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**WO 02/081749 A2**

(54) Title: METHYLATION ALTERED DNA SEQUENCES AS MARKERS ASSOCIATED WITH HUMAN CANCER

(57) Abstract: There is disclosed (103) novel methylation-altered DNA sequences ("marker sequences") that have distinct methylation patterns in cancer, compared to normal tissue. In many instances, these marker sequences represent novel sequences not found in the GenBank data base, and none of these marker sequences have previously been characterized with respect to their methylation pattern in human cancers including, but not limited to those of bladder and prostate. These (103) sequences have utility as diagnosis, prognostic and therapeutic markers in the treatment of human cancer, and as reagents in kits for detecting methylated CpG-containing nucleic acids.

## METHYLATION ALTERED DNA SEQUENCES AS MARKERS ASSOCIATED WITH HUMAN CANCER

### 5 **Cross-Reference to Related Applications**

This application claims priority to U.S. Patent Application Serial No. 09/699,243, filed October 27, 2000.

### **Technical Field of the Invention**

10 The present invention relates to novel human DNA sequences that exhibit altered methylation patterns (hypermethylation or hypomethylation) in cancer patients. These novel methylation-altered DNA sequences are useful as diagnostic, prognostic and therapeutic markers for human cancer.

### 15 **Background of the Invention**

The identification of early genetic changes in tumorigenesis is a primary focus in molecular cancer research. Characterization of the nature and pattern of cancer-associated genetic alterations will allow for early detection, diagnosis and treatment of cancer. Such genetic alterations in vertebrates fall generally into one of three categories: gain or loss of  
20 genetic material; mutation of genetic material; or methylation at cytosine residues in CpG dinucleotides within "CpG islands." Among these, DNA methylation is uniquely reversible, and changes in methylation state are known to affect gene expression (*e.g.*, transcriptional initiation of genes where CpG islands located at or near the promoter region) or genomic stability.

25 *Methylation of CpG dinucleotides within CpG islands.* DNA, in higher order eukaryotic organisms, is methylated only at cytosine residues located 5' to guanine residues in CpG dinucleotides. This covalent modification of the C-5 position of the cytosine base by the enzyme DNA (cytosine-5)-methyltransferase results in the formation of 5-methylcytosine (5-mCyt), and gives this base unique properties (*e.g.*, susceptibility to  
30 undergo spontaneous deamination). This enzymatic conversion is the only epigenetic modification of DNA known to exist in vertebrates, and is essential for normal embryonic development (Bird, A.P., *Cell* 70:5-8, 1992; Laird & Jaenisch, *Human Molecular Genetics* 3:1487-1495, 1994; Li et al., *Cell* 69:915-926, 1992).

The presence of 5-mCyt at CpG dinucleotides has resulted in the 5-fold depletion of  
35 this sequence in the genome during the course of vertebrate evolution (Schroeder & Gartler, *Proc. Nat. Acad. Sci. USA* 89:957-961, 1992), presumably due to spontaneous deamination of 5-mCyt to Thymidine. Certain areas of the genome, however, do not show such depletion,

and are referred to as “CpG islands” (Bird, A.P., *Nature* 321:209-213, 1986; Gardiner-Garden & Frommer, *J. Mol. Biol.* 196:261-282, 1987). These CpG islands comprise only approximately 1% of the vertebrate genome, yet account for about 15% of the total number of genomic CpG dinucleotides (Antequera & Bird, *Proc. Nat. Acad. Sci. USA* 90:11995-11999, 1993). CpG islands contain the expected (*i.e.*, the non-evolutionarily depleted) frequency of CpGs (with an Observed/Expected Ratio<sup>1</sup> >0.6), are GC-rich (with a GC Content<sup>2</sup> >0.5) and are typically between about 0.2 to about 1 kb in length.

*Methylation within CpG islands affects gene expression.* CpG islands are located upstream of many housekeeping and tissue-specific genes, but may also extend into gene coding regions (Cross & Bird, *Current Opinions in Genetics and Development* 5:309-314, 1995; Larsen et al., *Genomics* 13:1095-1107, 1992). The methylation of cytosines within CpG islands in somatic tissues is believed to affect gene expression. Methylation has been inversely correlated with gene activity and may lead to decreased gene expression by a variety of mechanisms including inhibition of transcription initiation (Bird, A.P., *Nature* 321:209-213, 1986; Delgado et al., *EMBO Journal* 17:2426-2435, 1998), disruption of local chromatin structure (Counts & Goodman, *Molecular Carcinogenesis* 11:185-188, 1994; Antequera et al., *Cell* 62:503-514, 1990), and recruitment of proteins that interact specifically with methylated sequences and thereby directly or indirectly prevent transcription factor binding (Bird, A.P., *Cell* 70:5-8, 1992; Counts & Goodman, *Molecular Carcinogenesis* 11:185-188, 1994; Cedar, H., *Cell* 53:3-4, 1988). Many studies have demonstrated the effect of methylation of CpG islands on gene expression (e.g., the *CDKN2A/p16* gene; Gonzalez-Zulueta et al., *Cancer Research* 55:4531-4535, 1995), but most CpG islands on autosomal genes remain unmethylated in the germline, and methylation of these islands is usually independent of gene expression. Tissue-specific genes are typically unmethylated in the respective target organs but are methylated in the germline and in non-expressing adult tissues, while CpG islands of constitutively expressed housekeeping genes are normally unmethylated in the germline and in somatic tissues.

*Methylation within CpG islands affects the expression of genes involved in cancer.* Data from a group of studies show the presence of altered methylation in cancer cells relative to non-cancerous cells. These studies show not only alteration of the overall genomic levels of DNA methylation, but also changes in the distribution of methyl groups. For example, abnormal methylation of CpG islands that are associated with tumor suppressor genes or oncogenes within a cell may cause altered gene expression. Such altered gene expression may provide a population of cells with a selective growth advantage and thereby result in selection of these cells to the detriment of the organism (*i.e.*, cancer).

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<sup>1</sup> Calculated as: [number of CpG sites / (number of C bases X number of G bases)] X band length for each fragment.

<sup>2</sup> Calculated as: (number of C bases + number of G bases) / band length for each fragment.

*Insufficient correlative data.* Unfortunately, the mere knowledge of the basic existence of altered methylation of CpG dinucleotides within CpG islands of cancer cells relative to normal cells, or of the fact that in particular instances such methylation changes result in altered gene expression (or chromatin structure or stability), is inadequate to allow for effective diagnostic, prognostic and therapeutic application of this knowledge. This is because only a limited number of CpG islands have been characterized, and thus there is insufficient knowledge, as to which particular CpG islands, among many, are actually involved in, or show significant correlation with cancer or the etiology thereof. Moreover, complex methylation patterns, involving a plurality of methylation-altered DNA sequences, including those that may have the sequence composition to qualify as CpG islands, may exist in particular cancers.

Therefore there is a need in the art to identify and characterize specific methylation altered DNA sequences, and to correlate them with cancer to allow for their diagnostic, prognostic and therapeutic application.

### **Summary of the Invention**

The present invention provides for a diagnostic or prognostic assay for cancer, comprising: obtaining a tissue sample from a test tissue; performing a methylation assay on DNA derived from the tissue sample, wherein the methylation assay determines the methylation state of a CpG dinucleotide within a DNA sequence of the DNA, and wherein the DNA sequence is a sequence selected from the group consisting of sequences of SEQ ID NOS:1-103, sequences having a nucleotide sequence at least 90% identical to sequences of SEQ ID NOS:1-103, CpG island sequences associated with sequences of SEQ ID NOS:1-103, CpG island sequences associated with sequences having a nucleotide sequence at least 90% identical to sequences of SEQ ID NOS:1-103, and combinations thereof, wherein the CpG island sequence associated with the sequence of the particular SEQ ID NO is that contiguous sequence of genomic DNA that encompasses at least one nucleotide of the particular SEQ ID NO sequence, and satisfies the criteria of having both a frequency of CpG dinucleotides corresponding to an Observed/Expected Ratio  $>0.6$ , and a GC Content  $>0.5$ ; and determining a diagnosis or prognosis based, at least in part, upon the methylation state of the CpG dinucleotide within the DNA sequence. Preferably, the DNA sequence is a sequence selected from the group consisting of CpG island sequences associated with sequences of SEQ ID NOS:1-103, CpG island sequences associated with sequences having a nucleotide sequence at least 90% identical to sequences of SEQ ID NOS:1-103, and combinations thereof. Preferably, the DNA sequence is a sequence selected from the group consisting of CpG island sequences associated with sequences of SEQ ID NOS: 2, 4, 6, 7, 9-16, 19, 20, 22-33, 35-43, 48, 51-55, 59, 60, 64, 71, 76, 78-81, 84 and 87-90, and combinations thereof. Preferably, the methylation assay procedure is selected from the group

consisting of MethyLight, MS-SnuPE (methylation-sensitive single nucleotide primer extension), MSP (methylation-specific PCR), MCA (methylated CpG island amplification), COBRA (combined bisulfite restriction analysis), and combinations thereof. Preferably, the methylation state of the CpG dinucleotide within the DNA sequence is that of

5 hypermethylation, hypomethylation or normal methylation. Preferably, the cancer is selected from the group consisting of bladder cancer, prostate cancer, colon cancer, lung cancer, renal cancer, leukemia, breast cancer, uterine cancer, astrocytoma, glioblastoma, and neuroblastoma. Preferably, the cancer is bladder cancer, or prostate cancer.

The present invention further provides a kit useful for the detection of a methylated  
10 CpG-containing nucleic acid comprising a carrier means containing one or more containers comprising: a container containing a probe or primer which hybridizes to any region of a sequence selected from the group consisting of SEQ ID NOS:1-103, and sequences having a nucleotide sequence at least 90% identical to sequences of SEQ ID NOS:1-103; and  
15 additional standard methylation assay reagents required to affect detection of methylated CpG-containing nucleic acid based on the probe or primer. Preferably, the additional standard methylation assay reagents are standard reagents for performing a methylation assay from the group consisting of MethyLight, MS-SNuPE, MSP, MCA, COBRA, and combinations thereof. Preferably, the probe or primer comprises at least about 12 to 15  
20 nucleotides of a sequence selected from the group consisting of SEQ ID NOS:1-103, and sequences having a nucleotide sequence at least 90% identical to sequences of SEQ ID NOS:1-103.

The present invention further provides an isolated nucleic acid molecule comprising a methylated or unmethylated polynucleotide sequence selected from the group consisting of  
25 SEQ ID NO:1, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:18, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:32, SEQ ID NO:34, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:42, SEQ ID NO:44, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:62, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:74, SEQ ID NO:76, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:86, SEQ ID NO:90, SEQ ID NO:92, SEQ ID NO:97,  
30 and SEQ ID NO:100. Preferably the nucleic acid is methylated. Preferably, the nucleic acid is unmethylated.

## Detailed Description of the Invention

### 35 Definitions:

“GC Content” refers, within a particular DNA sequence, to the [(number of C bases + number of G bases) / band length for each fragment].

“Observed/Expected Ratio” (“O/E Ratio”) refers to the frequency of CpG

dinucleotides within a particular DNA sequence, and corresponds to the [number of CpG sites / (number of C bases X number of G bases)] X band length for each fragment.

“**CpG Island**” refers to a contiguous region of genomic DNA that satisfies the criteria of (1) having a frequency of CpG dinucleotides corresponding to an  
5 “Observed/Expected Ratio” >0.6), and (2) having a “GC Content” >0.5. CpG islands are typically, but not always, between about 0.2 to about 1 kb in length. A CpG island sequence associated with a particular SEQ ID NO sequence of the present invention is that contiguous sequence of genomic DNA that encompasses at least one nucleotide of the particular SEQ ID NO sequence, and satisfies the criteria of having both a frequency of CpG dinucleotides  
10 corresponding to an Observed/Expected Ratio >0.6), and a GC Content >0.5.

“**Methylation state**” refers to the presence or absence of 5-methylcytosine (“5-mCyt”) at one or a plurality of CpG dinucleotides within a DNA sequence.

“**Hypermethylation**” refers to the methylation state corresponding to an *increased* presence of 5-mCyt at one or a plurality of CpG dinucleotides within a DNA sequence of a  
15 test DNA sample, relative to the amount of 5-mCyt found at corresponding CpG dinucleotides within a normal control DNA sample.

“**Hypomethylation**” refers to the methylation state corresponding to a *decreased* presence of 5-mCyt at one or a plurality of CpG dinucleotides within a DNA sequence of a  
20 test DNA sample, relative to the amount of 5-mCyt found at corresponding CpG dinucleotides within a normal control DNA sample.

“**Methylation assay**” refers to any assay for determining the methylation state of a CpG dinucleotide within a sequence of DNA.

“**MS.AP-PCR**” (Methylation-Sensitive Arbitrarily-Primed Polymerase Chain Reaction) refers to the art-recognized technology that allows for a global scan of the genome  
25 using CG-rich primers to focus on the regions most likely to contain CpG dinucleotides, and described by Gonzalgo et al., *Cancer Research* 57:594-599, 1997.

“**MethyLight**” refers to the art-recognized fluorescence-based real-time PCR technique described by Eads et al., *Cancer Res.* 59:2302-2306, 1999.

“**Ms-SNuPE**” (Methylation-sensitive Single Nucleotide Primer Extension) refers to  
30 the art-recognized assay described by Gonzalgo & Jones, *Nucleic Acids Res.* 25:2529-2531, 1997.

“**MSP**” (Methylation-specific PCR) refers to the art-recognized methylation assay described by Herman et al. *Proc. Natl. Acad. Sci. USA* 93:9821-9826, 1996, and by US Patent No. 5,786,146.

35 “**COBRA**” (Combined Bisulfite Restriction Analysis) refers to the art-recognized methylation assay described by Xiong & Laird, *Nucleic Acids Res.* 25:2532-2534, 1997.

“**MCA**” (Methylated CpG Island Amplification) refers to the methylation assay described by Toyota et al., *Cancer Res.* 59:2307-12, 1999, and in WO 00/26401A1.

## Overview

The present invention provides for 103 DNA sequences (*i.e.*, “marker sequences”) having distinct methylation patterns in cancer, as compared to normal tissue. These methylation-altered DNA sequence embodiments correspond to 103 DNA fragments isolated from bladder and prostate cancer patients, and in many instances, represent novel sequences not found in the GenBank database. *None* of the instant sequence embodiments have previously been characterized with respect to their methylation pattern in human cancers including, but not limited to, those of the bladder and prostate. The significance of such methylation patterns lies in the value of altered fragments as potential prognostic, diagnostic and therapeutic markers in the treatment of human cancers.

## Identification of Methylation-altered Marker Sequences in Genomic DNA

The MS.AP-PCR technique was used to scan the genomes of bladder or prostate cancer patients for DNA methylation changes relative to normal individuals, because the pattern is known to be highly conserved. A total of 103 DNA sequence embodiments (methylation-altered DNA sequences; “marker sequences”) were isolated and characterized as having distinct methylation patterns in cancer, as compared to normal tissue.

*Methods for the Identification of Marker Sequences in Genomic DNA.* There are a variety of art-recognized genome scanning methods that have been used to identify altered methylation sites in cancer cells. For example, one method involves restriction landmark genomic scanning (Kawai et al., *Mol. Cell. Biol.* 14:7421-7427, 1994), another involves MCA (methylated CpG island amplification; Toyota et al., *Cancer Res.* 59:2307-12, 1999), and yet another involves MS.AP-PCR (Methylation-Sensitive Arbitrarily-Primed Polymerase Chain Reaction; Gonzalzo et al., *Cancer Res.* 57:594-599, 1997), which allows for a global scan of the genome using CG-rich primers to focus on the regions most likely to contain CpG dinucleotides. The MS.AP-PCR technique used in the present invention is a rapid and efficient method to screen (“scan”) for altered methylation patterns in genomic DNA and to isolate specific sequences associated with these changes.

Briefly, genomic DNA from the tissue of bladder or prostate cancer patients was prepared using standard, art-recognized methods. Restriction enzymes (*e.g.*, HpaII) with different sensitivities to cytosine methylation in their recognition sites were used to digest these genomic DNAs prior to arbitrarily primed PCR amplification with GC-rich primers. Fragments that showed differential methylation (*e.g.*, *hypermethylation* or *hypomethylation*, based on the methylation sensitivity of the restriction enzyme, or upon DNA sequence analysis or Ms-SNuPE analysis; Gonzalzo & Jones, *Nucleic Acids Res* 25:2529-2531, 1997) were cloned and sequenced after resolving the PCR products on high-resolution polyacrylamide gels. The cloned fragments were used as probes for Southern blot analysis to

confirm differential methylation of these regions in the tissue. Methods for DNA cloning, sequencing, PCR, high-resolution polyacrylamide gel resolution and Southern blot analysis are well known by those of ordinary skill in the relevant art.

*Results.* A total of 500 DNA fragments that underwent either hypermethylation (an increase in the level of methylation relative to normal) or hypomethylation (a decrease in the level of methylation relative to normal) were isolated from the scanned patients genomic DNA. A total of 178 of these fragments were sequenced, of which 103 were *novel* in that they corresponded to DNA loci whose methylation pattern had not previously been characterized. The corresponding sequences are disclosed as [SEQ ID NOS:1-103], wherein for certain sequences, the letter “n” refers to an undetermined nucleotide base.

***Novel marker sequences identified by MS.AP-PCR.*** Table I shows an *overall* summary of methylation patterns and sequence data corresponding to the 103 DNA fragments identified by MS.AP-PCR. A total of 103 fragments were sequenced following identification as becoming either hypermethylated (gain of methylation; noted as having a hypermethylation pattern) or hypomethylated (loss of methylation; noted as having a hypomethylation pattern) relative to normal tissue. For the fragments of each category, the “Average GC Content” is shown, calculated as (number of C bases + number of G bases)/band length for each fragment, as well as the average Observed/Expected Ratio (“O/E Ratio”), calculated as [number of CpG sites/(number of C bases X number of G bases)] X band length for each fragment. Additionally, the percent of fragments that qualify as CpG islands is listed, and corresponds to the percentage of all fragments within each category that have sequence compositions that satisfy the criteria of having a “GC Content” >0.5 and an “O/E Ratio” >0.6.

