acid residues may be any

one of the following groups: STA, NEQK, NHQK, NDEQ, QHRK, MILV, MILF, HY, FYW, wherein the single letter amino acid codes are grouped by those amino acids that may be substituted for each other. Likewise, the "weak" group of conserved residues may be any one of the following: CSA, ATV, SAG, STNK, STPA, SGND, SNDEQK, NDEQHK, NEQHRK, VLIM, HFY, wherein the letters within each group represent the single letter amino acid code.

In one embodiment, a mutant FCTR<sub>X</sub> protein can be assayed for (i) the ability to form protein:protein interactions with other FCTR<sub>X</sub> proteins, other cell-surface proteins, or biologically-active portions thereof, (ii) complex formation between a mutant FCTR<sub>X</sub> protein and an FCTR<sub>X</sub> ligand; or (iii) the ability of a mutant FCTR<sub>X</sub> protein to bind to an intracellular target protein or biologically-active portion thereof; (e.g. avidin proteins).

In yet another embodiment, a mutant FCTR<sub>X</sub> protein can be assayed for the ability to regulate a specific biological function (e.g., regulation of insulin release).

### Antisense Nucleic Acids

Another aspect of the invention pertains to isolated antisense nucleic acid molecules that are hybridizable to or complementary to the nucleic acid molecule comprising the nucleotide sequence of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, or fragments, analogs or derivatives thereof. An "antisense" nucleic acid comprises a nucleotide sequence that is complementary to a "sense" nucleic acid encoding a protein (e.g., complementary to the coding strand of a double-stranded cDNA molecule or complementary to an mRNA sequence). In specific aspects, antisense nucleic acid molecules are provided that comprise a sequence complementary to at least about 10, 25, 50, 100, 250 or 500 nucleotides or an entire FCTR<sub>X</sub> coding strand, or to only a portion thereof. Nucleic acid molecules encoding fragments, homologs, derivatives and analogs of an FCTR<sub>X</sub> protein of SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25; or antisense nucleic acids complementary to an FCTR<sub>X</sub> nucleic acid sequence of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, are additionally provided.

In one embodiment, an antisense nucleic acid molecule is antisense to a "coding region" of the coding strand of a nucleotide sequence encoding an FCTR<sub>X</sub> protein. The term "coding region" refers to the region of the nucleotide sequence comprising codons which are translated into amino acid residues. In another embodiment, the antisense nucleic acid molecule is antisense to a "noncoding region" of the coding strand of a nucleotide sequence encoding the FCTR<sub>X</sub> protein. The term "noncoding region" refers to 5' and 3' sequences

which flank the coding region that are not translated into amino acids (*i.e.*, also referred to as 5' and 3' untranslated regions).

Given the coding strand sequences encoding the FCTR<sub>X</sub> protein disclosed herein, antisense nucleic acids of the invention can be designed according to the rules of Watson and Crick or Hoogsteen base pairing. The antisense nucleic acid molecule can be complementary to the entire coding region of FCTR<sub>X</sub> mRNA, but more preferably is an oligonucleotide that is antisense to only a portion of the coding or noncoding region of FCTR<sub>X</sub> mRNA. For example, the antisense oligonucleotide can be complementary to the region surrounding the translation start site of FCTR<sub>X</sub> mRNA. An antisense oligonucleotide can be, for example, about 5, 10, 15, 20, 25, 30, 35, 40, 45 or 50 nucleotides in length. An antisense nucleic acid of the invention can be constructed using chemical synthesis or enzymatic ligation reactions using procedures known in the art. For example, an antisense nucleic acid (*e.g.*, an antisense oligonucleotide) can be chemically synthesized using naturally-occurring nucleotides or variously modified nucleotides designed to increase the biological stability of the molecules or to increase the physical stability of the duplex formed between the antisense and sense nucleic acids (*e.g.*, phosphorothioate derivatives and acridine substituted nucleotides can be used).

Examples of modified nucleotides that can be used to generate the antisense nucleic acid include: 5-fluorouracil, 5-bromouracil, 5-chlorouracil, 5-iodouracil, hypoxanthine, xanthine, 4-acetylcytosine, 5-(carboxyhydroxymethyl) uracil, 5-carboxymethylaminomethyl-2-thiouridine, 5-carboxymethylaminomethyluracil, dihydrouracil, beta-D-galactosylqueosine, inosine, N6-isopentenyladenine, 1-methylguanine, 1-methylinosine, 2,2-dimethylguanine, 2-methyladenine, 2-methylguanine, 3-methylcytosine, 5-methylcytosine, N6-adenine, 7-methylguanine, 5-methylaminomethyluracil, 5-methoxyaminomethyl-2-thiouracil, beta-D-mannosylqueosine, 5'-methoxycarboxymethyluracil, 5-methoxyuracil, 2-methylthio-N6-isopentenyladenine, uracil-5-oxyacetic acid (*v*), wybutoxosine, pseudouracil, queosine, 2-thiocytosine, 5-methyl-2-thiouracil, 2-thiouracil, 4-thiouracil, 5-methyluracil, uracil-5-oxyacetic acid methylester, uracil-5-oxyacetic acid (*v*), 5-methyl-2-thiouracil, 3-(3-amino-3-N-2-carboxypropyl) uracil, (acp3)<sub>w</sub>, and 2,6-diaminopurine. Alternatively, the antisense nucleic acid can be produced biologically using an expression vector into which a nucleic acid has been subcloned in an antisense orientation (*i.e.*, RNA transcribed from the inserted nucleic acid will be of an antisense orientation to a target nucleic acid of interest, described further in the following subsection).

The antisense nucleic acid molecules of the invention are typically administered to a subject or generated *in situ* such that they hybridize with or bind to cellular mRNA and/or

genomic DNA encoding an FCTR<sub>X</sub> protein to thereby inhibit expression of the protein (*e.g.*, by inhibiting transcription and/or translation). The hybridization can be by conventional nucleotide complementarity to form a stable duplex, or, for example, in the case of an antisense nucleic acid molecule that binds to DNA duplexes, through specific interactions in the major groove of the double helix. An example of a route of administration of antisense nucleic acid molecules of the invention includes direct injection at a tissue site. Alternatively, antisense nucleic acid molecules can be modified to target selected cells and then administered systemically. For example, for systemic administration, antisense molecules can be modified such that they specifically bind to receptors or antigens expressed on a selected cell surface (*e.g.*, by linking the antisense nucleic acid molecules to peptides or antibodies that bind to cell surface receptors or antigens). The antisense nucleic acid molecules can also be delivered to cells using the vectors described herein. To achieve sufficient nucleic acid molecules, vector constructs in which the antisense nucleic acid molecule is placed under the control of a strong pol II or pol III promoter are preferred.

In yet another embodiment, the antisense nucleic acid molecule of the invention is an  $\alpha$ -anomeric nucleic acid molecule. An  $\alpha$ -anomeric nucleic acid molecule forms specific double-stranded hybrids with complementary RNA in which, contrary to the usual  $\beta$ -units, the strands run parallel to each other. See, *e.g.*, Gaultier, *et al.*, 1987. *Nucl. Acids Res.* **15**: 6625-6641. The antisense nucleic acid molecule can also comprise a 2'-*o*-methylribonucleotide (see, *e.g.*, Inoue, *et al.* 1987. *Nucl. Acids Res.* **15**: 6131-6148) or a chimeric RNA-DNA analogue (see, *e.g.*, Inoue, *et al.*, 1987. *FEBS Lett.* **215**: 327-330).

#### **Ribozymes and PNA Moieties**

Nucleic acid modifications include, by way of non-limiting example, modified bases, and nucleic acids whose sugar phosphate backbones are modified or derivatized. These modifications are carried out at least in part to enhance the chemical stability of the modified nucleic acid, such that they may be used, for example, as antisense binding nucleic acids in therapeutic applications in a subject.

In one embodiment, an antisense nucleic acid of the invention is a ribozyme. Ribozymes are catalytic RNA molecules with ribonuclease activity that are capable of cleaving a single-stranded nucleic acid, such as an mRNA, to which they have a complementary region. Thus, ribozymes (*e.g.*, hammerhead ribozymes as described in Haselhoff and Gerlach 1988. *Nature* 334: 585-591) can be used to catalytically cleave FCTR<sub>X</sub> mRNA transcripts to thereby inhibit translation of FCTR<sub>X</sub> mRNA. A ribozyme having specificity for an FCTR<sub>X</sub>-encoding nucleic acid can be designed based upon the nucleotide

sequence of an FCTR<sub>X</sub> cDNA disclosed herein (*i.e.*, SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24). For example, a derivative of a *Tetrahymena* L-19 IVS RNA can be constructed in which the nucleotide sequence of the active site is complementary to the nucleotide sequence to be cleaved in an FCTR<sub>X</sub>-encoding mRNA. See, *e.g.*, U.S. Patent  
5 4,987,071 to Cech, *et al.* and U.S. Patent 5,116,742 to Cech, *et al.* FCTR<sub>X</sub> mRNA can also be used to select a catalytic RNA having a specific ribonuclease activity from a pool of RNA molecules. See, *e.g.*, Bartel *et al.*, (1993) *Science* 261:1411-1418.

Alternatively, FCTR<sub>X</sub> gene expression can be inhibited by targeting nucleotide sequences complementary to the regulatory region of the FCTR<sub>X</sub> nucleic acid (*e.g.*, the  
10 FCTR<sub>X</sub> promoter and/or enhancers) to form triple helical structures that prevent transcription of the FCTR<sub>X</sub> gene in target cells. See, *e.g.*, Helene, 1991. *Anticancer Drug Des.* 6: 569-84; Helene, *et al.* 1992. *Ann. N.Y. Acad. Sci.* 660: 27-36; Maher, 1992. *Bioassays* 14: 807-15.

In various embodiments, the FCTR<sub>X</sub> nucleic acids can be modified at the base moiety, sugar moiety or phosphate backbone to improve, *e.g.*, the stability, hybridization, or solubility  
15 of the molecule. For example, the deoxyribose phosphate backbone of the nucleic acids can be modified to generate peptide nucleic acids. See, *e.g.*, Hyrup, *et al.*, 1996. *Bioorg Med Chem* 4: 5-23. As used herein, the terms "peptide nucleic acids" or "PNAs" refer to nucleic acid mimics (*e.g.*, DNA mimics) in which the deoxyribose phosphate backbone is replaced by a pseudopeptide backbone and only the four natural nucleobases are retained. The neutral  
20 backbone of PNAs has been shown to allow for specific hybridization to DNA and RNA under conditions of low ionic strength. The synthesis of PNA oligomers can be performed using standard solid phase peptide synthesis protocols as described in Hyrup, *et al.*, 1996. *supra*; Perry-O'Keefe, *et al.*, 1996. *Proc. Natl. Acad. Sci. USA* 93: 14670-14675.

PNAs of FCTR<sub>X</sub> can be used in therapeutic and diagnostic applications. For example,  
25 PNAs can be used as antisense or antigene agents for sequence-specific modulation of gene expression by, *e.g.*, inducing transcription or translation arrest or inhibiting replication. PNAs of FCTR<sub>X</sub> can also be used, for example, in the analysis of single base pair mutations in a gene (*e.g.*, PNA directed PCR clamping; as artificial restriction enzymes when used in combination with other enzymes, *e.g.*, S<sub>1</sub> nucleases (*see*, Hyrup, *et al.*, 1996. *supra*); or as  
30 probes or primers for DNA sequence and hybridization (*see*, Hyrup, *et al.*, 1996, *supra*; Perry-O'Keefe, *et al.*, 1996. *supra*).

In another embodiment, PNAs of FCTR<sub>X</sub> can be modified, *e.g.*, to enhance their stability or cellular uptake, by attaching lipophilic or other helper groups to PNA, by the formation of PNA-DNA chimeras, or by the use of liposomes or other techniques of drug

delivery known in the art. For example, PNA-DNA chimeras of FCTR<sub>X</sub> can be generated that may combine the advantageous properties of PNA and DNA. Such chimeras allow DNA recognition enzymes (*e.g.*, RNase H and DNA polymerases) to interact with the DNA portion while the PNA portion would provide high binding affinity and specificity. PNA-DNA

5 chimeras can be linked using linkers of appropriate lengths selected in terms of base stacking, number of bonds between the nucleobases, and orientation (*see*, Hyrup, *et al.*, 1996. *supra*). The synthesis of PNA-DNA chimeras can be performed as described in Hyrup, *et al.*, 1996. *supra* and Finn, *et al.*, 1996. *Nucl Acids Res* 24: 3357-3363. For example, a DNA chain can be synthesized on a solid support using standard phosphoramidite coupling chemistry, and

10 modified nucleoside analogs, *e.g.*, 5'-(4-methoxytrityl)amino-5'-deoxy-thymidine phosphoramidite, can be used between the PNA and the 5' end of DNA. *See, e.g.*, Mag, *et al.*, 1989. *Nucl Acid Res* 17: 5973-5988. PNA monomers are then coupled in a stepwise manner to produce a chimeric molecule with a 5' PNA segment and a 3' DNA segment. *See, e.g.*, Finn, *et al.*, 1996. *supra*. Alternatively, chimeric molecules can be synthesized with a 5' DNA

15 segment and a 3' PNA segment. *See, e.g.*, Petersen, *et al.*, 1975. *Bioorg. Med. Chem. Lett.* 5: 1119-11124.

In other embodiments, the oligonucleotide may include other appended groups such as peptides (*e.g.*, for targeting host cell receptors *in vivo*), or agents facilitating transport across the cell membrane (*see, e.g.*, Letsinger, *et al.*, 1989. *Proc. Natl. Acad. Sci. U.S.A.* 86: 6553-6556; Lemaitre, *et al.*, 1987. *Proc. Natl. Acad. Sci.* 84: 648-652; PCT Publication No. WO88/09810) or the blood-brain barrier (*see, e.g.*, PCT Publication No. WO 89/10134). In addition, oligonucleotides can be modified with hybridization triggered cleavage agents (*see, e.g.*, Krol, *et al.*, 1988. *BioTechniques* 6:958-976) or intercalating agents (*see, e.g.*, Zon, 1988. *Pharm. Res.* 5: 539-549). To this end, the oligonucleotide may be conjugated to another

25 molecule, *e.g.*, a peptide, a hybridization triggered cross-linking agent, a transport agent, a hybridization-triggered cleavage agent, and the like.

### FCTR<sub>X</sub> Polypeptides

A polypeptide according to the invention includes a polypeptide including the amino acid sequence of FCTR<sub>X</sub> polypeptides whose sequences are provided in SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25. The invention also includes a mutant or variant protein any of whose residues may be changed from the corresponding residues shown in SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25, while still encoding a protein that maintains its FCTR<sub>X</sub> activities and physiological functions, or a functional fragment thereof.

30

In general, an FCTR<sub>X</sub> variant that preserves FCTR<sub>X</sub>-like function includes any variant in which residues at a particular position in the sequence have been substituted by other amino acids, and further include the possibility of inserting an additional residue or residues between two residues of the parent protein as well as the possibility of deleting one or more residues from the parent sequence. Any amino acid substitution, insertion, or deletion is encompassed by the invention. In favorable circumstances, the substitution is a conservative substitution as defined above.

One aspect of the invention pertains to isolated FCTR<sub>X</sub> proteins, and biologically-active portions thereof, or derivatives, fragments, analogs or homologs thereof. Also provided are polypeptide fragments suitable for use as immunogens to raise anti-FCTR<sub>X</sub> antibodies. In one embodiment, native FCTR<sub>X</sub> proteins can be isolated from cells or tissue sources by an appropriate purification scheme using standard protein purification techniques. In another embodiment, FCTR<sub>X</sub> proteins are produced by recombinant DNA techniques. Alternative to recombinant expression, an FCTR<sub>X</sub> protein or polypeptide can be synthesized chemically using standard peptide synthesis techniques.

An "isolated" or "purified" polypeptide or protein or biologically-active portion thereof is substantially free of cellular material or other contaminating proteins from the cell or tissue source from which the FCTR<sub>X</sub> protein is derived, or substantially free from chemical precursors or other chemicals when chemically synthesized. The language "substantially free of cellular material" includes preparations of FCTR<sub>X</sub> proteins in which the protein is separated from cellular components of the cells from which it is isolated or recombinantly-produced. In one embodiment, the language "substantially free of cellular material" includes preparations of FCTR<sub>X</sub> proteins having less than about 30% (by dry weight) of non-FCTR<sub>X</sub> proteins (also referred to herein as a "contaminating protein"), more preferably less than about 20% of non-FCTR<sub>X</sub> proteins, still more preferably less than about 10% of non-FCTR<sub>X</sub> proteins, and most preferably less than about 5% of non-FCTR<sub>X</sub> proteins. When the FCTR<sub>X</sub> protein or biologically-active portion thereof is recombinantly-produced, it is also preferably substantially free of culture medium, *i.e.*, culture medium represents less than about 20%, more preferably less than about 10%, and most preferably less than about 5% of the volume of the FCTR<sub>X</sub> protein preparation.

The language "substantially free of chemical precursors or other chemicals" includes preparations of FCTR<sub>X</sub> proteins in which the protein is separated from chemical precursors or other chemicals that are involved in the synthesis of the protein. In one embodiment, the language "substantially free of chemical precursors or other chemicals" includes preparations

of FCTR proteins having less than about 30% (by dry weight) of chemical precursors or non-FCTR chemicals, more preferably less than about 20% chemical precursors or non-FCTR chemicals, still more preferably less than about 10% chemical precursors or non-FCTR chemicals, and most preferably less than about 5% chemical precursors or non-FCTR chemicals.

Biologically-active portions of FCTR proteins include peptides comprising amino acid sequences sufficiently homologous to or derived from the amino acid sequences of the FCTR proteins (*e.g.*, the amino acid sequence shown in SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25) that include fewer amino acids than the full-length FCTR proteins, and exhibit at least one activity of an FCTR protein. Typically, biologically-active portions comprise a domain or motif with at least one activity of the FCTR protein. A biologically-active portion of an FCTR protein can be a polypeptide which is, for example, 10, 25, 50, 100 or more amino acid residues in length.

Moreover, other biologically-active portions, in which other regions of the protein are deleted, can be prepared by recombinant techniques and evaluated for one or more of the functional activities of a native FCTR protein.

In an embodiment, the FCTR protein has an amino acid sequence shown in SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25. In other embodiments, the FCTR protein is substantially homologous to SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25, and retains the functional activity of the protein of SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25, yet differs in amino acid sequence due to natural allelic variation or mutagenesis, as described in detail, below. Accordingly, in another embodiment, the FCTR protein is a protein that comprises an amino acid sequence at least about 45% homologous to the amino acid sequence of SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25, and retains the functional activity of the FCTR proteins of SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25.

#### *Determining Homology Between Two or More Sequences*

To determine the percent homology of two amino acid sequences or of two nucleic acids, the sequences are aligned for optimal comparison purposes (*e.g.*, gaps can be introduced in the sequence of a first amino acid or nucleic acid sequence for optimal alignment with a second amino or nucleic acid sequence). The amino acid residues or nucleotides at corresponding amino acid positions or nucleotide positions are then compared. When a position in the first sequence is occupied by the same amino acid residue or nucleotide as the corresponding position in the second sequence, then the molecules are homologous at that

position (*i.e.*, as used herein amino acid or nucleic acid "homology" is equivalent to amino acid or nucleic acid "identity").

The nucleic acid sequence homology may be determined as the degree of identity between two sequences. The homology may be determined using computer programs known in the art, such as GAP software provided in the GCG program package. *See*, Needleman and Wunsch, 1970. *J Mol Biol* 48: 443-453. Using GCG GAP software with the following settings for nucleic acid sequence comparison: GAP creation penalty of 5.0 and GAP extension penalty of 0.3, the coding region of the analogous nucleic acid sequences referred to above exhibits a degree of identity preferably of at least 70%, 75%, 80%, 85%, 90%, 95%, 98%, or 99%, with the CDS (encoding) part of the DNA sequence shown in SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24.

The term "sequence identity" refers to the degree to which two polynucleotide or polypeptide sequences are identical on a residue-by-residue basis over a particular region of comparison. The term "percentage of sequence identity" is calculated by comparing two optimally aligned sequences over that region of comparison, determining the number of positions at which the identical nucleic acid base (*e.g.*, A, T, C, G, U, or I, in the case of nucleic acids) occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the region of comparison (*i.e.*, the window size), and multiplying the result by 100 to yield the percentage of sequence identity. The term "substantial identity" as used herein denotes a characteristic of a polynucleotide sequence, wherein the polynucleotide comprises a sequence that has at least 80 percent sequence identity, preferably at least 85 percent identity and often 90 to 95 percent sequence identity, more usually at least 99 percent sequence identity as compared to a reference sequence over a comparison region.

#### Chimeric and Fusion Proteins

The invention also provides FCTR<sub>X</sub> chimeric or fusion proteins. As used herein, an FCTR<sub>X</sub> "chimeric protein" or "fusion protein" comprises an FCTR<sub>X</sub> polypeptide operatively-linked to a non-FCTR<sub>X</sub> polypeptide. An "FCTR<sub>X</sub> polypeptide" refers to a polypeptide having an amino acid sequence corresponding to an FCTR<sub>X</sub> protein (SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25), whereas a "non-FCTR<sub>X</sub> polypeptide" refers to a polypeptide having an amino acid sequence corresponding to a protein that is not substantially homologous to the FCTR<sub>X</sub> protein, *e.g.*, a protein that is different from the FCTR<sub>X</sub> protein and that is derived from the same or a different organism. Within an FCTR<sub>X</sub> fusion protein the FCTR<sub>X</sub> polypeptide can correspond to all or a portion of an FCTR<sub>X</sub> protein. In one embodiment, an

FCTR<sub>X</sub> fusion protein comprises at least one biologically-active portion of an FCTR<sub>X</sub> protein. In another embodiment, an FCTR<sub>X</sub> fusion protein comprises at least two biologically-active portions of an FCTR<sub>X</sub> protein. In yet another embodiment, an FCTR<sub>X</sub> fusion protein comprises at least three biologically-active portions of an FCTR<sub>X</sub> protein.

5 Within the fusion protein, the term "operatively-linked" is intended to indicate that the FCTR<sub>X</sub> polypeptide and the non-FCTR<sub>X</sub> polypeptide are fused in-frame with one another. The non-FCTR<sub>X</sub> polypeptide can be fused to the N-terminus or C-terminus of the FCTR<sub>X</sub> polypeptide.

In one embodiment, the fusion protein is a GST-FCTR<sub>X</sub> fusion protein in which the  
10 FCTR<sub>X</sub> sequences are fused to the C-terminus of the GST (glutathione S-transferase) sequences. Such fusion proteins can facilitate the purification of recombinant FCTR<sub>X</sub> polypeptides.

In another embodiment, the fusion protein is an FCTR<sub>X</sub> protein containing a heterologous signal sequence at its N-terminus. In certain host cells (*e.g.*, mammalian host  
15 cells), expression and/or secretion of FCTR<sub>X</sub> can be increased through use of a heterologous signal sequence.

In yet another embodiment, the fusion protein is an FCTR<sub>X</sub>-immunoglobulin fusion protein in which the FCTR<sub>X</sub> sequences are fused to sequences derived from a member of the immunoglobulin protein family. The FCTR<sub>X</sub>-immunoglobulin fusion proteins of the  
20 invention can be incorporated into pharmaceutical compositions and administered to a subject to inhibit an interaction between an FCTR<sub>X</sub> ligand and an FCTR<sub>X</sub> protein on the surface of a cell, to thereby suppress FCTR<sub>X</sub>-mediated signal transduction *in vivo*. The FCTR<sub>X</sub>-immunoglobulin fusion proteins can be used to affect the bioavailability of an FCTR<sub>X</sub> cognate ligand. Inhibition of the FCTR<sub>X</sub> ligand/FCTR<sub>X</sub> interaction may be useful therapeutically for  
25 both the treatment of proliferative and differentiative disorders, as well as modulating (*e.g.* promoting or inhibiting) cell survival. Moreover, the FCTR<sub>X</sub>-immunoglobulin fusion proteins of the invention can be used as immunogens to produce anti-FCTR<sub>X</sub> antibodies in a subject, to purify FCTR<sub>X</sub> ligands, and in screening assays to identify molecules that inhibit the interaction of FCTR<sub>X</sub> with an FCTR<sub>X</sub> ligand.

30 An FCTR<sub>X</sub> chimeric or fusion protein of the invention can be produced by standard recombinant DNA techniques. For example, DNA fragments coding for the different polypeptide sequences are ligated together in-frame in accordance with conventional techniques, *e.g.*, by employing blunt-ended or stagger-ended termini for ligation, restriction enzyme digestion to provide for appropriate termini, filling-in of cohesive ends as appropriate,

alkaline phosphatase treatment to avoid undesirable joining, and enzymatic ligation. In another embodiment, the fusion gene can be synthesized by conventional techniques including automated DNA synthesizers. Alternatively, PCR amplification of gene fragments can be carried out using anchor primers that give rise to complementary overhangs between two consecutive gene fragments that can subsequently be annealed and reamplified to generate a chimeric gene sequence (*see, e.g.,* Ausubel, *et al.* (eds.) CURRENT PROTOCOLS IN MOLECULAR BIOLOGY, John Wiley & Sons, 1992). Moreover, many expression vectors are commercially available that already encode a fusion moiety (*e.g.,* a GST polypeptide). An FCTR<sub>X</sub>-encoding nucleic acid can be cloned into such an expression vector such that the fusion moiety is linked in-frame to the FCTR<sub>X</sub> protein.

#### *FCTR<sub>X</sub> Agonists and Antagonists*

The invention also pertains to variants of the FCTR<sub>X</sub> proteins that function as either FCTR<sub>X</sub> agonists (*i.e.,* mimetics) or as FCTR<sub>X</sub> antagonists. Variants of the FCTR<sub>X</sub> protein can be generated by mutagenesis (*e.g.,* discrete point mutation or truncation of the FCTR<sub>X</sub> protein). An agonist of the FCTR<sub>X</sub> protein can retain substantially the same, or a subset of, the biological activities of the naturally occurring form of the FCTR<sub>X</sub> protein. An antagonist of the FCTR<sub>X</sub> protein can inhibit one or more of the activities of the naturally occurring form of the FCTR<sub>X</sub> protein by, for example, competitively binding to a downstream or upstream member of a cellular signaling cascade which includes the FCTR<sub>X</sub> protein. Thus, specific biological effects can be elicited by treatment with a variant of limited function. In one embodiment, treatment of a subject with a variant having a subset of the biological activities of the naturally occurring form of the protein has fewer side effects in a subject relative to treatment with the naturally occurring form of the FCTR<sub>X</sub> proteins.

Variants of the FCTR<sub>X</sub> proteins that function as either FCTR<sub>X</sub> agonists (*i.e.,* mimetics) or as FCTR<sub>X</sub> antagonists can be identified by screening combinatorial libraries of mutants (*e.g.,* truncation mutants) of the FCTR<sub>X</sub> proteins for FCTR<sub>X</sub> protein agonist or antagonist activity. In one embodiment, a variegated library of FCTR<sub>X</sub> variants is generated by combinatorial mutagenesis at the nucleic acid level and is encoded by a variegated gene library. A variegated library of FCTR<sub>X</sub> variants can be produced by, for example, enzymatically ligating a mixture of synthetic oligonucleotides into gene sequences such that a degenerate set of potential FCTR<sub>X</sub> sequences is expressible as individual polypeptides, or alternatively, as a set of larger fusion proteins (*e.g.,* for phage display) containing the set of FCTR<sub>X</sub> sequences therein. There are a variety of methods which can be used to produce libraries of potential FCTR<sub>X</sub> variants from a degenerate oligonucleotide sequence. Chemical

synthesis of a degenerate gene sequence can be performed in an automatic DNA synthesizer, and the synthetic gene then ligated into an appropriate expression vector. Use of a degenerate set of genes allows for the provision, in one mixture, of all of the sequences encoding the desired set of potential FCTR<sub>X</sub> sequences. Methods for synthesizing degenerate

5 oligonucleotides are well-known within the art. See, e.g., Narang, 1983. *Tetrahedron* 39: 3; Itakura, et al., 1984. *Annu. Rev. Biochem.* 53: 323; Itakura, et al., 1984. *Science* 198: 1056; Ike, et al., 1983. *Nucl. Acids Res.* 11: 477.

#### *Polypeptide Libraries*

In addition, libraries of fragments of the FCTR<sub>X</sub> protein coding sequences can be used  
10 to generate a variegated population of FCTR<sub>X</sub> fragments for screening and subsequent selection of variants of an FCTR<sub>X</sub> protein. In one embodiment, a library of coding sequence fragments can be generated by treating a double stranded PCR fragment of an FCTR<sub>X</sub> coding sequence with a nuclease under conditions wherein nicking occurs only about once per molecule, denaturing the double stranded DNA, renaturing the DNA to form double-stranded  
15 DNA that can include sense/antisense pairs from different nicked products, removing single stranded portions from reformed duplexes by treatment with S<sub>1</sub> nuclease, and ligating the resulting fragment library into an expression vector. By this method, expression libraries can be derived which encodes N-terminal and internal fragments of various sizes of the FCTR<sub>X</sub> proteins.

20 Various techniques are known in the art for screening gene products of combinatorial libraries made by point mutations or truncation, and for screening cDNA libraries for gene products having a selected property. Such techniques are adaptable for rapid screening of the gene libraries generated by the combinatorial mutagenesis of FCTR<sub>X</sub> proteins. The most widely used techniques, which are amenable to high throughput analysis, for screening large  
25 gene libraries typically include cloning the gene library into replicable expression vectors, transforming appropriate cells with the resulting library of vectors, and expressing the combinatorial genes under conditions in which detection of a desired activity facilitates isolation of the vector encoding the gene whose product was detected. Recursive ensemble mutagenesis (REM), a new technique that enhances the frequency of functional mutants in the  
30 libraries, can be used in combination with the screening assays to identify FCTR<sub>X</sub> variants. See, e.g., Arkin and Yourvan, 1992. *Proc. Natl. Acad. Sci. USA* 89: 7811-7815; Delgrave, et al., 1993. *Protein Engineering* 6:327-331.

## Anti-FCTR<sub>X</sub> Antibodies

The invention encompasses antibodies and antibody fragments, such as F<sub>ab</sub> or (F<sub>ab</sub>)<sub>2</sub>, that bind immunospecifically to any of the FCTR<sub>X</sub> polypeptides of said invention.

An isolated FCTR<sub>X</sub> protein, or a portion or fragment thereof, can be used as an immunogen to generate antibodies that bind to FCTR<sub>X</sub> polypeptides using standard techniques for polyclonal and monoclonal antibody preparation. The full-length FCTR<sub>X</sub> proteins can be used or, alternatively, the invention provides antigenic peptide fragments of FCTR<sub>X</sub> proteins for use as immunogens. The antigenic FCTR<sub>X</sub> peptides comprises at least 4 amino acid residues of the amino acid sequence shown in SEQ ID NO NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25, and encompasses an epitope of FCTR<sub>X</sub> such that an antibody raised against the peptide forms a specific immune complex with FCTR<sub>X</sub>. Preferably, the antigenic peptide comprises at least 6, 8, 10, 15, 20, or 30 amino acid residues. Longer antigenic peptides are sometimes preferable over shorter antigenic peptides, depending on use and according to methods well known to someone skilled in the art.