Thus, of these 103 fragments identified by MS.AP-PCR, 60 showed hypermethylation (Table I, upper row; Table II, [SEQ ID NOS:1-60]) while 43 showed hypomethylation (Table I, lower row; Table II, [SEQ ID NOS:61-103]). Moreover, 55 (43 hypermethylated, and 12 hypomethylated) of the 103 fragments correspond to CpG islands (*i.e.*, fulfill the criteria of a GC content >0.5 and an Observed/Expected Ratio >0.6;), whereas the other 48 (17 hypermethylated and 31 hypomethylated) fragments do not meet the criteria for CpG islands (*see* Table II).

**TABLE I. Summary of 103 DNA Fragments Identified by MS.AP-PCR**

DNA Fragment Type	Methylation Pattern (relative to normal)	Number of Fragments (103 total)	Average GC Content	Average O/E Ratio	Percent that correspond to CpG Islands
Hypermethylated Fragments	Hyper-methylation	60	0.54	0.72	72%
Hypomethylated Fragments	Hypo-methylation	43	0.52	0.48	28%



Table II shows a summary of methylation pattern and sequence data for each individual sequence embodiment ([SEQ ID NOS:1-103]), corresponding to the 103 DNA fragments identified by MS.AP-PCR. Data for the 103 fragments was divided into either hypermethylated ([SEQ ID NOS:1-60]) or hypomethylated ([SEQ ID NOS:61-103]) categories. Table II also lists, for each sequence embodiment, the corresponding "Fragment Name," fragment "Size" (in base pairs; "bp"), "GC Content," Observed/Expected Ratio ("O/E Ratio"), "Description" (*i.e.*, as a CpG island if criteria are met), "Inventor Initials" (IDCM = Isabel D.C. Markl, JC = Jonathan Cheng, GL = Gangning Liang, HF = Hualin Fu, YT = Yoshitaka Tomigahara), "Cancer Source," and "Chromosome Match" to the GenBank database. A dash ("-") indicates that no GenBank chromosome match existed, or that only a low-scoring partial match was found. Averages of the "GC Content" and "O/E Ratio," along with the percent of fragments that are CpG islands, are listed after the last member of both the hypermethylated and hypomethylated categories.

Therefore, the present invention provides for 103 DNA fragments and corresponding marker sequence embodiments (*i.e.*, methylation-altered DNA sequences) that are useful in cancer prognostic, diagnostic and therapeutic applications.

Additionally, at least 55 of these 103 sequences correspond to CpG islands (based on GC Content and O/E ratio); namely [SEQ ID NOS:2, 4, 6, 7, 9-16, 19, 20, 22-33, 35-43, 48, 51-55, 59, 60, 64, 71, 76, 78-81, 84 and 87-90]. Thus, based on the fact that the methylation state of a portion of a given CpG island is generally representative of the island as a whole, the present invention further encompassed the novel use of the 55 CpG islands associated with [SEQ ID NOS:2, 4, 6, 7, 9-16, 19, 20, 22-33, 35-43, 48, 51-55, 59, 60, 64, 71, 76, 78-81, 84 and 87-90] in cancer prognostic, diagnostic and therapeutic applications, where a CpG island sequence associated with the sequence of a particular SEQ ID NO is that contiguous sequence of genomic DNA that encompasses at least one nucleotide of the particular SEQ ID NO sequence, and satisfies the criteria of having both a frequency of CpG dinucleotides corresponding to an Observed/Expected Ratio >0.6, and a GC Content >0.5.

**TABLE II. Summary of MS.AP-PCR Fragments Sequenced**

Methylation Pattern	Fragment Name	Size (bp)	GC Content	O/E Ratio	Description	Inventor Initials	Cancer Source	Chromosome Matches	[SEQ ID NO]
Hyper-methylation Category	11-1A	510	0.44	0.74		IDCM	Bladder	-	1
	14-3B	313	0.58	0.74	CpG Island	IDCM	Bladder	2	2
	18-2B	165	0.57	0.45		IDCM	Bladder	7	3
	24-1B	601	0.51	0.72	CpG Island	IDCM	Bladder	Xp11	4
	26-1B	801	0.48	0.56		IDCM	Bladder	-	5
	26-2C	204	0.50	0.63	CpG Island	IDCM	Bladder	-	6
	30-3D	205	0.55	1.25	CpG Island	IDCM	Bladder	14	7
	32-3E	597	0.57	0.10		IDCM	Bladder	20q12-13.1	8
	34-2B	500	0.62	0.66	CpG Island	IDCM	Bladder	20	9
	34-4B	343	0.70	0.81	CpG Island	IDCM	Bladder	-	10

Methylation Pattern	Fragment Name	Size (bp)	GC Content	O/E Ratio	Description	Inventor Initials	Cancer Source	Chromosome Matches	[SEQ ID NO]
	34-5D	291	0.62	0.96	CpG Island	IDCM	Bladder	9	11
	34-6A	266	0.64	0.93	CpG Island	IDCM	Bladder	-	12
	35-1C	553	0.64	0.63	CpG Island	IDCM	Bladder	-	13
	36-2D	156	0.60	0.58	CpG Island	IDCM	Bladder	10	14
	38-1A	300	0.70	0.80	CpG Island	IDCM	Bladder	10	15
	38-2B	196	0.56	0.89	CpG Island	IDCM	Bladder	15	16
	7-8E	299	0.59	0.39		IDCM	Bladder	17q21-22	17
	83-4B	363	0.54	0.49		IDCM	Bladder	-	18
	84-1D	322	0.55	0.90	CpG Island	IDCM	Bladder	7	19
	101-3E	255	0.57	0.83	CpG Island	IDCM	Bladder	17	20
	M1-5A	406	0.45	0.96		IDCM	Bladder	1	21
	U2-8E	210	0.56	0.61	CpG Island	IDCM	Bladder	2	22
	U12-1A	310	0.56	0.81	CpG Island	IDCM	Bladder	2	23
	U7-4A	305	0.59	0.80	CpG Island	IDCM	Bladder	-	24
	NU9-5A	379	0.67	0.83	CpG Island	JC	Bladder	-	25
	3-17-8-B	625	0.48	0.72	CpG Island	GL	Bladder	18	26
	4-10-4-A	499	0.55	0.30	CpG Island	GL	Bladder	7	27
	1-1-1-A	561	0.58	0.98	CpG Island	GL	Bladder	20	28
	3-17-8-A	717	0.50	0.68	CpG Island	GL	Bladder	17	29
	G145-H	280	0.50	1.10	CpG Island	GL	Bladder	11	30
	1-1-1-D	270	0.50	0.60	CpG Island	GL	Bladder	2	31
	1-1-1-C	347	0.65	1.25	CpG Island	GL	Bladder	-	32
	G178-A	342	0.55	0.85	CpG Island	GL	Bladder	2	33
	34-A	370	0.62	0.44		HF	Prostate	-	34
	34-D	213	0.53	0.74	CpG Island	HF	Prostate	2	35
	35-D	173	0.56	0.66	CpG Island	HF	Prostate	3	36
	36-A	369	0.67	0.70	CpG Island	HF	Prostate	-	37
	40-A	123	0.60	1.16	CpG Island	HF	Prostate	-	38
	91-1	450	0.64	0.86	CpG Island	YT	Bladder	5 or 16q24.3	39
	93-2	593	0.51	0.68	CpG Island	YT	Bladder	Xp11	40
	93-3	457	0.52	0.94	CpG Island	YT	Bladder	Xp22.1-22.3	41
	94-8	211	0.66	0.96	CpG Island	YT	Bladder	-	42
	95-5	141	0.63	0.79	CpG Island	YT	Bladder	14	43
	97-5	559	0.56	0.40		YT	Bladder	-	44
	98-1	433	0.46	0.96		YT	Bladder	1	45
	100-1	487	0.59	0.58		YT	Bladder	14	46
	100-2	403	0.60	0.47		YT	Bladder	3	47
	100-6	155	0.57	0.99	CpG Island	YT	Bladder	20	48
	4-2	256	0.57	0.40		YT	Bladder	7	49
	5-8	224	0.47	0.96		YT	Bladder	5	50
	6-4	313	0.70	0.82	CpG Island	YT	Bladder	-	51
	7-6	385	0.70	0.88	CpG Island	YT	Bladder	-	52
	13-3	307	0.59	0.89	CpG Island	YT	Bladder	10	53
	15-2	182	0.62	0.92	CpG Island	YT	Bladder	13	54
	23-2	523	0.54	0.87	CpG Island	YT	Bladder	Xp22.1-22.3	55
	39-2	795	0.46	0.64		YT	Bladder	13	56
	40-2	438	0.62	0.51		YT	Bladder	10	57
	41-3	611	0.47	0.70		YT	Bladder	18	58
	105-4	291	0.58	0.71	CpG Island	YT	Bladder	5	59
	107-8	226	0.53	0.96	CpG Island	YT	Bladder	11	60
<i>AVERAGE</i>			<i>0.54</i>	<i>0.72</i>	<i>72% islands</i>				
Hypo-methylation Category	14-2B	580	0.55	0.51		IDCM	Bladder	2	61
	16-1B	633	0.56	0.39		IDCM	Bladder	-	62
	18-1B	703	0.45	0.35		IDCM	Bladder	17	63

Methylation Pattern	Fragment Name	Size (bp)	GC Content	O/E Ratio	Description	Inventor Initials	Cancer Source	Chromosome Matches	[SEQ ID NO]
	19-1B	420	0.66	0.87	CpG Island	IDCM	Bladder	-	64
	20-1B	496	0.61	0.59		IDCM	Bladder	-	65
	21-2C	637	0.60	0.33		IDCM	Bladder	9q34	66
	29-1A	595	0.55	0.27		IDCM	Bladder	Xp11.23	67
	29-2B	580	0.47	0.77		IDCM	Bladder	-	68
	32-1A	589	0.59	0.48		IDCM	Bladder	-	69
	34-1B	450	0.42	0.46		IDCM	Bladder	-	70
	34-3B	432	0.70	0.61	CpG Island	IDCM	Bladder	-	71
	32-2B	748	0.47	0.24		IDCM	Bladder	2	72
	32-4B	599	0.57	0.15		IDCM	Bladder	20q12-13.1	73
	32-5B	614	0.58	0.20		IDCM	Bladder	-	74
	33-1A	552	0.54	0.32		IDCM	Bladder	10	75
	5-1E	501	0.61	1.04	CpG Island	IDCM	Bladder	-	76
	6-1A	826	0.55	0.36		IDCM	Bladder	22q13.32-13.33	77
	7-5D	433	0.59	0.85	CpG Island	IDCM	Bladder	5	78
	8-7C	424	0.58	0.83	CpG Island	IDCM	Bladder	5	79
	30-6D	285	0.63	0.72	CpG Island	IDCM	Bladder	1	80
	66-2E	401	0.54	0.82	CpG Island	IDCM	Bladder	16	81
	78-1C	268	0.54	0.41		IDCM	Bladder	-	82
	97-2E	989	0.53	0.16		IDCM	Bladder	-	83
	M1-8C	250	0.64	0.99	CpG Island	IDCM	Bladder	-	84
	M2-5A	402	0.50	0.45		IDCM	Bladder	5	85
	M1-4P	595	0.43	0.41		IDCM	Bladder	-	86
	M12-10A	304	0.53	0.76	CpG Island	IDCM	Bladder	7	87
	M12-12C	296	0.51	0.64	CpG Island	IDCM	Bladder	17	88
	M2-8M	220	0.67	0.62	CpG Island	IDCM	Bladder	6q27	89
	NU4-3A	273	0.63	1.02	CpG Island	JC	Bladder	-	90
	NU5-2A	361	0.44	0.73		JC	Bladder	6q14.3-15	91
	88-5	462	0.62	0.39		YT	Bladder	-	92
	90-1	591	0.66	0.45		YT	Bladder	19	93
	91-3	279	0.58	0.45		YT	Bladder	5 or 16q24.3	94
	91-4	351	0.55	0.30		YT	Bladder	18q23	95
	91-7	171	0.61	0.59		YT	Bladder	11	96
	89-3	743	0.55	0.43		YT	Bladder	-	97
	94-2	589	0.53	0.41		YT	Bladder	22q13.31-13.32	98
	94-3	538	0.53	0.49		YT	Bladder	5 or 18	99
	94-4	486	0.61	0.57		YT	Bladder	-	100
	94-5	450	0.60	0.45		YT	Bladder	1p36.2-36.3	101
	94-6	292	0.58	0.32		YT	Bladder	8 or 9	102
	96-4	395	0.63	0.54		YT	Bladder	9	103
<i>AVERAGE</i>			0.52	0.48	28% islands				

**Diagnostic and Prognostic Assays for Cancer.** The present invention provides for diagnostic and prognostic cancer assays based on determination of the methylation state of one or more of the disclosed 103 methylation-altered DNA sequence embodiments. Typically, such assays involve obtaining a tissue sample from a test tissue, performing a methylation assay on DNA derived from the tissue sample, and making a diagnosis or prognosis based thereon.

The methylation assay is used to determine the methylation state of one or a plurality of CpG dinucleotide within a DNA sequence of the DNA sample. According to the present invention, possible methylation states include *hypermethylation* and *hypomethylation*, relative to a normal state (*i.e.*, non-cancerous control state). Hypermethylation and hypomethylation refer to the methylation states corresponding to an *increased* or *decreased*, respectively, presence 5-methylcytosine (“5-mCyt”) at one or a plurality of CpG dinucleotides within a DNA sequence of the test sample, relative to the amount of 5-mCyt found at corresponding CpG dinucleotides within a normal control DNA sample.

A diagnosis or prognosis is based, at least in part, upon the determined methylation state of the sample DNA sequence compared to control data obtained from normal, non-cancerous tissue.

**Methylation Assay Procedures.** Various methylation assay procedures are known in the art, and can be used in conjunction with the present invention. These assays allow for determination of the methylation state of one or a plurality of CpG dinucleotides (*e.g.*, CpG islands) within a DNA sequence. Such assays involve, among other techniques, DNA sequencing of bisulfite-treated DNA, PCR (for sequence-specific amplification), Southern blot analysis, use of methylation-sensitive restriction enzymes, etc.

For example, genomic sequencing has been simplified for analysis of DNA methylation patterns and 5-methylcytosine distribution by using bisulfite treatment (Frommer et al., *Proc. Natl. Acad. Sci. USA* 89:1827-1831, 1992). Additionally, restriction enzyme digestion of PCR products amplified from bisulfite-converted DNA is used, *e.g.*, the method described by Sadri & Hornsby (*Nucl. Acids Res.* 24:5058-5059, 1996), or COBRA (Combined Bisulfite Restriction Analysis) (Xiong & Laird, *Nucleic Acids Res.* 25:2532-2534, 1997).

**COBRA.** COBRA analysis is a quantitative methylation assay useful for determining DNA methylation levels at specific gene loci in small amounts of genomic DNA (Xiong & Laird, *Nucleic Acids Res.* 25:2532-2534, 1997). Briefly, restriction enzyme digestion is used to reveal methylation-dependent sequence differences in PCR products of sodium bisulfite-treated DNA. Methylation-dependent sequence differences are first introduced into the genomic DNA by standard bisulfite treatment according to the procedure described by Frommer et al. (*Proc. Natl. Acad. Sci. USA* 89:1827-1831, 1992). PCR amplification of the bisulfite converted DNA is then performed using primers specific for the interested CpG islands, followed by restriction endonuclease digestion, gel electrophoresis, and detection using specific, labeled hybridization probes. Methylation levels in the original DNA sample are represented by the relative amounts of digested and undigested PCR product in a linearly quantitative fashion across a wide spectrum of DNA methylation levels. In addition, this technique can be reliably applied to DNA obtained from microdissected paraffin-embedded tissue samples. Typical reagents (*e.g.*, as might be found in a typical COBRA-based kit) for

COBRA analysis may include, but are not limited to: PCR primers for specific gene (or methylation-altered DNA sequence or CpG island); restriction enzyme and appropriate buffer; gene-hybridization oligo; control hybridization oligo; kinase labeling kit for oligo probe; and radioactive nucleotides. Additionally, bisulfite conversion reagents may include:  
5 DNA denaturation buffer; sulfonation buffer; DNA recovery reagents or kit (*e.g.*, precipitation, ultrafiltration, affinity column); desulfonation buffer; and DNA recovery components.

Preferably, assays such as “MethyLight” (a fluorescence-based real-time PCR technique) (Eads et al., *Cancer Res.* 59:2302-2306, 1999), Ms-SNuPE (Methylation-sensitive  
10 Single Nucleotide Primer Extension) reactions (Gonzalogo & Jones, *Nucleic Acids Res.* 25:2529-2531, 1997), methylation-specific PCR (“MSP”; Herman et al., *Proc. Natl. Acad. Sci. USA* 93:9821-9826, 1996; US Patent No. 5,786,146), and methylated CpG island amplification (“MCA”; Toyota et al., *Cancer Res.* 59:2307-12, 1999) are used alone or in combination with other of these methods.

15 ***MethyLight.*** The MethyLight assay is a high-throughput quantitative methylation assay that utilizes fluorescence-based real-time PCR (TaqMan ®) technology that requires no further manipulations after the PCR step (Eads et al., *Cancer Res.* 59:2302-2306, 1999). Briefly, the MethyLight process begins with a mixed sample of genomic DNA that is converted, in a sodium bisulfite reaction, to a mixed pool of methylation-dependent sequence  
20 differences according to standard procedures (the bisulfite process converts unmethylated cytosine residues to uracil). Fluorescence-based PCR is then performed either in an “unbiased” (with primers that do not overlap known CpG methylation sites) PCR reaction, or in a “biased” (with PCR primers that overlap known CpG dinucleotides) reaction. Sequence discrimination can occur either at the level of the amplification process or at the level of the  
25 fluorescence detection process, or both.