In certain embodiments of the invention, at least one epitope encompassed by the antigenic peptide is a region of FCTR<sub>X</sub> that is located on the surface of the protein (*e.g.*, a hydrophilic region). As a means for targeting antibody production, hydropathy plots showing regions of hydrophilicity and hydrophobicity may be generated by any method well known in the art, including, for example, the Kyte Doolittle or the Hopp Woods methods, either with or without Fourier transformation (*see, e.g.*, Hopp and Woods, 1981. *Proc. Nat. Acad. Sci. USA* 78: 3824-3828; Kyte and Doolittle, 1982. *J. Mol. Biol.* 157: 105-142, each incorporated herein by reference in their entirety).

As disclosed herein, FCTR<sub>X</sub> protein sequences of SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25, or derivatives, fragments, analogs or homologs thereof, may be utilized as immunogens in the generation of antibodies that immunospecifically-bind these protein components. The term "antibody" as used herein refers to immunoglobulin molecules and immunologically-active portions of immunoglobulin molecules, *i.e.*, molecules that contain an antigen binding site that specifically-binds (immunoreacts with) an antigen, such as FCTR<sub>X</sub>. Such antibodies include, but are not limited to, polyclonal, monoclonal, chimeric, single chain, F<sub>ab</sub> and F<sub>(ab)</sub><sub>2</sub> fragments, and an F<sub>ab</sub> expression library. In a specific embodiment, antibodies to human FCTR<sub>X</sub> proteins are disclosed. Various procedures known within the art may be used for the production of polyclonal or monoclonal antibodies to an FCTR<sub>X</sub> protein sequence of SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25, or a derivative, fragment, analog or homolog thereof. Some of these proteins are discussed below.

For the production of polyclonal antibodies, various suitable host animals (*e.g.*, rabbit, goat, mouse or other mammal) may be immunized by injection with the native protein, or a synthetic variant thereof, or a derivative of the foregoing. An appropriate immunogenic preparation can contain, for example, recombinantly-expressed FCTR<sub>X</sub> protein or a  
5 chemically-synthesized FCTR<sub>X</sub> polypeptide. The preparation can further include an adjuvant. Various adjuvants used to increase the immunological response include, but are not limited to, Freund's (complete and incomplete), mineral gels (*e.g.*, aluminum hydroxide), surface active substances (*e.g.*, lysolecithin, pluronic polyols, polyanions, peptides, oil emulsions, dinitrophenol, etc.), human adjuvants such as *Bacille Calmette-Guerin* and *Corynebacterium*  
10 *parvum*, or similar immunostimulatory agents. If desired, the antibody molecules directed against FCTR<sub>X</sub> can be isolated from the mammal (*e.g.*, from the blood) and further purified by well known techniques, such as protein A chromatography to obtain the IgG fraction.

The term "monoclonal antibody" or "monoclonal antibody composition", as used herein, refers to a population of antibody molecules that contain only one species of an antigen  
15 binding site capable of immunoreacting with a particular epitope of FCTR<sub>X</sub>. A monoclonal antibody composition thus typically displays a single binding affinity for a particular FCTR<sub>X</sub> protein with which it immunoreacts. For preparation of monoclonal antibodies directed towards a particular FCTR<sub>X</sub> protein, or derivatives, fragments, analogs or homologs thereof, any technique that provides for the production of antibody molecules by continuous cell line  
20 culture may be utilized. Such techniques include, but are not limited to, the hybridoma technique (*see, e.g.*, Kohler & Milstein, 1975. *Nature* 256: 495-497); the trioma technique; the human B-cell hybridoma technique (*see, e.g.*, Kozbor, *et al.*, 1983. *Immunol. Today* 4: 72) and the EBV hybridoma technique to produce human monoclonal antibodies (*see, e.g.*, Cole, *et al.*, 1985. In: MONOCLONAL ANTIBODIES AND CANCER THERAPY, Alan R. Liss, Inc., pp. 77-96).  
25 Human monoclonal antibodies may be utilized in the practice of the invention and may be produced by using human hybridomas (*see, e.g.*, Cote, *et al.*, 1983. *Proc Natl Acad Sci USA* 80: 2026-2030) or by transforming human B-cells with Epstein Barr Virus *in vitro* (*see, e.g.*, Cole, *et al.*, 1985. In: MONOCLONAL ANTIBODIES AND CANCER THERAPY, Alan R. Liss, Inc., pp. 77-96). Each of the above citations is incorporated herein by reference in their entirety.

30 According to the invention, techniques can be adapted for the production of single-chain antibodies specific to an FCTR<sub>X</sub> protein (*see, e.g.*, U.S. Patent No. 4,946,778). In addition, methods can be adapted for the construction of F<sub>ab</sub> expression libraries (*see, e.g.*, Huse, *et al.*, 1989. *Science* 246: 1275-1281) to allow rapid and effective identification of monoclonal F<sub>ab</sub> fragments with the desired specificity for an FCTR<sub>X</sub> protein or derivatives,

fragments, analogs or homologs thereof. Non-human antibodies can be "humanized" by techniques well known in the art. *See, e.g.*, U.S. Patent No. 5,225,539. Antibody fragments that contain the idiotype to an FCTR<sub>X</sub> protein may be produced by techniques known in the art including, but not limited to: (i) an F<sub>(ab')<sub>2</sub></sub> fragment produced by pepsin digestion of an antibody molecule; (ii) an F<sub>ab</sub> fragment generated by reducing the disulfide bridges of an F<sub>(ab')<sub>2</sub></sub> fragment; (iii) an F<sub>ab</sub> fragment generated by the treatment of the antibody molecule with papain and a reducing agent; and (iv) F<sub>v</sub> fragments.

Additionally, recombinant anti-FCTR<sub>X</sub> antibodies, such as chimeric and humanized monoclonal antibodies, comprising both human and non-human portions, which can be made using standard recombinant DNA techniques, are within the scope of the invention. Such chimeric and humanized monoclonal antibodies can be produced by recombinant DNA techniques known in the art, for example using methods described in International Application No. PCT/US86/02269; European Patent Application No. 184,187; European Patent Application No. 171,496; European Patent Application No. 173,494; PCT International Publication No. WO 86/01533; U.S. Patent No. 4,816,567; U.S. Pat. No. 5,225,539; European Patent Application No. 125,023; Better, *et al.*, 1988. *Science* 240: 1041-1043; Liu, *et al.*, 1987. *Proc. Natl. Acad. Sci. USA* 84: 3439-3443; Liu, *et al.*, 1987. *J. Immunol.* 139: 3521-3526; Sun, *et al.*, 1987. *Proc. Natl. Acad. Sci. USA* 84: 214-218; Nishimura, *et al.*, 1987. *Cancer Res.* 47: 999-1005; Wood, *et al.*, 1985. *Nature* 314 :446-449; Shaw, *et al.*, 1988. *J. Natl. Cancer Inst.* 80: 1553-1559; Morrison(1985) *Science* 229:1202-1207; Oi, *et al.* (1986) *BioTechniques* 4:214; Jones, *et al.*, 1986. *Nature* 321: 552-525; Verhoeyan, *et al.*, 1988. *Science* 239: 1534; and Beidler, *et al.*, 1988. *J. Immunol.* 141: 4053-4060. Each of the above citations are incorporated herein by reference in their entirety.

In one embodiment, methods for the screening of antibodies that possess the desired specificity include, but are not limited to, enzyme-linked immunosorbent assay (ELISA) and other immunologically-mediated techniques known within the art. In a specific embodiment, selection of antibodies that are specific to a particular domain of an FCTR<sub>X</sub> protein is facilitated by generation of hybridomas that bind to the fragment of an FCTR<sub>X</sub> protein possessing such a domain. Thus, antibodies that are specific for a desired domain within an FCTR<sub>X</sub> protein, or derivatives, fragments, analogs or homologs thereof, are also provided herein.

Anti-FCTR<sub>X</sub> antibodies may be used in methods known within the art relating to the localization and/or quantitation of an FCTR<sub>X</sub> protein (*e.g.*, for use in measuring levels of the FCTR<sub>X</sub> protein within appropriate physiological samples, for use in diagnostic methods, for

use in imaging the protein, and the like). In a given embodiment, antibodies for FCTR<sub>X</sub> proteins, or derivatives, fragments, analogs or homologs thereof, that contain the antibody derived binding domain, are utilized as pharmacologically-active compounds (hereinafter "Therapeutics").

5           An anti-FCTR<sub>X</sub> antibody (*e.g.*, monoclonal antibody) can be used to isolate an FCTR<sub>X</sub> polypeptide by standard techniques, such as affinity chromatography or immunoprecipitation. An anti-FCTR<sub>X</sub> antibody can facilitate the purification of natural FCTR<sub>X</sub> polypeptide from cells and of recombinantly-produced FCTR<sub>X</sub> polypeptide expressed in host cells. Moreover, an anti-FCTR<sub>X</sub> antibody can be used to detect FCTR<sub>X</sub> protein (*e.g.*,  
10   in a cellular lysate or cell supernatant) in order to evaluate the abundance and pattern of expression of the FCTR<sub>X</sub> protein. Anti-FCTR<sub>X</sub> antibodies can be used diagnostically to monitor protein levels in tissue as part of a clinical testing procedure, *e.g.*, to, for example, determine the efficacy of a given treatment regimen. Detection can be facilitated by coupling (*i.e.*, physically linking) the antibody to a detectable substance. Examples of detectable  
15   substances include various enzymes, prosthetic groups, fluorescent materials, luminescent materials, bioluminescent materials, and radioactive materials. Examples of suitable enzymes include horseradish peroxidase, alkaline phosphatase,  $\beta$ -galactosidase, or acetylcholinesterase; examples of suitable prosthetic group complexes include streptavidin/biotin and avidin/biotin; examples of suitable fluorescent materials include umbelliferone, fluorescein, fluorescein  
20   isothiocyanate, rhodamine, dichlorotriazinylamine fluorescein, dansyl chloride or phycoerythrin; an example of a luminescent material includes luminol; examples of bioluminescent materials include luciferase, luciferin, and aequorin, and examples of suitable radioactive material include  $^{125}\text{I}$ ,  $^{131}\text{I}$ ,  $^{35}\text{S}$  or  $^3\text{H}$ .

### **FCTR<sub>X</sub> Recombinant Expression Vectors and Host Cells**

25           Another aspect of the invention pertains to vectors, preferably expression vectors, containing a nucleic acid encoding an FCTR<sub>X</sub> protein, or derivatives, fragments, analogs or homologs thereof. As used herein, the term "vector" refers to a nucleic acid molecule capable of transporting another nucleic acid to which it has been linked. One type of vector is a "plasmid", which refers to a circular double stranded DNA loop into which additional DNA  
30   segments can be ligated. Another type of vector is a viral vector, wherein additional DNA segments can be ligated into the viral genome. Certain vectors are capable of autonomous replication in a host cell into which they are introduced (*e.g.*, bacterial vectors having a bacterial origin of replication and episomal mammalian vectors). Other vectors (*e.g.*,

non-episomal mammalian vectors) are integrated into the genome of a host cell upon introduction into the host cell, and thereby are replicated along with the host genome. Moreover, certain vectors are capable of directing the expression of genes to which they are operatively-linked. Such vectors are referred to herein as "expression vectors". In general, expression vectors of utility in recombinant DNA techniques are often in the form of plasmids. In the present specification, "plasmid" and "vector" can be used interchangeably as the plasmid is the most commonly used form of vector. However, the invention is intended to include such other forms of expression vectors, such as viral vectors (*e.g.*, replication defective retroviruses, adenoviruses and adeno-associated viruses), which serve equivalent functions.

The recombinant expression vectors of the invention comprise a nucleic acid of the invention in a form suitable for expression of the nucleic acid in a host cell, which means that the recombinant expression vectors include one or more regulatory sequences, selected on the basis of the host cells to be used for expression, that is operatively-linked to the nucleic acid sequence to be expressed. Within a recombinant expression vector, "operably-linked" is intended to mean that the nucleotide sequence of interest is linked to the regulatory sequence(s) in a manner that allows for expression of the nucleotide sequence (*e.g.*, in an *in vitro* transcription/translation system or in a host cell when the vector is introduced into the host cell).

The term "regulatory sequence" is intended to include promoters, enhancers and other expression control elements (*e.g.*, polyadenylation signals). Such regulatory sequences are described, for example, in Goeddel, GENE EXPRESSION TECHNOLOGY: METHODS IN ENZYMOLOGY 185, Academic Press, San Diego, Calif. (1990). Regulatory sequences include those that direct constitutive expression of a nucleotide sequence in many types of host cell and those that direct expression of the nucleotide sequence only in certain host cells (*e.g.*, tissue-specific regulatory sequences). It will be appreciated by those skilled in the art that the design of the expression vector can depend on such factors as the choice of the host cell to be transformed, the level of expression of protein desired, etc. The expression vectors of the invention can be introduced into host cells to thereby produce proteins or peptides, including fusion proteins or peptides, encoded by nucleic acids as described herein (*e.g.*, FCTRX proteins, mutant forms of FCTRX proteins, fusion proteins, etc.).

The recombinant expression vectors of the invention can be designed for expression of FCTRX proteins in prokaryotic or eukaryotic cells. For example, FCTRX proteins can be expressed in bacterial cells such as *Escherichia coli*, insect cells (using baculovirus expression vectors) yeast cells or mammalian cells. Suitable host cells are discussed further in Goeddel,

GENE EXPRESSION TECHNOLOGY: METHODS IN ENZYMOLOGY 185, Academic Press, San Diego, Calif. (1990). Alternatively, the recombinant expression vector can be transcribed and translated *in vitro*, for example using T7 promoter regulatory sequences and T7 polymerase.

Expression of proteins in prokaryotes is most often carried out in *Escherichia coli* with  
5 vectors containing constitutive or inducible promoters directing the expression of either fusion or non-fusion proteins. Fusion vectors add a number of amino acids to a protein encoded therein, usually to the amino terminus of the recombinant protein. Such fusion vectors typically serve three purposes: (i) to increase expression of recombinant protein; (ii) to increase the solubility of the recombinant protein; and (iii) to aid in the purification of the  
10 recombinant protein by acting as a ligand in affinity purification. Often, in fusion expression vectors, a proteolytic cleavage site is introduced at the junction of the fusion moiety and the recombinant protein to enable separation of the recombinant protein from the fusion moiety subsequent to purification of the fusion protein. Such enzymes, and their cognate recognition sequences, include Factor Xa, thrombin and enterokinase. Typical fusion expression vectors  
15 include pGEX (Pharmacia Biotech Inc; Smith and Johnson, 1988. *Gene* 67: 31-40), pMAL (New England Biolabs, Beverly, Mass.) and pRIT5 (Pharmacia, Piscataway, N.J.) that fuse glutathione S-transferase (GST), maltose E binding protein, or protein A, respectively, to the target recombinant protein.

Examples of suitable inducible non-fusion *E. coli* expression vectors include pTrc  
20 (Amrann *et al.*, (1988) *Gene* 69:301-315) and pET 11d (Studier *et al.*, GENE EXPRESSION TECHNOLOGY: METHODS IN ENZYMOLOGY 185, Academic Press, San Diego, Calif. (1990) 60-89).

One strategy to maximize recombinant protein expression in *E. coli* is to express the protein in a host bacteria with an impaired capacity to proteolytically cleave the recombinant  
25 protein. See, e.g., Gottesman, GENE EXPRESSION TECHNOLOGY: METHODS IN ENZYMOLOGY 185, Academic Press, San Diego, Calif. (1990) 119-128. Another strategy is to alter the nucleic acid sequence of the nucleic acid to be inserted into an expression vector so that the individual codons for each amino acid are those preferentially utilized in *E. coli* (see, e.g., Wada, *et al.*, 1992. *Nucl. Acids Res.* 20: 2111-2118). Such alteration of nucleic acid  
30 sequences of the invention can be carried out by standard DNA synthesis techniques.

In another embodiment, the FCTRX expression vector is a yeast expression vector. Examples of vectors for expression in yeast *Saccharomyces cerevisiae* include pYepSec1 (Baldari, *et al.*, 1987. *EMBO J.* 6: 229-234), pMFa (Kurjan and Herskowitz, 1982. *Cell* 30:

933-943), pJRY88 (Schultz *et al.*, 1987. *Gene* 54: 113-123), pYES2 (Invitrogen Corporation, San Diego, Calif.), and picZ (Invitrogen Corp, San Diego, Calif.).

Alternatively, FCTR<sub>X</sub> can be expressed in insect cells using baculovirus expression vectors. Baculovirus vectors available for expression of proteins in cultured insect cells (*e.g.*,  
5 SF9 cells) include the pAc series (Smith, *et al.*, 1983. *Mol. Cell. Biol.* 3: 2156-2165) and the pVL series (Lucklow and Summers, 1989. *Virology* 170: 31-39).

In yet another embodiment, a nucleic acid of the invention is expressed in mammalian cells using a mammalian expression vector. Examples of mammalian expression vectors include pCDM8 (Seed, 1987. *Nature* 329: 840) and pMT2PC (Kaufman, *et al.*, 1987. *EMBO J.* 6: 187-195). When used in mammalian cells, the expression vector's control functions are  
10 often provided by viral regulatory elements. For example, commonly used promoters are derived from polyoma, adenovirus 2, cytomegalovirus, and simian virus 40. For other suitable expression systems for both prokaryotic and eukaryotic cells see, *e.g.*, Chapters 16 and 17 of Sambrook, *et al.*, MOLECULAR CLONING: A LABORATORY MANUAL. 2nd ed., Cold Spring  
15 Harbor Laboratory, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y., 1989.

In another embodiment, the recombinant mammalian expression vector is capable of directing expression of the nucleic acid preferentially in a particular cell type (*e.g.*, tissue-specific regulatory elements are used to express the nucleic acid). Tissue-specific regulatory elements are known in the art. Non-limiting examples of suitable tissue-specific  
20 promoters include the albumin promoter (liver-specific; Pinkert, *et al.*, 1987. *Genes Dev.* 1: 268-277), lymphoid-specific promoters (Calame and Eaton, 1988. *Adv. Immunol.* 43: 235-275), in particular promoters of T cell receptors (Winoto and Baltimore, 1989. *EMBO J.* 8: 729-733) and immunoglobulins (Banerji, *et al.*, 1983. *Cell* 33: 729-740; Queen and Baltimore, 1983. *Cell* 33: 741-748), neuron-specific promoters (*e.g.*, the neurofilament  
25 promoter; Byrne and Ruddle, 1989. *Proc. Natl. Acad. Sci. USA* 86: 5473-5477), pancreas-specific promoters (Edlund, *et al.*, 1985. *Science* 230: 912-916), and mammary gland-specific promoters (*e.g.*, milk whey promoter; U.S. Pat. No. 4,873,316 and European Application Publication No. 264,166). Developmentally-regulated promoters are also encompassed, *e.g.*, the murine hox promoters (Kessel and Gruss, 1990. *Science* 249: 374-379)  
30 and the  $\alpha$ -fetoprotein promoter (Campes and Tilghman, 1989. *Genes Dev.* 3: 537-546).

The invention further provides a recombinant expression vector comprising a DNA molecule of the invention cloned into the expression vector in an antisense orientation. That is, the DNA molecule is operatively-linked to a regulatory sequence in a manner that allows for expression (by transcription of the DNA molecule) of an RNA molecule that is antisense to

FCTR<sub>X</sub> mRNA. Regulatory sequences operatively linked to a nucleic acid cloned in the antisense orientation can be chosen that direct the continuous expression of the antisense RNA molecule in a variety of cell types, for instance viral promoters and/or enhancers, or regulatory sequences can be chosen that direct constitutive, tissue specific or cell type specific expression of antisense RNA. The antisense expression vector can be in the form of a recombinant plasmid, phagemid or attenuated virus in which antisense nucleic acids are produced under the control of a high efficiency regulatory region, the activity of which can be determined by the cell type into which the vector is introduced. For a discussion of the regulation of gene expression using antisense genes *see, e.g.,* Weintraub, *et al.*, "Antisense RNA as a molecular tool for genetic analysis," *Reviews-Trends in Genetics*, Vol. 1(1) 1986.

Another aspect of the invention pertains to host cells into which a recombinant expression vector of the invention has been introduced. The terms "host cell" and "recombinant host cell" are used interchangeably herein. It is understood that such terms refer not only to the particular subject cell but also to the progeny or potential progeny of such a cell. Because certain modifications may occur in succeeding generations due to either mutation or environmental influences, such progeny may not, in fact, be identical to the parent cell, but are still included within the scope of the term as used herein.

A host cell can be any prokaryotic or eukaryotic cell. For example, FCTR<sub>X</sub> protein can be expressed in bacterial cells such as *E. coli*, insect cells, yeast or mammalian cells (such as Chinese hamster ovary cells (CHO) or COS cells). Other suitable host cells are known to those skilled in the art.

Vector DNA can be introduced into prokaryotic or eukaryotic cells via conventional transformation or transfection techniques. As used herein, the terms "transformation" and "transfection" are intended to refer to a variety of art-recognized techniques for introducing foreign nucleic acid (*e.g.,* DNA) into a host cell, including calcium phosphate or calcium chloride co-precipitation, DEAE-dextran-mediated transfection, lipofection, or electroporation. Suitable methods for transforming or transfecting host cells can be found in Sambrook, *et al.* (MOLECULAR CLONING: A LABORATORY MANUAL. 2nd ed., Cold Spring Harbor Laboratory, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y., 1989), and other laboratory manuals.

For stable transfection of mammalian cells, it is known that, depending upon the expression vector and transfection technique used, only a small fraction of cells may integrate the foreign DNA into their genome. In order to identify and select these integrants, a gene that encodes a selectable marker (*e.g.,* resistance to antibiotics) is generally introduced into the

host cells along with the gene of interest. Various selectable markers include those that confer resistance to drugs, such as G418, hygromycin and methotrexate. Nucleic acid encoding a selectable marker can be introduced into a host cell on the same vector as that encoding FCTR<sub>X</sub> or can be introduced on a separate vector. Cells stably transfected with the introduced nucleic acid can be identified by drug selection (*e.g.*, cells that have incorporated the selectable marker gene will survive, while the other cells die).

A host cell of the invention, such as a prokaryotic or eukaryotic host cell in culture, can be used to produce (*i.e.*, express) FCTR<sub>X</sub> protein. Accordingly, the invention further provides methods for producing FCTR<sub>X</sub> protein using the host cells of the invention. In one embodiment, the method comprises culturing the host cell of invention (into which a recombinant expression vector encoding FCTR<sub>X</sub> protein has been introduced) in a suitable medium such that FCTR<sub>X</sub> protein is produced. In another embodiment, the method further comprises isolating FCTR<sub>X</sub> protein from the medium or the host cell.

### Transgenic FCTR<sub>X</sub> Animals

The host cells of the invention can also be used to produce non-human transgenic animals. For example, in one embodiment, a host cell of the invention is a fertilized oocyte or an embryonic stem cell into which FCTR<sub>X</sub> protein-coding sequences have been introduced. Such host cells can then be used to create non-human transgenic animals in which exogenous FCTR<sub>X</sub> sequences have been introduced into their genome or homologous recombinant animals in which endogenous FCTR<sub>X</sub> sequences have been altered. Such animals are useful for studying the function and/or activity of FCTR<sub>X</sub> protein and for identifying and/or evaluating modulators of FCTR<sub>X</sub> protein activity. As used herein, a "transgenic animal" is a non-human animal, preferably a mammal, more preferably a rodent such as a rat or mouse, in which one or more of the cells of the animal includes a transgene. Other examples of transgenic animals include non-human primates, sheep, dogs, cows, goats, chickens, amphibians, etc. A transgene is exogenous DNA that is integrated into the genome of a cell from which a transgenic animal develops and that remains in the genome of the mature animal, thereby directing the expression of an encoded gene product in one or more cell types or tissues of the transgenic animal. As used herein, a "homologous recombinant animal" is a non-human animal, preferably a mammal, more preferably a mouse, in which an endogenous FCTR<sub>X</sub> gene has been altered by homologous recombination between the endogenous gene and an exogenous DNA molecule introduced into a cell of the animal, *e.g.*, an embryonic cell of the animal, prior to development of the animal.

A transgenic animal of the invention can be created by introducing FCTR<sub>X</sub>-encoding nucleic acid into the male pronuclei of a fertilized oocyte (*e.g.*, by microinjection, retroviral infection) and allowing the oocyte to develop in a pseudopregnant female foster animal. The human FCTR<sub>X</sub> cDNA sequences of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, can be introduced as a transgene into the genome of a non-human animal.

Alternatively, a non-human homologue of the human FCTR<sub>X</sub> gene, such as a mouse FCTR<sub>X</sub> gene, can be isolated based on hybridization to the human FCTR<sub>X</sub> cDNA (described further *supra*) and used as a transgene. Intronic sequences and polyadenylation signals can also be included in the transgene to increase the efficiency of expression of the transgene. A

tissue-specific regulatory sequence(s) can be operably-linked to the FCTR<sub>X</sub> transgene to direct expression of FCTR<sub>X</sub> protein to particular cells. Methods for generating transgenic animals via embryo manipulation and microinjection, particularly animals such as mice, have become conventional in the art and are described, for example, in U.S. Patent Nos. 4,736,866; 4,870,009; and 4,873,191; and Hogan, 1986. In: MANIPULATING THE MOUSE EMBRYO, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y. Similar methods are used for production of other transgenic animals. A transgenic founder animal can be identified based upon the presence of the FCTR<sub>X</sub> transgene in its genome and/or expression of FCTR<sub>X</sub> mRNA in tissues or cells of the animals. A transgenic founder animal can then be used to breed additional animals carrying the transgene. Moreover, transgenic animals carrying a transgene-encoding FCTR<sub>X</sub> protein can further be bred to other transgenic animals carrying other transgenes.

To create a homologous recombinant animal, a vector is prepared which contains at least a portion of an FCTR<sub>X</sub> gene into which a deletion, addition or substitution has been introduced to thereby alter, *e.g.*, functionally disrupt, the FCTR<sub>X</sub> gene. The FCTR<sub>X</sub> gene can be a human gene (*e.g.*, the cDNA of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24), but more preferably, is a non-human homologue of a human FCTR<sub>X</sub> gene. For example, a mouse homologue of human FCTR<sub>X</sub> gene of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, can be used to construct a homologous recombination vector suitable for altering an endogenous FCTR<sub>X</sub> gene in the mouse genome. In one embodiment, the vector is designed such that, upon homologous recombination, the endogenous FCTR<sub>X</sub> gene is functionally disrupted (*i.e.*, no longer encodes a functional protein; also referred to as a "knock out" vector).

Alternatively, the vector can be designed such that, upon homologous recombination, the endogenous FCTR<sub>X</sub> gene is mutated or otherwise altered but still encodes functional

protein (*e.g.*, the upstream regulatory region can be altered to thereby alter the expression of the endogenous FCTR<sub>X</sub> protein). In the homologous recombination vector, the altered portion of the FCTR<sub>X</sub> gene is flanked at its 5'- and 3'-termini by additional nucleic acid of the FCTR<sub>X</sub> gene to allow for homologous recombination to occur between the exogenous FCTR<sub>X</sub> gene  
5 carried by the vector and an endogenous FCTR<sub>X</sub> gene in an embryonic stem cell. The additional flanking FCTR<sub>X</sub> nucleic acid is of sufficient length for successful homologous recombination with the endogenous gene. Typically, several kilobases of flanking DNA (both at the 5'- and 3'-termini) are included in the vector. *See, e.g.*, Thomas, *et al.*, 1987. *Cell* 51: 503 for a description of homologous recombination vectors. The vector is then introduced into  
10 an embryonic stem cell line (*e.g.*, by electroporation) and cells in which the introduced FCTR<sub>X</sub> gene has homologously-recombined with the endogenous FCTR<sub>X</sub> gene are selected. *See, e.g.*, Li, *et al.*, 1992. *Cell* 69: 915.

The selected cells are then injected into a blastocyst of an animal (*e.g.*, a mouse) to form aggregation chimeras. *See, e.g.*, Bradley, 1987. In: TERATOCARCINOMAS AND  
15 EMBRYONIC STEM CELLS: A PRACTICAL APPROACH, Robertson, ed. IRL, Oxford, pp. 113-152. A chimeric embryo can then be implanted into a suitable pseudopregnant female foster animal and the embryo brought to term. Progeny harboring the homologously-recombined DNA in their germ cells can be used to breed animals in which all cells of the animal contain the homologously-recombined DNA by germline transmission of the transgene. Methods for  
20 constructing homologous recombination vectors and homologous recombinant animals are described further in Bradley, 1991. *Curr. Opin. Biotechnol.* 2: 823-829; PCT International Publication Nos.: WO 90/11354; WO 91/01140; WO 92/0968; and WO 93/04169.

In another embodiment, transgenic non-humans animals can be produced that contain selected systems that allow for regulated expression of the transgene. One example of such a  
25 system is the cre/loxP recombinase system of bacteriophage P1. For a description of the cre/loxP recombinase system, *See, e.g.*, Lakso, *et al.*, 1992. *Proc. Natl. Acad. Sci. USA* 89: 6232-6236. Another example of a recombinase system is the FLP recombinase system of *Saccharomyces cerevisiae*. *See, O'Gorman, et al.*, 1991. *Science* 251:1351-1355. If a cre/loxP recombinase system is used to regulate expression of the transgene, animals containing  
30 transgenes encoding both the Cre recombinase and a selected protein are required. Such animals can be provided through the construction of "double" transgenic animals, *e.g.*, by mating two transgenic animals, one containing a transgene encoding a selected protein and the other containing a transgene encoding a recombinase.

Clones of the non-human transgenic animals described herein can also be produced according to the methods described in Wilmut, *et al.*, 1997. *Nature* 385: 810-813. In brief, a cell (*e.g.*, a somatic cell) from the transgenic animal can be isolated and induced to exit the growth cycle and enter G<sub>0</sub> phase. The quiescent cell can then be fused, *e.g.*, through the use of electrical pulses, to an enucleated oocyte from an animal of the same species from which the quiescent cell is isolated. The reconstructed oocyte is then cultured such that it develops to morula or blastocyte and then transferred to pseudopregnant female foster animal. The offspring borne of this female foster animal will be a clone of the animal from which the cell (*e.g.*, the somatic cell) is isolated.

## 10 **Pharmaceutical Compositions**

The FCTR<sub>X</sub> nucleic acid molecules, FCTR<sub>X</sub> proteins, and anti-FCTR<sub>X</sub> antibodies (also referred to herein as "active compounds") of the invention, and derivatives, fragments, analogs and homologs thereof, can be incorporated into pharmaceutical compositions suitable for administration. Such compositions typically comprise the nucleic acid molecule, protein, or antibody and a pharmaceutically acceptable carrier. As used herein, "pharmaceutically acceptable carrier" is intended to include any and all solvents, dispersion media, coatings, antibacterial and antifungal agents, isotonic and absorption delaying agents, and the like, compatible with pharmaceutical administration. Suitable carriers are described in the most recent edition of Remington's Pharmaceutical Sciences, a standard reference text in the field, which is incorporated herein by reference. Preferred examples of such carriers or diluents include, but are not limited to, water, saline, finger's solutions, dextrose solution, and 5% human serum albumin. Liposomes and non-aqueous vehicles such as fixed oils may also be used. The use of such media and agents for pharmaceutically active substances is well known in the art. Except insofar as any conventional media or agent is incompatible with the active compound, use thereof in the compositions is contemplated. Supplementary active compounds can also be incorporated into the compositions.

A pharmaceutical composition of the invention is formulated to be compatible with its intended route of administration. Examples of routes of administration include parenteral, *e.g.*, intravenous, intradermal, subcutaneous, oral (*e.g.*, inhalation), transdermal (*i.e.*, topical), transmucosal, and rectal administration. Solutions or suspensions used for parenteral, intradermal, or subcutaneous application can include the following components: a sterile diluent such as water for injection, saline solution, fixed oils, polyethylene glycols, glycerine, propylene glycol or other synthetic solvents; antibacterial agents such as benzyl alcohol or

5 methyl parabens; antioxidants such as ascorbic acid or sodium bisulfite; chelating agents such as ethylenediaminetetraacetic acid (EDTA); buffers such as acetates, citrates or phosphates, and agents for the adjustment of tonicity such as sodium chloride or dextrose. The pH can be adjusted with acids or bases, such as hydrochloric acid or sodium hydroxide. The parenteral preparation can be enclosed in ampoules, disposable syringes or multiple dose vials made of glass or plastic.

10 Pharmaceutical compositions suitable for injectable use include sterile aqueous solutions (where water soluble) or dispersions and sterile powders for the extemporaneous preparation of sterile injectable solutions or dispersion. For intravenous administration, suitable carriers include physiological saline, bacteriostatic water, Cremophor EL™ (BASF, Parsippany, N.J.) or phosphate buffered saline (PBS). In all cases, the composition must be sterile and should be fluid to the extent that easy syringeability exists. It must be stable under the conditions of manufacture and storage and must be preserved against the contaminating action of microorganisms such as bacteria and fungi. The carrier can be a solvent or  
15 dispersion medium containing, for example, water, ethanol, polyol (for example, glycerol, propylene glycol, and liquid polyethylene glycol, and the like), and suitable mixtures thereof. The proper fluidity can be maintained, for example, by the use of a coating such as lecithin, by the maintenance of the required particle size in the case of dispersion and by the use of surfactants. Prevention of the action of microorganisms can be achieved by various  
20 antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, ascorbic acid, thimerosal, and the like. In many cases, it will be preferable to include isotonic agents, for example, sugars, polyalcohols such as manitol, sorbitol, sodium chloride in the composition. Prolonged absorption of the injectable compositions can be brought about by including in the composition an agent which delays absorption, for example, aluminum  
25 monostearate and gelatin.

Sterile injectable solutions can be prepared by incorporating the active compound (*e.g.*, an FCTR<sub>X</sub> protein or anti-FCTR<sub>X</sub> antibody) in the required amount in an appropriate solvent with one or a combination of ingredients enumerated above, as required, followed by filtered sterilization. Generally, dispersions are prepared by incorporating the active compound into a  
30 sterile vehicle that contains a basic dispersion medium and the required other ingredients from those enumerated above. In the case of sterile powders for the preparation of sterile injectable solutions, methods of preparation are vacuum drying and freeze-drying that yields a powder of the active ingredient plus any additional desired ingredient from a previously sterile-filtered solution thereof.

Oral compositions generally include an inert diluent or an edible carrier. They can be enclosed in gelatin capsules or compressed into tablets. For the purpose of oral therapeutic administration, the active compound can be incorporated with excipients and used in the form of tablets, troches, or capsules. Oral compositions can also be prepared using a fluid carrier  
5 for use as a mouthwash, wherein the compound in the fluid carrier is applied orally and swished and expectorated or swallowed. Pharmaceutically compatible binding agents, and/or adjuvant materials can be included as part of the composition. The tablets, pills, capsules, troches and the like can contain any of the following ingredients, or compounds of a similar nature: a binder such as microcrystalline cellulose, gum tragacanth or gelatin; an excipient  
10 such as starch or lactose, a disintegrating agent such as alginic acid, Primogel, or corn starch; a lubricant such as magnesium stearate or Sterotes; a glidant such as colloidal silicon dioxide; a sweetening agent such as sucrose or saccharin; or a flavoring agent such as peppermint, methyl salicylate, or orange flavoring.

For administration by inhalation, the compounds are delivered in the form of an  
15 aerosol spray from pressured container or dispenser which contains a suitable propellant, *e.g.*, a gas such as carbon dioxide, or a nebulizer.

Systemic administration can also be by transmucosal or transdermal means. For transmucosal or transdermal administration, penetrants appropriate to the barrier to be permeated are used in the formulation. Such penetrants are generally known in the art, and  
20 include, for example, for transmucosal administration, detergents, bile salts, and fusidic acid derivatives. Transmucosal administration can be accomplished through the use of nasal sprays or suppositories. For transdermal administration, the active compounds are formulated into ointments, salves, gels, or creams as generally known in the art.

The compounds can also be prepared in the form of suppositories (*e.g.*, with  
25 conventional suppository bases such as cocoa butter and other glycerides) or retention enemas for rectal delivery.

In one embodiment, the active compounds are prepared with carriers that will protect the compound against rapid elimination from the body, such as a controlled release formulation, including implants and microencapsulated delivery systems. Biodegradable,  
30 biocompatible polymers can be used, such as ethylene vinyl acetate, polyanhydrides, polyglycolic acid, collagen, polyorthoesters, and polylactic acid. Methods for preparation of such formulations will be apparent to those skilled in the art. The materials can also be obtained commercially from Alza Corporation and Nova Pharmaceuticals, Inc. Liposomal suspensions (including liposomes targeted to infected cells with monoclonal antibodies to viral

antigens) can also be used as pharmaceutically acceptable carriers. These can be prepared according to methods known to those skilled in the art, for example, as described in U.S. Patent No. 4,522,811.

It is especially advantageous to formulate oral or parenteral compositions in dosage unit form for ease of administration and uniformity of dosage. Dosage unit form as used herein refers to physically discrete units suited as unitary dosages for the subject to be treated; each unit containing a predetermined quantity of active compound calculated to produce the desired therapeutic effect in association with the required pharmaceutical carrier. The specification for the dosage unit forms of the invention are dictated by and directly dependent on the unique characteristics of the active compound and the particular therapeutic effect to be achieved, and the limitations inherent in the art of compounding such an active compound for the treatment of individuals.

The nucleic acid molecules of the invention can be inserted into vectors and used as gene therapy vectors. Gene therapy vectors can be delivered to a subject by, for example, intravenous injection, local administration (*see, e.g.*, U.S. Patent No. 5,328,470) or by stereotactic injection (*see, e.g.*, Chen, *et al.*, 1994. *Proc. Natl. Acad. Sci. USA* 91: 3054-3057). The pharmaceutical preparation of the gene therapy vector can include the gene therapy vector in an acceptable diluent, or can comprise a slow release matrix in which the gene delivery vehicle is imbedded. Alternatively, where the complete gene delivery vector can be produced intact from recombinant cells, *e.g.*, retroviral vectors, the pharmaceutical preparation can include one or more cells that produce the gene delivery system.

The pharmaceutical compositions can be included in a container, pack, or dispenser together with instructions for administration.

### Screening and Detection Methods

The isolated nucleic acid molecules of the invention can be used to express FCTR<sub>X</sub> protein (*e.g.*, via a recombinant expression vector in a host cell in gene therapy applications), to detect FCTR<sub>X</sub> mRNA (*e.g.*, in a biological sample) or a genetic lesion in an FCTR<sub>X</sub> gene, and to modulate FCTR<sub>X</sub> activity, as described further, below. In addition, the FCTR<sub>X</sub> proteins can be used to screen drugs or compounds that modulate the FCTR<sub>X</sub> protein activity or expression as well as to treat disorders characterized by insufficient or excessive production of FCTR<sub>X</sub> protein or production of FCTR<sub>X</sub> protein forms that have decreased or aberrant activity compared to FCTR<sub>X</sub> wild-type protein (*e.g.*; diabetes (regulates insulin release); obesity (binds and transport lipids); metabolic disturbances associated with obesity, the

metabolic syndrome X as well as anorexia and wasting disorders associated with chronic diseases and various cancers, and infectious disease (possesses anti-microbial activity) and the various dyslipidemias. In addition, the anti-FCTR<sub>X</sub> antibodies of the invention can be used to detect and isolate FCTR<sub>X</sub> proteins and modulate FCTR<sub>X</sub> activity. In yet a further aspect, the invention can be used in methods to influence appetite, absorption of nutrients and the disposition of metabolic substrates in both a positive and negative fashion.

The invention further pertains to novel agents identified by the screening assays described herein and uses thereof for treatments as described, *supra*.

### ***Screening Assays***

The invention provides a method (also referred to herein as a "screening assay") for identifying modulators, *i.e.*, candidate or test compounds or agents (*e.g.*, peptides, peptidomimetics, small molecules or other drugs) that bind to FCTR<sub>X</sub> proteins or have a stimulatory or inhibitory effect on, *e.g.*, FCTR<sub>X</sub> protein expression or FCTR<sub>X</sub> protein activity. The invention also includes compounds identified in the screening assays described herein.

In one embodiment, the invention provides assays for screening candidate or test compounds which bind to or modulate the activity of the membrane-bound form of an FCTR<sub>X</sub> protein or polypeptide or biologically-active portion thereof. The test compounds of the invention can be obtained using any of the numerous approaches in combinatorial library methods known in the art, including: biological libraries; spatially addressable parallel solid phase or solution phase libraries; synthetic library methods requiring deconvolution; the "one-bead one-compound" library method; and synthetic library methods using affinity chromatography selection. The biological library approach is limited to peptide libraries, while the other four approaches are applicable to peptide, non-peptide oligomer or small molecule libraries of compounds. *See, e.g., Lam, 1997. Anticancer Drug Design 12: 145.*

A "small molecule" as used herein, is meant to refer to a composition that has a molecular weight of less than about 5 kD and most preferably less than about 4 kD. Small molecules can be, *e.g.*, nucleic acids, peptides, polypeptides, peptidomimetics, carbohydrates, lipids or other organic or inorganic molecules. Libraries of chemical and/or biological mixtures, such as fungal, bacterial, or algal extracts, are known in the art and can be screened with any of the assays of the invention.

Examples of methods for the synthesis of molecular libraries can be found in the art, for example in: DeWitt, *et al.*, 1993. *Proc. Natl. Acad. Sci. U.S.A.* 90: 6909; Erb, *et al.*, 1994. *Proc. Natl. Acad. Sci. U.S.A.* 91: 11422; Zuckermann, *et al.*, 1994. *J. Med. Chem.* 37: 2678; Cho, *et al.*, 1993. *Science* 261: 1303; Carrell, *et al.*, 1994. *Angew. Chem. Int. Ed. Engl.* 33:

2059; Carell, *et al.*, 1994. *Angew. Chem. Int. Ed. Engl.* 33: 2061; and Gallop, *et al.*, 1994. *J. Med. Chem.* 37: 1233.

Libraries of compounds may be presented in solution (*e.g.*, Houghten, 1992. *Biotechniques* 13: 412-421), or on beads (Lam, 1991. *Nature* 354: 82-84), on chips (Fodor, 1993. *Nature* 364: 555-556), bacteria (Ladner, U.S. Patent No. 5,223,409), spores (Ladner, U.S. Patent 5,233,409), plasmids (Cull, *et al.*, 1992. *Proc. Natl. Acad. Sci. USA* 89: 1865-1869) or on phage (Scott and Smith, 1990. *Science* 249: 386-390; Devlin, 1990. *Science* 249: 404-406; Cwirla, *et al.*, 1990. *Proc. Natl. Acad. Sci. U.S.A.* 87: 6378-6382; Felici, 1991. *J. Mol. Biol.* 222: 301-310; Ladner, U.S. Patent No. 5,233,409.).

In one embodiment, an assay is a cell-based assay in which a cell which expresses a membrane-bound form of FCTR<sub>X</sub> protein, or a biologically-active portion thereof, on the cell surface is contacted with a test compound and the ability of the test compound to bind to an FCTR<sub>X</sub> protein determined. The cell, for example, can be of mammalian origin or a yeast cell. Determining the ability of the test compound to bind to the FCTR<sub>X</sub> protein can be accomplished, for example, by coupling the test compound with a radioisotope or enzymatic label such that binding of the test compound to the FCTR<sub>X</sub> protein or biologically-active portion thereof can be determined by detecting the labeled compound in a complex. For example, test compounds can be labeled with <sup>125</sup>I, <sup>35</sup>S, <sup>14</sup>C, or <sup>3</sup>H, either directly or indirectly, and the radioisotope detected by direct counting of radioemission or by scintillation counting. Alternatively, test compounds can be enzymatically-labeled with, for example, horseradish peroxidase, alkaline phosphatase, or luciferase, and the enzymatic label detected by determination of conversion of an appropriate substrate to product. In one embodiment, the assay comprises contacting a cell which expresses a membrane-bound form of FCTR<sub>X</sub> protein, or a biologically-active portion thereof, on the cell surface with a known compound which binds FCTR<sub>X</sub> to form an assay mixture, contacting the assay mixture with a test compound, and determining the ability of the test compound to interact with an FCTR<sub>X</sub> protein, wherein determining the ability of the test compound to interact with an FCTR<sub>X</sub> protein comprises determining the ability of the test compound to preferentially bind to FCTR<sub>X</sub> protein or a biologically-active portion thereof as compared to the known compound.

In another embodiment, an assay is a cell-based assay comprising contacting a cell expressing a membrane-bound form of FCTR<sub>X</sub> protein, or a biologically-active portion thereof, on the cell surface with a test compound and determining the ability of the test compound to modulate (*e.g.*, stimulate or inhibit) the activity of the FCTR<sub>X</sub> protein or biologically-active portion thereof. Determining the ability of the test compound to modulate

the activity of FCTR<sub>X</sub> or a biologically-active portion thereof can be accomplished, for example, by determining the ability of the FCTR<sub>X</sub> protein to bind to or interact with an FCTR<sub>X</sub> target molecule. As used herein, a "target molecule" is a molecule with which an FCTR<sub>X</sub> protein binds or interacts in nature, for example, a molecule on the surface of a cell which expresses an FCTR<sub>X</sub> interacting protein, a molecule on the surface of a second cell, a molecule in the extracellular milieu, a molecule associated with the internal surface of a cell membrane or a cytoplasmic molecule. An FCTR<sub>X</sub> target molecule can be a non-FCTR<sub>X</sub> molecule or an FCTR<sub>X</sub> protein or polypeptide of the invention. In one embodiment, an FCTR<sub>X</sub> target molecule is a component of a signal transduction pathway that facilitates transduction of an extracellular signal (*e.g.* a signal generated by binding of a compound to a membrane-bound FCTR<sub>X</sub> molecule) through the cell membrane and into the cell. The target, for example, can be a second intercellular protein that has catalytic activity or a protein that facilitates the association of downstream signaling molecules with FCTR<sub>X</sub>.

Determining the ability of the FCTR<sub>X</sub> protein to bind to or interact with an FCTR<sub>X</sub> target molecule can be accomplished by one of the methods described above for determining direct binding. In one embodiment, determining the ability of the FCTR<sub>X</sub> protein to bind to or interact with an FCTR<sub>X</sub> target molecule can be accomplished by determining the activity of the target molecule. For example, the activity of the target molecule can be determined by detecting induction of a cellular second messenger of the target (*i.e.* intracellular Ca<sup>2+</sup>, diacylglycerol, IP<sub>3</sub>, etc.), detecting catalytic/enzymatic activity of the target on an appropriate substrate, detecting the induction of a reporter gene (comprising an FCTR<sub>X</sub>-responsive regulatory element operatively linked to a nucleic acid encoding a detectable marker, *e.g.*, luciferase), or detecting a cellular response, for example, cell survival, cellular differentiation, or cell proliferation.

In yet another embodiment, an assay of the invention is a cell-free assay comprising contacting an FCTR<sub>X</sub> protein or biologically-active portion thereof with a test compound and determining the ability of the test compound to bind to the FCTR<sub>X</sub> protein or biologically-active portion thereof. Binding of the test compound to the FCTR<sub>X</sub> protein can be determined either directly or indirectly as described above. In one such embodiment, the assay comprises contacting the FCTR<sub>X</sub> protein or biologically-active portion thereof with a known compound which binds FCTR<sub>X</sub> to form an assay mixture, contacting the assay mixture with a test compound, and determining the ability of the test compound to interact with an FCTR<sub>X</sub> protein, wherein determining the ability of the test compound to interact with an FCTR<sub>X</sub>

protein comprises determining the ability of the test compound to preferentially bind to FCTR<sub>X</sub> or biologically-active portion thereof as compared to the known compound.

In still another embodiment, an assay is a cell-free assay comprising contacting FCTR<sub>X</sub> protein or biologically-active portion thereof with a test compound and determining the ability of the test compound to modulate (*e.g.* stimulate or inhibit) the activity of the FCTR<sub>X</sub> protein or biologically-active portion thereof. Determining the ability of the test compound to modulate the activity of FCTR<sub>X</sub> can be accomplished, for example, by determining the ability of the FCTR<sub>X</sub> protein to bind to an FCTR<sub>X</sub> target molecule by one of the methods described above for determining direct binding. In an alternative embodiment, determining the ability of the test compound to modulate the activity of FCTR<sub>X</sub> protein can be accomplished by determining the ability of the FCTR<sub>X</sub> protein further modulate an FCTR<sub>X</sub> target molecule. For example, the catalytic/enzymatic activity of the target molecule on an appropriate substrate can be determined as described, *supra*.

In yet another embodiment, the cell-free assay comprises contacting the FCTR<sub>X</sub> protein or biologically-active portion thereof with a known compound which binds FCTR<sub>X</sub> protein to form an assay mixture, contacting the assay mixture with a test compound, and determining the ability of the test compound to interact with an FCTR<sub>X</sub> protein, wherein determining the ability of the test compound to interact with an FCTR<sub>X</sub> protein comprises determining the ability of the FCTR<sub>X</sub> protein to preferentially bind to or modulate the activity of an FCTR<sub>X</sub> target molecule.

The cell-free assays of the invention are amenable to use of both the soluble form or the membrane-bound form of FCTR<sub>X</sub> protein. In the case of cell-free assays comprising the membrane-bound form of FCTR<sub>X</sub> protein, it may be desirable to utilize a solubilizing agent such that the membrane-bound form of FCTR<sub>X</sub> protein is maintained in solution. Examples of such solubilizing agents include non-ionic detergents such as n-octylglucoside, n-dodecylglucoside, n-dodecylmaltoside, octanoyl-N-methylglucamide, decanoyl-N-methylglucamide, Triton<sup>®</sup> X-100, Triton<sup>®</sup> X-114, Thesit<sup>®</sup>, Isotridecypoly(ethylene glycol ether)<sub>n</sub>, N-dodecyl--N,N-dimethyl-3-ammonio-1-propane sulfonate, 3-(3-cholamidopropyl) dimethylamminiol-1-propane sulfonate (CHAPS), or 3-(3-cholamidopropyl)dimethylamminiol-2-hydroxy-1-propane sulfonate (CHAPSO).

In more than one embodiment of the above assay methods of the invention, it may be desirable to immobilize either FCTR<sub>X</sub> protein or its target molecule to facilitate separation of complexed from uncomplexed forms of one or both of the proteins, as well as to accommodate automation of the assay. Binding of a test compound to FCTR<sub>X</sub> protein, or interaction of

FCTR<sub>X</sub> protein with a target molecule in the presence and absence of a candidate compound, can be accomplished in any vessel suitable for containing the reactants. Examples of such vessels include microtiter plates, test tubes, and micro-centrifuge tubes. In one embodiment, a fusion protein can be provided that adds a domain that allows one or both of the proteins to be bound to a matrix. For example, GST-FCTR<sub>X</sub> fusion proteins or GST-target fusion proteins can be adsorbed onto glutathione sepharose beads (Sigma Chemical, St. Louis, MO) or glutathione derivatized microtiter plates, that are then combined with the test compound or the test compound and either the non-adsorbed target protein or FCTR<sub>X</sub> protein, and the mixture is incubated under conditions conducive to complex formation (*e.g.*, at physiological conditions for salt and pH). Following incubation, the beads or microtiter plate wells are washed to remove any unbound components, the matrix immobilized in the case of beads, complex determined either directly or indirectly, for example, as described, *supra*. Alternatively, the complexes can be dissociated from the matrix, and the level of FCTR<sub>X</sub> protein binding or activity determined using standard techniques.

Other techniques for immobilizing proteins on matrices can also be used in the screening assays of the invention. For example, either the FCTR<sub>X</sub> protein or its target molecule can be immobilized utilizing conjugation of biotin and streptavidin. Biotinylated FCTR<sub>X</sub> protein or target molecules can be prepared from biotin-NHS (N-hydroxy-succinimide) using techniques well-known within the art (*e.g.*, biotinylation kit, Pierce Chemicals, Rockford, Ill.), and immobilized in the wells of streptavidin-coated 96 well plates (Pierce Chemical). Alternatively, antibodies reactive with FCTR<sub>X</sub> protein or target molecules, but which do not interfere with binding of the FCTR<sub>X</sub> protein to its target molecule, can be derivatized to the wells of the plate, and unbound target or FCTR<sub>X</sub> protein trapped in the wells by antibody conjugation. Methods for detecting such complexes, in addition to those described above for the GST-immobilized complexes, include immunodetection of complexes using antibodies reactive with the FCTR<sub>X</sub> protein or target molecule, as well as enzyme-linked assays that rely on detecting an enzymatic activity associated with the FCTR<sub>X</sub> protein or target molecule.

In another embodiment, modulators of FCTR<sub>X</sub> protein expression are identified in a method wherein a cell is contacted with a candidate compound and the expression of FCTR<sub>X</sub> mRNA or protein in the cell is determined. The level of expression of FCTR<sub>X</sub> mRNA or protein in the presence of the candidate compound is compared to the level of expression of FCTR<sub>X</sub> mRNA or protein in the absence of the candidate compound. The candidate compound can then be identified as a modulator of FCTR<sub>X</sub> mRNA or protein expression

based upon this comparison. For example, when expression of FCTR<sub>X</sub> mRNA or protein is greater (*i.e.*, statistically significantly greater) in the presence of the candidate compound than in its absence, the candidate compound is identified as a stimulator of FCTR<sub>X</sub> mRNA or protein expression. Alternatively, when expression of FCTR<sub>X</sub> mRNA or protein is less  
5 (statistically significantly less) in the presence of the candidate compound than in its absence, the candidate compound is identified as an inhibitor of FCTR<sub>X</sub> mRNA or protein expression. The level of FCTR<sub>X</sub> mRNA or protein expression in the cells can be determined by methods described herein for detecting FCTR<sub>X</sub> mRNA or protein.

In yet another aspect of the invention, the FCTR<sub>X</sub> proteins can be used as "bait  
10 proteins" in a two-hybrid assay or three hybrid assay (*see, e.g.*, U.S. Patent No. 5,283,317; Zervos, *et al.*, 1993. *Cell* 72: 223-232; Madura, *et al.*, 1993. *J. Biol. Chem.* 268: 12046-12054; Bartel, *et al.*, 1993. *Biotechniques* 14: 920-924; Iwabuchi, *et al.*, 1993. *Oncogene* 8: 1693-1696; and Brent WO 94/10300), to identify other proteins that bind to or interact with FCTR<sub>X</sub> ("FCTR<sub>X</sub>-binding proteins" or "FCTR<sub>X</sub>-bp") and modulate FCTR<sub>X</sub> activity. Such  
15 FCTR<sub>X</sub>-binding proteins are also likely to be involved in the propagation of signals by the FCTR<sub>X</sub> proteins as, for example, upstream or downstream elements of the FCTR<sub>X</sub> pathway.

The two-hybrid system is based on the modular nature of most transcription factors, which consist of separable DNA-binding and activation domains. Briefly, the assay utilizes two different DNA constructs. In one construct, the gene that codes for FCTR<sub>X</sub> is fused to a  
20 gene encoding the DNA binding domain of a known transcription factor (*e.g.*, GAL-4). In the other construct, a DNA sequence, from a library of DNA sequences, that encodes an unidentified protein ("prey" or "sample") is fused to a gene that codes for the activation domain of the known transcription factor. If the "bait" and the "prey" proteins are able to interact, *in vivo*, forming an FCTR<sub>X</sub>-dependent complex, the DNA-binding and activation  
25 domains of the transcription factor are brought into close proximity. This proximity allows transcription of a reporter gene (*e.g.*, LacZ) that is operably linked to a transcriptional regulatory site responsive to the transcription factor. Expression of the reporter gene can be detected and cell colonies containing the functional transcription factor can be isolated and used to obtain the cloned gene that encodes the protein which interacts with FCTR<sub>X</sub>.

30 The invention further pertains to novel agents identified by the aforementioned screening assays and uses thereof for treatments as described herein.

### ***Detection Assays***

Portions or fragments of the cDNA sequences identified herein (and the corresponding complete gene sequences) can be used in numerous ways as polynucleotide reagents. By way of example, and not of limitation, these sequences can be used to: (i) map their respective  
5 genes on a chromosome; and, thus, locate gene regions associated with genetic disease; (ii) identify an individual from a minute biological sample (tissue typing); and (iii) aid in forensic identification of a biological sample. Some of these applications are described in the subsections, below.

### **Chromosome Mapping**

10 Once the sequence (or a portion of the sequence) of a gene has been isolated, this sequence can be used to map the location of the gene on a chromosome. This process is called chromosome mapping. Accordingly, portions or fragments of the FCTRX sequences, SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, or fragments or derivatives thereof, can be used to map the location of the FCTRX genes, respectively, on a chromosome. The  
15 mapping of the FCTRX sequences to chromosomes is an important first step in correlating these sequences with genes associated with disease.

Briefly, FCTRX genes can be mapped to chromosomes by preparing PCR primers (preferably 15-25 bp in length) from the FCTRX sequences. Computer analysis of the FCTRX sequences can be used to rapidly select primers that do not span more than one exon  
20 in the genomic DNA, thus complicating the amplification process. These primers can then be used for PCR screening of somatic cell hybrids containing individual human chromosomes. Only those hybrids containing the human gene corresponding to the FCTRX sequences will yield an amplified fragment.

Somatic cell hybrids are prepared by fusing somatic cells from different mammals  
25 (e.g., human and mouse cells). As hybrids of human and mouse cells grow and divide, they gradually lose human chromosomes in random order, but retain the mouse chromosomes. By using media in which mouse cells cannot grow, because they lack a particular enzyme, but in which human cells can, the one human chromosome that contains the gene encoding the needed enzyme will be retained. By using various media, panels of hybrid cell lines can be  
30 established. Each cell line in a panel contains either a single human chromosome or a small number of human chromosomes, and a full set of mouse chromosomes, allowing easy mapping of individual genes to specific human chromosomes. See, e.g., D'Eustachio, *et al.*, 1983. *Science* 220: 919-924. Somatic cell hybrids containing only fragments of human

chromosomes can also be produced by using human chromosomes with translocations and deletions.

PCR mapping of somatic cell hybrids is a rapid procedure for assigning a particular sequence to a particular chromosome. Three or more sequences can be assigned per day using a single thermal cycler. Using the FCTR<sub>X</sub> sequences to design oligonucleotide primers, sub-localization can be achieved with panels of fragments from specific chromosomes.

Fluorescence *in situ* hybridization (FISH) of a DNA sequence to a metaphase chromosomal spread can further be used to provide a precise chromosomal location in one step. Chromosome spreads can be made using cells whose division has been blocked in metaphase by a chemical like colcemid that disrupts the mitotic spindle. The chromosomes can be treated briefly with trypsin, and then stained with Giemsa. A pattern of light and dark bands develops on each chromosome, so that the chromosomes can be identified individually. The FISH technique can be used with a DNA sequence as short as 500 or 600 bases. However, clones larger than 1,000 bases have a higher likelihood of binding to a unique chromosomal location with sufficient signal intensity for simple detection. Preferably 1,000 bases, and more preferably 2,000 bases, will suffice to get good results at a reasonable amount of time. For a review of this technique, see, Verma, *et al.*, HUMAN CHROMOSOMES: A MANUAL OF BASIC TECHNIQUES (Pergamon Press, New York 1988).

Reagents for chromosome mapping can be used individually to mark a single chromosome or a single site on that chromosome, or panels of reagents can be used for marking multiple sites and/or multiple chromosomes. Reagents corresponding to noncoding regions of the genes actually are preferred for mapping purposes. Coding sequences are more likely to be conserved within gene families, thus increasing the chance of cross hybridizations during chromosomal mapping.

Once a sequence has been mapped to a precise chromosomal location, the physical position of the sequence on the chromosome can be correlated with genetic map data. Such data are found, *e.g.*, in McKusick, MENDELIAN INHERITANCE IN MAN, available on-line through Johns Hopkins University Welch Medical Library). The relationship between genes and disease, mapped to the same chromosomal region, can then be identified through linkage analysis (co-inheritance of physically adjacent genes), described in, *e.g.*, Egeland, *et al.*, 1987. *Nature*, 325: 783-787.

Moreover, differences in the DNA sequences between individuals affected and unaffected with a disease associated with the FCTR<sub>X</sub> gene, can be determined. If a mutation is observed in some or all of the affected individuals but not in any unaffected individuals,

then the mutation is likely to be the causative agent of the particular disease. Comparison of affected and unaffected individuals generally involves first looking for structural alterations in the chromosomes, such as deletions or translocations that are visible from chromosome spreads or detectable using PCR based on that DNA sequence. Ultimately, complete  
5 sequencing of genes from several individuals can be performed to confirm the presence of a mutation and to distinguish mutations from polymorphisms.

### **Tissue Typing**

The FCTRX sequences of the invention can also be used to identify individuals from minute biological samples. In this technique, an individual's genomic DNA is digested with  
10 one or more restriction enzymes, and probed on a Southern blot to yield unique bands for identification. The sequences of the invention are useful as additional DNA markers for RFLP ("restriction fragment length polymorphisms," described in U.S. Patent No. 5,272,057).

Furthermore, the sequences of the invention can be used to provide an alternative technique that determines the actual base-by-base DNA sequence of selected portions of an  
15 individual's genome. Thus, the FCTRX sequences described herein can be used to prepare two PCR primers from the 5'- and 3'-termini of the sequences. These primers can then be used to amplify an individual's DNA and subsequently sequence it.

Panels of corresponding DNA sequences from individuals, prepared in this manner, can provide unique individual identifications, as each individual will have a unique set of such  
20 DNA sequences due to allelic differences. The sequences of the invention can be used to obtain such identification sequences from individuals and from tissue. The FCTRX sequences of the invention uniquely represent portions of the human genome. Allelic variation occurs to some degree in the coding regions of these sequences, and to a greater degree in the noncoding regions. It is estimated that allelic variation between individual humans occurs with a  
25 frequency of about once per each 500 bases. Much of the allelic variation is due to single nucleotide polymorphisms (SNPs), which include restriction fragment length polymorphisms (RFLPs).