The MethyLight may assay be used as a quantitative test for methylation patterns in the genomic DNA sample, wherein sequence discrimination occurs at the level of probe hybridization. In this quantitative version, the PCR reaction provides for unbiased amplification in the presence of a fluorescent probe that overlaps a particular putative  
30 methylation site. An unbiased control for the amount of input DNA is provided by a reaction in which neither the primers, nor the probe overlies any CpG dinucleotides. Alternatively, a qualitative test for genomic methylation is achieved by probing of the biased PCR pool with either control oligonucleotides that do not “cover” known methylation sites (a fluorescence-based version of the “MSP” technique), or with oligonucleotides covering potential  
35 methylation sites.

The MethyLight process can be used with a “TaqMan®” probe in the amplification process. For example, double-stranded genomic DNA is treated with sodium bisulfite and subjected to one of two sets of PCR reactions using TaqMan® probes; *e.g.*, with either

biased primers and TaqMan® probe, or unbiased primers and TaqMan® probe. The TaqMan® probe is dual-labeled with fluorescent “reporter” and “quencher” molecules, and is designed to be specific for a relatively high GC content region so that it melts out at about 10 °C higher temperature in the PCR cycle than the forward or reverse primers. This allows the TaqMan® probe to remain fully hybridized during the PCR annealing/extension step. As the Taq polymerase enzymatically synthesizes a new strand during PCR, it will eventually reach the annealed TaqMan® probe. The Taq polymerase 5’ to 3’ endonuclease activity will then displace the TaqMan® probe by digesting it to release the fluorescent reporter molecule for quantitative detection of its now unquenched signal using a real-time fluorescent detection system.

Typical reagents (*e.g.*, as might be found in a typical MethyLight-based kit) for MethyLight analysis may include, but are not limited to: PCR primers for specific gene (or methylation-altered DNA sequence or CpG island); TaqMan® probes; optimized PCR buffers and deoxynucleotides; and Taq polymerase.

**Ms-SNuPE.** The Ms-SNuPE technique is a quantitative method for assessing methylation differences at specific CpG sites based on bisulfite treatment of DNA, followed by single-nucleotide primer extension (Gonzalvo & Jones, *Nucleic Acids Res.* 25:2529-2531, 1997). Briefly, genomic DNA is reacted with sodium bisulfite to convert unmethylated cytosine to uracil while leaving 5-methylcytosine unchanged. Amplification of the desired target sequence is then performed using PCR primers specific for bisulfite-converted DNA, and the resulting product is isolated and used as a template for methylation analysis at the CpG site(s) of interest. Small amounts of DNA can be analyzed (*e.g.*, microdissected pathology sections), and it avoids utilization of restriction enzymes for determining the methylation status at CpG sites. Typical reagents (*e.g.*, as might be found in a typical Ms-SNuPE-based kit) for Ms-SNuPE analysis may include, but are not limited to: PCR primers for specific gene (or methylation-altered DNA sequence or CpG island); optimized PCR buffers and deoxynucleotides; gel extraction kit; positive control primers; Ms-SNuPE primers for specific gene; reaction buffer (for the Ms-SNuPE reaction); and radioactive nucleotides. Additionally, bisulfite conversion reagents may include: DNA denaturation buffer; sulfonation buffer; DNA recovery reagents or kit (*e.g.*, precipitation, ultrafiltration, affinity column); desulfonation buffer; and DNA recovery components.

**MSP.** MSP (methylation-specific PCR) allows for assessing the methylation status of virtually any group of CpG sites within a CpG island, independent of the use of methylation-sensitive restriction enzymes (Herman et al. *Proc. Natl. Acad. Sci. USA* 93:9821-9826, 1996; US Patent No. 5,786,146). Briefly, DNA is modified by sodium bisulfite converting all unmethylated, but not methylated cytosines to uracil, and subsequently amplified with primers specific for methylated versus unmethylated DNA. MSP requires only small quantities of DNA, is sensitive to 0.1% methylated alleles of a given CpG island locus, and

can be performed on DNA extracted from paraffin-embedded samples. Typical reagents (e.g., as might be found in a typical MSP-based kit) for MSP analysis may include, but are not limited to: methylated and unmethylated PCR primers for specific gene (or methylation-altered DNA sequence or CpG island), optimized PCR buffers and deoxynucleotides, and  
5 specific probes.

**MCA.** The MCA technique is a method that can be used to screen for altered methylation patterns in genomic DNA, and to isolate specific sequences associated with these changes (Toyota et al., *Cancer Res.* 59:2307-12, 1999). Briefly, restriction enzymes with different sensitivities to cytosine methylation in their recognition sites are used to digest  
10 genomic DNAs from primary tumors, cell lines, and normal tissues prior to arbitrarily primed PCR amplification. Fragments that show differential methylation are cloned and sequenced after resolving the PCR products on high-resolution polyacrylamide gels. The cloned fragments are then used as probes for Southern analysis to confirm differential methylation of these regions. Typical reagents (e.g., as might be found in a typical MCA -based kit) for  
15 MCA analysis may include, but are not limited to: PCR primers for arbitrary priming Genomic DNA; PCR buffers and nucleotides, restriction enzymes and appropriate buffers; gene-hybridization oligos or probes; control hybridization oligos or probes.

**Kits for Detection of Methylated CpG-containing Nucleic Acid.** The reagents required to perform one or more art-recognized methylation assays (including those identified  
20 above) are combined with primers or probes comprising the sequences of SEQ ID NOS:1-103, or portions thereof, to determine the methylation state of CpG-containing nucleic acids. For example, the MethyLight, Ms-SNuPE, MCA, COBRA, and MSP methylation assays could be used alone or in combination, along with primers or probes comprising the sequences of SEQ ID NOS:1-103, or portions thereof, to determine the methylation state of a  
25 CpG dinucleotide within a genomic sequence corresponding to SEQ ID NOS:1-103, or to CpG island sequences associated with sequences of SEQ ID NOS:1-103, where the CpG island sequence associated with the sequence of the particular SEQ ID NO is that contiguous sequence of genomic DNA that encompasses at least one nucleotide of the particular SEQ ID NO sequence, and satisfies the criteria of having both a frequency of CpG dinucleotides  
30 corresponding to an Observed/Expected Ratio >0.6, and a GC Content >0.5.

We claim:

1. A diagnostic or prognostic assay for cancer, comprising:
  - (a) obtaining a tissue sample from a test tissue;
  - (b) performing a methylation assay on DNA derived from the tissue sample,
- 5 wherein the methylation assay determines the methylation state of a CpG dinucleotide within a DNA sequence of the DNA, and wherein the DNA sequence is a sequence selected from the group consisting of sequences of SEQ ID NOS:1-103, sequences having a nucleotide sequence at least 90% identical to sequences of SEQ ID NOS:1-103, CpG island sequences associated with sequences of SEQ ID NOS:1-103, CpG island sequences associated with
- 10 sequences having a nucleotide sequence at least 90% identical to sequences of SEQ ID NOS:1-103, and combinations thereof, wherein the CpG island sequence associated with the sequence of the particular SEQ ID NO is that contiguous sequence of genomic DNA that encompasses at least one nucleotide of the particular SEQ ID NO sequence, and satisfies the criteria of having both a frequency of CpG dinucleotides corresponding to an
- 15 Observed/Expected Ratio  $>0.6$ , and a GC Content  $>0.5$ ; and
  - (c) determining a diagnosis or prognosis based, at least in part, upon the methylation state of the CpG dinucleotide within the DNA sequence.
2. The diagnostic or prognostic assay of claim 1 wherein the DNA sequence is a sequence selected from the group consisting of CpG island sequences associated with
- 20 sequences of SEQ ID NOS:1-103, CpG island sequences associated with sequences having a nucleotide sequence at least 90% identical to sequences of SEQ ID NOS:1-103, and combinations thereof.
3. The diagnostic or prognostic assay of claim 2 wherein the DNA sequence is a sequence selected from the group consisting of CpG island sequences associated with
- 25 sequences of SEQ ID NOS: 2, 4, 6, 7, 9-16, 19, 20, 22-33, 35-43, 48, 51-55, 59, 60, 64, 71, 76, 78-81, 84 and 87-90, and combinations thereof.
4. The diagnostic or prognostic assay of claim 1 wherein the methylation assay procedure is selected from the group consisting of MethyLight, MS-SNuPE, MSP MCA, COBRA, and combinations thereof.
- 30 5. The diagnostic or prognostic assay of claim 1 wherein the methylation state of the CpG dinucleotide within the DNA sequence is that of hypermethylation, hypomethylation or normal methylation.
6. The diagnostic or prognostic assay of claim 1 wherein the cancer is selected from the group consisting of bladder cancer, prostate cancer, colon cancer, lung cancer, renal
- 35 cancer, leukemia, breast cancer, uterine cancer, astrocytoma, glioblastoma, and neuroblastoma.
7. A kit useful for the detection of a methylated CpG-containing nucleic acid comprising a carrier means containing one or more containers comprising:



(a) a container containing a probe or primer which hybridizes to any region of a sequence selected from the group consisting of SEQ ID NOS:1-103, and sequences having a nucleotide sequence at least 90% identical to sequences of SEQ ID NOS:1-103; and

5 (b) additional standard methylation assay reagents required to affect detection of methylated CpG-containing nucleic acid based, at least in part, on the probe or primer.

8. The kit of claim 7, wherein the additional standard methylation assay reagents are standard reagents for performing a methylation assay from the group consisting of MethyLight, MS-SNuPE, MSP MCA, COBRA, and combinations thereof.

9. The kit of claim 7, wherein the probe or primer comprises at least about 12 to  
10 15 nucleotides of a sequence selected from the group consisting of SEQ ID NOS:1-103, and sequences having a nucleotide sequence at least 90% identical to sequences of SEQ ID NOS:1-103.

10. An isolated nucleic acid molecule comprising a methylated or unmethylated polynucleotide sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:5,  
15 SEQ ID NO:6, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:18, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:32, SEQ ID NO:34, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:42, SEQ ID NO:44, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:62, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:74, SEQ ID NO:76, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID  
20 NO:86, SEQ ID NO:90, SEQ ID NO:92, SEQ ID NO:97, and SEQ ID NO:100.

11. The nucleic acid of claim 10, wherein the nucleic acid is methylated.

12. The nucleic acid of claim 10, wherein the nucleic acid is unmethylated.

## SEQUENCE LISTING

<110> University of Southern California  
Markl, Isabel  
Tomigahara, Yoshitaka  
Liang, Gangning  
Fu, Hualin  
Jones, Peter

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 caggccgct gagatggttc tagtcccttt gagtatacag acccttctctg tgcattgacc 120  
 gacacagctc ggcccggatc ccgaaatgaa cgtttctacc ttcggaacgc tgcgtctcgg 180  
 atccttctga acccgcacgt cgcaa 205

<210> 8  
 <211> 597  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> unsure  
 <222> position is 361 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 382 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 513 nucleotides  
 <223> "n" refers to an undetermined base

<400> 8  
 gaccatgaaa togtgtggct ctagcccctt ctgggcctct tgttggaat gaagccactc 60  
 taaagcgccc cctgttattc agagggctcc ccagctgcca tgatatgtgt atggggaggg 120  
 catagcaggt ccttttgccc cggcagccat tcttctgctc acaaggggct ggctctgggg 180  
 acagggatgt ctttgtcadc agtgaccact aatccccctc ctcatggcc tccagggctg 240  
 ctccccttca ctctcttggt tgaagttgta ggggctgagg ttaccctgag aaacacctgt 300  
 tcttgagacc catagacca accttgagaga tgcaggggga gccactggct gggctctgca 360  
 ngtggggcca gctgatcccc anctgctggc acctccaggc atccacagag cttggagtcc 420  
 cagccacatt tcctccttgg ccttagaggg agaggaagtc ctttgattgc ctagtccaag 480  
 atccctttat ttctgcctt gggattatgg ggnagcaagc catgcccttc atgggaagct 540  
 gttctccctt cctcgggggtt gggctctggcc tcagctcggg caacagtcac gatgggc 597

<210> 9  
 <211> 500  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> unsure  
 <222> position is 10 nucleotides  
 <223> "n" refers to an undetermined base

<400> 9

gccaaacgcn ataccctctg cggggtgaga atgcgggccc gcccggtcc tcccgtgagg 60  
 ccagggcctc ctgttctcct agacacccca aggagccaac tcctccgcag aagttccccg 120  
 cttctgctct tatttccaag cttegcgctt tctacaaact ccctggtgcc ttgactttga 180  
 tttccagccg tgggtgagggt cagagtgaac cccggcgcgc tccccgacgg catccccgca 240  
 caccaggata ggagaaattg gagggcctgg ggcctcgggc tccgcagtgc tcggaggaag 300  
 aacccacogc ggggtccgca agggaaagtg aagaggcccc ggatttttcc aaagcgctgg 360  
 ccaggacccc gaaggaaggg gaggagtcaac ctgaagccgg ggaaggcccc ttgggtgctc 420  
 tgccttggat ccttatgttc actgactttc gcgaccctg gaggggggca aatccgcgct 480  
 gtttccccca acttggcttc 500

<210> 10  
 <211> 343  
 <212> DNA  
 <213> Homo sapiens

<400> 10  
 gccaacccac accagtacct gggaccgggg ggagcccggg cgggccgcta aaccgggctg 60  
 gctggcgcca gggctccggg aggtgcgggc cggcggggaa gccgtgatgg gaagcgactc 120  
 tgtccagga gtgtccttca ccaccacact cctcacgtcc aggcagtgat cgacggcctg 180  
 gcggcacctt cacagcgggc ccatagcacg gggccacaca cgtcccctga gcttagcctg 240  
 ggcacattcg tctgccgccc agggcttaag ccagtctgca gcccgcgccc cgtcactcgg 300  
 acgcaagtcc gtcgtccgct ctgccacgcg gccgctaagc cga 343

<210> 11  
 <211> 291  
 <212> DNA  
 <213> Homo sapiens

<400> 11  
 gtccctacaca ctccgcacac aacgcggccg gtgttaagtc tccaaacgcc ccgagagctc 60  
 caaggaccgc gcgcgcgaag gcgccgtagc aagtgggcac acaccagaca ccacccccgc 120  
 gtgttccgcg ggagaagcca gtgcacacat cctcccgcaa ggcggggttg ccagtgcaac 180  
 acaggaatcc tgcccttttt ctagaaaagc cccctcccc actttccctc caatacactc 240  
 acctgogtct caacagtttc cttcttgccg tacacgcggc cgctaagccg a 291

<210> 12  
 <211> 266

<212> DNA  
 <213> Homo sapiens

<400> 12  
 gtccggatca gtttccccgg ccaggtcgct tcccggctctc aaccatttcg cgctctgctc 60  
 tgtccgctgg tttgtccctg cccggttcct ctccccgggc ctgtcagcct ccgcttctct 120  
 ggaggttcct gggactcatc tctgatccac cgtcttgcgt tctctgggcg catcgacttc 180  
 tctccatctt cgggctcact cctgactccc tcgctgccgc ccccgggggt ttccacgcgt 240  
 gtctctaacc gcggccgcta agccga 266

<210> 13  
 <211> 553  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> unsure  
 <222> position is 497 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 513 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 517 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 519 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 527 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 546 nucleotides  
 <223> "n" refers to an undetermined base

<400> 13  
 gatcctggtc catcgaacc ttgtgtgcat cggttagtgc ttctgggcg tttgctteta 60  
 gccgacgctg acagtggagt gccagaaaga gggagaggac cgtcatggct actctgcccc 120  
 tgggtgcacc atgcgctctc ccccggcacc ggcgaggcga aacgtttcgc tagtccccgg 180



gaggcccctc ggtcagggca gcagcatccc tgcacctct cgcaggtgg tctccccgac 240  
gccacaggtg gccagcaggg cgcggtggg ggcaggagcg cctctcccct gccaggcct 300  
cccgtcctt ctggagcgc tgtggcggg tggagagaca gccttctaca gctagtctag 360  
ctcggcgcgg ttcccgtctg tggcctccta atcccacagc cacagcgcct tctcttaacc 420  
tccctcgggtg ggcttaaagc ctcccgttcc ttctgtctca ttctttctgc tccctcccc 480  
cgaaaccccc agatganagc tgggaacctg gnccantna ctgagcnaac agtggtgacg 540  
ggccgnggcc caa 553

<210> 14  
<211> 156  
<212> DNA  
<213> Homo sapiens

<400> 14  
gcgcacacag tgggtacaag gatgagctcg gtgtaaggaa tggaaagccc ccagtctaaa 60  
ccaccgcccc ctagacacgg gtgaaaacct gcctaaaagc taactcaggc agtgactcta 120  
tcaccggaag gggccctggg ccgcgcccca agccga 156

<210> 15  
<211> 300  
<212> DNA  
<213> Homo sapiens

<220>  
<221> unsure  
<222> position is 117 nucleotides  
<223> "n" refers to an undetermined base

<220>  
<221> unsure  
<222> position is 154 nucleotides  
<223> "n" refers to an undetermined base

<220>  
<221> unsure  
<222> position is 163 nucleotides  
<223> "n" refers to an undetermined base

<400> 15  
gttcacagcc cataaggtgg gggtgcccg aacctgaaac ggagcctgag ccaggatcct 60  
gcaaccaaag tctgaagcgc cccccggtgg gggccgagag cgctgcaggc aggtggnggc 120  
gcggggcagg cgggcgggcg aaggagctc cggntacgca ganaacgcgg agcgcgccct 180

tcccacctgc gcgagggcat cctgcccggg ggaggaaagg cgggagtccg aggcgggtcg 240  
 gattcccagc cagctccctc ctcacaggag gcggcccatt atccggcgtc gcaaagccga 300

<210> 16  
 <211> 196  
 <212> DNA  
 <213> Homo sapiens

<400> 16  
 ggcgcccagc aggggagcga gggaggaggg tgcagaaaga ggctccgaaa ttgggggaaa 60  
 ctgacccgtg cttctctacc ttcggaggtg ggacagttgc acgaagtgct agttagaccg 120  
 gatcagttgg aactgacgga ggactgcaaa gaagaaacta aaatagacgt cgaaagcctg 180  
 tcctcggcgt cgcaaa 196

<210> 17  
 <211> 299  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> unsure  
 <222> position is 21 nucleotides  
 <223> "n" refers to an undetermined base

<400> 17  
 acaccaggag aggggaagaa nccagcacct accgacaggg gtggagctgg gtcaagaatg 60  
 gtgtggtccc tgctttgggg gaatgctggg gaggtagaaa gcccttcta acggggcgtc 120  
 actgcaatta ctgcttcctc tttcccataa aactccccct agtgtatcag aacccccaaag 180  
 gagtttcagt aagcggttct tctgttgtct cgggctgaga ctccagggga acctcaagct 240  
 cacatggccc tggccggggc cctgggcagg agcaggcgag aggtctgcgc ggccgctaa 299

<210> 18  
 <211> 363  
 <212> DNA  
 <213> Homo sapiens

<400> 18  
 gggatgtgt tacacatccg agataactac acaggcatcg accctgtcca cccggggatg 60  
 ctagaggggc tgcgctgggt ttactccagg ccatgggtgag agccaccgtg aacacagggc 120  
 tctctcctct gagctgcaga agctctgtgc cctgtcccct gccacaagtc acagactttc 180  
 ttcatgtgtt ttacctcatg ttaatgaagg agatcttctc caggggcttg atctagtggg 240

aaacagagga gggggggatt ttaaatttca gtccgtccaa ccctgtagat ctgctgtcct 300  
 acagtaacgt aaaggatcac caggtaaaac gctgcttctc ccggacgccg ccccgcaagc 360  
 cga 363

<210> 19  
 <211> 322  
 <212> DNA  
 <213> Homo sapiens

<400> 19  
 ccggcccgtc cctcttaata tggcctcagt tccgaaaacc acagaataga accgcgggtcc 60  
 tattccatta ttcctagctg aggtatccag gcggtctgga cctgctttga aactcctaat 120  
 tttttcaaag taaacgcttc gggctgcagg aactcagct aagagcatca gggggcgccc 180  
 aagaggcaag gggcggggat gggtggtggc tgcctctgtg gcagaccgcc cggccgctcc 240  
 caagatccaa ctacgagctt ttaactgca gcaactttaa tatacgctat tggagctgga 300  
 attaccgagg ccgctaagcc ga 322

<210> 20  
 <211> 255  
 <212> DNA  
 <213> Homo sapiens

<400> 20  
 taataagata ccaaatcggg cgagaaacga aaagctcctg gcctccgtat ttggggccag 60  
 agacaccgca gggagtcagg tccccgccga caaatcgga gaggcctgcg ggagttagcc 120  
 agataatgct ctccctgtcc taccggtccc caccaatttg ccttttacct gccgcagagc 180  
 ttgcttgaac caaagggggt tgcggtcttc tcctctcaa cttgcatcc ccaggccttc 240  
 gcgtcccga gccga 255

<210> 21  
 <211> 406  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> unsure  
 <222> position is 6 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 7 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 18 nucleotides  
 <223> "n" refers to an undetermined base

<400> 21  
 atgtgnnaag gctcgcntc catttctctt ttctctctc tccctctctc atgtgcggtc 60  
 tccctcaaca tccaaaccaa cggagtgcgt ctgaggtgaa atcgtgccag acttagagac 120  
 ggctgccagg tttctctcaa gtcttggctt aacaaaagaa agcaaattac aaaaatggaa 180  
 attttcaaac tagcgttcag tggattcaa atcgacgttt gggtagcgca caggcacaga 240  
 ccgcattcgt gctatcttct gattaaaatg atacaaaaa tacctccttg ctttggtttt 300  
 cgtcttcgaa aacgacttct ttcttctctc taatttcccc ctacttttg ggagcggcaa 360  
 acccctgacc actctagaat tgctaacatt tggaccggcg tcgcaa 406

<210> 22  
 <211> 210  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> unsure  
 <222> position is 10 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 13 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 14 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 25 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 40 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 46 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 47 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 50 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 76 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 95 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 207 nucleotides  
 <223> "n" refers to an undetermined base

<400> 22  
 gcacggttcgn gcnncgtgta ccatnagctg ccaactggan gcaccnnggn aagggtgggg 60  
 gcctcctgga gacttngggg agagggatag ccgntaaag ctctgtcct ttctataggc 120  
 ataagcgggt ggtcaccacg gattggggat cccgaatccc tggctccaga tagacttaat 180  
 gaagaagcac ctggatccgg gccgcncaa 210

<210> 23  
 <211> 310  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> unsure  
 <222> position is 9 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 11 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 32 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 79 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 80 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 120 nucleotides  
 <223> "n" refers to an undetermined base

<400> 23  
 tcacgcttnc naaggctctg aatcctgagg gncagatctc caagaaggag ggaggctggt 60  
 cctagttccc gaggtcctnn actaggtcta gatcactggg taaaagaagg ggagcggcan 120  
 cacgtatggg gtaggcgctc tcactactca catctcgaga cctttgccgg cgtagggctg 180  
 tccgggggga acgacccgcc ttttccggta tcggttgta tggcggcgcc cagcccagcc 240  
 tggttttttc cggtagccaa ttgaactaac aaccccgttc cctttaggac taatctgtca 300  
 cgtcggcgca 310

<210> 24  
 <211> 304  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> unsure  
 <222> position is 13 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 74 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 266 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 269 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure

<222> position is 292 nucleotides  
 <223> "n" refers to an undetermined base

<400> 24  
 ctctggtctg tgntggatac gcgtggttctt ctgctggagtt aaagggtcgg ggacgggggt 60  
 tctggactta ccanagcaat tccagccggt gggcgtttgg cagtcactta aggaggtagg 120  
 gaaagcagcg agcttcaccg ggcgggctac gatgagtagc atgacgggca gcagcagcag 180  
 ccagcaaaag ccctcgcaaa gtgtccagct gctgcactgc cgcggggact cccacagcac 240  
 catgactagt tcgtgcgact ctgcancanc aaacggcttc cgaggaacac angatcgcg 300  
 gggca 304

<210> 25  
 <211> 379  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> unsure  
 <222> position is 6 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 10 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 13 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 19 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 21 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 31 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 113 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 184 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 206 nucleotides  
 <223> "n" refers to an undetermined base

<400> 25  
 aaaacncatn tgnagagcnc ntcggcagag ncgcagctgg ctgacccagg agaaggcgcg 60  
 ctgggtgtgg ctgggacggc caaggccgcg gcttcccgcg tgggatgcg ctntggcgca 120  
 aagctggtcc cggcggggcc aggcgtttgt gggcgggtga cgggatcta ggccttccgc 180  
 tcgngattcc tcttgggctg tctttncggg tttggactcg cctgccaggc tgtgtgcagg 240  
 gttcccgctg cctctggccg gcaggcgtcc gggctgcagg tgggccggca ggcaggtgtt 300  
 agcgggaagg gagcacaggt agcgaggtgg gatcggcgac ctggctaggg tgtcggcaga 360  
 atggaatgcg cggccgcta 379

<210> 26  
 <211> 625  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> unsure  
 <222> position is 8 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 18 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 50 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 64 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 609 nucleotides  
 <223> "n" refers to an undetermined base



<220>  
 <221> unsure  
 <222> position is 616 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 618 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 621 nucleotides  
 <223> "n" refers to an undetermined base

<400> 26  
 gggacgcag ccagggantt tgatccgttt tgaatgaaaa gaaagagaan ccaaaccaaa 60  
 cctntcagtc atccaaaacc ttcaggcttc caggagggtt ttgctataat tttctctaag 120  
 catgactggt tctgggggag gggaaagggg tggttgtatt tactgaaaat tcaaatcgaa 180  
 ataataaatg gccaaatttg gacacttacg gacccaaaca gttttgctca cgccagagaa 240  
 accgagagca cagggttgc gtgaagccta tctcggcaga aggcaacatt ctaataaagc 300  
 ccgtgggaaa acagattaca ttttcgcat gaataagtca tgcagtgaaa aatattgcct 360  
 acagcctgtc gacttatatt attatcacgt ttttcaactc ggcgtgagga gggagaggag 420  
 tgttcatatt tgactaggaa ttgcaggatc gatgcaaact ccagggcagc agccagactg 480  
 gcatatgtgg ggctctcggg ttactttctc tgtatgtcgc gggtgagagg aacagcgagg 540  
 acaatttagc gcaaacacac gaagggtcgg atctcaaggg ggcagcgctg ggagaaaggt 600  
 tagggctgna gagcgnanag ncaaa 625

<210> 27  
 <211> 499  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> unsure  
 <222> position is 2 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 7 nucleotides  
 <223> "n" refers to an undetermined base

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<400> 27
gnctccncgt tcccctcggg cggaacggag gcaactttcc ggagtctatt tttgtaaga      60
caatcaactc caataactga gctgaagttt ttgtttaaaa agaaaaaat ctgataagtg      120
atgattttac ctacttgtgg aactagatt tcaattagga aggttttttt aaacggcttt      180
ttgtaacttc gctgcaggaa gcaggtttgt ttctttttct tttcttttta agagaagggtg      240
tatttcaactg gtgcaatggc ttggcacctc cggggcctgg gaggacctca gacctcccca      300
gccctggggtt tctccgtctt caagaccaac taggaagggt caagcgggga gagggagtgg      360
agggtcaggt gagatctcag agctgccccg gccggcccc gtctctttct acctcctctt      420
ccagagaacc agcggctcac accttctca acgcaggaca tgctcggcgg ccaaagccga      480
attctgcaga tatccatca                                                    499

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<210> 28
<211> 561
<212> DNA
<213> Homo sapiens

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<220>
<221> unsure
<222> position is 20 nucleotides
<223> "n" refers to an undetermined base

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<220>
<221> unsure
<222> position is 21 nucleotides
<223> "n" refers to an undetermined base

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<220>
<221> unsure
<222> position is 23 nucleotides
<223> "n" refers to an undetermined base

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<220>
<221> unsure
<222> position is 26 nucleotides
<223> "n" refers to an undetermined base

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<220>
<221> unsure
<222> position is 39 nucleotides
<223> "n" refers to an undetermined base

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<220>
<221> unsure
<222> position is 40 nucleotides
<223> "n" refers to an undetermined base

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<220>

```

<221> unsure  
 <222> position is 44 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 49 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 65 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 80 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 98 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 107 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 471 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 484 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 544 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 559 nucleotides  
 <223> "n" refers to an undetermined base

<400> 28  
 gggcgattgt tattcaaacn ngntanctct ctgcggggnn gagnaatgng ggcctcgcac 60  
 ggctncatcc ccgtcgagcn cagggcctcc ctgttctnct agacatncca aggagccaac 120  
 tcctccgcag aagttccccg cttctgctct tatttccaag cttcgcgctt tctacaaact 180

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ccctgttgcc ttgactttga tttccagccg tggtgagggt cagagtgaac cccggcgcgc      240
tccccgacgg catccccgca caccaggata ggagaaattg gagggcctgg gcctcggctc      300
ccgcagtcgt cggaggaaga acccaccgcg gggcccccaa gggaaagtga agaggcccgg      360
gattttttcca aagcgctgcc aggaccccgga aggaagggga ggagtcacct gaagccgggg      420
aagctccttg ggtgctctcc ttggatcctt atgttcaactg actttcgcga ngccccctgg      480
aggnggaaaaa tccgcgctgt ttcccccaac ttaacttcac gcggccgcta agccgaattc      540
tgongaaatc attacactng c                                                    561

```

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<210> 29
<211> 717
<212> DNA
<213> Homo sapiens

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<220>
<221> unsure
<222> position is 643 nucleotides
<223> "n" refers to an undetermined base

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<220>
<221> unsure
<222> position is 651 nucleotides
<223> "n" refers to an undetermined base

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<400> 29
actotccgcg gtntontggt gcctcacagg aggtggggct ccctccacc ggtccccagg      60
cctctccctc tgcccgagct tcccggctct gcctccttcg cctcgcctgc ctgccgact      120
ctgaaccctg ctcctcttct aactaaaagt cagtgtttta tttcctccgc agtccaatgc      180
ccgcgtttta ccttatcca taagaagggc ttcatttatg gcaagacagg acagccaggt      240
aataagggcc tctgcacacg cgggccatt ggaggggagg aactgcgaag tcttcccga      300
agagcttcct ggagagaagg ggaacgagcc agcgtttatt gagcatctat tatactaagc      360
atctgcttgg cagttcacga cggtcgcatt tttcctcct tacagcgatc cctattgtgt      420
cgcttgcttt aaagcctcac agctcacaaa gggctgggat ttattccaga tctctctctc      480
agatgccatc tcacttccag gtgtctctgc tgctttgaac gcgggaaacc cacgcaaagg      540
agtgatttcc aaggccttct gtttgggaata tctttaatcc tccccttatt aactggaaaa      600
actccaagc atccttcagg gctcagctca aatgtccttt atntctgcag ngaaactttc      660
ccaaggaaaa ttagttacac agctaatttt agataaattg agccagttga tagaatt      717

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<210> 30  
 <211> 280  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> unsure  
 <222> position is 30 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 189 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 192 nucleotides  
 <223> "n" refers to an undetermined base

<400> 30  
 tgatggatat ctgcagaatt cgggctttgn gacgccgggc acgcagtagg gaaaacagta 60  
 ttaaaacgcc ctacagaaaa tctcggcgaa gtccccggag aactctggtt tctaagatca 120  
 gctggggcgca ctttctccgg gacgtccctt cttctcggtc tcagcgcctt cctgccctca 180  
 gccgcgcng tnttgttttg gtggcaaact gaaataagaa atggaaatat attggccttt 240  
 gctgctgcca gggatgagag gttgttgacg tcggcgcaaa 280

<210> 31  
 <211> 270  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> unsure  
 <222> position is 2 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 5 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 6 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 8 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
<221> unsure  
<222> position is 9 nucleotides  
<223> "n" refers to an undetermined base

<220>  
<221> unsure  
<222> position is 11 nucleotides  
<223> "n" refers to an undetermined base

<220>  
<221> unsure  
<222> position is 12 nucleotides  
<223> "n" refers to an undetermined base

<220>  
<221> unsure  
<222> position is 24 nucleotides  
<223> "n" refers to an undetermined base

<220>  
<221> unsure  
<222> position is 26 nucleotides  
<223> "n" refers to an undetermined base

<220>  
<221> unsure  
<222> position is 27 nucleotides  
<223> "n" refers to an undetermined base

<220>  
<221> unsure  
<222> position is 29 nucleotides  
<223> "n" refers to an undetermined base

<220>  
<221> unsure  
<222> position is 33 nucleotides  
<223> "n" refers to an undetermined base

<220>  
<221> unsure  
<222> position is 36 nucleotides  
<223> "n" refers to an undetermined base

<220>  
<221> unsure  
<222> position is 227 nucleotides  
<223> "n" refers to an undetermined base

<220>  
<221> unsure  
<222> position is 244 nucleotides  
<223> "n" refers to an undetermined base

<220>

<221> unsure  
 <222> position is 245 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 264 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 265 nucleotides  
 <223> "n" refers to an undetermined base

<400> 31  
 gnggngngna nncggcgatg gatntnngna ganttnngtg atggatatct gcagaattcg 60  
 gcttagcggc cggaacaaa gagcgaacca aaggatgctt cgaattttta aaacggaatc 120  
 tctgcacca aatgcaggac tggtgactta aggagctgcg aagtctgatt taccgggctt 180  
 actctcgacc tgccccccac cccagctca gggggacctt tttatcntga acgccagagc 240  
 tacnaccaa gtcgggtggc cacnnccaaa 270

<210> 32  
 <211> 347  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> unsure  
 <222> position is 7 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 8 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 11 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 50 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 309 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 313 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 322 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 325 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 331 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 336 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 337 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 338 nucleotides  
 <223> "n" refers to an undetermined base

<400> 32  
 tttggannta ngggggcgtg gcgtggatcc agtttcccc gcccaggtcn gcttcccgg 60  
 ctcaaccatt tcgcgctctg ctctgtccgc tggtttgtcc ctgcccggtt cctctcccc 120  
 ggctgtcag cctccgcttc tctggagggt cctgggactc atctctgatc caccgtcttg 180  
 cgttctctgg gcgcatcgac ttctctccat cttcgggctc actcctgact ccctcgtgc 240  
 cgccccgggg gtttccacgc gtgtctctaa ccgcgccgc taagccgaat tctgcagata 300  
 tccatcacng aantctgcag anatncatcg nccaannca ccgact 347

<210> 33  
 <211> 342  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> unsure  
 <222> position is 193 nucleotides