Each of the sequences described herein can, to some degree, be used as a standard against which DNA from an individual can be compared for identification purposes. Because  
30 greater numbers of polymorphisms occur in the noncoding regions, fewer sequences are necessary to differentiate individuals. The noncoding sequences can comfortably provide positive individual identification with a panel of perhaps 10 to 1,000 primers that each yield a noncoding amplified sequence of 100 bases. If predicted coding sequences, such as those in

SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, are used, a more appropriate number of primers for positive individual identification would be 500-2,000.

### Predictive Medicine

The invention also pertains to the field of predictive medicine in which diagnostic assays, prognostic assays, pharmacogenomics, and monitoring clinical trials are used for prognostic (predictive) purposes to thereby treat an individual prophylactically. Accordingly, one aspect of the invention relates to diagnostic assays for determining FCTR<sub>X</sub> protein and/or nucleic acid expression as well as FCTR<sub>X</sub> activity, in the context of a biological sample (*e.g.*, blood, serum, cells, tissue) to thereby determine whether an individual is afflicted with a disease or disorder, or is at risk of developing a disorder, associated with aberrant FCTR<sub>X</sub> expression or activity. The disorders include Also within the scope of the invention is the use of a Therapeutic in the manufacture of a medicament for treating or preventing disorders or syndromes including, *e.g.*, Colorectal cancer, adenomatous polyposis coli, myelogenous leukemia, congenital neonatal alloimmune thrombocytopenia, multiple human solid malignancies, malignant ovarian tumours particularly at the interface between epithelia and stroma, malignant brain tumors, mammary tumors, human gliomas, astrocytomas, mixed glioma/astrocytomas, renal cells carcinoma, breast adenocarcinoma, ovarian cancer, melanomas, renal cell carcinoma, clear cell and granular cell carcinomas, autocrine/paracrine stimulation of tumor cell proliferation, autocrine/paracrine stimulation of tumor cell survival and tumor cell resistance to cytotoxic therapy, paranechmal and basement membrane invasion and motility of tumor cells thereby contributing to metastasis, tumor-mediated immunosuppression of T-cell mediated immune effector cells and pathways resulting in tumor escape from immune surveillance, neurological disorders, neurodegenerative disorders, nerve trauma, familial myelodysplastic syndrome, Charcot-Marie-Tooth neuropathy, demyelinating Gardner syndrome, familial myelodysplastic syndrome; mental health conditions, immunological disorders, allergy and infection, asthma, bronchial asthma, Avellino type eosinophilia, lung diseases, reproductive disorders, male infertility, female reproductive system disorders, male and female reproductive diseases, hemangioma, deafness, glycoprotein Ia deficiency, desmoid disease, turcot syndrome, liver cirrhosis, hepatitis C, gastric disorders, pancreatic diseases like diabetes, *Schistosoma mansoni* infection, Spinocerebellar ataxia, *Plasmodium falciparum* parasitemia, Corneal dystrophy -Groenouw type I, Corneal dystrophy - lattice type I, and Reis-Bucklers corneal dystrophy. The invention also provides for prognostic (or predictive) assays for determining whether an individual is at risk of developing a disorder associated with FCTR<sub>X</sub> protein, nucleic acid expression or activity. For example,

mutations in an FCTR<sub>X</sub> gene can be assayed in a biological sample. Such assays can be used for prognostic or predictive purpose to thereby prophylactically treat an individual prior to the onset of a disorder characterized by or associated with FCTR<sub>X</sub> protein, nucleic acid expression, or biological activity.

5 Another aspect of the invention provides methods for determining FCTR<sub>X</sub> protein, nucleic acid expression or activity in an individual to thereby select appropriate therapeutic or prophylactic agents for that individual (referred to herein as "pharmacogenomics"). Pharmacogenomics allows for the selection of agents (*e.g.*, drugs) for therapeutic or prophylactic treatment of an individual based on the genotype of the individual (*e.g.*, the  
10 genotype of the individual examined to determine the ability of the individual to respond to a particular agent.)

Yet another aspect of the invention pertains to monitoring the influence of agents (*e.g.*, drugs, compounds) on the expression or activity of FCTR<sub>X</sub> in clinical trials.

These and other agents are described in further detail in the following sections.

#### 15 ***Diagnostic Assays***

An exemplary method for detecting the presence or absence of FCTR<sub>X</sub> in a biological sample involves obtaining a biological sample from a test subject and contacting the biological sample with a compound or an agent capable of detecting FCTR<sub>X</sub> protein or nucleic acid (*e.g.*, mRNA, genomic DNA) that encodes FCTR<sub>X</sub> protein such that the presence of FCTR<sub>X</sub> is  
20 detected in the biological sample. An agent for detecting FCTR<sub>X</sub> mRNA or genomic DNA is a labeled nucleic acid probe capable of hybridizing to FCTR<sub>X</sub> mRNA or genomic DNA. The nucleic acid probe can be, for example, a full-length FCTR<sub>X</sub> nucleic acid, such as the nucleic acid of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, or a portion thereof, such as an oligonucleotide of at least 15, 30, 50, 100, 250 or 500 nucleotides in length and  
25 sufficient to specifically hybridize under stringent conditions to FCTR<sub>X</sub> mRNA or genomic DNA. Other suitable probes for use in the diagnostic assays of the invention are described herein.

An agent for detecting FCTR<sub>X</sub> protein is an antibody capable of binding to FCTR<sub>X</sub> protein, preferably an antibody with a detectable label. Antibodies can be polyclonal, or more  
30 preferably, monoclonal. An intact antibody, or a fragment thereof (*e.g.*, Fab or F(ab')<sub>2</sub>) can be used. The term "labeled", with regard to the probe or antibody, is intended to encompass direct labeling of the probe or antibody by coupling (*i.e.*, physically linking) a detectable substance to the probe or antibody, as well as indirect labeling of the probe or antibody by reactivity with another reagent that is directly labeled. Examples of indirect labeling include

detection of a primary antibody using a fluorescently-labeled secondary antibody and end-labeling of a DNA probe with biotin such that it can be detected with fluorescently-labeled streptavidin. The term "biological sample" is intended to include tissues, cells and biological fluids isolated from a subject, as well as tissues, cells and fluids present within a subject. That is, the detection method of the invention can be used to detect FCTR<sub>X</sub> mRNA, protein, or genomic DNA in a biological sample *in vitro* as well as *in vivo*. For example, *in vitro* techniques for detection of FCTR<sub>X</sub> mRNA include Northern hybridizations and *in situ* hybridizations. *In vitro* techniques for detection of FCTR<sub>X</sub> protein include enzyme linked immunosorbent assays (ELISAs), Western blots, immunoprecipitations, and immunofluorescence. *In vitro* techniques for detection of FCTR<sub>X</sub> genomic DNA include Southern hybridizations. Furthermore, *in vivo* techniques for detection of FCTR<sub>X</sub> protein include introducing into a subject a labeled anti-FCTR<sub>X</sub> antibody. For example, the antibody can be labeled with a radioactive marker whose presence and location in a subject can be detected by standard imaging techniques.

In one embodiment, the biological sample contains protein molecules from the test subject. Alternatively, the biological sample can contain mRNA molecules from the test subject or genomic DNA molecules from the test subject. A preferred biological sample is a peripheral blood leukocyte sample isolated by conventional means from a subject.

In another embodiment, the methods further involve obtaining a control biological sample from a control subject, contacting the control sample with a compound or agent capable of detecting FCTR<sub>X</sub> protein, mRNA, or genomic DNA, such that the presence of FCTR<sub>X</sub> protein, mRNA or genomic DNA is detected in the biological sample, and comparing the presence of FCTR<sub>X</sub> protein, mRNA or genomic DNA in the control sample with the presence of FCTR<sub>X</sub> protein, mRNA or genomic DNA in the test sample.

The invention also encompasses kits for detecting the presence of FCTR<sub>X</sub> in a biological sample. For example, the kit can comprise: a labeled compound or agent capable of detecting FCTR<sub>X</sub> protein or mRNA in a biological sample; means for determining the amount of FCTR<sub>X</sub> in the sample; and means for comparing the amount of FCTR<sub>X</sub> in the sample with a standard. The compound or agent can be packaged in a suitable container. The kit can further comprise instructions for using the kit to detect FCTR<sub>X</sub> protein or nucleic acid.

#### *Prognostic Assays*

The diagnostic methods described herein can furthermore be utilized to identify subjects having or at risk of developing a disease or disorder associated with aberrant FCTR<sub>X</sub> expression or activity. For example, the assays described herein, such as the preceding

diagnostic assays or the following assays, can be utilized to identify a subject having or at risk of developing a disorder associated with FCTR<sub>X</sub> protein, nucleic acid expression or activity. Alternatively, the prognostic assays can be utilized to identify a subject having or at risk for developing a disease or disorder. Thus, the invention provides a method for identifying a disease or disorder associated with aberrant FCTR<sub>X</sub> expression or activity in which a test sample is obtained from a subject and FCTR<sub>X</sub> protein or nucleic acid (*e.g.*, mRNA, genomic DNA) is detected, wherein the presence of FCTR<sub>X</sub> protein or nucleic acid is diagnostic for a subject having or at risk of developing a disease or disorder associated with aberrant FCTR<sub>X</sub> expression or activity. As used herein, a "test sample" refers to a biological sample obtained from a subject of interest. For example, a test sample can be a biological fluid (*e.g.*, serum), cell sample, or tissue.

Furthermore, the prognostic assays described herein can be used to determine whether a subject can be administered an agent (*e.g.*, an agonist, antagonist, peptidomimetic, protein, peptide, nucleic acid, small molecule, or other drug candidate) to treat a disease or disorder associated with aberrant FCTR<sub>X</sub> expression or activity. For example, such methods can be used to determine whether a subject can be effectively treated with an agent for a disorder. Thus, the invention provides methods for determining whether a subject can be effectively treated with an agent for a disorder associated with aberrant FCTR<sub>X</sub> expression or activity in which a test sample is obtained and FCTR<sub>X</sub> protein or nucleic acid is detected (*e.g.*, wherein the presence of FCTR<sub>X</sub> protein or nucleic acid is diagnostic for a subject that can be administered the agent to treat a disorder associated with aberrant FCTR<sub>X</sub> expression or activity).

The methods of the invention can also be used to detect genetic lesions in an FCTR<sub>X</sub> gene, thereby determining if a subject with the lesioned gene is at risk for a disorder characterized by aberrant cell proliferation and/or differentiation. In various embodiments, the methods include detecting, in a sample of cells from the subject, the presence or absence of a genetic lesion characterized by at least one of an alteration affecting the integrity of a gene encoding an FCTR<sub>X</sub>-protein, or the misexpression of the FCTR<sub>X</sub> gene. For example, such genetic lesions can be detected by ascertaining the existence of at least one of: (i) a deletion of one or more nucleotides from an FCTR<sub>X</sub> gene; (ii) an addition of one or more nucleotides to an FCTR<sub>X</sub> gene; (iii) a substitution of one or more nucleotides of an FCTR<sub>X</sub> gene, (iv) a chromosomal rearrangement of an FCTR<sub>X</sub> gene; (v) an alteration in the level of a messenger RNA transcript of an FCTR<sub>X</sub> gene, (vi) aberrant modification of an FCTR<sub>X</sub> gene, such as of the methylation pattern of the genomic DNA, (vii) the presence of a non-wild-type splicing

pattern of a messenger RNA transcript of an FCTR<sub>X</sub> gene, (viii) a non-wild-type level of an FCTR<sub>X</sub> protein, (ix) allelic loss of an FCTR<sub>X</sub> gene, and (x) inappropriate post-translational modification of an FCTR<sub>X</sub> protein. As described herein, there are a large number of assay techniques known in the art which can be used for detecting lesions in an FCTR<sub>X</sub> gene. A preferred biological sample is a peripheral blood leukocyte sample isolated by conventional means from a subject. However, any biological sample containing nucleated cells may be used, including, for example, buccal mucosal cells.

In certain embodiments, detection of the lesion involves the use of a probe/primer in a polymerase chain reaction (PCR) (*see, e.g.*, U.S. Patent Nos. 4,683,195 and 4,683,202), such as anchor PCR or RACE PCR, or, alternatively, in a ligation chain reaction (LCR) (*see, e.g.*, Landegran, *et al.*, 1988. *Science* 241: 1077-1080; and Nakazawa, *et al.*, 1994. *Proc. Natl. Acad. Sci. USA* 91: 360-364), the latter of which can be particularly useful for detecting point mutations in the FCTR<sub>X</sub>-gene (*see*, Abravaya, *et al.*, 1995. *Nucl. Acids Res.* 23: 675-682). This method can include the steps of collecting a sample of cells from a patient, isolating nucleic acid (*e.g.*, genomic, mRNA or both) from the cells of the sample, contacting the nucleic acid sample with one or more primers that specifically hybridize to an FCTR<sub>X</sub> gene under conditions such that hybridization and amplification of the FCTR<sub>X</sub> gene (if present) occurs, and detecting the presence or absence of an amplification product, or detecting the size of the amplification product and comparing the length to a control sample. It is anticipated that PCR and/or LCR may be desirable to use as a preliminary amplification step in conjunction with any of the techniques used for detecting mutations described herein.

Alternative amplification methods include: self sustained sequence replication (*see*, Guatelli, *et al.*, 1990. *Proc. Natl. Acad. Sci. USA* 87: 1874-1878), transcriptional amplification system (*see*, Kwoh, *et al.*, 1989. *Proc. Natl. Acad. Sci. USA* 86: 1173-1177); Q $\beta$  Replicase (*see*, Lizardi, *et al.*, 1988. *BioTechnology* 6: 1197), or any other nucleic acid amplification method, followed by the detection of the amplified molecules using techniques well known to those of skill in the art. These detection schemes are especially useful for the detection of nucleic acid molecules if such molecules are present in very low numbers.

In an alternative embodiment, mutations in an FCTR<sub>X</sub> gene from a sample cell can be identified by alterations in restriction enzyme cleavage patterns. For example, sample and control DNA is isolated, amplified (optionally), digested with one or more restriction endonucleases, and fragment length sizes are determined by gel electrophoresis and compared. Differences in fragment length sizes between sample and control DNA indicates mutations in the sample DNA. Moreover, the use of sequence specific ribozymes (*see, e.g.*, U.S. Patent

No. 5,493,531) can be used to score for the presence of specific mutations by development or loss of a ribozyme cleavage site.

In other embodiments, genetic mutations in FCTRX can be identified by hybridizing a sample and control nucleic acids, *e.g.*, DNA or RNA, to high-density arrays containing  
5 hundreds or thousands of oligonucleotide probes. *See, e.g.*, Cronin, *et al.*, 1996. *Human Mutation* 7: 244-255; Kozal, *et al.*, 1996. *Nat. Med.* 2: 753-759. For example, genetic mutations in FCTRX can be identified in two dimensional arrays containing light-generated DNA probes as described in Cronin, *et al.*, *supra*. Briefly, a first hybridization array of probes can be used to scan through long stretches of DNA in a sample and control to identify base  
10 changes between the sequences by making linear arrays of sequential overlapping probes. This step allows the identification of point mutations. This is followed by a second hybridization array that allows the characterization of specific mutations by using smaller, specialized probe arrays complementary to all variants or mutations detected. Each mutation array is composed of parallel probe sets, one complementary to the wild-type gene and the  
15 other complementary to the mutant gene.

In yet another embodiment, any of a variety of sequencing reactions known in the art can be used to directly sequence the FCTRX gene and detect mutations by comparing the sequence of the sample FCTRX with the corresponding wild-type (control) sequence. Examples of sequencing reactions include those based on techniques developed by Maxim and  
20 Gilbert, 1977. *Proc. Natl. Acad. Sci. USA* 74: 560 or Sanger, 1977. *Proc. Natl. Acad. Sci. USA* 74: 5463. It is also contemplated that any of a variety of automated sequencing procedures can be utilized when performing the diagnostic assays (*see, e.g.*, Naeve, *et al.*, 1995. *Biotechniques* 19: 448), including sequencing by mass spectrometry (*see, e.g.*, PCT International Publication No. WO 94/16101; Cohen, *et al.*, 1996. *Adv. Chromatography* 36:  
25 127-162; and Griffin, *et al.*, 1993. *Appl. Biochem. Biotechnol.* 38: 147-159).

Other methods for detecting mutations in the FCTRX gene include methods in which protection from cleavage agents is used to detect mismatched bases in RNA/RNA or RNA/DNA heteroduplexes. *See, e.g.*, Myers, *et al.*, 1985. *Science* 230: 1242. In general, the art technique of "mismatch cleavage" starts by providing heteroduplexes of formed by  
30 hybridizing (labeled) RNA or DNA containing the wild-type FCTRX sequence with potentially mutant RNA or DNA obtained from a tissue sample. The double-stranded duplexes are treated with an agent that cleaves single-stranded regions of the duplex such as which will exist due to basepair mismatches between the control and sample strands. For instance, RNA/DNA duplexes can be treated with RNase and DNA/DNA hybrids treated with

S<sub>1</sub> nuclease to enzymatically digesting the mismatched regions. In other embodiments, either DNA/DNA or RNA/DNA duplexes can be treated with hydroxylamine or osmium tetroxide and with piperidine in order to digest mismatched regions. After digestion of the mismatched regions, the resulting material is then separated by size on denaturing polyacrylamide gels to determine the site of mutation. See, e.g., Cotton, *et al.*, 1988. *Proc. Natl. Acad. Sci. USA* 85: 4397; Saleeba, *et al.*, 1992. *Methods Enzymol.* 217: 286-295. In an embodiment, the control DNA or RNA can be labeled for detection.

In still another embodiment, the mismatch cleavage reaction employs one or more proteins that recognize mismatched base pairs in double-stranded DNA (so called "DNA mismatch repair" enzymes) in defined systems for detecting and mapping point mutations in FCTR<sub>X</sub> cDNAs obtained from samples of cells. For example, the mutY enzyme of *E. coli* cleaves A at G/A mismatches and the thymidine DNA glycosylase from HeLa cells cleaves T at G/T mismatches. See, e.g., Hsu, *et al.*, 1994. *Carcinogenesis* 15: 1657-1662. According to an exemplary embodiment, a probe based on an FCTR<sub>X</sub> sequence, e.g., a wild-type FCTR<sub>X</sub> sequence, is hybridized to a cDNA or other DNA product from a test cell(s). The duplex is treated with a DNA mismatch repair enzyme, and the cleavage products, if any, can be detected from electrophoresis protocols or the like. See, e.g., U.S. Patent No. 5,459,039.

In other embodiments, alterations in electrophoretic mobility will be used to identify mutations in FCTR<sub>X</sub> genes. For example, single strand conformation polymorphism (SSCP) may be used to detect differences in electrophoretic mobility between mutant and wild type nucleic acids. See, e.g., Orita, *et al.*, 1989. *Proc. Natl. Acad. Sci. USA*: 86: 2766; Cotton, 1993. *Mutat. Res.* 285: 125-144; Hayashi, 1992. *Genet. Anal. Tech. Appl.* 9: 73-79. Single-stranded DNA fragments of sample and control FCTR<sub>X</sub> nucleic acids will be denatured and allowed to renature. The secondary structure of single-stranded nucleic acids varies according to sequence, the resulting alteration in electrophoretic mobility enables the detection of even a single base change. The DNA fragments may be labeled or detected with labeled probes. The sensitivity of the assay may be enhanced by using RNA (rather than DNA), in which the secondary structure is more sensitive to a change in sequence. In one embodiment, the subject method utilizes heteroduplex analysis to separate double stranded heteroduplex molecules on the basis of changes in electrophoretic mobility. See, e.g., Keen, *et al.*, 1991. *Trends Genet.* 7: 5.

In yet another embodiment, the movement of mutant or wild-type fragments in polyacrylamide gels containing a gradient of denaturant is assayed using denaturing gradient gel electrophoresis (DGGE). See, e.g., Myers, *et al.*, 1985. *Nature* 313: 495. When DGGE is

used as the method of analysis, DNA will be modified to insure that it does not completely denature, for example by adding a GC clamp of approximately 40 bp of high-melting GC-rich DNA by PCR. In a further embodiment, a temperature gradient is used in place of a denaturing gradient to identify differences in the mobility of control and sample DNA. *See,*

5 *e.g.*, Rosenbaum and Reissner, 1987. *Biophys. Chem.* 265: 12753.

Examples of other techniques for detecting point mutations include, but are not limited to, selective oligonucleotide hybridization, selective amplification, or selective primer extension. For example, oligonucleotide primers may be prepared in which the known mutation is placed centrally and then hybridized to target DNA under conditions that permit  
10 hybridization only if a perfect match is found. *See, e.g.*, Saiki, *et al.*, 1986. *Nature* 324: 163; Saiki, *et al.*, 1989. *Proc. Natl. Acad. Sci. USA* 86: 6230. Such allele specific oligonucleotides are hybridized to PCR amplified target DNA or a number of different mutations when the oligonucleotides are attached to the hybridizing membrane and hybridized with labeled target DNA.

15 Alternatively, allele specific amplification technology that depends on selective PCR amplification may be used in conjunction with the instant invention. Oligonucleotides used as primers for specific amplification may carry the mutation of interest in the center of the molecule (so that amplification depends on differential hybridization; *see, e.g.*, Gibbs, *et al.*, 1989. *Nucl. Acids Res.* 17: 2437-2448) or at the extreme 3'-terminus of one primer where,  
20 under appropriate conditions, mismatch can prevent, or reduce polymerase extension (*see, e.g.*, Prossner, 1993. *Tibtech.* 11: 238). In addition it may be desirable to introduce a novel restriction site in the region of the mutation to create cleavage-based detection. *See, e.g.*, Gasparini, *et al.*, 1992. *Mol. Cell Probes* 6: 1. It is anticipated that in certain embodiments amplification may also be performed using *Taq* ligase for amplification. *See, e.g.*, Barany,  
25 1991. *Proc. Natl. Acad. Sci. USA* 88: 189. In such cases, ligation will occur only if there is a perfect match at the 3'-terminus of the 5' sequence, making it possible to detect the presence of a known mutation at a specific site by looking for the presence or absence of amplification.

The methods described herein may be performed, for example, by utilizing pre-packaged diagnostic kits comprising at least one probe nucleic acid or antibody reagent  
30 described herein, which may be conveniently used, *e.g.*, in clinical settings to diagnose patients exhibiting symptoms or family history of a disease or illness involving an FCTR<sub>X</sub> gene.

Furthermore, any cell type or tissue, preferably peripheral blood leukocytes, in which FCTR<sub>X</sub> is expressed may be utilized in the prognostic assays described herein. However, any

biological sample containing nucleated cells may be used, including, for example, buccal mucosal cells.

### ***Pharmacogenomics***

Agents, or modulators that have a stimulatory or inhibitory effect on FCTR<sub>X</sub> activity (e.g., FCTR<sub>X</sub> gene expression), as identified by a screening assay described herein can be administered to individuals to treat (prophylactically or therapeutically) disorders (The disorders include metabolic disorders, Also within the scope of the invention is the use of a Therapeutic in the manufacture of a medicament for treating or preventing disorders or syndromes including, e.g., Colorectal cancer, adenomatous polyposis coli, myelogenous leukemia, congenital neonatal alloimmune thrombocytopenia, multiple human solid malignancies, malignant ovarian tumours particularly at the interface between epithelia and stroma, malignant brain tumors, mammary tumors, human gliomas, astrocytomas, mixed glioma/astrocytomas, renal cells carcinoma, breast adenocarcinoma, ovarian cancer, melanomas, renal cell carcinoma, clear cell and granular cell carcinomas, autocrine/paracrine stimulation of tumor cell proliferation, autocrine/paracrine stimulation of tumor cell survival and tumor cell resistance to cytotoxic therapy, paranechmal and basement membrane invasion and motility of tumor cells thereby contributing to metastasis, tumor-mediated immunosuppression of T-cell mediated immune effector cells and pathways resulting in tumor escape from immune surveillance, neurological disorders, neurodegenerative disorders, nerve trauma, familial myelodysplastic syndrome, Charcot-Marie-Tooth neuropathy, demyelinating Gardner syndrome, familial myelodysplastic syndrome; mental health conditions, immunological disorders, allergy and infection, asthma, bronchial asthma, Avellino type eosinophilia, lung diseases, reproductive disorders, male infertility, female reproductive system disorders, male and female reproductive diseases, hemangioma, deafness, glycoprotein Ia deficiency, desmoid disease, turcot syndrome, liver cirrhosis, hepatitis C, gastric disorders, pancreatic diseases like diabetes, Schistosoma mansoni infection, Spinocerebellar ataxia, Plasmodium falciparum parasitemia, Corneal dystrophy -Groenouw type I, Corneal dystrophy - lattice type I, and Reis-Bucklers corneal dystrophy) In conjunction with such treatment, the pharmacogenomics (*i.e.*, the study of the relationship between an individual's genotype and that individual's response to a foreign compound or drug) of the individual may be considered. Differences in metabolism of therapeutics can lead to severe toxicity or therapeutic failure by altering the relation between dose and blood concentration of the pharmacologically active drug. Thus, the pharmacogenomics of the individual permits the selection of effective agents (e.g., drugs) for prophylactic or therapeutic treatments based on a consideration of the

individual's genotype. Such pharmacogenomics can further be used to determine appropriate dosages and therapeutic regimens. Accordingly, the activity of FCTR<sub>X</sub> protein, expression of FCTR<sub>X</sub> nucleic acid, or mutation content of FCTR<sub>X</sub> genes in an individual can be determined to thereby select appropriate agent(s) for therapeutic or prophylactic treatment of the individual.

Pharmacogenomics deals with clinically significant hereditary variations in the response to drugs due to altered drug disposition and abnormal action in affected persons. See *e.g.*, Eichelbaum, 1996. *Clin. Exp. Pharmacol. Physiol.*, 23: 983-985; Linder, 1997. *Clin. Chem.*, 43: 254-266. In general, two types of pharmacogenetic conditions can be differentiated. Genetic conditions transmitted as a single factor altering the way drugs act on the body (altered drug action) or genetic conditions transmitted as single factors altering the way the body acts on drugs (altered drug metabolism). These pharmacogenetic conditions can occur either as rare defects or as polymorphisms. For example, glucose-6-phosphate dehydrogenase (G6PD) deficiency is a common inherited enzymopathy in which the main clinical complication is hemolysis after ingestion of oxidant drugs (anti-malarials, sulfonamides, analgesics, nitrofurans) and consumption of fava beans.

As an illustrative embodiment, the activity of drug metabolizing enzymes is a major determinant of both the intensity and duration of drug action. The discovery of genetic polymorphisms of drug metabolizing enzymes (*e.g.*, N-acetyltransferase 2 (NAT 2) and cytochrome P450 enzymes CYP2D6 and CYP2C19) has provided an explanation as to why some patients do not obtain the expected drug effects or show exaggerated drug response and serious toxicity after taking the standard and safe dose of a drug. These polymorphisms are expressed in two phenotypes in the population, the extensive metabolizer (EM) and poor metabolizer (PM). The prevalence of PM is different among different populations. For example, the gene coding for CYP2D6 is highly polymorphic and several mutations have been identified in PM, which all lead to the absence of functional CYP2D6. Poor metabolizers of CYP2D6 and CYP2C19 quite frequently experience exaggerated drug response and side effects when they receive standard doses. If a metabolite is the active therapeutic moiety, PM show no therapeutic response, as demonstrated for the analgesic effect of codeine mediated by its CYP2D6-formed metabolite morphine. At the other extreme are the so called ultra-rapid metabolizers who do not respond to standard doses. Recently, the molecular basis of ultra-rapid metabolism has been identified to be due to CYP2D6 gene amplification.

Thus, the activity of FCTR<sub>X</sub> protein, expression of FCTR<sub>X</sub> nucleic acid, or mutation content of FCTR<sub>X</sub> genes in an individual can be determined to thereby select appropriate

agent(s) for therapeutic or prophylactic treatment of the individual. In addition, pharmacogenetic studies can be used to apply genotyping of polymorphic alleles encoding drug-metabolizing enzymes to the identification of an individual's drug responsiveness phenotype. This knowledge, when applied to dosing or drug selection, can avoid adverse reactions or therapeutic failure and thus enhance therapeutic or prophylactic efficiency when treating a subject with an FCTR<sub>X</sub> modulator, such as a modulator identified by one of the exemplary screening assays described herein.

### ***Monitoring of Effects During Clinical Trials***

Monitoring the influence of agents (*e.g.*, drugs, compounds) on the expression or activity of FCTR<sub>X</sub> (*e.g.*, the ability to modulate aberrant cell proliferation and/or differentiation) can be applied not only in basic drug screening, but also in clinical trials. For example, the effectiveness of an agent determined by a screening assay as described herein to increase FCTR<sub>X</sub> gene expression, protein levels, or upregulate FCTR<sub>X</sub> activity, can be monitored in clinical trials of subjects exhibiting decreased FCTR<sub>X</sub> gene expression, protein levels, or downregulated FCTR<sub>X</sub> activity. Alternatively, the effectiveness of an agent determined by a screening assay to decrease FCTR<sub>X</sub> gene expression, protein levels, or downregulate FCTR<sub>X</sub> activity, can be monitored in clinical trials of subjects exhibiting increased FCTR<sub>X</sub> gene expression, protein levels, or upregulated FCTR<sub>X</sub> activity. In such clinical trials, the expression or activity of FCTR<sub>X</sub> and, preferably, other genes that have been implicated in, for example, a cellular proliferation or immune disorder can be used as a "read out" or markers of the immune responsiveness of a particular cell.

By way of example, and not of limitation, genes, including FCTR<sub>X</sub>, that are modulated in cells by treatment with an agent (*e.g.*, compound, drug or small molecule) that modulates FCTR<sub>X</sub> activity (*e.g.*, identified in a screening assay as described herein) can be identified. Thus, to study the effect of agents on cellular proliferation disorders, for example, in a clinical trial, cells can be isolated and RNA prepared and analyzed for the levels of expression of FCTR<sub>X</sub> and other genes implicated in the disorder. The levels of gene expression (*i.e.*, a gene expression pattern) can be quantified by Northern blot analysis or RT-PCR, as described herein, or alternatively by measuring the amount of protein produced, by one of the methods as described herein, or by measuring the levels of activity of FCTR<sub>X</sub> or other genes. In this manner, the gene expression pattern can serve as a marker, indicative of the physiological response of the cells to the agent. Accordingly, this response state may be determined before, and at various points during, treatment of the individual with the agent.