<223> "n" refers to an undetermined base

<220>

<221> unsure

<222> position is 299 nucleotides

<223> "n" refers to an undetermined base

<220>

<221> unsure

<222> position is 300 nucleotides

<223> "n" refers to an undetermined base

<220>

<221> unsure

<222> position is 301 nucleotides

<223> "n" refers to an undetermined base

<220>

<221> unsure

<222> position is 302 nucleotides

<223> "n" refers to an undetermined base

<220>

<221> unsure

<222> position is 325 nucleotides

<223> "n" refers to an undetermined base

<220>

<221> unsure

<222> position is 328 nucleotides

<223> "n" refers to an undetermined base

<220>

<221> unsure

<222> position is 337 nucleotides

<223> "n" refers to an undetermined base

<220>

<221> unsure

<222> position is 338 nucleotides

<223> "n" refers to an undetermined base

<220>

<221> unsure

<222> position is 339 nucleotides

<223> "n" refers to an undetermined base

<400> 33

gtagggcgcc gccgtgacag attagtccta aagggaacgg ggttgtagt tcaattggct 60

accggaaaa accaggctgg gctgggccc cgccatgaca accgataccg gaaaaggcgg 120

gtcgttccc ccggacagcc ctacgccggc aaaggtctcg agatgtgagt agtgagagcg 180

cctaccccat acngtcggcc ggctcccctt cttttacca gtgatctaga cctagtctag 240

gacctogga actaggacca gcctccctcc ttcttgaga tctgaccctc aggattcann 300

nnctttgctc acgagctcca acccnacnca tccaaannnc aa 342

<210> 34  
 <211> 370  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> unsure  
 <222> position is 325 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 343 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 361 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 368 nucleotides  
 <223> "n" refers to an undetermined base

<400> 34  
 cattgtttac tttcgtctaa acgcggtgga agcccatgga agaaagcggg tagcagcaag 60  
 gcagagccct gctccctctg cagccccagc tcccagcgcc ctgggctttc caggcacctg 120  
 tccgggtagg ggattgaggg ccgtggccag gcccgcaact tcttgctagc cgcagctggc 180  
 cacatgcca tctgaccctc cgagttctcc tctaaaaatg gggctgacag ccgtacctc 240  
 acaaagtcca caccgggctc aaccgntgc ctctctccc aacaggactc tgccaccctc 300  
 cctcaggatg cctgagggcc ccganctgca cctggccagc cantttgtga atgaggcctg 360  
 nggggcgntt 370

<210> 35  
 <211> 213  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> unsure  
 <222> position is 8 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure

<222> position is 10 nucleotides  
 <223> "n" refers to an undetermined base

<400> 35  
 aaaatacnan taaagcgatg cttcgaattt ttaaaacgga atctctgcac ccaaatgcag 60  
 gactggtgac ttaaggagct gcgaagtctg atttaccggc ctactctoga cctgcccccc 120  
 acccccagct caggggacct ttgtctgaa cgccagagct actgaccagg tcggggggcc 180  
 gcggcccaag cgaattctg cagatatcca tca 213

<210> 36  
 <211> 173  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> unsure  
 <222> position is 4 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 5 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 100 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 109 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 123 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 144 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 156 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 160 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 162 nucleotides  
 <223> "n" refers to an undetermined base

<400> 36  
 gacnncgggt ttgtgtgtaa cagggtcagt ccccgatatct actttgcgaa agcttcgagg 60  
 cgagcgtgaa gtcaagggct gcggtggatg ggggtaaaan gcctcctcnt cccactgcct 120  
 genccgtctt ggggtaacct ctancccca cccgnggtn cnccttaatg ctc 173

<210> 37  
 <211> 369  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> unsure  
 <222> position is 22 nucleotides  
 <223> "n" refers to an undetermined base

<400> 37  
 tcaactgtgcc ggggtctctcc tncccgggtcc aactccetta cttgtcctca tctctgtccc 60  
 caaggtccgt gacccgcgga ggtgatgggg gggataggag agccccaggg accgcagagg 120  
 tgacacaatc gcccgcccgt cctccctcgc tgggagccga ttcagcctgt gccgagcctc 180  
 tcccttcgcy tgctctgcy cacagcggty gcaccgcagg actccgggty cccccgggct 240  
 ctccatcggg aagccggcaa atgcgcttcc tcagccagac cgcggcgggg tgggggcggg 300  
 gggggcgga gttgaaatac tgggacagaa acacctgcc gtcccaaggg acggaact 360  
 ggatgcaa 369

<210> 38  
 <211> 123  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> unsure  
 <222> position is 20 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 29 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure

<222> position is 41 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 87 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 108 nucleotides  
 <223> "n" refers to an undetermined base

<400> 38  
 gtcccttcgc cccgcttttn ctttcccna ggtcccagcg nccgaaccgg cggatgtcca 60  
 cgaaacatag ggcgagccgg gggccangcg gggccgtgta aaatctcntg tggtcatttt 120  
 gtg 123

<210> 39  
 <211> 450  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> unsure  
 <222> position is 32 nucleotides  
 <223> "n" refers to an undetermined base

<400> 39  
 ctagccctgg aagagaatcc gaggctcagc cntgctgcag caccaggac actgcatccc 60  
 agcacctgcc cgaagatcag cccaggaccc aaaggaaagc aggctccaag ctccccggaa 120  
 gccaaagaaa ataggaaaac atatcctgcc ccggggacac cttctggaac tatgaccaca 180  
 tgcaactgac cttccggaac aatcaccgca tgcacctgac ctcccggaac tgtcaccacc 240  
 gcgcgcacct gacctcccgg cactgtcacg accgcgcgca cctgacctcc cggcaactgtc 300  
 atcaccgcgc gcacctcacc tcccggaact gtcaccaccg cgcgcacctg acctcccggc 360  
 actgtcacga ccgcgcgcac ctgacctccc ggaactgtca tcaccaggcg cacctgacct 420  
 cccggcaactg tcacgaccgc gcgcacctca 450

<210> 40  
 <211> 593  
 <212> DNA  
 <213> Homo sapiens

<400> 40  
 ggaccaagct gggtaaactg ccgacagctc cattgggcag catgtccacc cctgatgacc 60

aaatcccacc aaacgtgcag ctggcaactcg gccgcctttg tttccttccc ctagaataaa 120  
 actccgctgc tttcccacgt tcttgagca gcagccggaa taaagcgccc atggccttgc 180  
 cctttgagtc tcggaggatg tttgccactc caacaatgga cttttaaata attcaggggt 240  
 caaaaggcgt gtgtgtgggg ggggagaaaa gttacaaatc agcacttgaa accgaacaca 300  
 aacaaaaatc aaacaaatcc gaactaatat aacaaatcaa aactttgatc tttagaagaa 360  
 aacttcaacc ttaatgcttc caggaggaaa gcagaaagga taatgactga attgtgaaaa 420  
 cgagccaaaa tgttccacca ctgatgtcac acacacctat gactccctgc acagatccac 480  
 ggtcccgggc gctgaatccc cgcaaccctc tgcgcccaca gaggttaaac tctcgtctgt 540  
 ggcgacttcc gcttctggc ctaaactctga caogcagcag tcccccgcg gca 593

<210> 41  
 <211> 457  
 <212> DNA  
 <213> Homo sapiens

<400> 41  
 accaccaacc aaatagggcc tttcctgtta acgaccacgc ggcaaggggg ccgggcctc 60  
 gcacgcctcg acggcctccc ccaactccaaa gggactccga tttcgcagga tctcccgcct 120  
 cccgcctctg ctcccacac cctacgtttt tctcttctc ctcatctacg tatttacaat 180  
 aaaacagcga agctgcacag tctgtctcta aatcaaacgc ggttaccatc aaagcctcag 240  
 actctatgtc tcaaccgcaa aaggctctgac aggaaatcaa ctcgggagtt tgtcaattct 300  
 ttaaaactcaa agctctgtta acgaaatctg gatctttctc cgtcctccac ctgcctcccc 360  
 tgacaggaga atgactgtaa aaggatcctg tctgccccga aagtcagcac caagcacttc 420  
 acaaattgtc aaatctcaaa agcttacacg cgcggca 457

<210> 42  
 <211> 211  
 <212> DNA  
 <213> Homo sapiens

<400> 42  
 gcctgacctg aatgacgcgc atgttgaggc cggctctctg cggcagctgc tcgaggatgt 60  
 ggcgggtggg cttgggtgta gcagcgaagg cggccttcag cgtctccagc tgcttggtct 120  
 tgatgggtgt gcgcggtccc cgcgcttgg cggccagggt ctggctgtca ttctcgttgc 180  
 taccgccttc cttgtccgac acgtcggcgc a 211

<210> 43  
 <211> 141  
 <212> DNA  
 <213> Homo sapiens

<400> 43  
 aaatcatctc cgggggcccga gcacggacac gtcacagacc cgtgagttcc ccagcgccgt 60  
 gccgggaggt caggggcgct gaaagaagga agaattcagc cacctctcag catccctggt 120  
 acctcgagga cgcgcctctc a 141

<210> 44  
 <211> 559  
 <212> DNA  
 <213> Homo sapiens

<400> 44  
 acccactttc cattaacact aaataaaacg catccatgga tttcctctcc attccgagggc 60  
 aacaggagtg catggcacat tgcctactc cctgaagct cttcgctaac ctaagactcc 120  
 aggggtgagga agttagctgg agctttttaa agtgcattc caaagagaat tttgctcaca 180  
 ccatgagagc cccaagaaa caccagggcc cccttagatg ccgagacca cgccctccag 240  
 gaataagccg caccctctgc ccagcagatc cttgcgcgag tagccctctt tccctggggc 300  
 taatcaagtg catgccacat gtcaccactc tcagctggca attcttcctc agaggcgcag 360  
 actttcacgg aatccccagc aggggggggtt aagagattca ggggaggccc cgcccggtgc 420  
 ttccacaaaa gtcgctttac cgtggctcgt gtccctgcggc cccaaggggg tagcctggga 480  
 cgtgtattgg gagggcatag aggtccttc caggacaagc tgccagcctc cagtggggcaa 540  
 ccatgtgaga ggcaaaatt 559

<210> 45  
 <211> 433  
 <212> DNA  
 <213> Homo sapiens

<400> 45  
 gcgaacagca caaaggcttc attcctacga gagattaagt tttagagcaa atggacacga 60  
 tcgttaaaga atttgatatt tccatgtaaa ctgcattagc aggttatgcg atccaaaactc 120  
 acaggaacaa ctccaactct cggccatgcc ctatttcattg tctagatttg ttttaaccgac 180  
 ttacatcata atccaagaat acgaactaca gtatattctt acagcaaagt tattccttaa 240  
 aagcaaaacc gagccacctt tgaaaacacg cacacacatt atccacggca ctaaaacccc 300  
 agtcttgacc gagaaagacc aacaacttg gggggaagaa aacaacttca gagccagagc 360

tcccaaagca gaaagcgctg ggggctgaag ggcacacgag gttccgctcc cgggcgaacg 420  
 ggcggcgtcg caa 433

<210> 46  
 <211> 487  
 <212> DNA  
 <213> Homo sapiens

<400> 46  
 cccttagtat tccatgagcc accatthttcc ccacgatccc tccagcctga acgatcacat 60  
 cctactgtgg accacgactc tcccagcagc gggcgthtaa tatccagtta gcaggttctc 120  
 accacccccct cgctggctcg aatacagcat ctgcaccgag ttcccagaaa tcgtcaacct 180  
 agcaaattccc ttaattggtg gacatgaaaa tccagggtt tgtgctgtaa taacagagtc 240  
 ctgggggctt ggggagthtg tgccgcttg agctcaggtt tctgggacag aggctgagcg 300  
 cagggcaggg aggcaggtct cacctggcac ctcccagagt cctcgccgag cagatggaag 360  
 cagaggctct cgcgcccggc ccccgccggg agacctctct ctctttccct cggcctgctc 420  
 tgccctctcc cgccttctcc ctgtctgac cttctctgct gtcatttct ttgtcctcgc 480  
 gccccga 487

<210> 47  
 <211> 403  
 <212> DNA  
 <213> Homo sapiens

<400> 47  
 gtcatataag cacaaccatt cccagggcca cctggatgc atcagatcag tcccccaact 60  
 ggtgaccaca atggctggct cagagtgcct ttgaacagac aggagaaaca gacttcttgg 120  
 agggaggggac cttcccacag ggaatggcca aggagctagg tcttcagggc ttgcatggcg 180  
 tggagtgtgt gctcaggtgc acagtgaagc aaacctgagg ggacttgggc cctgctcct 240  
 ccagcacaca cgcacccttt cgccgtcaca tccggggcac ccaccctgg aatatgtgag 300  
 cgcacttgg ccagccacga gttccagggc caggaagtcg tgcttctcgt tcaggcgccc 360  
 gttgtagaag agcagcccgc tctgctgcac tctcgcgtcc cga 403

<210> 48  
 <211> 155  
 <212> DNA  
 <213> Homo sapiens



<400> 48  
 ggcgtggaga ggagggggca gaaactcagc cgcccctacg tttgctaaac tgcgtccgcc 60  
 agggggcgta tttttctaaa acgcacaaga cgtttcgtgg gttatcgatg gtctcttgag 120  
 cctccttgac tgatggggat tgaccgggcg ggata 155

<210> 49  
 <211> 256  
 <212> DNA  
 <213> Homo sapiens

<400> 49  
 tctactgagc ttttctttaa gtggaaccag aagtgcctggg atgagaggga aaggatggga 60  
 gtgcgtocaa aggtggacag caggtcccca tccttgggtgg gagtgagact ggacggcatc 120  
 ccccgaaag gtggtttggg ccttggacaa ggctagaggc aggagtccat gatgcagaga 180  
 tgacacagtg cccctccgcg tgtgagtcca cgaaggtcac tactgaggct ttgtgcttgt 240  
 aaaaggccgc cccgca 256

<210> 50  
 <211> 224  
 <212> DNA  
 <213> Homo sapiens

<400> 50  
 tgcggggtcg tgggggaacc ggcgggagct gttcgtggc cggcctcact ggagtaggaa 60  
 ttttagatga aactgagtcc gtttctcctt gaaggcaggc agtattctta gatctactat 120  
 tcatttaaaa agaaggaaaa gaaaaaaaaa tgactgctac ttactgagaa gaaaatttct 180  
 gttctctcc gattccgctg atcccgcctt atccgcgcac ctca 224

<210> 51  
 <211> 313  
 <212> DNA  
 <213> Homo sapiens

<400> 51  
 gtggctggga cggcccaggc cgcggttcc cgcgtgggga tgcgctgtgg cgcagagctg 60  
 gtcccggcgg ggccaggcgt ttgtgggagg gtgacgggga tctagggctt ccgctcgtga 120  
 ttctcttgg gctgtcttcc cgggtttgga ctgcctgcc cggctgtgtg cagggttccc 180  
 gctgcctctg gccggcaggc gtccgggctg caggtgggcc gccaggcagg tgtagcggg 240  
 aaggagcac aggtagcgag gtgggatcgg cgacctggct aggggtgctgg cagaatggaa 300  
 tgcgcgccg cta 313

<210> 52  
 <211> 385  
 <212> DNA  
 <213> Homo sapiens

<400> 52  
 tacgtttgcgc attcatttctg ccgacaccct agccggtcgc cgatgccacc tcgctacctg 60  
 tgctcccttc ccgctaacac ctgcttgcgc gccacactgc agccccggacg cctgccggcc 120  
 agagggcagcg ggaaccctgc acacagccgg gcaggcgagt ccaaaccggg aaagacagcc 180  
 caagaggaat cacgagcgga agccctagat ccccgtcacc cgcccacaaa cgcttggccc 240  
 cgccgggacc agctctgcgc cacagcgcat ccccacgcgg gaagccgcgg cctggggcgt 300  
 cccagccaca cccagcgcgc cttctccagg gtcagccagc tgcggctctg ccgaagcgct 360  
 cctccgctcc tttctcgcgc cccga 385

<210> 53  
 <211> 307  
 <212> DNA  
 <213> Homo sapiens

<400> 53  
 aacccggctc ggttcggcaa ggttcagggg gacaaggtag agaaggctgg ggtgagcaag 60  
 aagtcggggcg gccgatcgtc agggccacga gcctcgcctt gccttcttgg aatcccaccc 120  
 aactttaaag gcccaaagat cctgaaaatt ccgaaagcga aactgcgggc tggctccag 180  
 aagtttgaga acggtctccc aggctttcca gcgtcgtccc gggattctcg gacaccacaa 240  
 acgccatcaa ccacgagcac cgggtgtccgt ggctattgcc ccgaatggtc cccatccgcg 300  
 tccccta 307

<210> 54  
 <211> 182  
 <212> DNA  
 <213> Homo sapiens

<400> 54  
 cgatgtcgaa gccgtttggg gggaaacagcg gtttccaagt tcctgctgac ttgagaagcc 60  
 tctgcggggtt tccgaatctc cggcgcactc ctgggcgcgc tgcgggagct gtagctcagc 120  
 cagccagggg gtagcgggctt tcatccgccg ggaggagtct ttcgagttca atcgcggggg 180  
 ca 182

<210> 55  
 <211> 523  
 <212> DNA  
 <213> Homo sapiens

<400> 55  
 tcgggtttga tccgccccaa ccaaataagg cctttcctgt taacgaccac gcggaagg 60  
 ggccggggccc tgcacgcct cgacggcctc cccactcca aagggactcc gatttcgcag 120  
 gatctccgc ctccgcctc tgctcccaac accctacgtt tttctcttcc tcctcattta 180  
 cgtatttaca ataaaacagc gaagctgcac agtctgtctc taaatcaaac gcggttacca 240  
 tcaaagcctc agactctatg tctcaaccgc aaaaggctctg acaggaaatc aactcgggag 300  
 tttgtcaatt ctttaaactc aaagctctgt taacgaaatc tggatcctc ctgcctcccc 360  
 acctgcctcc cctgacagga gaatgactgt aaaaggatcc tgcctgctccc gaaagtcagc 420  
 accaagcact tcacaaattg tcaaatctca aaagcttaca cgcgcgggca ctccggaaag 480  
 gctgtgggga ccacccaaag cccccctc cacaccgcg gca 523