In one embodiment, the invention provides a method for monitoring the effectiveness of treatment of a subject with an agent (*e.g.*, an agonist, antagonist, protein, peptide, peptidomimetic, nucleic acid, small molecule, or other drug candidate identified by the screening assays described herein) comprising the steps of (i) obtaining a pre-administration sample from a subject prior to administration of the agent; (ii) detecting the level of expression of an FCTR<sub>X</sub> protein, mRNA, or genomic DNA in the preadministration sample; (iii) obtaining one or more post-administration samples from the subject; (iv) detecting the level of expression or activity of the FCTR<sub>X</sub> protein, mRNA, or genomic DNA in the post-administration samples; (v) comparing the level of expression or activity of the FCTR<sub>X</sub> protein, mRNA, or genomic DNA in the pre-administration sample with the FCTR<sub>X</sub> protein, mRNA, or genomic DNA in the post administration sample or samples; and (vi) altering the administration of the agent to the subject accordingly. For example, increased administration of the agent may be desirable to increase the expression or activity of FCTR<sub>X</sub> to higher levels than detected, *i.e.*, to increase the effectiveness of the agent. Alternatively, decreased administration of the agent may be desirable to decrease expression or activity of FCTR<sub>X</sub> to lower levels than detected, *i.e.*, to decrease the effectiveness of the agent.

### Methods of Treatment

The invention provides for both prophylactic and therapeutic methods of treating a subject at risk of (or susceptible to) a disorder or having a disorder associated with aberrant FCTR<sub>X</sub> expression or activity. The disorders include cardiomyopathy, atherosclerosis, hypertension, congenital heart defects, aortic stenosis, atrial septal defect (ASD), atrioventricular (A-V) canal defect, ductus arteriosus, pulmonary stenosis, subaortic stenosis, ventricular septal defect (VSD), valve diseases, tuberous sclerosis, scleroderma, obesity, transplantation, adrenoleukodystrophy, congenital adrenal hyperplasia, prostate cancer, neoplasm; adenocarcinoma, lymphoma, uterus cancer, fertility, hemophilia, hypercoagulation, idiopathic thrombocytopenic purpura, immunodeficiencies, graft versus host disease, AIDS, bronchial asthma, Crohn's disease; multiple sclerosis, treatment of Albright Hereditary Osteodystrophy, and other diseases, disorders and conditions of the like.

These methods of treatment will be discussed more fully, below.

### Disease and Disorders

Diseases and disorders that are characterized by increased (relative to a subject not suffering from the disease or disorder) levels or biological activity may be treated with Therapeutics that antagonize (*i.e.*, reduce or inhibit) activity. Therapeutics that antagonize

activity may be administered in a therapeutic or prophylactic manner. Therapeutics that may be utilized include, but are not limited to: (i) an aforementioned peptide, or analogs, derivatives, fragments or homologs thereof; (ii) antibodies to an aforementioned peptide; (iii) nucleic acids encoding an aforementioned peptide; (iv) administration of antisense nucleic acid and nucleic acids that are "dysfunctional" (*i.e.*, due to a heterologous insertion within the coding sequences of coding sequences to an aforementioned peptide) that are utilized to "knockout" endogenous function of an aforementioned peptide by homologous recombination (*see, e.g.*, Capecchi, 1989. *Science* 244: 1288-1292); or (v) modulators (*i.e.*, inhibitors, agonists and antagonists, including additional peptide mimetic of the invention or antibodies specific to a peptide of the invention) that alter the interaction between an aforementioned peptide and its binding partner.

Diseases and disorders that are characterized by decreased (relative to a subject not suffering from the disease or disorder) levels or biological activity may be treated with Therapeutics that increase (*i.e.*, are agonists to) activity. Therapeutics that upregulate activity may be administered in a therapeutic or prophylactic manner. Therapeutics that may be utilized include, but are not limited to, an aforementioned peptide, or analogs, derivatives, fragments or homologs thereof; or an agonist that increases bioavailability.

Increased or decreased levels can be readily detected by quantifying peptide and/or RNA, by obtaining a patient tissue sample (*e.g.*, from biopsy tissue) and assaying it *in vitro* for RNA or peptide levels, structure and/or activity of the expressed peptides (or mRNAs of an aforementioned peptide). Methods that are well-known within the art include, but are not limited to, immunoassays (*e.g.*, by Western blot analysis, immunoprecipitation followed by sodium dodecyl sulfate (SDS) polyacrylamide gel electrophoresis, immunocytochemistry, etc.) and/or hybridization assays to detect expression of mRNAs (*e.g.*, Northern assays, dot blots, *in situ* hybridization, and the like).

#### *Prophylactic Methods*

In one aspect, the invention provides a method for preventing, in a subject, a disease or condition associated with an aberrant FCTR<sub>X</sub> expression or activity, by administering to the subject an agent that modulates FCTR<sub>X</sub> expression or at least one FCTR<sub>X</sub> activity. Subjects at risk for a disease that is caused or contributed to by aberrant FCTR<sub>X</sub> expression or activity can be identified by, for example, any or a combination of diagnostic or prognostic assays as described herein. Administration of a prophylactic agent can occur prior to the manifestation of symptoms characteristic of the FCTR<sub>X</sub> aberrancy, such that a disease or disorder is prevented or, alternatively, delayed in its progression. Depending upon the type of FCTR<sub>X</sub>

aberrancy, for example, an FCTR<sub>X</sub> agonist or FCTR<sub>X</sub> antagonist agent can be used for treating the subject. The appropriate agent can be determined based on screening assays described herein. The prophylactic methods of the invention are further discussed in the following subsections.

5           *Therapeutic Methods*

Another aspect of the invention pertains to methods of modulating FCTR<sub>X</sub> expression or activity for therapeutic purposes. The modulatory method of the invention involves contacting a cell with an agent that modulates one or more of the activities of FCTR<sub>X</sub> protein activity associated with the cell. An agent that modulates FCTR<sub>X</sub> protein activity can be an agent as described herein, such as a nucleic acid or a protein, a naturally-occurring cognate ligand of an FCTR<sub>X</sub> protein, a peptide, an FCTR<sub>X</sub> peptidomimetic, or other small molecule. In one embodiment, the agent stimulates one or more FCTR<sub>X</sub> protein activity. Examples of such stimulatory agents include active FCTR<sub>X</sub> protein and a nucleic acid molecule encoding FCTR<sub>X</sub> that has been introduced into the cell. In another embodiment, the agent inhibits one or more FCTR<sub>X</sub> protein activity. Examples of such inhibitory agents include antisense FCTR<sub>X</sub> nucleic acid molecules and anti-FCTR<sub>X</sub> antibodies. These modulatory methods can be performed *in vitro* (e.g., by culturing the cell with the agent) or, alternatively, *in vivo* (e.g., by administering the agent to a subject). As such, the invention provides methods of treating an individual afflicted with a disease or disorder characterized by aberrant expression or activity of an FCTR<sub>X</sub> protein or nucleic acid molecule. In one embodiment, the method involves administering an agent (e.g., an agent identified by a screening assay described herein), or combination of agents that modulates (e.g., up-regulates or down-regulates) FCTR<sub>X</sub> expression or activity. In another embodiment, the method involves administering an FCTR<sub>X</sub> protein or nucleic acid molecule as therapy to compensate for reduced or aberrant FCTR<sub>X</sub> expression or activity.

Stimulation of FCTR<sub>X</sub> activity is desirable in situations in which FCTR<sub>X</sub> is abnormally downregulated and/or in which increased FCTR<sub>X</sub> activity is likely to have a beneficial effect. One example of such a situation is where a subject has a disorder characterized by aberrant cell proliferation and/or differentiation (e.g., cancer or immune associated disorders). Another example of such a situation is where the subject has a gestational disease (e.g., preclampsia).

**Determination of the Biological Effect of the Therapeutic**

In various embodiments of the invention, suitable *in vitro* or *in vivo* assays are performed to determine the effect of a specific Therapeutic and whether its administration is indicated for treatment of the affected tissue.

5 In various specific embodiments, *in vitro* assays may be performed with representative cells of the type(s) involved in the patient's disorder, to determine if a given Therapeutic exerts the desired effect upon the cell type(s). Compounds for use in therapy may be tested in suitable animal model systems including, but not limited to rats, mice, chicken, cows, monkeys, rabbits, and the like, prior to testing in human subjects. Similarly, for *in vivo*  
10 testing, any of the animal model system known in the art may be used prior to administration to human subjects.

**Prophylactic and Therapeutic Uses of the Compositions of the Invention**

The FCTR<sub>X</sub> nucleic acids and proteins of the invention are useful in potential prophylactic and therapeutic applications implicated in a variety of disorders including, but not  
15 limited to: Also within the scope of the invention is the use of a Therapeutic in the manufacture of a medicament for treating or preventing disorders or syndromes including, *e.g.*, Colorectal cancer, adenomatous polyposis coli, myelogenous leukemia, congenital neonatal alloimmune thrombocytopenia, multiple human solid malignancies, malignant ovarian tumours particularly at the interface between epithelia and stroma, malignant brain  
20 tumors, mammary tumors, human gliomas, astrocytomas, mixed glioma/astrocytomas, renal cells carcinoma, breast adenocarcinoma, ovarian cancer, melanomas, renal cell carcinoma, clear cell and granular cell carcinomas, autocrine/paracrine stimulation of tumor cell proliferation, autocrine/paracrine stimulation of tumor cell survival and tumor cell resistance to cytotoxic therapy, paranechmal and basement membrane invasion and motility of tumor  
25 cells thereby contributing to metastasis, tumor-mediated immunosuppression of T-cell mediated immune effector cells and pathways resulting in tumor escape from immune surveillance, neurological disorders, neurodegenerative disorders, nerve trauma, familial myelodysplastic syndrome, Charcot-Marie-Tooth neuropathy, demyelinating Gardner syndrome, familial myelodysplastic syndrome; mental health conditions, immunological  
30 disorders, allergy and infection, asthma, bronchial asthma, Avellino type eosinophilia, lung diseases, reproductive disorders, male infertility, female reproductive system disorders, male and female reproductive diseases, hemangioma, deafness, glycoprotein Ia deficiency, desmoid disease, turcot syndrome, liver cirrhosis, hepatitis C, gastric disorders, pancreatic diseases like

diabetes, *Schistosoma mansoni* infection, Spinocerebellar ataxia, *Plasmodium falciparum* parasitemia, Corneal dystrophy -Groenouw type I, Corneal dystrophy - lattice type I, and Reis-Bucklers corneal dystrophy.

As an example, a cDNA encoding the FCTR<sub>X</sub> protein of the invention may be useful  
 5 in gene therapy, and the protein may be useful when administered to a subject in need thereof. By way of non-limiting example, the compositions of the invention will have efficacy for treatment of patients suffering from: Also within the scope of the invention is the use of a Therapeutic in the manufacture of a medicament for treating or preventing disorders or syndromes including, *e.g.*, Colorectal cancer, adenomatous polyposis coli, myelogenous  
 10 leukemia, congenital neonatal alloimmune thrombocytopenia, multiple human solid malignancies, malignant ovarian tumours particularly at the interface between epithelia and stroma, malignant brain tumors, mammary tumors, human gliomas, astrocytomas, mixed glioma/astrocytomas, renal cells carcinoma, breast adenocarcinoma, ovarian cancer, melanomas, renal cell carcinoma, clear cell and granular cell carcinomas, autocrine/paracrine  
 15 stimulation of tumor cell proliferation, autocrine/paracrine stimulation of tumor cell survival and tumor cell resistance to cytotoxic therapy, paraneoplastic and basement membrane invasion and motility of tumor cells thereby contributing to metastasis, tumor-mediated immunosuppression of T-cell mediated immune effector cells and pathways resulting in tumor escape from immune surveillance, neurological disorders, neurodegenerative disorders, nerve  
 20 trauma, familial myelodysplastic syndrome, Charcot-Marie-Tooth neuropathy, demyelinating Gardner syndrome, familial myelodysplastic syndrome; mental health conditions, immunological disorders, allergy and infection, asthma, bronchial asthma, Avellino type eosinophilia, lung diseases, reproductive disorders, male infertility, female reproductive system disorders, male and female reproductive diseases, hemangioma, deafness, glycoprotein  
 25 Ia deficiency, desmoid disease, Turcot syndrome, liver cirrhosis, hepatitis C, gastric disorders, pancreatic diseases like diabetes, *Schistosoma mansoni* infection, Spinocerebellar ataxia, *Plasmodium falciparum* parasitemia, Corneal dystrophy -Groenouw type I, Corneal dystrophy - lattice type I, and Reis-Bucklers corneal dystrophy.

Both the novel nucleic acid encoding the FCTR<sub>X</sub> protein, and the FCTR<sub>X</sub> protein of  
 30 the invention, or fragments thereof, may also be useful in diagnostic applications, wherein the presence or amount of the nucleic acid or the protein are to be assessed. A further use could be as an anti-bacterial molecule (*i.e.*, some peptides have been found to possess anti-bacterial properties). These materials are further useful in the generation of antibodies which

immunospecifically-bind to the novel substances of the invention for use in therapeutic or diagnostic methods.

## EXAMPLES

The following examples illustrate by way of non-limiting example various aspects of the invention.

The following examples illustrate by way of non-limiting example various aspects of the invention.

### Example 1: Method of Identifying the Nucleic Acids

The novel nucleic acids of the invention were identified by TblastN using a proprietary sequence file, run against the Genomic Daily Files made available by GenBank. The nucleic acids were further predicted by the proprietary software program GenScan™, including selection of exons. These were further modified by means of similarities using BLAST searches. The sequences were then manually corrected for apparent inconsistencies, thereby obtaining the sequences encoding the full-length proteins.

### Example 2. Quantitative expression analysis of FCTR2 in various cells and tissues

The quantitative expression of various clones was assessed using microtiter plates containing RNA samples from a variety of normal and pathology-derived cells, cell lines and tissues using real time quantitative PCR (RTQ PCR; TAQMAN®). RTQ PCR was performed on a Perkin-Elmer Biosystems ABI PRISM® 7700 Sequence Detection System. Various collections of samples are assembled on the plates, and referred to as Panel 1 (containing cells and cell lines from normal and cancer sources), Panel 2 (containing samples derived from tissues, in particular from surgical samples, from normal and cancer sources), Panel 3 (containing samples derived from a wide variety of cancer sources) and Panel 4 (containing cells and cell lines from normal cells and cells related to inflammatory conditions).

First, the RNA samples were normalized to constitutively expressed genes such as  $\beta$ -actin and GAPDH. RNA (~50 ng total or ~1 ng polyA+) was converted to cDNA using the TAQMAN® Reverse Transcription Reagents Kit (PE Biosystems, Foster City, CA; Catalog No. N808-0234) and random hexamers according to the manufacturer's protocol. Reactions were performed in 20 ul and incubated for 30 min. at 48°C. cDNA (5 ul) was then transferred to a separate plate for the TAQMAN® reaction using  $\beta$ -actin and GAPDH TAQMAN® Assay Reagents (PE Biosystems; Catalog Nos. 4310881E and 4310884E, respectively) and

TAQMAN® universal PCR Master Mix (PE Biosystems; Catalog No. 4304447) according to the manufacturer's protocol. Reactions were performed in 25  $\mu$ l using the following parameters: 2 min. at 50°C; 10 min. at 95°C; 15 sec. at 95°C/1 min. at 60°C (40 cycles). Results were recorded as CT values (cycle at which a given sample crosses a threshold level of fluorescence) using a log scale, with the difference in RNA concentration between a given sample and the sample with the lowest CT value being represented as 2 to the power of delta CT. The percent relative expression is then obtained by taking the reciprocal of this RNA difference and multiplying by 100. The average CT values obtained for  $\beta$ -actin and GAPDH were used to normalize RNA samples. The RNA sample generating the highest CT value required no further diluting, while all other samples were diluted relative to this sample according to their  $\beta$ -actin /GAPDH average CT values.

Normalized RNA (5  $\mu$ l) was converted to cDNA and analyzed via TAQMAN® using One Step RT-PCR Master Mix Reagents (PE Biosystems; Catalog No. 4309169) and gene-specific primers according to the manufacturer's instructions. Probes and primers were designed for each assay according to Perkin Elmer Biosystem's *Primer Express* Software package (version I for Apple Computer's Macintosh Power PC) or a similar algorithm using the target sequence as input. Default settings were used for reaction conditions and the following parameters were set before selecting primers: primer concentration = 250 nM, primer melting temperature ( $T_m$ ) range = 58°-60° C, primer optimal  $T_m$  = 59° C, maximum primer difference = 2° C, probe does not have 5' G, probe  $T_m$  must be 10° C greater than primer  $T_m$ , amplicon size 75 bp to 100 bp. The probes and primers selected (see below) were synthesized by SyntheGen (Houston, TX, USA). Probes were double purified by HPLC to remove uncoupled dye and evaluated by mass spectroscopy to verify coupling of reporter and quencher dyes to the 5' and 3' ends of the probe, respectively. Their final concentrations were: forward and reverse primers, 900 nM each, and probe, 200nM.

PCR conditions: Normalized RNA from each tissue and each cell line was spotted in each well of a 96 well PCR plate (Perkin Elmer Biosystems). PCR cocktails including two probes (a probe specific for the target clone and another gene-specific probe multiplexed with the target probe) were set up using 1X TaqMan™ PCR Master Mix for the PE Biosystems 7700, with 5 mM MgCl<sub>2</sub>, dNTPs (dA, G, C, U at 1:1:1:2 ratios), 0.25 U/ml AmpliTaq Gold™ (PE Biosystems), and 0.4 U/ $\mu$ l RNase inhibitor, and 0.25 U/ $\mu$ l reverse transcriptase. Reverse transcription was performed at 48° C for 30 minutes followed by amplification/PCR cycles as follows: 95° C 10 min, then 40 cycles of 95° C for 15 seconds, 60° C for 1 minute.

In the results for Panel 1, the following abbreviations are used:

ca. = carcinoma,

\* = established from metastasis,

met = metastasis,

s cell var = small cell variant,

non-s = non-sm = non-small,

squam = squamous,

pl. eff = pl effusion = pleural effusion,

glio = glioma,

astro = astrocytoma, and

neuro = neuroblastoma.

## Panel 2

The plates for Panel 2 generally include 2 control wells and 94 test samples composed of RNA or cDNA isolated from human tissue procured by surgeons working in close cooperation with the National Cancer Institute's Cooperative Human Tissue Network (CHTN) or the National Disease Research Initiative (NDRI). The tissues are derived from human malignancies and in cases where indicated many malignant tissues have "matched margins" obtained from noncancerous tissue just adjacent to the tumor. These are termed normal adjacent tissues and are denoted "NAT" in the results below. The tumor tissue and the "matched margins" are evaluated by two independent pathologists (the surgical pathologists and again by a pathologists at NDRI or CHTN). This analysis provides a gross histopathological assessment of tumor differentiation grade. Moreover, most samples include the original surgical pathology report that provides information regarding the clinical stage of the patient. These matched margins are taken from the tissue surrounding (i.e. immediately proximal) to the zone of surgery (designated "NAT", for normal adjacent tissue, in Table RR). In addition, RNA and cDNA samples were obtained from various human tissues derived from autopsies performed on elderly people or sudden death victims (accidents, etc.). These tissue were ascertained to be free of disease and were purchased from various commercial sources such as Clontech (Palo Alto, CA), Research Genetics, and Invitrogen.

RNA integrity from all samples is controlled for quality by visual assessment of agarose gel electropherograms using 28S and 18S ribosomal RNA staining intensity ratio as a

guide (2:1 to 2.5:1 28s:18s) and the absence of low molecular weight RNAs that would be indicative of degradation products. Samples are controlled against genomic DNA contamination by RTQ PCR reactions run in the absence of reverse transcriptase using probe and primer sets designed to amplify across the span of a single exon.

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**Panel 4**

Panel 4 includes samples on a 96 well plate (2 control wells, 94 test samples) composed of RNA (Panel 4r) or cDNA (Panel 4d) isolated from various human cell lines or tissues related to inflammatory conditions. Total RNA from control normal tissues such as colon and lung (Stratagene, La Jolla, CA) and thymus and kidney (Clontech) were employed. Total RNA from liver tissue from cirrhosis patients and kidney from lupus patients was obtained from BioChain (Biochain Institute, Inc., Hayward, CA). Intestinal tissue for RNA preparation from patients diagnosed as having Crohn's disease and ulcerative colitis was obtained from the National Disease Research Interchange (NDRI) (Philadelphia, PA).

Astrocytes, lung fibroblasts, dermal fibroblasts, coronary artery smooth muscle cells, small airway epithelium, bronchial epithelium, microvascular dermal endothelial cells, microvascular lung endothelial cells, human pulmonary aortic endothelial cells, human umbilical vein endothelial cells were all purchased from Clonetics (Walkersville, MD) and grown in the media supplied for these cell types by Clonetics. These primary cell types were activated with various cytokines or combinations of cytokines for 6 and/or 12-14 hours, as indicated. The following cytokines were used; IL-1 beta at approximately 1-5 ng/ml, TNF alpha at approximately 5-10 ng/ml, IFN gamma at approximately 20-50 ng/ml, IL-4 at approximately 5-10 ng/ml, IL-9 at approximately 5-10 ng/ml, IL-13 at approximately 5-10 ng/ml. Endothelial cells were sometimes starved for various times by culture in the basal media from Clonetics with 0.1% serum.

Mononuclear cells were prepared from blood of employees at CuraGen Corporation, using Ficoll. LAK cells were prepared from these cells by culture in DMEM 5% FCS (Hyclone), 100  $\mu$ M non essential amino acids (Gibco/Life Technologies, Rockville, MD), 1 mM sodium pyruvate (Gibco), mercaptoethanol  $5.5 \times 10^{-5}$  M (Gibco), and 10 mM Hepes (Gibco) and Interleukin 2 for 4-6 days. Cells were then either activated with 10-20 ng/ml PMA and 1-2  $\mu$ g/ml ionomycin, IL-12 at 5-10 ng/ml, IFN gamma at 20-50 ng/ml and IL-18 at

5-10 ng/ml for 6 hours. In some cases, mononuclear cells were cultured for 4-5 days in DMEM 5% FCS (Hyclone), 100  $\mu$ M non essential amino acids (Gibco), 1 mM sodium pyruvate (Gibco), mercaptoethanol  $5.5 \times 10^{-5}$  M (Gibco), and 10 mM Hepes (Gibco) with PHA (phytohemagglutinin) or PWM (pokeweed mitogen) at approximately 5  $\mu$ g/ml. Samples were taken at 24, 48 and 72 hours for RNA preparation. MLR (mixed lymphocyte reaction) samples were obtained by taking blood from two donors, isolating the mononuclear cells using Ficoll and mixing the isolated mononuclear cells 1:1 at a final concentration of approximately  $2 \times 10^6$  cells/ml in DMEM 5% FCS (Hyclone), 100  $\mu$ M non essential amino acids (Gibco), 1 mM sodium pyruvate (Gibco), mercaptoethanol ( $5.5 \times 10^{-5}$  M) (Gibco), and 10 mM Hepes (Gibco). The MLR was cultured and samples taken at various time points ranging from 1- 7 days for RNA preparation.

Monocytes were isolated from mononuclear cells using CD14 Miltenyi Beads, +ve VS selection columns and a Vario Magnet according to the manufacturer's instructions. Monocytes were differentiated into dendritic cells by culture in DMEM 5% fetal calf serum (FCS) (Hyclone, Logan, UT), 100  $\mu$ M non essential amino acids (Gibco), 1 mM sodium pyruvate (Gibco), mercaptoethanol  $5.5 \times 10^{-5}$  M (Gibco), and 10 mM Hepes (Gibco), 50 ng/ml GMCSF and 5 ng/ml IL-4 for 5-7 days. Macrophages were prepared by culture of monocytes for 5-7 days in DMEM 5% FCS (Hyclone), 100  $\mu$ M non essential amino acids (Gibco), 1 mM sodium pyruvate (Gibco), mercaptoethanol  $5.5 \times 10^{-5}$  M (Gibco), 10 mM Hepes (Gibco) and 10% AB Human Serum or MCSF at approximately 50 ng/ml. Monocytes, macrophages and dendritic cells were stimulated for 6 and 12-14 hours with lipopolysaccharide (LPS) at 100 ng/ml. Dendritic cells were also stimulated with anti-CD40 monoclonal antibody (Pharmingen) at 10  $\mu$ g/ml for 6 and 12-14 hours.

CD4 lymphocytes, CD8 lymphocytes and NK cells were also isolated from mononuclear cells using CD4, CD8 and CD56 Miltenyi beads, positive VS selection columns and a Vario Magnet according to the manufacturer's instructions. CD45RA and CD45RO CD4 lymphocytes were isolated by depleting mononuclear cells of CD8, CD56, CD14 and CD19 cells using CD8, CD56, CD14 and CD19 Miltenyi beads and +ve selection. Then CD45RO beads were used to isolate the CD45RO CD4 lymphocytes with the remaining cells being CD45RA CD4 lymphocytes. CD45RA CD4, CD45RO CD4 and CD8 lymphocytes were placed in DMEM 5% FCS (Hyclone), 100  $\mu$ M non essential amino acids (Gibco), 1 mM sodium pyruvate (Gibco), mercaptoethanol  $5.5 \times 10^{-5}$  M (Gibco), and 10 mM Hepes (Gibco).

and plated at  $10^6$  cells/ml onto Falcon 6 well tissue culture plates that had been coated overnight with 0.5  $\mu$ g/ml anti-CD28 (Pharmingen) and 3  $\mu$ g/ml anti-CD3 (OKT3, ATCC) in PBS. After 6 and 24 hours, the cells were harvested for RNA preparation. To prepare chronically activated CD8 lymphocytes, we activated the isolated CD8 lymphocytes for 4 days on anti-CD28 and anti-CD3 coated plates and then harvested the cells and expanded them in DMEM 5% FCS (Hyclone), 100  $\mu$ M non essential amino acids (Gibco), 1 mM sodium pyruvate (Gibco), mercaptoethanol  $5.5 \times 10^{-5}$  M (Gibco), and 10 mM Hepes (Gibco) and IL-2. The expanded CD8 cells were then activated again with plate bound anti-CD3 and anti-CD28 for 4 days and expanded as before. RNA was isolated 6 and 24 hours after the second activation and after 4 days of the second expansion culture. The isolated NK cells were cultured in DMEM 5% FCS (Hyclone), 100  $\mu$ M non essential amino acids (Gibco), 1 mM sodium pyruvate (Gibco), mercaptoethanol  $5.5 \times 10^{-5}$  M (Gibco), and 10 mM Hepes (Gibco) and IL-2 for 4-6 days before RNA was prepared.

To obtain B cells, tonsils were procured from NDRI. The tonsil was cut up with sterile dissecting scissors and then passed through a sieve. Tonsil cells were then spun down and resuspended at  $10^6$  cells/ml in DMEM 5% FCS (Hyclone), 100  $\mu$ M non essential amino acids (Gibco), 1 mM sodium pyruvate (Gibco), mercaptoethanol  $5.5 \times 10^{-5}$  M (Gibco), and 10 mM Hepes (Gibco). To activate the cells, we used PWM at 5  $\mu$ g/ml or anti-CD40 (Pharmingen) at approximately 10  $\mu$ g/ml and IL-4 at 5-10 ng/ml. Cells were harvested for RNA preparation at 24, 48 and 72 hours.

To prepare the primary and secondary Th1/Th2 and Tr1 cells, six-well Falcon plates were coated overnight with 10  $\mu$ g/ml anti-CD28 (Pharmingen) and 2  $\mu$ g/ml OKT3 (ATCC), and then washed twice with PBS. Umbilical cord blood CD4 lymphocytes (Poietic Systems, German Town, MD) were cultured at  $10^5$  -  $10^6$  cells/ml in DMEM 5% FCS (Hyclone), 100  $\mu$ M non essential amino acids (Gibco), 1 mM sodium pyruvate (Gibco), mercaptoethanol  $5.5 \times 10^{-5}$  M (Gibco), 10 mM Hepes (Gibco) and IL-2 (4 ng/ml). IL-12 (5 ng/ml) and anti-IL4 (1  $\mu$ g/ml) were used to direct to Th1, while IL-4 (5 ng/ml) and anti-IFN gamma (1  $\mu$ g/ml) were used to direct to Th2 and IL-10 at 5 ng/ml was used to direct to Tr1. After 4-5 days, the activated Th1, Th2 and Tr1 lymphocytes were washed once in DMEM and expanded for 4-7 days in DMEM 5% FCS (Hyclone), 100  $\mu$ M non essential amino acids (Gibco), 1 mM sodium pyruvate (Gibco), mercaptoethanol  $5.5 \times 10^{-5}$  M (Gibco), 10 mM Hepes (Gibco) and IL-2 (1

ng/ml). Following this, the activated Th1, Th2 and Tr1 lymphocytes were re-stimulated for 5 days with anti-CD28/OKT3 and cytokines as described above, but with the addition of anti-CD95L (1  $\mu$ g/ml) to prevent apoptosis. After 4-5 days, the Th1, Th2 and Tr1 lymphocytes were washed and then expanded again with IL-2 for 4-7 days. Activated Th1 and Th2 lymphocytes were maintained in this way for a maximum of three cycles. RNA was prepared from primary and secondary Th1, Th2 and Tr1 after 6 and 24 hours following the second and third activations with plate bound anti-CD3 and anti-CD28 mAbs and 4 days into the second and third expansion cultures in Interleukin 2.

The following leukocyte cells lines were obtained from the ATCC: Ramos, EOL-1, KU-812. EOL cells were further differentiated by culture in 0.1 mM dbcAMP at  $5 \times 10^5$  cells/ml for 8 days, changing the media every 3 days and adjusting the cell concentration to  $5 \times 10^5$  cells/ml. For the culture of these cells, we used DMEM or RPMI (as recommended by the ATCC), with the addition of 5% FCS (Hyclone), 100  $\mu$ M non essential amino acids (Gibco), 1 mM sodium pyruvate (Gibco), mercaptoethanol  $5.5 \times 10^{-5}$  M (Gibco), 10 mM Hepes (Gibco). RNA was either prepared from resting cells or cells activated with PMA at 10 ng/ml and ionomycin at 1  $\mu$ g/ml for 6 and 14 hours. Keratinocyte line CCD106 and an airway epithelial tumor line NCI-H292 were also obtained from the ATCC. Both were cultured in DMEM 5% FCS (Hyclone), 100  $\mu$ M non essential amino acids (Gibco), 1 mM sodium pyruvate (Gibco), mercaptoethanol  $5.5 \times 10^{-5}$  M (Gibco), and 10 mM Hepes (Gibco). CCD1106 cells were activated for 6 and 14 hours with approximately 5 ng/ml TNF alpha and 1 ng/ml IL-1 beta, while NCI-H292 cells were activated for 6 and 14 hours with the following cytokines: 5 ng/ml IL-4, 5 ng/ml IL-9, 5 ng/ml IL-13 and 25 ng/ml IFN gamma.

For these cell lines and blood cells, RNA was prepared by lysing approximately  $10^7$  cells/ml using Trizol (Gibco BRL). Briefly, 1/10 volume of bromochloropropane (Molecular Research Corporation) was added to the RNA sample, vortexed and after 10 minutes at room temperature, the tubes were spun at 14,000 rpm in a Sorvall SS34 rotor. The aqueous phase was removed and placed in a 15 ml Falcon Tube. An equal volume of isopropanol was added and left at -20 degrees C overnight. The precipitated RNA was spun down at 9,000 rpm for 15 min in a Sorvall SS34 rotor and washed in 70% ethanol. The pellet was redissolved in 300  $\mu$ l of RNase-free water and 35  $\mu$ l buffer (Promega) 5  $\mu$ l DTT, 7  $\mu$ l RNasin and 8  $\mu$ l DNase were added. The tube was incubated at 37 degrees C for 30 minutes to remove contaminating genomic DNA, extracted once with phenol chloroform and re-

precipitated with 1/10 volume of 3 M sodium acetate and 2 volumes of 100% ethanol. The RNA was spun down and placed in RNase free water. RNA was stored at -80 degrees C.

The above detailed procedures were carried out to obtain the taqman profiles of the clones in question.

Given below are the Primers and the Taqman results for the following clones:

58092213.0.36 – Probe Name: Ag809 (Table 9 and Table 10)

29692275.0.1 – Probe Name: Ag2773 (Table 11 and Table 12)

32125243.0.21 – Probe Name: Ag427 (Table 13 and Table 14)

27455183.0.19 – Probe Name: Ag1541 (Table 15 and Table 16, 17, 18)

**Table 8: Primer Design for Probe Ag809 (FCTR1)**

| Primer  | Sequences                               | TM   | Length | Start Pos | SEQID NO |
|---------|-----------------------------------------|------|--------|-----------|----------|
| Forward | 5'-ATGTGATCTTTGGCTGTGAAGT-3'            | 58.7 | 22     | 337       | 24       |
| Probe   | FAM-5'-CTACCCCATGGCCTCCATCGAGT-3'-TAMRA | 69.4 | 23     | 365       | 25       |
| Reverse | 5'-GGATGTCCAAGCCATCCTT-3'               | 59.9 | 19     | 393       | 26       |

**TABLE 9: TAQMAN RESULTS FOR FCTR1**

| Tissue_Name            | Panel 1 | Tissue_Name                          | Panel 2D | Tissue_Name                                 | Panel 4D |
|------------------------|---------|--------------------------------------|----------|---------------------------------------------|----------|
| Liver adenocarcinoma   | 79.6    | Normal Colon GENPAK 061003           | 6.8      | 93768_Secondary Th1_anti-CD28/anti-CD3      | 2.0      |
| Heart (fetal)          | 43.8    | 83219 CC Well to Mod Diff (ODO3866)  | 6.1      | 93769_Secondary Th2_anti-CD28/anti-CD3      | 1.5      |
| Pancreas               | 2.1     | 83220 CC NAT (ODO3866)               | 2.5      | 93770_Secondary Tr1_anti-CD28/anti-CD3      | 2.5      |
| Pancreatic ca. CAPAN 2 | 4.7     | 83221 CC Gr.2 rectosigmoid (ODO3868) | 0.9      | 93573_Secondary Th1_resting day 4-6 in IL-2 | 1.0      |
| Adrenal gland          | 2.3     | 83222 CC NAT (ODO3868)               | 1.2      | 93572_Secondary Th2_resting day 4-6 in IL-2 | 3.0      |
| Thyroid                | 6.5     | 83235 CC Mod Diff (ODO3920)          | 3.8      | 93571_Secondary Tr1_resting day 4-6 in IL-2 | 1.7      |
| Salivary gland         | 12.3    | 83236 CC NAT (ODO3920)               | 1.3      | 93568_primary Th1_anti-CD28/anti-CD3        | 0.4      |
| Pituitary gland        | 8.7     | 83237 CC Gr.2 ascend colon (ODO3921) | 6.9      | 93569_primary Th2_anti-CD28/anti-CD3        | 1.5      |
| Brain (fetal)          | 0.0     | 83238 CC NAT (ODO3921)               | 4.0      | 93570_primary Tr1_anti-CD28/anti-CD3        | 2.0      |
| Brain (whole)          | 3.0     | 83241 CC from                        | 1.2      | 93565_primary Th1_resting dy 4-6            | 5.4      |

|                                      |       |                                               |      |                                                             |      |
|--------------------------------------|-------|-----------------------------------------------|------|-------------------------------------------------------------|------|
|                                      |       | Partial<br>Hepatectomy<br>(ODO4309)           |      | in IL-2                                                     |      |
| Brain<br>(amygdala)                  | 2.4   | 83242 Liver NAT<br>(ODO4309)                  | 0.6  | 93566_primary Th2_resting dy 4-6<br>in IL-2                 | 3.1  |
| Brain<br>(cerebellum)                | 0.0   | 87472 Colon mets<br>to lung (OD04451-<br>01)  | 4.4  | 93567_primary Tr1_resting dy 4-6<br>in IL-2                 | 0.0  |
| Brain<br>(hippocampus)               | 13.0  | 87473 Lung NAT<br>(OD04451-02)                | 1.2  | 93351_CD45RA CD4<br>lymphocyte_anti-CD28/anti-CD3           | 11.2 |
| Brain (thalamus)                     | 3.0   | Normal Prostate<br>Clontech A+<br>6546-1      | 10.2 | 93352_CD45RO CD4<br>lymphocyte_anti-CD28/anti-CD3           | 1.2  |
| Cerebral Cortex                      | 2.3   | 84140 Prostate<br>Cancer<br>(OD04410)         | 41.8 | 93251_CD8 Lymphocytes_anti-<br>CD28/anti-CD3                | 0.9  |
| Spinal cord                          | 2.6   | 84141 Prostate<br>NAT (OD04410)               | 25.7 | 93353_chronic CD8 Lymphocytes<br>2ry_resting dy 4-6 in IL-2 | 0.0  |
| CNS ca.<br>(glio/astro) U87-<br>MG   | 12.1  | 87073 Prostate<br>Cancer<br>(OD04720-01)      | 11.0 | 93574_chronic CD8 Lymphocytes<br>2ry_activated CD3/CD28     | 0.6  |
| CNS ca.<br>(glio/astro) U-<br>118-MG | 100.0 | 87074 Prostate<br>NAT (OD04720-<br>02)        | 10.0 | 93354_CD4_none                                              | 1.1  |
| CNS ca. (astro)<br>SW1783            | 6.5   | Normal Lung<br>GENPAK 061010                  | 7.9  | 93252_Secondary<br>Th1/Th2/Tr1_anti-CD95 CH11               | 0.0  |
| CNS ca.* (neuro;<br>met ) SK-N-AS    | 52.1  | 83239 Lung Met<br>to Muscle<br>(ODO4286)      | 6.5  | 93103_LAK cells_resting                                     | 0.5  |
| CNS ca. (astro)<br>SF-539            | 12.6  | 83240 Muscle<br>NAT (ODO4286)                 | 2.6  | 93788_LAK cells_IL-2                                        | 0.0  |
| CNS ca. (astro)<br>SNB-75            | 11.9  | 84136 Lung<br>Malignant Cancer<br>(OD03126)   | 14.8 | 93787_LAK cells_IL-2+IL-12                                  | 0.7  |
| CNS ca.<br>(glio)SNB-19              | 0.0   | 84137 Lung NAT<br>(OD03126)                   | 3.2  | 93789_LAK cells_IL-2+IFN gamma                              | 1.1  |
| CNS ca.<br>(glio)U251                | 0.9   | 84871 Lung<br>Cancer<br>(OD04404)             | 2.1  | 93790_LAK cells_IL-2+ IL-18                                 | 0.3  |
| CNS ca. (glio)<br>SF-295             | 12.6  | 84872 Lung NAT<br>(OD04404)                   | 1.9  | 93104_LAK cells_PMA/ionomycin<br>and IL-18                  | 0.0  |
| Heart                                | 13.9  | 84875 Lung<br>Cancer<br>(OD04565)             | 0.3  | 93578_NK Cells IL-2_resting                                 | 1.3  |
| Skeletal muscle                      | 3.2   | 85950 Lung<br>Cancer<br>(OD04237-01)          | 1.3  | 93109_Mixed Lymphocyte<br>Reaction_Two Way MLR              | 0.5  |
| Bone marrow                          | 3.6   | 85970 Lung NAT<br>(OD04237-02)                | 2.6  | 93110_Mixed Lymphocyte<br>Reaction_Two Way MLR              | 0.5  |
| Thymus                               | 4.2   | 83255 Ocular Mel<br>Met to Liver<br>(ODO4310) | 0.1  | 93111_Mixed Lymphocyte<br>Reaction_Two Way MLR              | 2.7  |
| Spleen                               | 61.6  | 83256 Liver NAT<br>(ODO4310)                  | 0.6  | 93112_Mononuclear Cells<br>(PBMCs)_resting                  | 0.0  |
| Lymph node                           | 3.3   | 84139 Melanoma<br>Mets to Lung<br>(OD04321)   | 2.5  | 93113_Mononuclear Cells<br>(PBMCs)_PWM                      | 1.3  |
| Colorectal                           | 11.9  | 84138 Lung NAT<br>(OD04321)                   | 2.6  | 93114_Mononuclear Cells<br>(PBMCs)_PHA-L                    | 1.0  |
| Stomach                              | 28.3  | Normal Kidney<br>GENPAK 061008                | 5.6  | 93249_Ramos (B cell)_none                                   | 1.2  |

|                                     |      |                                             |      |                                                                              |     |
|-------------------------------------|------|---------------------------------------------|------|------------------------------------------------------------------------------|-----|
| Small intestine                     | 4.5  | 83786 Kidney Ca, Nuclear grade 2 (OD04338)  | 0.6  | 93250_Ramos (B cell)_ionomycin                                               | 2.3 |
| Colon ca. SW480                     | 46.7 | 83787 Kidney NAT (OD04338)                  | 3.7  | 93349_B lymphocytes_PWM                                                      | 4.3 |
| Colon ca.* (SW480 met)SW620         | 19.0 | 83788 Kidney Ca Nuclear grade 1/2 (OD04339) | 0.8  | 93350_B lymphocytes_CD40L and IL-4                                           | 1.4 |
| Colon ca. HT29                      | 5.3  | 83789 Kidney NAT (OD04339)                  | 3.1  | 92665_EOL-1 (Eosinophil)_dbcAMP differentiated                               | 7.2 |
| Colon ca. HCT-116                   | 5.0  | 83790 Kidney Ca, Clear cell type (OD04340)  | 1.5  | 93248_EOL-1 (Eosinophil)_dbcAMP/PMAionomycin                                 | 3.0 |
| Colon ca. CaCo-2                    | 49.3 | 83791 Kidney NAT (OD04340)                  | 5.1  | 93356_Dendritic Cells_none                                                   | 1.5 |
| 83219 CC Well to Mod Diff (ODO3866) | 3.0  | 83792 Kidney Ca, Nuclear grade 3 (OD04348)  | 14.5 | 93355_Dendritic Cells_LPS 100 ng/ml                                          | 0.7 |
| Colon ca. HCC-2998                  | 27.7 | 83793 Kidney NAT (OD04348)                  | 2.5  | 93775_Dendritic Cells_anti-CD40                                              | 0.5 |
| Gastric ca.* (liver met) NCI-N87    | 10.5 | 87474 Kidney Cancer (OD04622-01)            | 1.7  | 93774_Monocytes_resting                                                      | 0.5 |
| Bladder                             | 3.7  | 87475 Kidney NAT (OD04622-03)               | 2.0  | 93776_Monocytes_LPS 50 ng/ml                                                 | 0.0 |
| Trachea                             | 23.5 | 85973 Kidney Cancer (OD04450-01)            | 0.3  | 93581_Macrophages_resting                                                    | 1.3 |
| Kidney                              | 1.8  | 85974 Kidney NAT (OD04450-03)               | 2.0  | 93582_Macrophages_LPS 100 ng/ml                                              | 1.8 |
| Kidney (fetal)                      | 1.9  | Kidney Cancer Clontech 8120607              | 7.0  | 93098_HUVEC (Endothelial)_none                                               | 2.3 |
| Renal ca. 786-0                     | 7.0  | Kidney NAT Clontech 8120608                 | 1.5  | 93099_HUVEC (Endothelial)_starved                                            | 9.0 |
| Renal ca. A498                      | 6.8  | Kidney Cancer Clontech 8120613              | 2.0  | 93100_HUVEC (Endothelial)_IL-1b                                              | 1.2 |
| Renal ca.RXF 393                    | 4.7  | Kidney NAT Clontech 8120614                 | 4.1  | 93779_HUVEC (Endothelial)_IFN gamma                                          | 1.4 |
| Renal ca.ACHN                       | 9.8  | Kidney Cancer Clontech 9010320              | 2.2  | 93102_HUVEC (Endothelial)_TNF alpha + IFN gamma                              | 0.8 |
| Renal ca.UO-31                      | 1.3  | Kidney NAT Clontech 9010321                 | 3.5  | 93101_HUVEC (Endothelial)_TNF alpha + IL4                                    | 1.1 |
| Renal ca.TK-10                      | 0.6  | Normal Uterus GENPAK 061018                 | 3.1  | 93781_HUVEC (Endothelial)_IL-11                                              | 3.0 |
| Liver                               | 0.8  | Uterus Cancer GENPAK 064011                 | 17.6 | 93583_Lung Microvascular Endothelial Cells_none                              | 0.8 |
| Liver (fetal)                       | 1.1  | Normal Thyroid Clontech A+ 6570-1           | 3.7  | 93584_Lung Microvascular Endothelial Cells_TNFa (4 ng/ml) and IL1b (1 ng/ml) | 0.5 |
| Liver ca. (hepatoblast) HepG2       | 54.0 | Thyroid Cancer GENPAK 064010                | 1.2  | 92662_Microvascular Dermal endothelium_none                                  | 1.1 |
| Lung                                | 3.9  | Thyroid Cancer INVITROGEN A302152           | 0.6  | 92663_Microvascular Dermal endothelium_TNFa (4 ng/ml) and IL1b (1 ng/ml)     | 1.0 |
| Lung (fetal)                        | 9.0  | Thyroid NAT INVITROGEN A302153              | 2.6  | 93773_Bronchial epithelium_TNFa (4 ng/ml) and IL1b (1 ng/ml) **              | 0.0 |

|                                  |      |                                                         |      |                                                                 |      |
|----------------------------------|------|---------------------------------------------------------|------|-----------------------------------------------------------------|------|
| Lung ca. (small cell) LX-1       | 34.4 | Normal Breast GENPAK 061019                             | 3.4  | 93347_Small Airway Epithelium_none                              | 0.4  |
| Lung ca. (small cell) NCI-H69    | 3.0  | 84877 Breast Cancer (OD04566)                           | 0.9  | 93348_Small Airway Epithelium_TNFa (4 ng/ml) and IL1b (1 ng/ml) | 0.5  |
| Lung ca. (s.cell var.) SHP-77    | 13.0 | 85975 Breast Cancer (OD04590-01)                        | 67.8 | 92668_Coronary Artery SMC_resting                               | 5.8  |
| Lung ca. (large cell) NCI-H460   | 6.8  | 85976 Breast Cancer Mets (OD04590-03)                   | 51.1 | 92669_Coronary Artery SMC_TNFa (4 ng/ml) and IL1b (1 ng/ml)     | 2.3  |
| Lung ca. (non-sm. cell) A549     | 3.4  | 87070 Breast Cancer Metastasis (OD04655-05)             | 12.7 | 93107_astrocytes_resting                                        | 2.7  |
| Lung ca. (non-s.cell) NCI-H23    | 34.4 | GENPAK Breast Cancer 064006                             | 8.9  | 93108_astrocytes_TNFa (4 ng/ml) and IL1b (1 ng/ml)              | 0.0  |
| Lung ca (non-s.cell) HOP-62      | 10.5 | Breast Cancer Clontech 9100266                          | 6.2  | 92666_KU-812 (Basophil)_resting                                 | 6.8  |
| Lung ca. (non-s.cl) NCI-H522     | 47.6 | Breast NAT Clontech 9100265                             | 3.3  | 92667_KU-812 (Basophil)_PMA/ionoycin                            | 8.4  |
| Lung ca. (squam.) SW 900         | 4.7  | Breast Cancer INVITROGEN A209073                        | 3.4  | 93579_CCD1106 (Keratinocytes)_none                              | 1.6  |
| Lung ca. (squam.) NCI-H596       | 0.7  | Breast NAT INVITROGEN A2090734                          | 8.7  | 93580_CCD1106 (Keratinocytes)_TNFa and IFNg **                  | 1.4  |
| Mammary gland                    | 9.9  | Normal Liver GENPAK 061009                              | 1.1  | 93791_Liver Cirrhosis                                           | 4.2  |
| Breast ca.* (pl. effusion) MCF-7 | 5.6  | Liver Cancer GENPAK 064003                              | 0.6  | 93792_Lupus Kidney                                              | 1.9  |
| Breast ca.* (pl.ef) MDA-MB-231   | 21.3 | Liver Cancer Research Genetics RNA 1025                 | 0.6  | 93577_NCI-H292                                                  | 39.5 |
| Breast ca.* (pl. effusion) T47D  | 66.0 | Liver Cancer Research Genetics RNA 1026                 | 1.4  | 93358_NCI-H292_IL-4                                             | 39.0 |
| Breast ca. BT-549                | 7.6  | Paired Liver Cancer Tissue Research Genetics RNA 6004-T | 1.3  | 93360_NCI-H292_IL-9                                             | 65.5 |
| Breast ca.MDA-N                  | 18.7 | Paired Liver Tissue Research Genetics RNA 6004-N        | 1.3  | 93359_NCI-H292_IL-13                                            | 37.1 |
| Ovary                            | 12.1 | Paired Liver Cancer Tissue Research Genetics RNA 6005-T | 1.1  | 93357_NCI-H292_IFN gamma                                        | 31.9 |
| Ovarian ca.OVCAR-3               | 3.5  | Paired Liver Tissue Research Genetics RNA 6005-N        | 0.3  | 93777_HPAEC_-                                                   | 0.5  |
| Ovarian ca.OVCAR-4               | 4.0  | Normal Bladder GENPAK 061001                            | 5.9  | 93778_HPAEC_IL-1 beta/TNA alpha                                 | 1.2  |
| Ovarian ca. OVCAR-5              | 9.1  | Bladder Cancer Research                                 | 1.7  | 93254_Normal Human Lung Fibroblast_none                         | 42.3 |

|                                       |      |                                                  |       |                                                                              |       |
|---------------------------------------|------|--------------------------------------------------|-------|------------------------------------------------------------------------------|-------|
|                                       |      | Genetics RNA<br>1023                             |       |                                                                              |       |
| Ovarian ca.<br>OVCAR-8                | 12.7 | Bladder Cancer<br>INVITROGEN<br>A302173          | 1.9   | 93253_Normal Human Lung<br>Fibroblast_TNFa (4 ng/ml) and IL-<br>1b (1 ng/ml) | 17.8  |
| Ovarian<br>ca.IGROV-1                 | 9.8  | 87071 Bladder<br>Cancer<br>(OD04718-01)          | 2.0   | 93257_Normal Human Lung<br>Fibroblast_IL-4                                   | 100.0 |
| Ovarian ca.*<br>(ascites) SK-OV-<br>3 | 0.4  | 87072 Bladder<br>Normal Adjacent<br>(OD04718-03) | 3.3   | 93256_Normal Human Lung<br>Fibroblast_IL-9                                   | 72.7  |
| Uterus                                | 6.9  | Normal Ovary<br>Res. Gen.                        | 2.2   | 93255_Normal Human Lung<br>Fibroblast_IL-13                                  | 60.7  |
| Placenta                              | 4.6  | Ovarian Cancer<br>GENPAK 064008                  | 29.1  | 93258_Normal Human Lung<br>Fibroblast_IFN gamma                              | 81.8  |
| Prostate                              | 15.7 | 87492 Ovary<br>Cancer<br>(OD04768-07)            | 100.0 | 93106_Dermal Fibroblasts<br>CCD1070_resting                                  | 76.8  |
| Prostate ca.*<br>(bone met)PC-3       | 35.9 | 87493 Ovary NAT<br>(OD04768-08)                  | 2.2   | 93361_Dermal Fibroblasts<br>CCD1070_TNF alpha 4 ng/ml                        | 30.2  |
| Testis                                | 14.6 | Normal Stomach<br>GENPAK 061017                  | 13.1  | 93105_Dermal Fibroblasts<br>CCD1070_IL-1 beta 1 ng/ml                        | 38.2  |
| Melanoma<br>Hs688(A).T                | 13.5 | NAT Stomach<br>Clontech 9060359                  | 8.8   | 93772_dermal fibroblast_IFN<br>gamma                                         | 34.2  |
| Melanoma*<br>(met)<br>Hs688(B).T      | 71.2 | Gastric Cancer<br>Clontech<br>9060395            | 2.5   | 93771_dermal fibroblast_IL-4                                                 | 80.7  |
| Melanoma<br>UACC-62                   | 1.7  | NAT Stomach<br>Clontech 9060394                  | 9.7   | 93259_IBD Colitis 1**                                                        | 0.0   |
| Melanoma M14                          | 9.5  | Gastric Cancer<br>Clontech<br>9060397            | 15.9  | 93260_IBD Colitis 2                                                          | 0.3   |
| Melanoma LOX<br>IMVI                  | 2.4  | NAT Stomach<br>Clontech 9060396                  | 12.9  | 93261_IBD Crohns                                                             | 1.4   |
| Melanoma*<br>(met)SK-MEL-5            | 3.4  | Gastric Cancer<br>GENPAK 064005                  | 12.1  | 735010_Colon_normal                                                          | 35.6  |
| Adipose                               | 5.9  |                                                  |       | 735019_Lung_none                                                             | 11.0  |
|                                       |      |                                                  |       | 64028-1_Thymus_none                                                          | 5.8   |
|                                       |      |                                                  |       | 64030-1_Kidney_none                                                          | 9.7   |

Taqman results shown in Table 9 demonstrates that cFCTR1 is highly expressed by tumor cell lines and also overexpressed in tumor tissues, specifically breast and ovarian tumor compared to Normal Adjacent Tissues (NAT). There are reports that follistatin can act as a modulator of tumor growth and its expression also correlate with polycystic ovary syndrome, a benign form of ovarian tumor.

**Table 10: Primer Design for Probe Ag2773 (FCTR4)**

| Primer  | Sequences                                  | TM   | Length | Start Pos | SEQ ID<br>NO |
|---------|--------------------------------------------|------|--------|-----------|--------------|
| Forward | 5'-CCTTGCTTTGTCATATGCTGTT-3'               | 59.3 | 22     | 243       | 29           |
| Probe   | FAM-5'-CCCTTTGCCTGGAATATAAACTCTCA-3'-TAMRA | 64.6 | 26     | 265       | 30           |
| Reverse | 5'-AGAGGAAGCTTTCTGGAGAAGA-3'               | 58.9 | 22     | 313       | 31           |

TABLE 11: TAQMAN RESULTS FOR CLONE FCTR4

| Tissue_Name                   | Panel 1D | Tissue_Name                                 | Panel 2D | Tissue_Name                                              | Panel 4D |
|-------------------------------|----------|---------------------------------------------|----------|----------------------------------------------------------|----------|
| Liver adenocarcinoma          | 18.3     | Normal Colon GENPAK 061003                  | 41.2     | 93768_Secondary Th1_anti-CD28/anti-CD3                   | 12.7     |
| Heart (fetal)                 | 4.3      | 83219 CC Well to Mod Diff (ODO3866)         | 5.2      | 93769_Secondary Th2_anti-CD28/anti-CD3                   | 14.2     |
| Pancreas                      | 3.1      | 83220 CC NAT (ODO3866)                      | 2.5      | 93770_Secondary Tr1_anti-CD28/anti-CD3                   | 14.7     |
| Pancreatic ca.CAPAN 2         | 20.0     | 83221 CC Gr.2 rectosigmoid (ODO3868)        | 0.7      | 93573_Secondary Th1_resting day 4-6 in IL-2              | 4.7      |
| Adrenal gland                 | 7.4      | 83222 CC NAT (ODO3868)                      | 1.4      | 93572_Secondary Th2_resting day 4-6 in IL-2              | 3.5      |
| Thyroid                       | 6.8      | 83235 CC Mod Diff (ODO3920)                 | 14.0     | 93571_Secondary Tr1_resting day 4-6 in IL-2              | 7.0      |
| Salivary gland                | 2.5      | 83236 CC NAT (ODO3920)                      | 13.9     | 93568_primary Th1_anti-CD28/anti-CD3                     | 22.4     |
| Pituitary gland               | 5.7      | 83237 CC Gr.2 ascend colon (ODO3921)        | 16.2     | 93569_primary Th2_anti-CD28/anti-CD3                     | 16.3     |
| Brain (fetal)                 | 14.4     | 83238 CC NAT (ODO3921)                      | 5.2      | 93570_primary Tr1_anti-CD28/anti-CD3                     | 21.8     |
| Brain (whole)                 | 19.6     | 83241 CC from Partial Hepatectomy (ODO4309) | 13.9     | 93565_primary Th1_resting dy 4-6 in IL-2                 | 30.2     |
| Brain (amygdala)              | 3.7      | 83242 Liver NAT (ODO4309)                   | 12.7     | 93566_primary Th2_resting dy 4-6 in IL-2                 | 14.4     |
| Brain (cerebellum)            | 2.1      | 87472 Colon mets to lung (OD04451-01)       | 3.4      | 93567_primary Tr1_resting dy 4-6 in IL-2                 | 7.4      |
| Brain (hippocampus)           | 22.7     | 87473 Lung NAT (OD04451-02)                 | 1.5      | 93351_CD45RA CD4 lymphocyte_anti-CD28/anti-CD3           | 7.6      |
| Brain (thalamus)              | 7.4      | Normal Prostate Clontech A+ 6546-1          | 1.0      | 93352_CD45RO CD4 lymphocyte_anti-CD28/anti-CD3           | 11.1     |
| Cerebral Cortex               | 47.3     | 84140 Prostate Cancer (OD04410)             | 3.1      | 93251_CD8 Lymphocytes_anti-CD28/anti-CD3                 | 9.6      |
| Spinal cord                   | 8.3      | 84141 Prostate NAT (OD04410)                | 10.6     | 93353_chronic CD8 Lymphocytes 2ry_resting dy 4-6 in IL-2 | 9.7      |
| CNS ca. (glio/astro)U87-MG    | 19.9     | 87073 Prostate Cancer (OD04720-01)          | 9.7      | 93574_chronic CD8 Lymphocytes 2ry_activated CD3/CD28     | 6.2      |
| CNS ca. (glio/astro) U-118-MG | 57.0     | 87074 Prostate NAT (OD04720-02)             | 8.3      | 93354_CD4_none                                           | 6.4      |
| CNS ca. (astro) SW1783        | 10.0     | Normal Lung GENPAK 061010                   | 36.6     | 93252_Secondary Th1/Th2/Tr1_anti-CD95 CH11               | 9.3      |
| CNS ca.* (neuro; met )SK-N-AS | 44.8     | 83239 Lung Met to Muscle (ODO4286)          | 11.7     | 93103_LAK cells_resting                                  | 11.0     |
| CNS ca. (astro) SF-539        | 37.4     | 83240 Muscle NAT (ODO4286)                  | 3.4      | 93788_LAK cells_IL-2                                     | 10.4     |
| CNS ca. (astro) SNB-75        | 62.0     | 84136 Lung Malignant Cancer (OD03126)       | 15.1     | 93787_LAK cells_IL-2+IL-12                               | 7.4      |

|                                           |       |                                                   |      |                                                   |       |
|-------------------------------------------|-------|---------------------------------------------------|------|---------------------------------------------------|-------|
| CNS ca. (glio)<br>SNB-19                  | 24.8  | 84137 Lung NAT<br>(OD03126)                       | 17.4 | 93789_LAK cells_IL-2+IFN gamma                    | 11.6  |
| CNS ca. (glio)<br>U251                    | 40.3  | 84871 Lung<br>Cancer<br>(OD04404)                 | 5.0  | 93790_LAK cells_IL-2+ IL-18                       | 13.3  |
| CNS ca. (glio)<br>SF-295                  | 100.0 | 84872 Lung NAT<br>(OD04404)                       | 6.3  | 93104_LAK cells_PMA/ionomycin and<br>IL-18        | 4.8   |
| Heart                                     | 0.0   | 84875 Lung<br>Cancer<br>(OD04565)                 | 3.2  | 93578_NK Cells IL-2_resting                       | 6.2   |
| Skeletal muscle                           | 0.0   | 85950 Lung<br>Cancer<br>(OD04237-01)              | 15.8 | 93109_Mixed Lymphocyte<br>Reaction_Two Way MLR    | 12.3  |
| Bone marrow                               | 33.7  | 85970 Lung NAT<br>(OD04237-02)                    | 10.5 | 93110_Mixed Lymphocyte<br>Reaction_Two Way MLR    | 8.7   |
| Thymus                                    | 12.4  | 83255 Ocular Mel<br>Met to Liver<br>(ODO4310)     | 5.9  | 93111_Mixed Lymphocyte<br>Reaction_Two Way MLR    | 3.5   |
| Spleen                                    | 21.3  | 83256 Liver NAT<br>(ODO4310)                      | 3.6  | 93112_Mononuclear Cells<br>(PBMcs)_resting        | 4.5   |
| Lymph node                                | 13.4  | 84139 Melanoma<br>Mets to Lung<br>(OD04321)       | 10.6 | 93113_Mononuclear Cells<br>(PBMcs)_PWM            | 21.2  |
| Colorectal                                | 38.2  | 84138 Lung NAT<br>(OD04321)                       | 10.6 | 93114_Mononuclear Cells<br>(PBMcs)_PHA-L          | 8.9   |
| Stomach                                   | 9.9   | Normal Kidney<br>GENPAK 061008                    | 26.2 | 93249_Ramos (B cell)_none                         | 100.0 |
| Small intestine                           | 17.9  | 83786 Kidney<br>Ca, Nuclear grade<br>2 (OD04338)  | 22.2 | 93250_Ramos (B cell)_ionomycin                    | 28.7  |
| Colon ca.SW480                            | 27.7  | 83787 Kidney<br>NAT (OD04338)                     | 11.7 | 93349_B lymphocytes_PWM                           | 20.0  |
| Colon ca.*<br>(SW480<br>met)SW620         | 30.8  | 83788 Kidney Ca<br>Nuclear grade 1/2<br>(OD04339) | 45.1 | 93350_B lymphocytes_CD40L and IL-4                | 7.8   |
| Colon ca.HT29                             | 8.1   | 83789 Kidney<br>NAT (OD04339)                     | 14.8 | 92665_EOL-1 (Eosinophil)_dbcAMP<br>differentiated | 8.0   |
| Colon ca.HCT-<br>116                      | 35.4  | 83790 Kidney Ca,<br>Clear cell type<br>(OD04340)  | 26.6 | 93248_EOL-1<br>(Eosinophil)_dbcAMP/PMAionomycin   | 3.8   |
| Colon ca. CaCo-<br>2                      | 37.6  | 83791 Kidney<br>NAT (OD04340)                     | 10.4 | 93356_Dendritic Cells_none                        | 6.8   |
| 83219 CC Well<br>to Mod Diff<br>(ODO3866) | 17.8  | 83792 Kidney Ca,<br>Nuclear grade 3<br>(OD04348)  | 2.4  | 93355_Dendritic Cells_LPS 100 ng/ml               | 3.3   |
| Colon ca.HCC-<br>2998                     | 19.9  | 83793 Kidney<br>NAT (OD04348)                     | 18.8 | 93775_Dendritic Cells_anti-CD40                   | 6.3   |
| Gastric ca.*<br>(liver met) NCI-<br>N87   | 73.2  | 87474 Kidney<br>Cancer<br>(OD04622-01)            | 5.6  | 93774_Monocytes_resting                           | 10.6  |
| Bladder                                   | 43.2  | 87475 Kidney<br>NAT (OD04622-<br>03)              | 0.5  | 93776_Monocytes_LPS 50 ng/ml                      | 3.5   |
| Trachea                                   | 10.3  | 85973 Kidney<br>Cancer<br>(OD04450-01)            | 21.2 | 93581_Macrophages_resting                         | 7.6   |
| Kidney                                    | 9.2   | 85974 Kidney<br>NAT (OD04450-<br>03)              | 9.3  | 93582_Macrophages_LPS 100 ng/ml                   | 3.9   |
| Kidney (fetal)                            | 0.0   | Kidney Cancer<br>Clontech 8120607                 | 0.0  | 93098_HUVEC (Endothelial)_none                    | 8.5   |