<210> 56  
 <211> 795  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> unsure  
 <222> position is 741 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 762 nucleotides  
 <223> "n" refers to an undetermined base

<400> 56  
 tttactttct tccggctgac gtccatctcc tcaaatttct caggaatgtg gggaagctcc 60  
 tagccctgcc tgcctttcta gagggcttct tggatttgca gcttctaaca agttgctctc 120  
 gccacggaga agctgttatt atgacaaaat atttggggca ttatcaaaat cacacaggct 180  
 gctgggctgc tgtcggtttc tcgccagggc cagtaagcag ttacatttgg agttgctacg 240  
 tgttgtttgg gggccgggct gtggagagtg actgagccag ttttttcat ccaaatttct 300  
 gcaaattgaa ttaaccacaa ttctagtctc acctcccgtc tttaaaaaaa taagttgaag 360  
 aaaaggtaaa tattagagat aaggcagcat ctagtactg cggagaggca caagctggtg 420  
 ggcgagggtt gggggagtca gcaaagccct tcaaacctc cccgtttaat tttctggctg 480

tctctgcatc ctggtgccag aattccaaat gcttgagtc atttanaggt gcgagaactc 540  
 aaacgtcgtt ccaacttgaa aggggaccgt ttaacgttaa attccattag cacctaaatt 600  
 gtttcttaaa gacatccgct cagacacagg actcgaaagc gagcatttca tgcaaataaa 660  
 tttctcaaat tttaaacctt gttaaaagct tgtctcgcac ctcggtccc tccccttccc 720  
 cggaaganaa caataggccg ntggcgcac cccaacttcgg antaaatatt gacgggggaa 780  
 gttgctaaaa acatc 795

<210> 57  
 <211> 438  
 <212> DNA  
 <213> Homo sapiens

<400> 57  
 gcctgtgtgt aggggactgg aggtggggga acctgttctt ttcttgtgtc tgatcctggg 60  
 gctcgcttcc tgggtcctag aacagcagcc aggaocggaag aaactgttca cgttgcaccc 120  
 ctttctctaa gattcccagg ccaagagtag ctgcagaagg tggccctgaa tctatggcct 180  
 ccttctctct gcctgacccg gctagtggat ccggagaggg gaccagggag agctcctccg 240  
 agcagggggtc cttcgggaga cagagagggg tccaggctga gagaactctt caagcatggc 300  
 gagtctgcgt tatagaatcg ggcgggcggc tcaacttggg ggaagcacca agaagagctg 360  
 ggcgacctgg agcgcagaac cggctttggg gagccaccgg gcggggcagg ggtagcacgg 420  
 agcccggggc gcggccca 438

<210> 58  
 <211> 611  
 <212> DNA  
 <213> Homo sapiens

<400> 58  
 gcttccccct tcctttctcc cgcgctgccc cettgagatc cgacccttcg tgtgtttgog 60  
 ctaaattgtc ctgctgttc ctctcaccgg cgacatacag agaaagtaac cggagagccc 120  
 tacatatgcc agtctggctg ctgccctgga gtttgcacg atcctgcaat tcctagtcaa 180  
 atatgaacac tcctctccct cctcacgccg agttgaaaaa cgtgataata atataagtog 240  
 acaggctgta ggcaatattt ttcactgcat gacttattca tggcgaaaat gtaaactggt 300  
 ttcccacggg ctttattaga atgttgccct ctgccgagat aggcttcacg caagccctgt 360  
 gctctcagtt tctctggcgt gagcaaaact gtttgggtcc ataagtgtcc acatthggcc 420

atttattatt tcgatttgaa ttttcagtaa atacaaccac ccctttcccc tccccagaa 480  
 acagtcatgc ttagagaaaa ttatagcaaa acctccctgg aagcctgaag gttttggatg 540  
 actgagaggt ttggtttggg ttctctttct tttcattcaa aacggatcaa actccctggc 600  
 tcgcgtoccc a 611

<210> 59  
 <211> 291  
 <212> DNA  
 <213> Homo sapiens

<400> 59  
 gagtttgga ggcgccgat tccacaaagg agtaggcgcg gccagccgcc tccagccctg 60  
 agctcagtaa attcgggtgc ctgaatgctc ccttcctgct cttaccactg cgagctctct 120  
 tgggacagct ttctaggttc cactgcgacc tactttccgc tccctgagtg cttctttgct 180  
 gaaactgcag gcgaaaagat ctctttccca gaccgcagcg cactttgaga aggggctcaa 240  
 agtcgcccgc tctgaatccg gcaccggcaa ataggagtag ccgcatgcgc a 291

<210> 60  
 <211> 226  
 <212> DNA  
 <213> Homo sapiens

<400> 60  
 gaaaacagat aaaacgccct acagaaaatc tcggcgaagt cccggaggac tctggtttct 60  
 aagatcagct gggcgcactt tctccgggac gtcccttctt ctcggtctca ggccttctc 120  
 gccctcagcc ggcgcagct ttgttttggg gacaaactga aataagaaat ggaaatata 180  
 tggcctttgc tgctgccagg gatgagaggt tgttgacgct ggcgca 226

<210> 61  
 <211> 580  
 <212> DNA  
 <213> Homo sapiens

<400> 61  
 ctgtgatgca ctcgccgat ctcggtggca gctgcctcct tcatctccag tgacgcctgc 60  
 atgctgtcct aggcagtgtg aggagtgaag atgagatttg gcgcatcttt caacggagtc 120  
 tgagcaaagc taaagggtc cgattcgtgc aagccaaggg ctgcccctcc taccctgtcc 180  
 tccttgagga cctgtgctaa ggcttttctca tccaccagge caccatgggc tgcgttcaca 240  
 aggaatgctc cctgtotcat ctgctttata gtaaagtcac tgacgaggtg gtggttatgt 300

tcattgagat tgctgtgcaa cgagacacag tcaactctgat acagcaaacc ctgcaggggtg 360  
 tatcagggtc ccctctgcat gccctgggac ctctctatct tgtcctacaa gtaggggtca 420  
 taaaatacga cgctgaatcc aaaggccttg gctcaaaactg caaccgcctg cctcatgcaa 480  
 ccgaagccca tgaggcctag cgtcttccac gaatgagggc cactcccatg gccacctcga 540  
 gaatctgctc cacgctctga acccgcgcac ctcaagccga 580

<210> 62  
 <211> 633  
 <212> DNA  
 <213> Homo sapiens

<400> 62  
 gccagggaga agccctccac ggtgggctc ctcttagaca accagcacc cctgcaggca 60  
 ccctcgtctg gcagaatcag ccctttccca cctgcaggcc cttctcagcg cctctgactt 120  
 cccacacaca gcacaggtta caaactggtc cctggcagtg cactctagcg ggctctctc 180  
 acaagttctg cgggcctcgt ttcattgaaa gggggttg gattcctgct gcccttggat 240  
 ggcccctgcg cacgcacacc tctgagcggg cactgagcga gcgtggggag ctgctccctg 300  
 ggaactagge aggagctttt aaacaccctt acacacagcc attctgcggg aatacatgct 360  
 ttcccggtaa ggcttttact gttcattcca ggtaaattgg aagtcgcaca cccaagctc 420  
 caaatacaac tcgtttagctg gcaggctctt gaagccaatt ccttctgagg aaaatggaga 480  
 taatagcagc taccctccca ggtgactggg ggagaataaa gtggctgtgc atagtgggtg 540  
 ttgcagctgg tggctgctat tctcttcat tacagcttgt aaaaagggtg totagggcat 600  
 ttacacacag ataggccggg tggggtaagc cga 633

<210> 63  
 <211> 703  
 <212> DNA  
 <213> Homo sapiens

<400> 63  
 gcctatgaat ggatttataa ttgctttatt tttgtcccat ttagacagaa gtcagagaca 60  
 gaggagagaa ccaaaaaact tggatgtttc cgtaaaactag attcgtcaat cctcgataat 120  
 tgaaagtagt tccagtatgt cagccaccgg ggttccctgg ggagctaacc agtcctgaag 180  
 gaagtatgaa gaggaagagg aggtcttcag ttaaggggat gaatttgtgc agtcctaagc 240  
 cctgcaaagg tgctggaggg aggaagaagg gcaggaaata aaagatggaa gaaaatttgt 300  
 tttttatcca cttagagttt tatctttaat gatgggaaac agtgctgctc tcaggaaact 360

cagtgtggag atctaggagt tcacggttca tagtccatta ggagcaggaa aaggatagag 420  
 gacatttata aagtaacatc caagtccaaa gtaaaatggg ataaattggt tcccatgata 480  
 aaggctggct gagtaggtca ggaaaggtct tgtcagacca tatgtgctgt ttcaggctgc 540  
 ttcaaattct tttaggacag tgggtgatat gagtgaagac ggggcaggca ggccacatct 600  
 cttagaagag gaagtgatt gccacgtctc cttcctocat gctgatggca aggcgtgcgg 660  
 gctgtgttct cttgcagcca gcgtcccatg ctggcgggcc aaa 703

<210> 64  
 <211> 420  
 <212> DNA  
 <213> Homo sapiens

<400> 64  
 gtgacgtgcg gaatacacgt gatgtcgggg acaggagcgg gctgaagagg gcacgatccc 60  
 acgcggaggc caccctcac ccgggtagg agcccgtgc acttgctgtc gctcagcccg 120  
 ggcgctgcac cacggcagcc gccatgctgc ttaaagccgg tcatgtgac cgggagccag 180  
 ggtggaaggg gtccccgcgg gcaagccttc gacacgtgac ctgccaccg actacggaag 240  
 cctcttgggc gttccgcccg ggctcacatg tcatgtgac gccggccggg cgcggagta 300  
 accaggaact ttcccagacc ctgcgggtccc tggagcgtca aaaagagcgt ccccgtagt 360  
 aggtggagtc gcctgccctt ccgaatctca gctgtcttat ctggaacccc cacgcggcaa 420

<210> 65  
 <211> 496  
 <212> DNA  
 <213> Homo sapiens

<400> 65  
 gcgctgcacc aatntagagg gtagaaaag gagttagaag caaagaggaa aaaataaata 60  
 aacaggcaac aaaaacccaa cccagccagc ctgagccatt tgcattagtg ttcatttagg 120  
 aaattagcag acgggaaacg ctggggagtg gactgggccc cggccttggg gactgcagag 180  
 cccgctcagc cctgggtggc tgggcccaca tggctgtcgc caggagcaca ggaggacca 240  
 gaggtggccg aggagcctc gccgggtcc ggtatgggtc ctggcccctc acaggtgcga 300  
 gcctggccca gtgactgtgg acgctgtggg agagcaggcc tccgatacgc agggctggga 360  
 ctgctgacct ggaaggtggt gccgggcgtg tctggtgaag gcgccgttg cagctagaga 420  
 gagacggcgg atggggtgac gccataacc acggtcccag ttttgaggct tgacggtgac 480

ggaaaaggac gtcggc 496

<210> 66  
 <211> 637  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> unsure  
 <222> position is 612 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 627 nucleotides  
 <223> "n" refers to an undetermined base

<400> 66  
 cgccgagccg ggatgagcaa ggcttcctgg aggagagggc cggcctgagc ttggaaggat 60  
 ggggaggagc cactggctac aagggtgtag aggtgagaac cagtgtgacc tgcccatcgc 120  
 tggctgtctc tgggtcattc agctgaaatg gcatctctga gctgagagga gtgttgctctg 180  
 taaggagcta ggcacagccc cccagtagag gggcggccca ggcacagccc atagccgcag 240  
 acttagtgag tctagctagg gagacagtag aggggccc aa atgaggacac aggtcaccaa 300  
 aaatcctggc caggtcctgc cactacctgg ctacagcacc tgcccccccg agcctcagtt 360  
 tccccattg gtggaatgga gtgaggaaga cgogcctccc ggggctgcga tggagaattg 420  
 agtcagagtc tgggggtgct gggagggctg gggagcagcc tccctgagcc tcagtttccc 480  
 tggctgggga atgaggacct tgctcgtccc ccctcataag gggagagctgt caggaaagtg 540  
 ctttcaacgc tgagccattt cccagtgtg cacaattagc tttccagagg attttgggtg 600  
 attctagagc tngagggctg ggggatnggc ggccaaa 637

<210> 67  
 <211> 595  
 <212> DNA  
 <213> Homo sapiens

<400> 67  
 gccctgagct cttgagggcc totgcagttc ttgggacaat totgggacta tatctttggg 60  
 ccttgggtgag atctagaggc totaaagtct ttgggagggg tcctgagctc cgtggacggc 120  
 agggctcttg gcaactcactt gcattcttga ggggtgtggt tggcctcgtc cgtgcaggtg 180  
 tagaatttcc cctgtagaga ggatgtctgt caagtagggt cacccttcat cacactccc 240  
 cccagacccc tgccctggcat tccctccagt gtttgcccca ccttgaagag ctgcacccc 300



atgcaggcga acataaattg cagaagtgtg gtgacaatca tgatgtttcc gatggtccgg 360  
 atggccacaa atacacactg caccacatgc tgcgggcacc caagcatatg gctactgaac 420  
 actacaggcc acagtgggtca tggggcaggg actctgggtca tagatgcagc tgagggactt 480  
 gggctgggga catgtgggtga tgggtcaggg atgtatggtt agcaacatgt gttcaagagg 540  
 cagtgttatg ggctagagac gtgtgggcat ccaccaggaa taagtgtttg ccggg 595

<210> 68  
 <211> 580  
 <212> DNA  
 <213> Homo sapiens

<400> 68  
 gagtcaggac ggaggacgcg gcaggtcaca gagcccacca agtccgaagc tggaaagtca 60  
 gattctttga tattcaaagg tggatcatct gtgctttttt ttttttatca gtctctcaact 120  
 ttttatccat catctaattg tgacagctta tttgccttta taccataaga tggggagtag 180  
 ggttgagatg aaatccaagc atcgtttccc ttccccgatg gtcgcctccc tggggtgaga 240  
 cgttcgacgt gtcagacttc accaagagca tctcccgcct cggtgagta atgaacttgg 300  
 aaacgattta ctccggcact tggttcctgt ctccataaat gcggtgctt taaagggaat 360  
 gtaaaaaggg ctgtaaattg gtattgattg ccggtggtct tgaagaacct caactgagga 420  
 ttgaccgttc cttggagtga aggctccgca ttcagacgcc tttcgcctta cgtcatcata 480  
 attgagaagg gaaaggagac gtgttagttt cagtctgatt atttaccatc aaggcataaa 540  
 cacttctcag aggcagcgga acccattaaa ccggcccgtgta 580

<210> 69  
 <211> 589  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> unsure  
 <222> position is 559 nucleotides  
 <223> "n" refers to an undetermined base

<400> 69  
 acacgggggg caacctcttg cacctggctc cctgccctcg gtgccacgtt tccagggttc 60  
 ctccacgtcg caggctgtgt cagcctcgct ccttccactg cagaattgcg gtccacagcc 120  
 tggatgggcc actctccatg tatccacctg tccctccgtg gctgctgggc tgagtcgctt 180  
 ctgatgctaa caagaggcgt ccggctggac taaggccccg gaagctgaga actggagggc 240

aggtgcgggc atcgggcaga gcagctccag caggcaggac ctggggcctc caccctgcac 300  
 ccctgtgccc cgcgtgtggc ggaaccgccc cgaggggagg ctgtcaccac ggtgacaggc 360  
 agccccacgc gagcctgaga accctcagcc cacctttttc tgtaatcaca gcaggcatct 420  
 ctccggcaag tcaatccagt tccagctggt gctgcctccc ttgcctcatg ggctttattt 480  
 tagaactctg agcaataata aaaaagacgc taccgctac aatagatgtg gcagagaatc 540  
 tggctcttca cttcatcana gatcacctg aatgatggt tgttgtaa 589

<210> 70  
 <211> 748  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> unsure  
 <222> position is 10 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 412 nucleotides  
 <223> "n" refers to an undetermined base

<400> 70  
 gctacatctn ctctacattc taactaacac ttgttatfff ctgtttttgt ttgtttgfff 60  
 ttaatagcca ttctagtagg catgaagtgg tgtttgcctg ctttttttga tggagggtgga 120  
 ggaatagggg ggaattggtc cttaaccatc aattaagctg ggggccttag acctctgtga 180  
 attggctgtg acaatagcta aaggaggctg ctacctcata ctgaagagat gtttcctaag 240  
 tttgtcaccg gagagggcac cgaaccaact tattgtcttg gaggaagaa gcagcaaggc 300  
 agaagacttg aacttctcag agaaaaaaaa agtctacaga cttcatttta tgctgtcctc 360  
 acacactact gaaagctcta ccctggggac ctggcttgac ttctaaccta cncctgtggt 420  
 atttaggaag agctcccagc tgctctgagt ctcagtctcc caatcagtga aatggaggca 480  
 atagcacctg cctggctgca tcgccccaca gtgctgcaat gagcatccaa cgagagaaag 540  
 cttgtcacct gtgttgcaaa ctaagttaca caaatgcagg cagtagcagc tagaagaaaa 600  
 tggttgggaa tctgaaaaga attaaagccc cccatgaatt tcttctcag cctcctccaa 660  
 aagccagggg ctgcttcacc ccgcctccag gactgctcgc tccagcattt ccggcagctg 720  
 ctgacagaat gtatgttgcg gctgtccc 748

<210> 71  
 <211> 599  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> unsure  
 <222> position is 491 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 522 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 538 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 584 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 596 nucleotides  
 <223> "n" refers to an undetermined base

<400> 71  
 gatgactggt gcccgagctg aggccacgac ccaaccccga ggaagggaga acagcttccc 60  
 atgaagggca tggctgctgc ccataatcc cagggcagga aataaaggga tcttggacta 120  
 ggcaatcaaa ggacttctc tcctctaag gccaaggagg aatgtggct gggactccaa 180  
 gctctgtgga tgccctggagg tgccagcagc tggggatcag ctggccccac ctgcagagcc 240  
 agccagtggc cccoctgcat ctccaagggt gggcttatgg gctccaagaa caggtgtttc 300  
 tcagggtaac ctgagccct acaacttcaa ccaagagagt gaaggggagc agccctggag 360  
 gccaatgagg agggggatta gtggtcactg atgacaaaga catccctgtc ccagagacca 420  
 gccocttggt agcagaagaa tggctgccgg gcaaaaggac ctgctatgcc ctccccatac 480  
 acatatcatg nacctgggg accctctgaa taacaggggg cngctttaga gtggcttnat 540  
 taccaacaag aggccagaa gggctagagc acacgatttc atgntcggcc gcatgncaa 599

<210> 72  
 <211> 614  
 <212> DNA  
 <213> Homo sapiens

<400> 72  
 gtgCGctatc acgactgttg cccgagctga ggccagaccc aacccccgagg aagggagaaac 60  
 agcttcccat gaagggcatg gctgctgcca ccataatccc agggcaggaa ataaagggat 120  
 cttggactag gcaatcaaag gacttcctct ccctctaagg ccaaggagga aatgtggctg 180  
 ggactccaag ctctgtggat gcctggaggt gccagcagct ggggatcagc tggccccacc 240  
 tgcagagccc agccagtggc tccccctgca tctccaaggt tgggtctatg ggctccaaga 300  
 acaggtgttt ctCagggtaa cctcagcccc tacaacttca accaagagag tgaaggggag 360  
 cagccctgga ggccaatgag gagggggatt agtggtcact gatgacaaaag acatccctgt 420  
 ccccagagcc agccccttgt gagcagaaga atggctgccc gggcaaaaagg acctgctatg 480  
 ccctccccat acacatatca tggcagctgg ggagccctct gaataacagg gggcgcttta 540  
 gagtggcttc attaccaaca agaggcccag aaggggctag agccacacga tttcatggtc 600  
 ggccgcatgc gcaa 614

<210> 73  
 <211> 552  
 <212> DNA  
 <213> Homo sapiens

<400> 73  
 aagcGccccac agatggccaa gcatgtggag gagagcacia tattttatTTT aaatatccaa 60  
 atacgaacac attcccgcac ggcaccaaca gccgcctgaa cacgcccgat gccggcttgt 120  
 gctTTTTccg ttttTgtctag aaatttgggt Tgcactaaat tctcagctga atgaagatga 180  
 gaaggggctg gcagaggggg tggctccagc tctctgagaa cctggctcct tcccgggtgg 240  
 cagggagaga tggcccctgg ggagacgggg agggTgcact gcctcatgcc caaaccacca 300  
 gcttctagtt gagaaatcag aattttctct gcagaataag gaaaaagcat tgtcaccatg 360  
 attcacgtgg agctggccac actcaggaaa ttcaatgggg tcccacaggg gctccgaggg 420  
 ggaaggagag ggccctgggac atgcccctcc agccatcatg gaacaggatg ggcagggccg 480  
 gccctcactg ctctctaaca gtgaaaagcc acatctccac tttggaaaac acaggcatgt 540  
 gagagcctgg gg 552

<210> 74  
 <211> 450  
 <212> DNA  
 <213> Homo sapiens

<220>

<221> unsure  
 <222> position is 378 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 403 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 409 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 440 nucleotides  
 <223> "n" refers to an undetermined base

<400> 74  
 tggaggcttc gaggggaagtg aggttcctc ggacacccta gtgggaaggc tccacgcggt 60  
 aatggaacca cgctgtgaaa cctttgcctt tgggtgtcat ggtggaagca aatcttagaa 120  
 gacatttaat ttaaaaaatt cagttttaa aaatgttgac ttaaaaagca gttttgaaa 180  
 acaacctgga attagcctga gatcgatgcc aactcttagc agtctgtata ctaaacacag 240  
 ttaacaact gtagctgctg gcaagctgga accttttgt aaagaagcac ataaaaagga 300  
 cagaactggt ggaaggtgca ctggtcttc cacatcgcca ccaggcgtt tgaagcgtgc 360  
 tgctgacacg ctactcanat gcttctgaa gccaaacaat aanaaaaanc cccattgttt 420  
 ccottgctgg gttttaccn ccatggtgga 450

<210> 75  
 <211> 432  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> unsure  
 <222> position is 417 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 421 nucleotides  
 <223> "n" refers to an undetermined base

<400> 75  
 ggacaatgag gagggggtgc acgtggaatc cccacggata ggccggacgc cgggcaggag 60  
 cctttgcagg ggtgcacagc ctctctgga agccctggtc gctgcctggt gctgctgca 120

ccctgcgggc tccgcagcgg tggagccagg cctgaactgc ctgctcttgg ccccgctgc 180  
ggccctctgc cctttgtctt gcccggtggg cccggggcct caagctggcc cggggttcct 240  
gaagttagct gacgatgggc tggcctctgg ggctgggtcg tgggccttgt gcaactggccg 300  
ccacgtcacc agcgcagcgg ctaccgcggg tgctgctgga gacgcgggat gcccgggctc 360  
gggctgtgct ggatcccctg gcgctgcgaa ccccgtagcc cttccaatc gcgggncg 420  
nttaaagccc ga 432

<210> 76  
<211> 501  
<212> DNA  
<213> Homo sapiens

<220>  
<221> unsure  
<222> position is 18 nucleotides  
<223> "n" refers to an undetermined base

<400> 76  
gacgagacct agccggcncc atgcgcgcct tgagcctggc gaacagttcg gctggcgcga 60  
cgcgctgat gctcttcgtc cagatcatcc tgatcgacta gaccggcttc catccgagta 120  
cgtgctcgct cgatgcgatg tttcgcttgg tggcgaatgg gcaggtagcc ggatcaagcg 180  
tatcgagccg cccgattgca tcagccatga tggatacttt ctcggcagga gcaaggtggg 240  
atgacaggag atcctgcccc ggcacttcgc ccaatagcag ccagtccctt cccgcttcag 300  
tgacaacgtc gagcacagct gcccaaggaa cgcccgtcgt ggccagccac gatagccg 360  
ctgcctcgtc ctgcagttca ttcagggcac cggacaggtc ggtcttgaca aaaagaaccg 420  
ggcggcccctg ccgttgacag ccggaacacg gcggcatcag agcagccgat tgtctcgttg 480  
tgcccagtca tagccgaatt c 501

<210> 77  
<211> 826  
<212> DNA  
<213> Homo sapiens

<400> 77  
gcgcccctgtg gggatgacgc accatcctgt ttgtttgcac caagtcattt atctcgtgca 60  
ccccaggggg ccgtgggtccc tgccggggcca tcatgtctgc ttcccttatt tgggttttct 120  
gccccctcac ttcattttctc acttcgcttt tctccttat ccctttgcag tottgctttt 180  
gggggcattg ctgagccagt aatttgaggg acacctcgtg gagccctagt gtggagccgt 240

cagagcctgg gtaggattct ccgtggtgag gtgctcaggg agacacagga gcattccggc 300  
 gcctgttcct tgtgcacatc cgcaagtgtc tgcaagtgaga ggcatgggtc ccatcttgaa 360  
 tgccaacaat gtggcaccca caccctactt gatggggccg agccacagct ggccagggtg 420  
 accaccatgg acgtgccaga ggcatccgaa acccagctct tgcccagctg ttccactgcc 480  
 aactccagcg ttagcaaagc agctctccct tgctttgtct tctacagcag agaacagatt 540  
 aaaagagaag ctgcaggcag agaaatgcct cttggagcca gatgcccacaa aggatctctt 600  
 tgaacaaagg gttgctcagg tcagcgttag ttcttgcat caagcaacaa aatcagagat 660  
 gctaacagtt ctacagattca ctccaagtga agactcaaag ctggatttat aaatccccac 720  
 agagccgctg tgcaagagta gagggccggt ttcaggatga ggaagccctc ttggaagcac 780  
 cgtcctccgg ctaacaagcc tccaacctac tgtcggcagg gagaac 826

<210> 78  
 <211> 433  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> unsure  
 <222> position is 16 nucleotides  
 <223> "n" refers to an undetermined base

<400> 78  
 tgcgcagctc cgcgangtgc ccggcgggccc cgaccctcag actcgttgt ccctggagac 60  
 caaccctagc gaccaggctc tgccggatcc cgtcggggtt caactcctat tccgaaggtc 120  
 ctttctcccc taatcacaac acccactcgc ctctttttcc tcctcttct cagcttccac 180  
 cgccgaccgg gcagccccag ttacccgata acggtccca aggccccgtg ttacattct 240  
 ttcccactgg aagcagaaat tatcacgccc aaattcctac ctgccttccc tggattcctg 300  
 gtttcctaag aaacggggtt ggcccacccc tgggcgttcg aacagtccac agaagcgggc 360  
 aaaggaaaga cgactcagtc tttcccctcc gccaatctct tctccgggac cacagatccc 420  
 agaagtcacc gcg 433

<210> 79  
 <211> 424  
 <212> DNA  
 <213> Homo sapiens

<400> 79  
 ggcggggccc accctcagac tcgcttgtcc ctggagacca accctagcga ccaggctctg 60

ccggatcccg tcgggtttca actcctattc cgaaggtcct ttctccccta atcacaacac 120  
 ccaactgcct ctttttcttc ctcttctca gcttccaccg ccgaccgggc agccccagtt 180  
 aoccgataac ggctcccaag gccccgtgtt tacattcttt cccactggaa gcagaaatta 240  
 tcaogoccaa attcctacct gccttccctg gattcctggg ttcttaagaa acgggttttg 300  
 cccaccctg ggcgttcgaa cagtccacag aagcgggcaa aggaaagacg actcagtctt 360  
 tcccctccgc caatctcttc tccgggacca caaatcccag aagtcaccgc ggccgctaag 420  
 ccga 424

<210> 80  
 <211> 285  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> unsure  
 <222> position is 14 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 27 nucleotides  
 <223> "n" refers to an undetermined base

<400> 80  
 caaccggggg gcanaggcga tcaaaantgg ggtgcgctgt ggtgggagac acgtgtggcg 60  
 cgggtctcat tatccgccct tttcacttcc tggactggaa atggcagacc atatgatggc 120  
 aatgaaccac gggcgcttcc ccgacggcac caatgggctg caccatcacc ctgcccaccg 180  
 catgggcatg gggcagttcc cgagccccca tcaccaccag cagcagcagc cccagcacgc 240  
 cttcaacgcc ctaatgggag agcacatata ctacggcgcg ggcaa 285

<210> 81  
 <211> 401  
 <212> DNA  
 <213> Homo sapiens

<400> 81  
 cagatatgta tcctctctt tccaaccctg cgtccctttg aggcctggtc ggcgttccca 60  
 acctgcccct accccaccaa cccctgtccc tttggccatt agtcccggat tatctagcga 120  
 tgccccgtgt accgtctggc tttgctgttt actccgcgct cggccagttg aggccttttg 180  
 tattttattcc tgattttctc ataggggtaa agtgccttcg ggaggatagg acaagtccca 240



tcctgttcat acgaattaca gctcggactt cgggcccttt tacactgcct tttgtatctg 300  
 ttaacttgcg ctaaaaacga ttcgggttctt ttttttgagg aaggggggttg gggggcggag 360  
 actctgtcgc ccagtcctga gggccgcggc gcgcaagccg a 401

<210> 82  
 <211> 268  
 <212> DNA  
 <213> Homo sapiens

<400> 82  
 atagcgcgca caactgtgtc tcttaccag gcacatgcac tatccctgat cccgggtgcat 60  
 gatgggaatg tagtcctgca gcctgtgac caaagggctg ggagtgttta tgagacagca 120  
 tctctcagca agcaaagcaa ggctgcaca gccccgcctt ttcctccagt gaggcgcaact 180  
 gttcattaag gagtgttcat gagattacat tttccatcaa gccagccag tcacgcacag 240  
 ctctacctct tcctctgccg ccccgcaa 268

<210> 83  
 <211> 989  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> unsure  
 <222> position is 878 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 884 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 918 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 929 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 973 nucleotides  
 <223> "n" refers to an undetermined base

<400> 83

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gggtaatggg ggtgaacaga gagggatgcc gaggccagct tgtagtgtgg ctggttgtct      60
tgtccatcct atggcacaac cctgtcacca cccagatfff gttaggagtc ctcccccaac      120
ttgagagtgg aagctccttt ggcacaaaaa ggggttctgc atcatcccc agcccccagc      180
cctgagcctg ggtctggctc tgaactagac ctccatgaat gaatgcacag catcagtggg      240
gatccaccat catggggaaa tagtagatac aggaatgatt ttccaaccag attacagact      300
atttcaagcc cagccagagc ctaccaggcc aacattcccc aggettgtgc ctctccgagc      360
ctcagattgc tcatccttca aacgagggac agctctgctg gcattacctg aactctaggg      420
tcctttataa gctcagactc cagcttagag cacacattga gaggtgtctg cccccagag      480
ccacatacgt gcaacagagg gtggtccaga ccccttattg gtccccatgg ggtttgagag      540
agaagcctcc agaocagctc aacttctccc tcatctcact taggcctttg cccccagctc      600
ttaggagggt gtcaggtcac agtgccccat ttcttttctc ttccccagaa atcatgcggg      660
ggatacctgc tcagacagga ctttcatgaa agccaggctg tgaggtgtgt tggggaatgc      720
ataattgata ggccatcgtt cggaggccct cctggaggac caaaatgtaa tcagcagtgg      780
cgagcttggt caogacagga attcctttta catcctgggtg aggccaaaga cctggcaagc      840
aagtcctctt ggtcattaaa gaagcatcct gacttgangc agnncacctt aggtcactgc      900
agccacaaaa atctttgntg ctggattcna aagtaggcat tggggctggg atctgggctc      960
tggcatcctt gancgtgtcg ggggccaaa                                         989

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<210> 84
<211> 250
<212> DNA
<213> Homo sapiens

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<220>
<221> unsure
<222> position is 37 nucleotides
<223> "n" refers to an undetermined base

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<220>
<221> unsure
<222> position is 40 nucleotides
<223> "n" refers to an undetermined base

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<220>
<221> unsure
<222> position is 49 nucleotides
<223> "n" refers to an undetermined base

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<220>
<221> unsure
<222> position is 75 nucleotides
<223> "n" refers to an undetermined base

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<400> 84
cgggctcgaa acttogaaga ccgcggaacc cgaagcngcn cttggctcna atcgcttcgg      60

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ctcagaggcgc ccgtncgggt cacgtgaggt gggggcgggc cgaagagggg ggcctcccctc 120  
 ctccctgccgc agggttggcc gcaagtgcgc ttcaagaggc gcttgatgac ggттаатgтт 180  
 gcagcccgga agatgacttt tttctcctcc ttggggttgcg gcaggccgтт agtgggaggt 240  
 cgcgтccccga 250

<210> 85  
 <211> 402  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> unsure  
 <222> position is 224 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 265 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 382 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 390 nucleotides  
 <223> "n" refers to an undetermined base

<400> 85  
 ttctcccttg тcatcccctt accagagcca cagaaattat ccctgtgggc тcccttgтcc 60  
 тcactcggcc ttttctggag тtaagagatc caagccaact actgggtctg тtccctgгta 120  
 aaatcttagg ccggcgгtccc atccacccat ccccatgcct aggactттta agctggгcaac 180  
 ggtacctggg тttagттttc ccttcgtata тcactatctt cgтngcttac cттcttgгtc 240  
 cтаaagттoc accgatgгtc aaggngatta accactaaag тgcaсctgac actactcttg 300  
 acaaattgca gттgggaggt gagттgatga ctggccgгta aatcaaaaгt gcttatттtag 360  
 ggagtgaggg ggccccgгgc anaagccgan тtccagгaca ct 402

<210> 86  
 <211> 595  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> unsure

<222> position is 157 nucleotides  
<223> "n" refers to an undetermined base

<220>  
<221> unsure  
<222> position is 377 nucleotides  
<223> "n" refers to an undetermined base

<220>  
<221> unsure  
<222> position is 410 nucleotides  
<223> "n" refers to an undetermined base

<220>  
<221> unsure  
<222> position is 441 nucleotides  
<223> "n" refers to an undetermined base

<220>  
<221> unsure  
<222> position is 444 nucleotides  
<223> "n" refers to an undetermined base

<220>  
<221> unsure  
<222> position is 456 nucleotides  
<223> "n" refers to an undetermined base

<220>  
<221> unsure  
<222> position is 461 nucleotides  
<223> "n" refers to an undetermined base

<220>  
<221> unsure  
<222> position is 473 nucleotides  
<223> "n" refers to an undetermined base

<220>  
<221> unsure  
<222> position is 490 nucleotides  
<223> "n" refers to an undetermined base

<220>  
<221> unsure  
<222> position is 525 nucleotides  
<223> "n" refers to an undetermined base

<220>  
<221> unsure  
<222> position is 532 nucleotides  
<223> "n" refers to an undetermined base

<220>  
<221> unsure  
<222> position is 534 nucleotides  
<223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 541 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 572 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 575 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 583 nucleotides  
 <223> "n" refers to an undetermined base