|                                       |      |                                                      |      |                                                                                    |      |
|---------------------------------------|------|------------------------------------------------------|------|------------------------------------------------------------------------------------|------|
| Renal ca.786-0                        | 53.6 | Kidney NAT<br>Clontech 8120608                       | 0.9  | 93099_HUVEC (Endothelial)_starved                                                  | 17.9 |
| Renal ca. A498                        | 36.1 | Kidney Cancer<br>Clontech 8120613                    | 0.0  | 93100_HUVEC (Endothelial)_IL-1b                                                    | 6.0  |
| Renal ca.RXF<br>393                   | 31.6 | Kidney NAT<br>Clontech 8120614                       | 0.9  | 93779_HUVEC (Endothelial)_IFN<br>gamma                                             | 7.8  |
| Renal ca.ACHN                         | 21.6 | Kidney Cancer<br>Clontech 9010320                    | 2.7  | 93102_HUVEC (Endothelial)_TNF<br>alpha + IFN gamma                                 | 5.7  |
| Renal ca.UO-31                        | 28.7 | Kidney NAT<br>Clontech 9010321                       | 5.0  | 93101_HUVEC (Endothelial)_TNF<br>alpha + IL4                                       | 5.6  |
| Renal ca.TK-10                        | 7.0  | Normal Uterus<br>GENPAK 061018                       | 5.3  | 93781_HUVEC (Endothelial)_IL-11                                                    | 4.9  |
| Liver                                 | 14.2 | Uterus Cancer<br>GENPAK 064011                       | 9.0  | 93583_Lung Microvascular Endothelial<br>Cells_none                                 | 4.9  |
| Liver (fetal)                         | 14.5 | Normal Thyroid<br>Clontech A+<br>6570-1              | 3.4  | 93584_Lung Microvascular Endothelial<br>Cells_TNFa (4 ng/ml) and IL1b (1<br>ng/ml) | 4.9  |
| Liver ca.<br>(hepatoblast)<br>HepG2   | 59.9 | Thyroid Cancer<br>GENPAK 064010                      | 1.8  | 92662_Microvascular Dermal<br>endothelium_none                                     | 8.6  |
| Lung                                  | 17.8 | Thyroid Cancer<br>INVITROGEN<br>A302152              | 3.6  | 92663_Microvascular Dermal<br>endothelium_TNFa (4 ng/ml) and IL1b<br>(1 ng/ml)     | 6.0  |
| Lung (fetal)                          | 9.6  | Thyroid NAT<br>INVITROGEN<br>A302153                 | 4.9  | 93773_Bronchial epithelium_TNFa (4<br>ng/ml) and IL1b (1 ng/ml) **                 | 0.9  |
| Lung ca. (small<br>cell) LX-1         | 70.2 | Normal Breast<br>GENPAK 061019                       | 8.5  | 93347_Small Airway Epithelium_none                                                 | 1.3  |
| Lung ca. (small<br>cell) NCI-H69      | 29.9 | 84877 Breast<br>Cancer<br>(OD04566)                  | 1.5  | 93348_Small Airway Epithelium_TNFa<br>(4 ng/ml) and IL1b (1 ng/ml)                 | 13.2 |
| Lung ca. (s.cell<br>var.) SHP-77      | 3.9  | 85975 Breast<br>Cancer<br>(OD04590-01)               | 23.8 | 92668_Coronary Artery SMC_resting                                                  | 3.4  |
| Lung ca. (large<br>cell)NCI-H460      | 2.0  | 85976 Breast<br>Cancer Mets<br>(OD04590-03)          | 24.5 | 92669_Coronary Artery SMC_TNFa (4<br>ng/ml) and IL1b (1 ng/ml)                     | 2.0  |
| Lung ca. (non-<br>sm. cell) A549      | 28.5 | 87070 Breast<br>Cancer<br>Metastasis<br>(OD04655-05) | 12.9 | 93107_astrocytes_resting                                                           | 4.7  |
| Lung ca. (non-<br>s.cell) NCI-H23     | 36.1 | GENPAK Breast<br>Cancer 064006                       | 11.8 | 93108_astrocytes_TNFa (4 ng/ml) and<br>IL1b (1 ng/ml)                              | 1.9  |
| Lung ca (non-<br>s.cell) HOP-62       | 29.9 | Breast Cancer<br>Clontech 9100266                    | 3.2  | 92666_KU-812 (Basophil)_resting                                                    | 5.8  |
| Lung ca. (non-<br>s.cl) NCI-H522      | 17.2 | Breast NAT<br>Clontech 9100265                       | 1.8  | 92667_KU-812<br>(Basophil)_PMA/ionoycin                                            | 12.0 |
| Lung ca.<br>(squam.) SW<br>900        | 63.7 | Breast Cancer<br>INVITROGEN<br>A209073               | 11.0 | 93579_CCD1106 (Keratinocytes)_none                                                 | 4.9  |
| Lung ca.<br>(squam.) NCI-<br>H596     | 10.0 | Breast NAT<br>INVITROGEN<br>A2090734                 | 7.1  | 93580_CCD1106<br>(Keratinocytes)_TNFa and IFNg **                                  | 0.3  |
| Mammary gland                         | 4.6  | Normal Liver<br>GENPAK 061009                        | 8.8  | 93791_Liver Cirrhosis                                                              | 1.8  |
| Breast ca.* (pl.<br>effusion) MCF-7   | 0.0  | Liver Cancer<br>GENPAK 064003                        | 4.9  | 93792_Lupus Kidney                                                                 | 1.6  |
| Breast ca.*<br>(pl.ef) MDA-MB-<br>231 | 38.7 | Liver Cancer<br>Research<br>Genetics RNA<br>1025     | 1.0  | 93577_NCI-H292                                                                     | 11.1 |

|                                 |      |                                                         |       |                                                                       |      |
|---------------------------------|------|---------------------------------------------------------|-------|-----------------------------------------------------------------------|------|
| Breast ca.* (pl. effusion) T47D | 0.0  | Liver Cancer Research Genetics RNA 1026                 | 0.8   | 93358_NCI-H292_IL-4                                                   | 12.2 |
| Breast ca.BT-549                | 4.6  | Paired Liver Cancer Tissue Research Genetics RNA 6004-T | 3.0   | 93360_NCI-H292_IL-9                                                   | 7.6  |
| Breast ca.MDA-N                 | 19.0 | Paired Liver Tissue Research Genetics RNA 6004-N        | 7.3   | 93359_NCI-H292_IL-13                                                  | 6.1  |
| Ovary                           | 1.7  | Paired Liver Cancer Tissue Research Genetics RNA 6005-T | 0.2   | 93357_NCI-H292_IFN gamma                                              | 5.8  |
| Ovarian ca.OVCAR-3              | 4.8  | Paired Liver Tissue Research Genetics RNA 6005-N        | 0.0   | 93777_HPAEC_-                                                         | 6.8  |
| Ovarian ca.OVCAR-4              | 0.0  | Normal Bladder GENPAK 061001                            | 19.8  | 93778_HPAEC_IL-1 beta/TNA alpha                                       | 5.4  |
| Ovarian ca.OVCAR-5              | 39.0 | Bladder Cancer Research Genetics RNA 1023               | 3.1   | 93254_Normal Human Lung Fibroblast_none                               | 2.1  |
| Ovarian ca.OVCAR-8              | 36.6 | Bladder Cancer INVITROGEN A302173                       | 9.9   | 93253_Normal Human Lung Fibroblast_TNFa (4 ng/ml) and IL-1b (1 ng/ml) | 1.9  |
| Ovarian ca.IGROV-1              | 0.0  | 87071 Bladder Cancer (OD04718-01)                       | 6.6   | 93257_Normal Human Lung Fibroblast_IL-4                               | 3.6  |
| Ovarian ca.* (ascites) SK-OV-3  | 65.5 | 87072 Bladder Normal Adjacent (OD04718-03)              | 4.0   | 93256_Normal Human Lung Fibroblast_IL-9                               | 3.3  |
| Uterus                          | 1.6  | Normal Ovary Res. Gen.                                  | 0.3   | 93255_Normal Human Lung Fibroblast_IL-13                              | 2.3  |
| Placenta                        | 8.9  | Ovarian Cancer GENPAK 064008                            | 6.8   | 93258_Normal Human Lung Fibroblast_IFN gamma                          | 2.9  |
| Prostate                        | 0.0  | 87492 Ovary Cancer (OD04768-07)                         | 100.0 | 93106_Dermal Fibroblasts CCD1070_resting                              | 5.6  |
| Prostate ca.* (bone met)PC-3    | 9.2  | 87493 Ovary NAT (OD04768-08)                            | 3.6   | 93361_Dermal Fibroblasts CCD1070_TNF alpha 4 ng/ml                    | 17.4 |
| Testis                          | 29.5 | Normal Stomach GENPAK 061017                            | 8.6   | 93105_Dermal Fibroblasts CCD1070_IL-1 beta 1 ng/ml                    | 3.8  |
| Melanoma Hs688(A).T             | 14.3 | NAT Stomach Clontech 9060359                            | 0.7   | 93772_dermal fibroblast_IFN gamma                                     | 2.6  |
| Melanoma* (met) Hs688(B).T      | 22.9 | Gastric Cancer Clontech 9060395                         | 3.9   | 93771_dermal fibroblast_IL-4                                          | 3.4  |
| Melanoma UACC-62                | 9.7  | NAT Stomach Clontech 9060394                            | 5.3   | 93259_IBD Colitis 1**                                                 | 0.2  |
| Melanoma M14                    | 12.7 | Gastric Cancer Clontech 9060397                         | 13.2  | 93260_IBD Colitis 2                                                   | 0.4  |
| Melanoma LOX IMVI               | 4.5  | NAT Stomach Clontech 9060396                            | 1.1   | 93261_IBD Crohns                                                      | 0.3  |
| Melanoma*                       | 21.8 | Gastric Cancer                                          | 23.0  | 735010_Colon_normal                                                   | 3.3  |

|                |     |               |  |                     |      |
|----------------|-----|---------------|--|---------------------|------|
| (met) SK-MEL-5 |     | GENPAK 064005 |  |                     |      |
| Adipose        | 6.7 |               |  | 735019_Lung_none    | 3.9  |
|                |     |               |  | 64028-1_Thymus_none | 7.7  |
|                |     |               |  | 64030-1_Kidney_none | 21.8 |

Table 12 shows the taqman results of clone FCTR4 indicating overexpression in ovarian cancer as compared to Normal Adjacent Tissue (NAT). In addition, increased expression is demonstrated by ovarian tumor cell line suggesting that antibodies could be used to treat ovarian tumors.

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**Table 13: Primer Design for Probe Ag427 (FCTR5)**

| Primer  | Sequences                             | Length | Start Po | SEQ ID NO |
|---------|---------------------------------------|--------|----------|-----------|
| Forward | 5'-GAGCTACAGGCAGCCTCGAGT-3'           | 21     | 443      | 32        |
| Probe   | TET-5'-TGGCCCAGCTGACCCTGCTCA-3'-TAMRA | 21     |          | 33        |
| Reverse | 5'-GGCTACGTCAGTGGGTTTGG-3'            | 20     | 449      | 34        |

**Table 14: Taqman results for FCTR5**

10

| Tissue_Name                 | Panel 1 | Tissue_Name                                              | Panel 4D |
|-----------------------------|---------|----------------------------------------------------------|----------|
| Endothelial cells           | 10.7    | 93768_Secondary Th1_anti-CD28/anti-CD3                   | 15.9     |
| Endothelial cells (treated) | 15.2    | 93769_Secondary Th2_anti-CD28/anti-CD3                   | 14.7     |
| Pancreas                    | 16.2    | 93770_Secondary Tr1_anti-CD28/anti-CD3                   | 21.9     |
| Pancreatic ca.CAPAN 2       | 10.5    | 93573_Secondary Th1_resting day 4-6 in IL-2              | 12.3     |
| Adipose                     | 45.1    | 93572_Secondary Th2_resting day 4-6 in IL-2              | 16.2     |
| Adrenal gland               | 61.6    | 93571_Secondary Tr1_resting day 4-6 in IL-2              | 16.2     |
| Thyroid                     | 13.1    | 93568_primary Th1_anti-CD28/anti-CD3                     | 13.9     |
| Salavary gland              | 33.7    | 93569_primary Th2_anti-CD28/anti-CD3                     | 14.6     |
| Pituitary gland             | 15.8    | 93570_primary Tr1_anti-CD28/anti-CD3                     | 26.2     |
| Brain (fetal)               | 7.2     | 93565_primary Th1_resting dy 4-6 in IL-2                 | 56.3     |
| Brain (whole)               | 6.3     | 93566_primary Th2_resting dy 4-6 in IL-2                 | 27.7     |
| Brain (amygdala)            | 8.4     | 93567_primary Tr1_resting dy 4-6 in IL-2                 | 31.6     |
| Brain (cerebellum)          | 6.8     | 93351_CD45RA CD4 lymphocyte_anti-CD28/anti-CD3           | 12.1     |
| Brain (hippocampus)         | 7.9     | 93352_CD45RO CD4 lymphocyte_anti-CD28/anti-CD3           | 17.1     |
| Brain (substantia nigra)    | 9.5     | 93251_CD8 Lymphocytes_anti-CD28/anti-CD3                 | 9.1      |
| Brain (thalamus)            | 7.9     | 93353_chronic CD8 Lymphocytes 2ry_resting dy 4-6 in IL-2 | 13.4     |
| Brain (hypothalamus)        | 23.0    | 93574_chronic CD8 Lymphocytes 2ry_activated CD3/CD28     | 9.2      |
| Spinal cord                 | 9.5     | 93354_CD4_none                                           | 7.6      |

|                                  |       |                                                                              |      |
|----------------------------------|-------|------------------------------------------------------------------------------|------|
| CNS ca. (glio/astro)U87-MG       | 12.6  | 93252_Secondary Th1/Th2/Tr1_anti-CD95 CH11                                   | 20.2 |
| CNS ca. (glio/astro)U-118-MG     | 11.6  | 93103_LAK cells_resting                                                      | 57.0 |
| CNS ca. (astro)SW1783            | 4.3   | 93788_LAK cells_IL-2                                                         | 18.8 |
| CNS ca.* (neuro; met )SK-N-AS    | 10.4  | 93787_LAK cells_IL-2+IL-12                                                   | 14.2 |
| CNS ca. (astro) SF-539           | 11.6  | 93789_LAK cells_IL-2+IFN gamma                                               | 20.9 |
| CNS ca. (astro) SNB-75           | 4.4   | 93790_LAK cells_IL-2+ IL-18                                                  | 14.8 |
| CNS ca. (glio)SNB-19             | 31.6  | 93104_LAK cells_PMA/ionomycin and IL-18                                      | 12.9 |
| CNS ca. (glio)U251               | 17.3  | 93578_NK Cells IL-2_resting                                                  | 17.4 |
| CNS ca. (glio)SF-295             | 20.9  | 93109_Mixed Lymphocyte Reaction_Two Way MLR                                  | 43.5 |
| Heart                            | 14.3  | 93110_Mixed Lymphocyte Reaction_Two Way MLR                                  | 19.3 |
| Skeletal muscle                  | 11.7  | 93111_Mixed Lymphocyte Reaction_Two Way MLR                                  | 12.6 |
| Bone marrow                      | 21.9  | 93112_Mononuclear Cells (PBMCs)_resting                                      | 8.7  |
| Thymus                           | 20.9  | 93113_Mononuclear Cells (PBMCs)_PWM                                          | 28.5 |
| Spleen                           | 23.8  | 93114_Mononuclear Cells (PBMCs)_PHA-L                                        | 26.2 |
| Lymph node                       | 24.2  | 93249_Ramos (B cell)_none                                                    | 0.3  |
| Colon (ascending)                | 17.2  | 93250_Ramos (B cell)_ionomycin                                               | 1.2  |
| Stomach                          | 11.1  | 93349_B lymphocytes_PWM                                                      | 25.7 |
| Small intestine                  | 21.5  | 93350_B lymphocytes_CD40L and IL-4                                           | 13.0 |
| Colon ca.SW480                   | 12.2  | 92665_EOL-1 (Eosinophil)_dbcAMP differentiated                               | 26.4 |
| Colon ca.* (SW480 met)SW620      | 8.6   | 93248_EOL-1 (Eosinophil)_dbcAMP/PMAionomycin                                 | 11.4 |
| Colon ca.HT29                    | 16.2  | 93356_Dendritic Cells_none                                                   | 40.3 |
| Colon ca.HCT-116                 | 8.1   | 93355_Dendritic Cells_LPS 100 ng/ml                                          | 33.0 |
| Colon ca.CaCo-2                  | 22.1  | 93775_Dendritic Cells_anti-CD40                                              | 20.5 |
| Colon ca.HCT-15                  | 18.6  | 93774_Monocytes_resting                                                      | 23.3 |
| Colon ca.HCC-2998                | 21.9  | 93776_Monocytes_LPS 50 ng/ml                                                 | 6.9  |
| Gastric ca.* (liver met) NCI-N87 | 42.9  | 93581_Macrophages_resting                                                    | 14.7 |
| Bladder                          | 95.3  | 93582_Macrophages_LPS 100 ng/ml                                              | 64.6 |
| Trachea                          | 18.3  | 93098_HUVEC (Endothelial)_none                                               | 6.8  |
| Kidney                           | 25.7  | 93099_HUVEC (Endothelial)_starved                                            | 13.9 |
| Kidney (fetal)                   | 15.8  | 93100_HUVEC (Endothelial)_IL-1b                                              | 7.5  |
| Renal ca.786-0                   | 16.5  | 93779_HUVEC (Endothelial)_IFN gamma                                          | 27.7 |
| Renal ca.A498                    | 16.5  | 93102_HUVEC (Endothelial)_TNF alpha + IFN gamma                              | 11.8 |
| Renal ca.RXF 393                 | 7.4   | 93101_HUVEC (Endothelial)_TNF alpha + IL4                                    | 6.7  |
| Renal ca.ACHN                    | 11.9  | 93781_HUVEC (Endothelial)_IL-11                                              | 10.4 |
| Renal ca.UO-31                   | 15.8  | 93583_Lung Microvascular Endothelial Cells_none                              | 8.8  |
| Renal ca.TK-10                   | 28.7  | 93584_Lung Microvascular Endothelial Cells_TNFa (4 ng/ml) and IL1b (1 ng/ml) | 8.6  |
| Liver                            | 100.0 | 92662_Microvascular Dermal endothelium_none                                  | 22.1 |
| Liver (fetal)                    | 81.8  | 92663_Microvascular Dermal endothelium_TNFa (4 ng/ml) and IL1b (1 ng/ml)     | 18.7 |
| Liver ca. (hepatoblast) HepG2    | 28.3  | 93773_Bronchial epithelium_TNFa (4 ng/ml) and IL1b (1 ng/ml) **              | 35.4 |
| Lung                             | 10.7  | 93347_Small Airway Epithelium_none                                           | 10.9 |
| Lung (fetal)                     | 10.9  | 93348_Small Airway Epithelium_TNFa (4 ng/ml) and IL1b (1 ng/ml)              | 50.0 |

|                                  |      |                                                                       |       |
|----------------------------------|------|-----------------------------------------------------------------------|-------|
| Lung ca. (small cell) LX-1       | 24.3 | 92668_Coronary Artery SMC_resting                                     | 27.9  |
| Lung ca. (small cell) NCI-H69    | 41.5 | 92669_Coronary Artery SMC_TNFa (4 ng/ml) and IL1b (1 ng/ml)           | 25.4  |
| Lung ca. (s.cell var.) SHP-77    | 4.6  | 93107_astrocytes_resting                                              | 7.4   |
| Lung ca. (large cell)NCI-H460    | 46.3 | 93108_astrocytes_TNFa (4 ng/ml) and IL1b (1 ng/ml)                    | 10.7  |
| Lung ca. (non-sm. cell) A549     | 45.4 | 92666_KU-812 (Basophil)_resting                                       | 3.2   |
| Lung ca. (non-s.cell) NCI-H23    | 54.3 | 92667_KU-812 (Basophil)_PMA/ionoycin                                  | 6.7   |
| Lung ca (non-s.cell) HOP-62      | 50.7 | 93579_CCD1106 (Keratinocytes)_none                                    | 12.2  |
| Lung ca. (non-s.cl) NCI-H522     | 38.4 | 93580_CCD1106 (Keratinocytes)_TNFa and IFNg **                        | 100.0 |
| Lung ca. (squam.) SW 900         | 30.8 | 93791_Liver Cirrhosis                                                 | 27.6  |
| Lung ca. (squam.) NCI-H596       | 15.5 | 93792_Lupus Kidney                                                    | 32.3  |
| Mammary gland                    | 65.5 | 93577_NCI-H292                                                        | 77.4  |
| Breast ca.* (pl. effusion) MCF-7 | 4.4  | 93358_NCI-H292_IL-4                                                   | 70.2  |
| Breast ca.* (pl.ef) MDA-MB-231   | 3.5  | 93360_NCI-H292_IL-9                                                   | 54.3  |
| Breast ca.* (pl. effusion)T47D   | 8.7  | 93359_NCI-H292_IL-13                                                  | 47.0  |
| Breast ca. BT-549                | 5.7  | 93357_NCI-H292_IFN gamma                                              | 52.9  |
| Breast ca.MDA-N                  | 16.6 | 93777_HPAEC_-                                                         | 23.8  |
| Ovary                            | 20.5 | 93778_HPAEC_IL-1 beta/TNA alpha                                       | 21.5  |
| Ovarian ca. OVCAR-3              | 21.6 | 93254_Normal Human Lung Fibroblast_none                               | 49.3  |
| Ovarian ca.OVCAR-4               | 8.3  | 93253_Normal Human Lung Fibroblast_TNFa (4 ng/ml) and IL-1b (1 ng/ml) | 40.3  |
| Ovarian ca.OVCAR-5               | 26.1 | 93257_Normal Human Lung Fibroblast_IL-4                               | 48.3  |
| Ovarian ca.OVCAR-8               | 48.0 | 93256_Normal Human Lung Fibroblast_IL-9                               | 29.3  |
| Ovarian ca.IGROV-1               | 9.3  | 93255_Normal Human Lung Fibroblast_IL-13                              | 73.7  |
| Ovarian ca.* (ascites)SK-OV-3    | 8.8  | 93258_Normal Human Lung Fibroblast_IFN gamma                          | 66.9  |
| Uterus                           | 13.4 | 93106_Dermal Fibroblasts CCD1070_resting                              | 20.2  |
| Placenta                         | 9.4  | 93361_Dermal Fibroblasts CCD1070_TNF alpha 4 ng/ml                    | 35.1  |
| Prostate                         | 21.3 | 93105_Dermal Fibroblasts CCD1070_IL-1 beta 1 ng/ml                    | 15.0  |
| Prostate ca.* (bone met)PC-3     | 17.7 | 93772_dermal fibroblast_IFN gamma                                     | 21.8  |
| Testis                           | 11.7 | 93771_dermal fibroblast_IL-4                                          | 21.2  |
| Melanoma Hs688(A).T              | 9.0  | 93259_IBD Colitis 1**                                                 | 8.8   |
| Melanoma* (met) Hs688(B).T       | 12.9 | 93260_IBD Colitis 2                                                   | 3.5   |
| Melanoma UACC-62                 | 12.4 | 93261_IBD Crohns                                                      | 1.3   |
| Melanoma M14                     | 9.5  | 735010_Colon_normal                                                   | 20.3  |
| Melanoma LOX IMVI                | 8.1  | 735019_Lung_none                                                      | 40.3  |
| Melanoma* (met) SK-MEL-5         | 8.8  | 64028-1_Thymus_none                                                   | 33.5  |
| Melanoma SK-MEL-28               | 8.0  | 64030-1_Kidney_none                                                   | 21.0  |

Taqman results in Table 14 show high expression of clone FCTR5 in bladder, liver and adrenal gland suggesting a possible role in the treatment of diseases involving these tissues.

**Table 15: Primer Design for Probe Ag1541 (FCTR6)**

| Primer  | Sequences                                   | TM   | Lengt | Start Pos. | EQ ID NO. |
|---------|---------------------------------------------|------|-------|------------|-----------|
| Forward | 5'-AGAAGAACACCCCAGGGATATA-3'                | 58.8 | 22    | 1076       | 35        |
| Probe   | FAM-5'-CCTCGTTGGTGAACCTACAACCTCTGG-3'-TAMRA | 67.9 | 26    | 1100       | 36        |
| Reverse | 5'-CCTCTAGCTGGGTCACCTTCTC-3'                | 59.5 | 22    | 1129       | 37        |

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**TABLE 16: TAQMAN RESULTS FOR FCTR6 (PANEL 1D)**

| Tissue_Name                   | Panel 1D |       |
|-------------------------------|----------|-------|
|                               | Run 1    | Run 2 |
| Liver adenocarcinoma          | 0.0      | 0.0   |
| Heart (fetal)                 | 0.0      | 0.0   |
| Pancreas                      | 0.0      | 0.0   |
| Pancreatic ca.CAPAN 2         | 0.0      | 0.0   |
| Adrenal gland                 | 0.0      | 0.0   |
| Thyroid                       | 0.0      | 0.0   |
| Salivary gland                | 0.0      | 0.0   |
| Pituitary gland               | 0.0      | 0.0   |
| Brain (fetal)                 | 0.5      | 0.4   |
| Brain (whole)                 | 1.1      | 1.7   |
| Brain (amygdala)              | 0.0      | 1.8   |
| Brain (cerebellum)            | 0.6      | 1.9   |
| Brain (hippocampus)           | 3.3      | 3.4   |
| Brain (thalamus)              | 1.0      | 1.2   |
| Cerebral Cortex               | 1.6      | 2.6   |
| Spinal cord                   | 2.5      | 0.4   |
| CNS ca. (glio/astro)U87-MG    | 0.0      | 0.0   |
| CNS ca. (glio/astro)U-118-MG  | 0.0      | 0.0   |
| CNS ca. (astro)SW1783         | 0.0      | 0.0   |
| CNS ca.* (neuro; met )SK-N-AS | 0.0      | 0.0   |
| CNS ca. (astro)SF-539         | 0.0      | 0.0   |
| CNS ca. (astro) SNB-75        | 0.7      | 0.0   |
| CNS ca. (glio)SNB-19          | 0.0      | 0.0   |
| CNS ca. (glio)U251            | 0.0      | 0.0   |
| CNS ca. (glio)SF-295          | 0.0      | 0.8   |
| Heart                         | 0.0      | 0.0   |
| Skeletal muscle               | 0.0      | 0.0   |
| Bone marrow                   | 0.0      | 0.0   |
| Thymus                        | 0.0      | 0.0   |
| Spleen                        | 0.0      | 0.0   |
| Lymph node                    | 0.0      | 0.0   |
| Colorectal                    | 0.0      | 0.6   |
| Stomach                       | 1.9      | 0.0   |
| Small intestine               | 0.0      | 1.0   |
| Colon ca. SW480               | 0.0      | 0.0   |
| Colon ca.* (SW480 met)SW620   | 0.0      | 0.0   |
| Colon ca. HT29                | 0.0      | 0.0   |
| Colon ca. HCT-116             | 0.6      | 0.4   |

|                                     |       |       |
|-------------------------------------|-------|-------|
| Colon ca.CaCo-2                     | 1.5   | 0.0   |
| 83219 CC Well to Mod Diff (ODO3866) | 0.0   | 0.0   |
| Colon ca.HCC-2998                   | 0.0   | 0.0   |
| Gastric ca.* (liver met) NCI-N87    | 1.2   | 0.0   |
| Bladder                             | 0.0   | 0.0   |
| Trachea                             | 0.0   | 0.4   |
| Kidney                              | 0.8   | 1.2   |
| Kidney (fetal)                      | 0.5   | 0.7   |
| Renal ca.786-0                      | 0.0   | 0.0   |
| Renal ca.A498                       | 0.0   | 0.0   |
| Renal ca.RXF 393                    | 0.0   | 0.0   |
| Renal ca.ACHN                       | 0.0   | 0.0   |
| Renal ca. UO-31                     | 0.0   | 0.0   |
| Renal ca.TK-10                      | 0.0   | 0.0   |
| Liver                               | 0.0   | 0.0   |
| Liver (fetal)                       | 0.2   | 0.0   |
| Liver ca. (hepatoblast) HepG2       | 0.0   | 0.0   |
| Lung                                | 0.0   | 0.0   |
| Lung (fetal)                        | 0.0   | 0.0   |
| Lung ca. (small cell) LX-1          | 1.7   | 2.3   |
| Lung ca. (small cell)NCI-H69        | 0.0   | 0.0   |
| Lung ca. (s.cell var.) SHP-77       | 1.3   | 2.5   |
| Lung ca. (large cell)NCI-H460       | 0.0   | 0.0   |
| Lung ca. (non-sm. cell) A549        | 0.0   | 0.0   |
| Lung ca. (non-s.cell) NCI-H23       | 1.2   | 0.4   |
| Lung ca (non-s.cell) HOP-62         | 0.0   | 0.0   |
| Lung ca. (non-s.cl) NCI-H522        | 0.0   | 0.0   |
| Lung ca. (squam.) SW 900            | 0.0   | 0.7   |
| Lung ca. (squam.) NCI-H596          | 0.0   | 1.3   |
| Mammary gland                       | 0.0   | 1.5   |
| Breast ca.* (pl. effusion) MCF-7    | 0.0   | 0.0   |
| Breast ca.* (pl.ef) MDA-MB-231      | 5.8   | 0.5   |
| Breast ca.* (pl. effusion) T47D     | 1.2   | 0.3   |
| Breast ca. BT-549                   | 0.5   | 0.0   |
| Breast ca. MDA-N                    | 0.0   | 0.0   |
| Ovary                               | 0.0   | 0.0   |
| Ovarian ca. OVCAR-3                 | 0.0   | 0.0   |
| Ovarian ca.OVCAR-4                  | 0.0   | 0.0   |
| Ovarian ca.OVCAR-5                  | 3.6   | 0.7   |
| Ovarian ca.OVCAR-8                  | 0.0   | 0.0   |
| Ovarian ca.IGROV-1                  | 0.0   | 0.0   |
| Ovarian ca.* (ascites) SK-OV-3      | 0.0   | 0.0   |
| Uterus                              | 0.0   | 0.0   |
| Placenta                            | 0.0   | 0.0   |
| Prostate                            | 0.0   | 0.7   |
| Prostate ca.* (bone met)PC-3        | 0.0   | 0.0   |
| Testis                              | 100.0 | 100.0 |
| Melanoma Hs688(A).T                 | 0.0   | 0.0   |
| Melanoma* (met) Hs688(B).T          | 0.0   | 0.0   |
| Melanoma UACC-62                    | 0.0   | 0.0   |
| Melanoma M14                        | 0.0   | 0.0   |
| Melanoma LOX IMVI                   | 0.0   | 0.0   |
| Melanoma* (met)SK-MEL-5             | 0.0   | 0.0   |
| Adipose                             | 0.5   | 0.0   |