<400> 86  
 gatcccagaa ggttctggag ccgagtatca gagtttgagc agcgagtcca gcctagcaga 60  
 agcgggtggt gaccggagac ttttcaatgg tgcaaatga cactgctt ttgacttggg 120  
 gatctgtccc ttgtggcacc agaagctaca acaggtncac ctggattcca gctctagctg 180  
 gactcggtaa ttgctaagtg ccagctctga agtctgtgat tccgtggaaa tccctttcaa 240  
 gcccaattc tgttttttat ggcctcttg tccaaacagt ttgacttgtg aactctgttt 300  
 ctgtcaagtt gacacttggg ctggcacc attcatgagc cagatgaaag cggctaaatg 360  
 cccgaaaaaa taaaggnttt tacctttttt ttgaaccatt ggtgagcatn taaaaaaatt 420  
 agggaaggta aaaccaacc nggncaaacc caactnaaca nttttttttt ccnaaacaag 480  
 ggggggctan tttttcactt ggaaaaaaa acaattttta ttgantcttg ananggtgga 540  
 naaccaaaat tttttgttgg gttgggttcc gnagnccgaa ttntgcaaat ttctt 595

<210> 87  
 <211> 304  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> unsure  
 <222> position is 279 nucleotides  
 <223> "n" refers to an undetermined base

<400> 87  
 cgtggcccga tgcattcagg gagccctctg tgttgccgc atagcaggtg tagttgccgg 60  
 catcctggat gaagacgggc gcgatctgta gacccccga ttcaagaagc atgaacctag 120

gaatccggac agagccactg gccagaatgt ggttttctaa agaacagtgg agaaaagagg 180  
 catgttacag tcgtaacgct tgaaggaaat gaagatagtg gttagagcca taagcaagta 240  
 atatggttcg gctccgtgtc cccacccaag tctcgtctng aattgcaatc cccacgtcgg 300  
 cgca 304

<210> 88  
 <211> 296  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> unsure  
 <222> position is 9 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 31 nucleotides  
 <223> "n" refers to an undetermined base

<400> 88  
 ggctttcngt aggagttaat ggggcattgg ngggtgggat ggcagggctg ccagcatctg 60  
 acccaggagg ctgggaggag gctgctgtgt gaatacacgc tcggcctctc acagtggctg 120  
 ccgccgcatt agccccttgt gcttcagga acagagcatc cgtgatggat gagactttaa 180  
 ttaaagtaat gagacattta taatcgcggt tatctccaaa attaggcctt ttagcaatta 240  
 ttctctggga atattcctcc ggtagatagc tcccttttta gaacaacgtc ggcgca 296

<210> 89  
 <211> 220  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> unsure  
 <222> position is 10 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 24 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 29 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 30 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 31 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 38 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 45 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 87 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 99 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 134 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 158 nucleotides  
 <223> "n" refers to an undetermined base

<400> 89  
 attggcccgn caggcgggaa acangctgnn nttctctnac cgttntccag cactgcccag 60  
 accaggagggc gcagggagag gaggggncag cggttccgng accgctcctc ccgctgtccc 120  
 tgctctccag cctntgcctc tgaggagcc cgcgggantt gcccaggcc cctgtcccca 180  
 cctgtggctc ccgtcctggt cgctcccggg gccgcgga 220

<210> 90  
 <211> 273  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> unsure

<222> position is 2 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 7 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 10 nucleotides  
 <223> "n" refers to an undetermined base

<400> 90  
 gnagggnggn ggtcgcggac gccggtgggc agttottggt cggatgatgtg ggttaaaaag 60  
 gactgcagcg aggagccggg gcggcgctcg gagtaatcac cggcggcatc aaaaagcgcc 120  
 atcatggcat cgaggtcgcy gtctgcttgg gagccggtgg cgccgccgcy caaggcagat 180  
 gcctgcagcg gcatatccag ctcggtagcy ctccatacct cccacaggat ttcttcaca 240  
 gaggttggg cttgtatagc ctgccgccc gca 273

<210> 91  
 <211> 361  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> unsure  
 <222> position is 10 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 12 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 212 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 218 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 356 nucleotides  
 <223> "n" refers to an undetermined base

<400> 91  
 acggcttctn tnctaagtga cacggtgtgt gaaattcggg tggggaggta gttctgtaaa 60



ctgogtctcc ccgccagcta aggaagttga gtgaagggag cgttgccgtc tgggaatcgt 120  
 agtcctcaca aaggcgtgag taggcggcaa ataaggattt gggtttagcc ttggggattc 180  
 actcctgtca aagctgtag agaagctccc anaactcnta aagtaacaga aactacttgc 240  
 ggcaacattt gtaacttoca cctggctcat tatcttccac tgttaccttg tgttctagat 300  
 aagttataat ttattotaca tatcgttcag aagtcttgtg cctgttccat attgtnagca 360  
 t 361

<210> 92  
 <211> 462  
 <212> DNA  
 <213> Homo sapiens

<400> 92  
 gctgccacaca ctggatggga aggaccggcg cctgcagcat ctgccctcca agccttcgta 60  
 gctccctcct tcctgcagga taaactctaa actccttagc acaacgtggg agccttctca 120  
 gagactgggt ccaaccctac tccagccgca gcctcccctc ctggccccac tgccacacc 180  
 ccgggcctcc ggccacactg agcctctccc ggtttcccag gatacaacac tcgcccattc 240  
 atagtgtggt gccttttgca cgtgctgttc ctctgcttgg ggatgctgtt ggtctttctc 300  
 agccaggtga agaggacgct gaatgtcacc tgcttgagta tcaggaccgg ggactgggcg 360  
 ctggacctag actcttggcc ctggagagaa gccctgcatg gggccgcagc ctgccccctg 420  
 ccctgctcac agaaaagctc agccttgtag ccgcgtggga ga 462

<210> 93  
 <211> 591  
 <212> DNA  
 <213> Homo sapiens

<400> 93  
 caaagtcacc tccacggtgc ggctcagcag ctcgccacac ttggtcatgg tgtcggggaa 60  
 ggcgccctcc agctgtaggt gggtagtggc agaacaggag ggtgagggga gagtccgaac 120  
 tgtccccact tggccgttcc ctccccactg gggggccctg agccagtggc ctctctctc 180  
 ggggcctccc cggaaggagc caaggtctgt ctgcgaggca ccggtccccg gccacggcca 240  
 tcagccccca gaggtggatc agggcatcac cccactcca cagctgaggc caggggggtca 300  
 gggaggcaac cagggcagac ctggaacctg gctctgagac aggacggccg agggcccctc 360  
 cactctccct ccctcggggg gggcactgac ctggacgcca aagatgtcct cacactgggtg 420

gcgtttgagt agggcccact cggacatctg gccctgcagc aggttggtgc agacggccat 480  
 ctctccacat gtcacatccg cccgaagcg cttgcagatc cgtcggaagg gcaggttccc 540  
 aactgcggg gggagcagga cagacacaca tgctcttgca cgcgcacctc a 591

<210> 94  
 <211> 279  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> unsure  
 <222> position is 3 nucleotides  
 <223> "n" refers to an undetermined base

<400> 94  
 ttntgagttt tggcctgccc acagtctagc cctggacaga gaatccgagg ctcagccatg 60  
 ctgcagcacc caggacactg catcccagca cctgcccga aatcagccca gggacccaaa 120  
 ggaaagcagg ctccaagctc cccggaagcc aaggaaaata ggaaaacata tcctgccccg 180  
 gggacacctt ctggaactat gaccacatgc acttgacctt ccggaacaat caccgcatgc 240  
 acctgacctc ccggaactgt caccaccgcg cgcacctca 279

<210> 95  
 <211> 351  
 <212> DNA  
 <213> Homo sapiens

<400> 95  
 cttttattat tgttaaactg caccagaaa acccttaact cttagacagc ggctctcatt 60  
 aagcaaaagg ggaggcacat gaagctccag gcagggccg gagggaaccg tgaagccaaa 120  
 ggctctggga gccccaggc acctgcgttt gcattttcat cctggaggag accaggcctc 180  
 tggggctgct ccccggggtg cagagaggag ggtctttct tgggtgtgaa catactcatt 240  
 gattcagtca cctgacctt gactccatgt attttgttga gtctggatgt gtgggtgtgct 300  
 ctgcccagca gctgggatcc acatgagcac agacatggtc cccccgcggc a 351

<210> 96  
 <211> 171  
 <212> DNA  
 <213> Homo sapiens

<400> 96  
 ttgagtgtcg cgtgaatacc taggggacac tcaggggaat gatggctccc ccgagaggta 60

aaggggtggaa agaaggggcc tcagcagggt aggtcttgct gggtccttct gtagggcgtc 120  
tgggagatag atccgtgggg ctctagggt cgcccctacc cggcgcgggc a 171

<210> 97  
<211> 743  
<212> DNA  
<213> Homo sapiens

<220>  
<221> unsure  
<222> position is 155 nucleotides  
<223> "n" refers to an undetermined base

<220>  
<221> unsure  
<222> position is 181 nucleotides  
<223> "n" refers to an undetermined base

<220>  
<221> unsure  
<222> position is 202 nucleotides  
<223> "n" refers to an undetermined base

<220>  
<221> unsure  
<222> position is 228 nucleotides  
<223> "n" refers to an undetermined base

<220>  
<221> unsure  
<222> position is 259 nucleotides  
<223> "n" refers to an undetermined base

<220>  
<221> unsure  
<222> position is 262 nucleotides  
<223> "n" refers to an undetermined base

<220>  
<221> unsure  
<222> position is 293 nucleotides  
<223> "n" refers to an undetermined base

<220>  
<221> unsure  
<222> position is 366 nucleotides  
<223> "n" refers to an undetermined base

<220>  
<221> unsure  
<222> position is 386 nucleotides  
<223> "n" refers to an undetermined base

<220>  
<221> unsure

<222> position is 388 nucleotides  
<223> "n" refers to an undetermined base

<220>  
<221> unsure  
<222> position is 447 nucleotides  
<223> "n" refers to an undetermined base

<220>  
<221> unsure  
<222> position is 470 nucleotides  
<223> "n" refers to an undetermined base

<220>  
<221> unsure  
<222> position is 484 nucleotides  
<223> "n" refers to an undetermined base

<220>  
<221> unsure  
<222> position is 502 nucleotides  
<223> "n" refers to an undetermined base

<220>  
<221> unsure  
<222> position is 512 nucleotides  
<223> "n" refers to an undetermined base

<220>  
<221> unsure  
<222> position is 516 nucleotides  
<223> "n" refers to an undetermined base

<220>  
<221> unsure  
<222> position is 590 nucleotides  
<223> "n" refers to an undetermined base

<220>  
<221> unsure  
<222> position is 664 nucleotides  
<223> "n" refers to an undetermined base

<220>  
<221> unsure  
<222> position is 667 nucleotides  
<223> "n" refers to an undetermined base

<220>  
<221> unsure  
<222> position is 673 nucleotides  
<223> "n" refers to an undetermined base

<220>  
<221> unsure  
<222> position is 695 nucleotides  
<223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 717 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 742 nucleotides  
 <223> "n" refers to an undetermined base

<400> 97  
 cctccctggc ccttgttccc aaggagcttc ccttgcccga gcctcttcgc cagtgacttc 60  
 tcactggacc attcctttac aaggagcctg ttttttgtgt ttttttttta cacctttttt 120  
 cttctatttc acagaaggaa caccggacgt ccctntgtga tggcagcagc catgctgcct 180  
 ntgtttccgc tcaggggttc tntgccacct ccaattccac ccagtctntt ggccctcggct 240  
 gggcttcggc tcccgcctnt gngccaaaaa ttgcaatgcc cgcggtcagg gcnctttgcg 300  
 gagtctcacc gcctgcggag gcttgattcc ctctccacag gcagcagcgt ttgatggccg 360  
 gtgacncccc cctttccaag cacatntntc atggcccctg aatgccactt acagggcgctc 420  
 cctccctgtg ctaagtgtg cctgganctt tgggtgtggc agcagcaaan acctctacct 480  
 ttgnggatgt tcgtttcggg gnggaaagac anatancaaa gttggctcgt aactgtaaag 540  
 tgtgctggga ggaaactgag gcagggaggg cctggtgcca ctggggagcn ctgccccgac 600  
 cccatgtgct tcccaggctc ccttgagacc acgtggatgg cgacttcctg accttgaggg 660  
 ccgngncct cantcctcat gctcgatggc gtcancctcc tcttggggaa atccaancat 720  
 tcctgacctg aaaatgcacc cnc 743

<210> 98  
 <211> 589  
 <212> DNA  
 <213> Homo sapiens

<400> 98  
 ttgccgcgct gataaaggaa gcgtctagaa ggtctcccca gccttcatca tctgagactt 60  
 ggctttcagc cccaaagcac taggccctgc tgtaacctt ccaccattaa cctttggtgc 120  
 tcttcaatta gcagcagcca ggggtccttg gcaggtatga gaatttgaa ggacagcccc 180  
 agggcatggc ccccggtgc agcaaaagtt ctaagtgttc ttctgttga aggaagccca 240  
 ggagatattg atcagctgca ggtgggggag gccccagatc ccaccctgc ctgcctccag 300  
 gagaaggttc tccatgggcc aaaatggagg cagagtccca ctttgctgg gcagctccct 360

gagcatggct ccctgtggac ggagctgagt gacgtcatga ctctaggcct caacaaaaga 420  
gctttgaaa atcccgatga ttcgaattgt attaaatcaa caaacatcgg gttgcacagt 480  
tactagaaaa cggagatctg cgtcatcact tactagacac gtgaccttga acggcgggctt 540  
ccccgtgtga aacagcaaag ttctgtaacc cccatgaacg cgctctca 589

<210> 99  
<211> 538  
<212> DNA  
<213> Homo sapiens

<400> 99  
tgccgcgtct gaccctactc tcacaaagac tttccaacta gcataattga gttaaatgg 60  
cccccaact cccttaattc aagctaaact tgcagtttaa caactatagg agtgatatct 120  
acacattaat gccacacttt aacatgccta aactacaca tgaacacgct tccgggtgct 180  
gttacatccc gctctctccc aagcacgaga cacaggcagg atgctgacgt cctgcttctc 240  
tgctgcgggc ggggaagtcaa gactccggat ttgctgcagg agttgccgtg gggatcctga 300  
cttcacgcag gagatggctg gcctctggaa gtgcctggcc cgtttatcct tgaaatctac 360  
ctgtgcagggt ggtccttgcc tcagcccctc aggacaacac aggtctttcc taagttacag 420  
ggagaccatc agattgtcgt gtccgagccc cctgaagtgg aaccacagt ctccattcag 480  
tctgccctca gtttccctcc cctctgcagg gccattgctg ctgtggacgc gcctctca 538

<210> 100  
<211> 486  
<212> DNA  
<213> Homo sapiens

<400> 100  
agaggtagaa aaaggagtta gaagcaaaga ggaaaaata aataaacagg caacaaaaac 60  
ccaaccacgc cagcctgagc catttgcatt agtgttcatt taggaaatta gcagacggga 120  
aacgctgggg agtgaggatgg gccccggcct tggggactgc agagcccgct cagccctggg 180  
tggtggggcc cacatgggct gtgccccagg agcacaggag gaccagagg gtggccgaga 240  
gagcctcgcc gggctccggt atgggtcctg gccctcaca ggtgcgagcc tggcccagtg 300  
actgtggacg ctgtgggaga gcaggcctcc gatacgagg gctgggactg ctgacctgga 360  
aggtggtgcc gggcgtgtct ggtgaaggcg ccgttggcag ctagagagag acggcggatg 420  
gggtgacgcc attacccacg gtcccagttt tgaggcttga cggtgacgga aaaggacgtc 480  
ggcgca 486

<210> 101  
 <211> 450  
 <212> DNA  
 <213> Homo sapiens

<400> 101  
 aattgaacca ggggtgcacgg ccagcgccag acacagtgag cttcatggca actccagttt 60  
 accggtgaga accatggggc cactcagaga ggcaaagagc ctcacccgag tgagtcctct 120  
 ggcttctccc cacctggggc gggccccagg ccgcgctgtg gttccctttc cagcgcgtcat 180  
 ccctgggtga tgggaggtgg gcattctgtt caaccttgtg ggtcagggag ccagggccag 240  
 tgtgcagatg agaagaggct gcggttactg gcgatgagag ggactgtccc cttcgtgggc 300  
 actttctctt ttgaggccag tgaaatgtgt tccctggggg tgtattcctg agaaggcctc 360  
 atttaaaggg agccgcaaaa ccaagtgggc ttagcaaaag cagtttgtca cctggcagca 420  
 cgtgtgagcc tcgcccggac ggcctctca 450

<210> 102  
 <211> 292  
 <212> DNA  
 <213> Homo sapiens

<400> 102  
 agcgcggcct ggcagattgc ccattaatga aactcagtgg gcagaggctg ctgagggaca 60  
 cggattccca ctccccgggg gagggggtgg aaatggcttc ctccctctgc ttccctacca 120  
 ccagtaatgg ggagctcacc atgcttagaa gactcttctt tgcatggagt tcgggcctcc 180  
 tccctgcacc taccacccta gtggcccaaa gtcttaaggc tgaaggtaa tcctgtgtcc 240  
 ttcagaagca aaggctgcaa ccgatacaca acagaggtgg ccagcgcggg ca 292

<210> 103  
 <211> 395  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> unsure  
 <222> position is 340 nucleotides  
 <223> "n" refers to an undetermined base

<220>  
 <221> unsure  
 <222> position is 367 nucleotides  
 <223> "n" refers to an undetermined base

<400> 103  
agagcttata cgcgcgagcac aagggagccg gggcctgggc cgccgtggga aggggctcct 60  
gccttccggg gacgcggtca gggaaagtcca gccggggtgc tctctgcaact gcgggtgccg 120  
ggctcggcag aggccaaccc ggcaaaacga gcaggatctc cgggccccac cctagtgggc 180  
tccgcctgcc ccaacaacca tcctgccatc ctccctgaga gacaggtgac tttcctctct 240  
gatgcggtgc atctgtcatc tgtctaacgg gccattccc cagtgaaaca ccccaacca 300  
aagacacgaa ggggaaggcg caagcttcta ccaagctcan tttgccatc tggtgccac 360  
ctgcctngta tttggtgact tggaggatag gaagg 395