Table 17: Taqman Results for FCTR6 (Panel 2D)

| Tissue_Name                                 | Panel 2D |       |
|---------------------------------------------|----------|-------|
|                                             | Run 1    | Run 2 |
| Normal Colon GENPAK 061003                  | 5.4      | 2.4   |
| 83219 CC Well to Mod Diff (ODO3866)         | 7.3      | 0.0   |
| 83220 CC NAT (ODO3866)                      | 5.8      | 1.5   |
| 83221 CC Gr.2 rectosigmoid (ODO3868)        | 3.4      | 0.0   |
| 83222 CC NAT (ODO3868)                      | 0.0      | 0.0   |
| 83235 CC Mod Diff (ODO3920)                 | 11.0     | 1.4   |
| 83236 CC NAT (ODO3920)                      | 0.0      | 0.0   |
| 83237 CC Gr.2 ascend colon (ODO3921)        | 6.2      | 2.5   |
| 83238 CC NAT (ODO3921)                      | 10.2     | 0.0   |
| 83241 CC from Partial Hepatectomy (ODO4309) | 3.6      | 0.0   |
| 83242 Liver NAT (ODO4309)                   | 0.0      | 2.4   |
| 87472 Colon mets to lung (OD04451-01)       | 7.2      | 4.4   |
| 87473 Lung NAT (OD04451-02)                 | 0.0      | 0.0   |
| Normal Prostate Clontech A+ 6546-1          | 4.8      | 2.9   |
| 84140 Prostate Cancer (OD04410)             | 3.5      | 0.0   |
| 84141 Prostate NAT (OD04410)                | 3.4      | 0.0   |
| 87073 Prostate Cancer (OD04720-01)          | 9.0      | 8.5   |
| 87074 Prostate NAT (OD04720-02)             | 0.0      | 0.0   |
| Normal Lung GENPAK 061010                   | 17.7     | 6.5   |
| 83239 Lung Met to Muscle (ODO4286)          | 0.0      | 2.3   |
| 83240 Muscle NAT (ODO4286)                  | 0.0      | 0.0   |
| 84136 Lung Malignant Cancer (OD03126)       | 6.5      | 5.7   |
| 84137 Lung NAT (OD03126)                    | 0.0      | 0.0   |
| 84871 Lung Cancer (OD04404)                 | 0.0      | 0.0   |
| 84872 Lung NAT (OD04404)                    | 0.0      | 0.0   |
| 84875 Lung Cancer (OD04565)                 | 0.0      | 0.0   |
| 85950 Lung Cancer (OD04237-01)              | 0.0      | 0.0   |
| 85970 Lung NAT (OD04237-02)                 | 0.0      | 0.0   |
| 83255 Ocular Mel Met to Liver (ODO4310)     | 4.3      | 0.0   |
| 83256 Liver NAT (ODO4310)                   | 0.0      | 0.0   |
| 84139 Melanoma Mets to Lung (OD04321)       | 0.0      | 0.0   |
| 84138 Lung NAT (OD04321)                    | 0.0      | 0.0   |
| Normal Kidney GENPAK 061008                 | 28.1     | 39.2  |
| 83786 Kidney Ca, Nuclear grade 2 (OD04338)  | 0.0      | 3.0   |
| 83787 Kidney NAT (OD04338)                  | 22.7     | 31.6  |
| 83788 Kidney Ca Nuclear grade 1/2 (OD04339) | 0.0      | 3.1   |
| 83789 Kidney NAT (OD04339)                  | 97.3     | 100.0 |
| 83790 Kidney Ca, Clear cell type (OD04340)  | 0.0      | 0.0   |
| 83791 Kidney NAT (OD04340)                  | 100.0    | 34.4  |
| 83792 Kidney Ca, Nuclear grade 3 (OD04348)  | 2.0      | 4.9   |
| 83793 Kidney NAT (OD04348)                  | 30.2     | 19.9  |
| 87474 Kidney Cancer (OD04622-01)            | 0.0      | 2.4   |
| 87475 Kidney NAT (OD04622-03)               | 8.4      | 7.2   |
| 85973 Kidney Cancer (OD04450-01)            | 0.0      | 0.0   |
| 85974 Kidney NAT (OD04450-03)               | 47.3     | 12.9  |
| Kidney Cancer Clontech 8120607              | 0.0      | 0.0   |
| Kidney NAT Clontech 8120608                 | 0.0      | 0.0   |
| Kidney Cancer Clontech 8120613              | 0.0      | 0.0   |
| Kidney NAT Clontech 8120614                 | 20.6     | 22.9  |
| Kidney Cancer Clontech 9010320              | 0.0      | 0.0   |
| Kidney NAT Clontech 9010321                 | 3.4      | 26.4  |
| Normal Uterus GENPAK 061018                 | 0.0      | 0.0   |
| Uterus Cancer GENPAK 064011                 | 14.9     | 0.0   |
| Normal Thyroid Clontech A+ 6570-1           | 0.0      | 0.0   |
| Thyroid Cancer GENPAK 064010                | 0.0      | 0.0   |
| Thyroid Cancer INVITROGEN A302152           | 0.0      | 0.0   |

|                                                         |      |      |
|---------------------------------------------------------|------|------|
| Thyroid NAT INVITROGEN A302153                          | 0.0  | 0.0  |
| Normal Breast GENPAK 061019                             | 5.2  | 3.5  |
| 84877 Breast Cancer (OD04566)                           | 0.0  | 0.0  |
| 85975 Breast Cancer (OD04590-01)                        | 0.0  | 0.0  |
| 85976 Breast Cancer Mets (OD04590-03)                   | 0.0  | 0.0  |
| 87070 Breast Cancer Metastasis (OD04655-05)             | 0.0  | 0.0  |
| GENPAK Breast Cancer 064006                             | 0.0  | 2.5  |
| Breast Cancer Clontech 9100266                          | 6.2  | 0.0  |
| Breast NAT Clontech 9100265                             | 0.0  | 0.0  |
| Breast Cancer INVITROGEN A209073                        | 1.5  | 2.5  |
| Breast NAT INVITROGEN A2090734                          | 24.3 | 26.2 |
| Normal Liver GENPAK 061009                              | 10.5 | 2.7  |
| Liver Cancer GENPAK 064003                              | 5.9  | 1.7  |
| Liver Cancer Research Genetics RNA 1025                 | 21.6 | 11.0 |
| Liver Cancer Research Genetics RNA 1026                 | 0.0  | 0.0  |
| Paired Liver Cancer Tissue Research Genetics RNA 6004-T | 3.3  | 13.5 |
| Paired Liver Tissue Research Genetics RNA 6004-N        | 3.2  | 1.4  |
| Paired Liver Cancer Tissue Research Genetics RNA 6005-T | 0.0  | 0.0  |
| Paired Liver Tissue Research Genetics RNA 6005-N        | 0.0  | 0.0  |
| Normal Bladder GENPAK 061001                            | 0.0  | 0.0  |
| Bladder Cancer Research Genetics RNA 1023               | 0.0  | 0.0  |
| Bladder Cancer INVITROGEN A302173                       | 4.6  | 2.3  |
| 87071 Bladder Cancer (OD04718-01)                       | 17.9 | 11.4 |
| 87072 Bladder Normal Adjacent (OD04718-03)              | 0.0  | 0.0  |
| Normal Ovary Res. Gen.                                  | 0.0  | 0.0  |
| Ovarian Cancer GENPAK 064008                            | 1.7  | 4.8  |
| 87492 Ovary Cancer (OD04768-07)                         | 0.0  | 2.1  |
| 87493 Ovary NAT (OD04768-08)                            | 0.0  | 0.0  |
| Normal Stomach GENPAK 061017                            | 3.3  | 2.9  |
| NAT Stomach Clontech 9060359                            | 0.0  | 0.0  |
| Gastric Cancer Clontech 9060395                         | 0.0  | 0.0  |
| NAT Stomach Clontech 9060394                            | 0.0  | 0.0  |
| Gastric Cancer Clontech 9060397                         | 0.0  | 0.0  |
| NAT Stomach Clontech 9060396                            | 0.0  | 0.0  |
| Gastric Cancer GENPAK 064005                            | 6.3  | 3.8  |

Table 18: Taqman Results for clone 27455183.0.19 (Panel 4D)

| Tissue_Name                                              | Panel 4D |       |
|----------------------------------------------------------|----------|-------|
|                                                          | Run 1    | Run 2 |
| 93768_Secondary Th1_anti-CD28/anti-CD3                   | 0.0      | 0.0   |
| 93769_Secondary Th2_anti-CD28/anti-CD3                   | 0.0      | 0.0   |
| 93770_Secondary Tr1_anti-CD28/anti-CD3                   | 13.5     | 17.1  |
| 93573_Secondary Th1_resting day 4-6 in IL-2              | 0.0      | 0.0   |
| 93572_Secondary Th2_resting day 4-6 in IL-2              | 0.0      | 0.0   |
| 93571_Secondary Tr1_resting day 4-6 in IL-2              | 0.0      | 0.0   |
| 93568_primary Th1_anti-CD28/anti-CD3                     | 0.0      | 0.0   |
| 93569_primary Th2_anti-CD28/anti-CD3                     | 0.0      | 0.0   |
| 93570_primary Tr1_anti-CD28/anti-CD3                     | 0.0      | 0.0   |
| 93565_primary Th1_resting dy 4-6 in IL-2                 | 0.0      | 0.0   |
| 93566_primary Th2_resting dy 4-6 in IL-2                 | 0.0      | 0.0   |
| 93567_primary Tr1_resting dy 4-6 in IL-2                 | 0.0      | 0.0   |
| 93351_CD45RA CD4 lymphocyte_anti-CD28/anti-CD3           | 0.0      | 0.0   |
| 93352_CD45RO CD4 lymphocyte_anti-CD28/anti-CD3           | 0.0      | 0.0   |
| 93251_CD8 Lymphocytes_anti-CD28/anti-CD3                 | 0.0      | 0.0   |
| 93353_chronic CD8 Lymphocytes 2ry_resting dy 4-6 in IL-2 | 0.0      | 0.0   |

|                                                                              |       |      |
|------------------------------------------------------------------------------|-------|------|
| 93574_chronic CD8 Lymphocytes 2ry_activated CD3/CD28                         | 0.0   | 0.0  |
| 93354_CD4_none                                                               | 5.8   | 0.0  |
| 93252_Secondary Th1/Th2/Tr1_anti-CD95 CH11                                   | 0.0   | 0.0  |
| 93103_LAK cells_resting                                                      | 0.0   | 0.0  |
| 93788_LAK cells_IL-2                                                         | 0.0   | 0.0  |
| 93787_LAK cells_IL-2+IL-12                                                   | 0.0   | 0.0  |
| 93789_LAK cells_IL-2+IFN gamma                                               | 0.0   | 0.0  |
| 93790_LAK cells_IL-2+ IL-18                                                  | 0.0   | 0.0  |
| 93104_LAK cells_PMA/ionomycin and IL-18                                      | 0.0   | 0.0  |
| 93578_NK Cells IL-2_resting                                                  | 0.0   | 0.0  |
| 93109_Mixed Lymphocyte Reaction_Two Way MLR                                  | 0.0   | 0.0  |
| 93110_Mixed Lymphocyte Reaction_Two Way MLR                                  | 0.0   | 0.0  |
| 93111_Mixed Lymphocyte Reaction_Two Way MLR                                  | 0.0   | 0.0  |
| 93112_Mononuclear Cells (PBMCs)_resting                                      | 0.0   | 0.0  |
| 93113_Mononuclear Cells (PBMCs)_PWM                                          | 0.0   | 0.0  |
| 93114_Mononuclear Cells (PBMCs)_PHA-L                                        | 0.0   | 0.0  |
| 93249_Ramos (B cell)_none                                                    | 0.0   | 38.2 |
| 93250_Ramos (B cell)_ionomycin                                               | 0.0   | 0.0  |
| 93349_B lymphocytes_PWM                                                      | 0.0   | 68.8 |
| 93350_B lymphocytes_CD40L and IL-4                                           | 31.0  | 0.0  |
| 92665_EOL-1 (Eosinophil)_dbcAMP differentiated                               | 0.0   | 0.0  |
| 93248_EOL-1 (Eosinophil)_dbcAMP/PMAionomycin                                 | 0.0   | 0.0  |
| 93356_Dendritic Cells_none                                                   | 0.0   | 0.0  |
| 93355_Dendritic Cells_LPS 100 ng/ml                                          | 0.0   | 0.0  |
| 93775_Dendritic Cells_anti-CD40                                              | 32.5  | 0.0  |
| 93774_Monocytes_resting                                                      | 0.0   | 0.0  |
| 93776_Monocytes_LPS 50 ng/ml                                                 | 0.0   | 0.0  |
| 93581_Macrophages_resting                                                    | 0.0   | 0.0  |
| 93582_Macrophages_LPS 100 ng/ml                                              | 0.0   | 0.0  |
| 93098_HUVEC (Endothelial)_none                                               | 0.0   | 0.0  |
| 93099_HUVEC (Endothelial)_starved                                            | 11.3  | 0.0  |
| 93100_HUVEC (Endothelial)_IL-1b                                              | 0.0   | 14.6 |
| 93779_HUVEC (Endothelial)_IFN gamma                                          | 0.0   | 0.0  |
| 93102_HUVEC (Endothelial)_TNF alpha + IFN gamma                              | 0.0   | 0.0  |
| 93101_HUVEC (Endothelial)_TNF alpha + IL4                                    | 0.0   | 0.0  |
| 93781_HUVEC (Endothelial)_IL-11                                              | 0.0   | 0.0  |
| 93583_Lung Microvascular Endothelial Cells_none                              | 0.0   | 0.0  |
| 93584_Lung Microvascular Endothelial Cells_TNFa (4 ng/ml) and IL1b (1 ng/ml) | 0.0   | 0.0  |
| 92662_Microvascular Dermal endothelium_none                                  | 0.0   | 0.0  |
| 92663_Microvascular Dermal endothelium_TNFa (4 ng/ml) and IL1b (1 ng/ml)     | 0.0   | 0.0  |
| 93773_Bronchial epithelium_TNFa (4 ng/ml) and IL1b (1 ng/ml) **              | 0.0   | 0.0  |
| 93347_Small Airway Epithelium_none                                           | 0.0   | 0.0  |
| 93348_Small Airway Epithelium_TNFa (4 ng/ml) and IL1b (1 ng/ml)              | 0.0   | 0.0  |
| 92668_Coronary Artery SMC_resting                                            | 0.0   | 0.0  |
| 92669_Coronary Artery SMC_TNFa (4 ng/ml) and IL1b (1 ng/ml)                  | 0.0   | 0.0  |
| 93107_astrocytes_resting                                                     | 0.0   | 0.0  |
| 93108_astrocytes_TNFa (4 ng/ml) and IL1b (1 ng/ml)                           | 0.0   | 0.0  |
| 92666_KU-812 (Basophil)_resting                                              | 0.0   | 40.3 |
| 92667_KU-812 (Basophil)_PMA/ionoycin                                         | 0.0   | 0.0  |
| 93579_CCD1106 (Keratinocytes)_none                                           | 0.0   | 0.0  |
| 93580_CCD1106 (Keratinocytes)_TNFa and IFNg **                               | 0.0   | 0.0  |
| 93791_Liver Cirrhosis                                                        | 100.0 | 99.3 |
| 93792_Lupus Kidney                                                           | 0.0   | 0.0  |
| 93577_NCI-H292                                                               | 0.0   | 0.0  |
| 93358_NCI-H292_IL-4                                                          | 0.0   | 0.0  |
| 93360_NCI-H292_IL-9                                                          | 10.6  | 0.0  |
| 93359_NCI-H292_IL-13                                                         | 0.0   | 65.5 |

|                                                                       |      |       |
|-----------------------------------------------------------------------|------|-------|
| 93357_NCI-H292_IFN gamma                                              | 0.0  | 24.8  |
| 93777_HPAEC_-                                                         | 0.0  | 0.0   |
| 93778_HPAEC_IL-1 beta/TNA alpha                                       | 0.0  | 0.0   |
| 93254_Normal Human Lung Fibroblast_none                               | 0.0  | 0.0   |
| 93253_Normal Human Lung Fibroblast_TNFa (4 ng/ml) and IL-1b (1 ng/ml) | 0.0  | 0.0   |
| 93257_Normal Human Lung Fibroblast_IL-4                               | 0.0  | 0.0   |
| 93256_Normal Human Lung Fibroblast_IL-9                               | 0.0  | 0.0   |
| 93255_Normal Human Lung Fibroblast_IL-13                              | 0.0  | 0.0   |
| 93258_Normal Human Lung Fibroblast_IFN gamma                          | 0.0  | 0.0   |
| 93106_Dermal Fibroblasts CCD1070_resting                              | 0.0  | 0.0   |
| 93361_Dermal Fibroblasts CCD1070_TNF alpha 4 ng/ml                    | 0.0  | 43.8  |
| 93105_Dermal Fibroblasts CCD1070_IL-1 beta 1 ng/ml                    | 0.0  | 0.0   |
| 93772_dermal fibroblast_IFN gamma                                     | 42.0 | 27.7  |
| 93771_dermal fibroblast_IL-4                                          | 10.7 | 90.1  |
| 93259_IBD Colitis 1**                                                 | 0.0  | 0.0   |
| 93260_IBD Colitis 2                                                   | 13.8 | 0.0   |
| 93261_IBD Crohns                                                      | 0.0  | 46.7  |
| 735010_Colon_normal                                                   | 15.6 | 0.0   |
| 735019_Lung_none                                                      | 12.9 | 16.8  |
| 64028-1_Thymus_none                                                   | 69.3 | 100.0 |
| 64030-1_Kidney_none                                                   | 0.0  | 0.0   |

Taqman results in Table 18 demonstrate that clone FCTR6 is differentially expressed in clear cell Renal cell carcinoma tissues versus the normal adjacent kidney tissues and thus could have a potential role in the treatment of renal cell carcinoma.

### EQUIVALENTS

Although particular embodiments have been disclosed herein in detail, this has been done by way of example for purposes of illustration only, and is not intended to be limiting with respect to the scope of the appended claims which follow. In particular, it is contemplated by the inventors that various substitutions, alterations, and modifications may be made to the invention without departing from the spirit and scope of the invention as defined by the claims. The choice of nucleic acid starting material, clone of interest, or library type is believed to be a matter of routine for a person of ordinary skill in the art with knowledge of the embodiments described herein. Other aspects, advantages, and modifications considered to be within the scope of the following claims.

**WHAT IS CLAIMED IS:**

1. An isolated polypeptide comprising an amino acid sequence selected from the group consisting of:
  - (a) a mature form of an amino acid sequence selected from the group consisting of SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25;
  - (b) a variant of a mature form of an amino acid sequence selected from the group consisting of SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25, wherein one or more amino acid residues in said variant differs from the amino acid sequence of said mature form, provided that said variant differs in no more than 15% of the amino acid residues from the amino acid sequence of said mature form;
  - (c) an amino acid sequence selected from the group consisting of SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25; and
  - (d) a variant of an amino acid sequence selected from the group consisting of SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25, wherein one or more amino acid residues in said variant differs from the amino acid sequence of said mature form, provided that said variant differs in no more than 15% of amino acid residues from said amino acid sequence.
2. The polypeptide of claim 1, wherein said polypeptide comprises the amino acid sequence of a naturally-occurring allelic variant of an amino acid sequence selected from the group consisting of SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25.
3. The polypeptide of claim 2, wherein said allelic variant comprises an amino acid sequence that is the translation of a nucleic acid sequence differing by a single nucleotide from a nucleic acid sequence selected from the group consisting of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24.
4. The polypeptide of claim 1, wherein the amino acid sequence of said variant comprises a conservative amino acid substitution.

5. An isolated nucleic acid molecule comprising a nucleic acid sequence encoding a polypeptide comprising an amino acid sequence selected from the group consisting of:

- (a) a mature form of an amino acid sequence selected from the group consisting of SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25;
- (b) a variant of a mature form of an amino acid sequence selected from the group consisting of SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25, wherein one or more amino acid residues in said variant differs from the amino acid sequence of said mature form, provided that said variant differs in no more than 15% of the amino acid residues from the amino acid sequence of said mature form;
- (c) an amino acid sequence selected from the group consisting of SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25;
- (d) a variant of an amino acid sequence selected from the group consisting of SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25, wherein one or more amino acid residues in said variant differs from the amino acid sequence of said mature form, provided that said variant differs in no more than 15% of amino acid residues from said amino acid sequence;
- (e) a nucleic acid fragment encoding at least a portion of a polypeptide comprising an amino acid sequence chosen from the group consisting of SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25, or a variant of said polypeptide, wherein one or more amino acid residues in said variant differs from the amino acid sequence of said mature form, provided that said variant differs in no more than 15% of amino acid residues from said amino acid sequence; and
- (f) a nucleic acid molecule comprising the complement of (a), (b), (c), (d) or (e).

6. The nucleic acid molecule of claim 5, wherein the nucleic acid molecule comprises the nucleotide sequence of a naturally-occurring allelic nucleic acid variant.

7. The nucleic acid molecule of claim 5, wherein the nucleic acid molecule encodes a polypeptide comprising the amino acid sequence of a naturally-occurring polypeptide variant.

8. The nucleic acid molecule of claim 5, wherein the nucleic acid molecule differs by a single nucleotide from a nucleic acid sequence selected from the group consisting of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24.

9. The nucleic acid molecule of claim 5, wherein said nucleic acid molecule comprises a nucleotide sequence selected from the group consisting of:
- (a) a nucleotide sequence selected from the group consisting of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24;
  - (b) a nucleotide sequence differing by one or more nucleotides from a nucleotide sequence selected from the group consisting of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, provided that no more than 20% of the nucleotides differ from said nucleotide sequence;
  - (c) a nucleic acid fragment of (a); and
  - (d) a nucleic acid fragment of (b).
10. The nucleic acid molecule of claim 5, wherein said nucleic acid molecule hybridizes under stringent conditions to a nucleotide sequence chosen from the group consisting of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, or a complement of said nucleotide sequence.
11. The nucleic acid molecule of claim 5, wherein the nucleic acid molecule comprises a nucleotide sequence selected from the group consisting of:
- (a) a first nucleotide sequence comprising a coding sequence differing by one or more nucleotide sequences from a coding sequence encoding said amino acid sequence, provided that no more than 20% of the nucleotides in the coding sequence in said first nucleotide sequence differ from said coding sequence;
  - (b) an isolated second polynucleotide that is a complement of the first polynucleotide; and
  - (c) a nucleic acid fragment of (a) or (b).
12. A vector comprising the nucleic acid molecule of claim 11.
13. The vector of claim 12, further comprising a promoter operably-linked to said nucleic acid molecule.
14. A cell comprising the vector of claim 12.
15. An antibody that binds immunospecifically to the polypeptide of claim 1.

16. The antibody of claim 15, wherein said antibody is a monoclonal antibody.
17. The antibody of claim 15, wherein the antibody is a humanized antibody.
18. A method for determining the presence or amount of the polypeptide of claim 1 in a sample, the method comprising:
  - (a) providing the sample;
  - (b) contacting the sample with an antibody that binds immunospecifically to the polypeptide; and
  - (c) determining the presence or amount of antibody bound to said polypeptide, thereby determining the presence or amount of polypeptide in said sample.
19. A method for determining the presence or amount of the nucleic acid molecule of claim 5 in a sample, the method comprising:
  - (a) providing the sample;
  - (b) contacting the sample with a probe that binds to said nucleic acid molecule; and
  - (c) determining the presence or amount of the probe bound to said nucleic acid molecule, thereby determining the presence or amount of the nucleic acid molecule in said sample.
20. The method of claim 19 wherein presence or amount of the nucleic acid molecule is used as a marker for cell or tissue type.
21. The method of claim 20 wherein the cell or tissue type is cancerous.
22. A method of identifying an agent that binds to a polypeptide of claim 1, the method comprising:
  - (a) contacting said polypeptide with said agent; and
  - (b) determining whether said agent binds to said polypeptide.
23. The method of claim 22 wherein the agent is a cellular receptor or a downstream effector.

24. A method for identifying an agent that modulates the expression or activity of the polypeptide of claim 1, the method comprising:

- (a) providing a cell expressing said polypeptide;
- (b) contacting the cell with said agent, and
- (c) determining whether the agent modulates expression or activity of said polypeptide,

whereby an alteration in expression or activity of said peptide indicates said agent modulates expression or activity of said polypeptide.

25. A method for modulating the activity of the polypeptide of claim 1, the method comprising contacting a cell sample expressing the polypeptide of said claim with a compound that binds to said polypeptide in an amount sufficient to modulate the activity of the polypeptide.

26. A method of treating or preventing a FCTR<sub>X</sub>-associated disorder, said method comprising administering to a subject in which such treatment or prevention is desired the polypeptide of claim 1 in an amount sufficient to treat or prevent said FCTR<sub>X</sub>-associated disorder in said subject.

27. The method of claim 26 wherein the disorder is a neurodegenerative disorder.

28. The method of claim 26 wherein the disorder is related to cell signal processing and metabolic pathway modulation.

29. The method of claim 26, wherein said subject is a human.

30. A method of treating or preventing a FCTR<sub>X</sub>-associated disorder, said method comprising administering to a subject in which such treatment or prevention is desired the nucleic acid of claim 5 in an amount sufficient to treat or prevent said FCTR<sub>X</sub>-associated disorder in said subject.

31. The method of claim 30 wherein the disorder is a neurodegenerative disorder.

32. The method of claim 30 wherein the disorder is related to cell signal processing and metabolic pathway modulation.

33. The method of claim 30, wherein said subject is a human.

34. A method of treating or preventing a FCTR<sub>X</sub>-associated disorder, said method comprising administering to a subject in which such treatment or prevention is desired the antibody of claim 15 in an amount sufficient to treat or prevent said FCTR<sub>X</sub>-associated disorder in said subject

35. The method of claim 34 wherein the disorder is selected from the group consisting of Also within the scope of the invention is the use of a Therapeutic in the manufacture of a medicament for treating or preventing disorders or syndromes including, *e.g.*, Colorectal cancer, adenomatous polyposis coli, myelogenous leukemia, congenital neonatal alloimmune thrombocytopenia, multiple human solid malignancies, malignant ovarian tumours particularly at the interface between epithelia and stroma, malignant brain tumors, mammary tumors, human gliomas, astrocytomas, mixed glioma/astrocytomas, renal cells carcinoma, breast adenocarcinoma, ovarian cancer, melanomas, renal cell carcinoma, clear cell and granular cell carcinomas, autocrine/paracrine stimulation of tumor cell proliferation, autocrine/paracrine stimulation of tumor cell survival and tumor cell resistance to cytotoxic therapy, paranechmal and basement membrane invasion and motility of tumor cells thereby contributing to metastasis, tumor-mediated immunosuppression of T-cell mediated immune effector cells and pathways resulting in tumor escape from immune surveillance, neurological disorders, neurodegenerative disorders, nerve trauma, familial myelodysplastic syndrome, Charcot-Marie-Tooth neuropathy, demyelinating Gardner syndrome, familial myelodysplastic syndrome; mental health conditions, immunological disorders, allergy and infection, asthma, bronchial asthma, Avellino type eosinophilia, lung diseases, reproductive disorders, male infertility, female reproductive system disorders, male and female reproductive diseases, hemangioma, deafness, glycoprotein Ia deficiency, desmoid disease, turcot syndrome, liver cirrhosis, hepatitis C, gastric disorders, pancreatic diseases like diabetes, Schistosoma mansoni infection, Spinocerebellar ataxia, Plasmodium falciparum parasitemia, Corneal dystrophy - Groenouw type I, Corneal dystrophy - lattice type I, and Reis-Bucklers corneal dystrophy.

36. The method of claim 34 wherein the disorder is related to cell signal processing and metabolic pathway modulation.

37. The method of claim 34, wherein the subject is a human.

38. A pharmaceutical composition comprising the polypeptide of claim 1 and a pharmaceutically-acceptable carrier.

39. A pharmaceutical composition comprising the nucleic acid molecule of claim 5 and a pharmaceutically-acceptable carrier.

40. A pharmaceutical composition comprising the antibody of claim 15 and a pharmaceutically-acceptable carrier.

41. A kit comprising in one or more containers, the pharmaceutical composition of claim 38.

42. A kit comprising in one or more containers, the pharmaceutical composition of claim 39.

43. A kit comprising in one or more containers, the pharmaceutical composition of claim 40.

44. A method for determining the presence of or predisposition to a disease associated with altered levels of the polypeptide of claim 1 in a first mammalian subject, the method comprising:

- (a) measuring the level of expression of the polypeptide in a sample from the first mammalian subject; and
- (b) comparing the amount of said polypeptide in the sample of step (a) to the amount of the polypeptide present in a control sample from a second mammalian subject known not to have, or not to be predisposed to, said disease;

wherein an alteration in the expression level of the polypeptide in the first subject as compared to the control sample indicates the presence of or predisposition to said disease.

45. The method of claim 44 wherein the predisposition is to cancers.

46. A method for determining the presence of or predisposition to a disease associated with altered levels of the nucleic acid molecule of claim 5 in a first mammalian subject, the method comprising:

- (a) measuring the amount of the nucleic acid in a sample from the first mammalian subject; and
- (b) comparing the amount of said nucleic acid in the sample of step (a) to the amount of the nucleic acid present in a control sample from a second mammalian subject known not to have or not be predisposed to, the disease;

wherein an alteration in the level of the nucleic acid in the first subject as compared to the control sample indicates the presence of or predisposition to the disease.

47. The method of claim 46 wherein the predisposition is to cancers.

48. A method of treating a pathological state in a mammal, the method comprising administering to the mammal a polypeptide in an amount that is sufficient to alleviate the pathological state, wherein the polypeptide is a polypeptide having an amino acid sequence at least 95% identical to a polypeptide comprising an amino acid sequence of at least one of SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25, or a biologically active fragment thereof.

49. A method of treating a pathological state in a mammal, the method comprising administering to the mammal the antibody of claim 15 in an amount sufficient to alleviate the pathological state.