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(54) Titre : MARQUEURS DE L'EXPRESSION GENIQUE POUR LA MALADIE DE CROHN
(54) Title: GENE EXPRESSION MARKERS FOR CROHN'S DISEASE

(57) Abrégé/Abstract:
The present invention relates to methods of gene expression profiling for inflammatory bowel disease pathogenesis, in which the differential expression in a test sample from a mammalian subject of one or more IBD markers relative to a control is determined, wherein the differential expression in the test sample is indicative of an IBD in the mammalian subject from which the test sample was obtained.

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(54) Title: GENE EXPRESSION MARKERS FOR CROHN'S DISEASE

(57) Abstract: The present invention relates to methods of gene expression profiling for inflammatory bowel disease pathogenesis, in which the differential expression in a test sample from a mammalian subject of one or more IBD markers relative to a control is determined, wherein the differential expression in the test sample is indicative of an IBD in the mammalian subject from which the test sample was obtained.

GENE EXPRESSION MARKERS FOR CROHN'S DISEASE

Field of the Invention

The present invention relates to gene expression profiles in inflammatory bowel disease pathogenesis, including use in the detection and diagnosis of inflammatory bowel disease.

Description of Related Art

Immune related and inflammatory diseases are the manifestation or consequence of fairly complex, often multiple interconnected biological pathways which in normal physiology are critical to respond to insult or injury, initiate repair from insult or injury, and mount innate and acquired defense against foreign organisms. Disease or pathology occurs when these normal physiological pathways cause additional insult or injury either as directly related to the intensity of the response, as a consequence of abnormal regulation or excessive stimulation, as a reaction to self, or as a combination of these.

Though the genesis of these diseases often involves multistep pathways and often multiple different biological systems/pathways, intervention at critical points in one or more of these pathways can have an ameliorative or therapeutic effect. Therapeutic intervention can occur by either antagonism of a detrimental process/pathway or stimulation of a beneficial process/pathway.

Many immune related diseases are known and have been extensively studied. Such diseases include immune-mediated inflammatory diseases, non-immune-mediated inflammatory diseases, infectious diseases, immunodeficiency diseases, neoplasia, *etc.*

The term inflammatory bowel disorder ("IBD") describes a group of chronic inflammatory disorders of unknown causes in which the intestine (bowel) becomes inflamed, often causing recurring cramps or diarrhea. The prevalence of IBD in the US is estimated to be about 200 per 100,000 population. Patients with IBD can be divided into two major groups, those with ulcerative colitis ("UC") and those with Crohn's disease ("CD"). Both UC and CD are chronic relapsing diseases and are complex clinical entities that occur in genetically susceptible individuals who are exposed to as yet poorly defined environmental stimuli. (Bonen and Cho, Gastroenterology. 2003; 124:521-536; Gaya et al. Lancet. 2006;367:1271-1284).

Clinically, IBD is characterized by diverse manifestations often resulting in a chronic, unpredictable course. Bloody diarrhea and abdominal pain are often accompanied by fever and weight loss. Anemia is common, as is severe fatigue. Joint manifestations ranging from arthralgia to acute arthritis as well as abnormalities in liver function are commonly associated with IBD. Patients with IBD also have an increased risk of colon carcinomas compared to the general population. During acute "attacks" of IBD, work and other normal activity are usually impossible, and often a patient is hospitalized.

Although the cause of IBD remains unknown, several factors such as genetic, infectious and immunologic susceptibility have been implicated. IBD is much more common in Caucasians, especially those of Jewish descent. The chronic inflammatory nature of the condition has prompted an intense search for a possible infectious cause. Although agents have been found which stimulate acute inflammation, none has been found to cause the chronic inflammation associated with IBD. The hypothesis that IBD is an autoimmune disease is supported by the previously mentioned extraintestinal manifestation of IBD as joint arthritis, and the known positive response to IBD by treatment with therapeutic agents such as adrenal glucocorticoids, cyclosporine and azathioprine, which are known to suppress immune response. In addition, the GI tract, more than any other organ of the body, is continuously exposed to potential antigenic substances such as proteins from food, bacterial byproducts (LPS), etc. The subtypes of IBD are UC and CD.

There is sufficient overlap in the diagnostic criteria for UC and CD that it is sometimes impossible to say which a given patient has; however, the type of lesion typically seen is different, as is the localization. UC mostly appears in the colon, proximal to the rectum, and the characteristic lesion is a superficial ulcer of the mucosa; CD can appear anywhere in the bowel, with occasional involvement of stomach, esophagus and duodenum, and the lesions are usually described as extensive linear fissures. CD differs from UC in that the inflammation extends through all layers of the intestinal wall and involves mesentery as well as lymph nodes. CD may affect any part of the alimentary canal from mouth to anus. The disease is often discontinuous, i.e., severely diseased segments of bowel are separated from apparently disease-free areas. In CD, the bowel wall also thickens which can lead to obstructions. In addition, fistulas and fissures are not uncommon.

The current therapy of IBD usually involves the administration of antiinflammatory or immunosuppressive agents, such as sulfasalazine, corticosteroids, 6-mercaptopurine/azathioprine, or cyclosporine, which usually bring only partial results. If anti-inflammatory/immunosuppressive therapies fail, colectomies are the last line of defense. The typical operation for CD not involving the rectum is resection (removal of a diseased segment of bowel) and anastomosis (reconnection) without an ostomy. Sections of the small or large intestine may be removed. About 30% of CD patients will need surgery within the first year after diagnosis. In the subsequent years, the rate is about 5% per year. Unfortunately, CD is characterized by a high rate of recurrence; about 5% of patients need a second surgery each year after initial surgery.

Refining a diagnosis of inflammatory bowel disease involves evaluating the progression status of the diseases using standard classification criteria. The classification systems used in IBD include the Truelove and Witts Index (Truelove S.C. and Witts, L.J. *Br Med J.* 1955;2:1041-1048), which classifies colitis as mild, moderate, or severe, as well as Lennard-Jones. (Lennard-Jones JE. Scand J Gastroenterol Suppl 1989;170:2-6) and the simple clinical colitis activity index (SCCAI). (Walmsley et. al. Gut. 1998;43:29-32) These systems track such variables as daily bowel movements, rectal bleeding, temperature, heart rate, hemoglobin levels, erythrocyte sedimentation rate, weight, hematocrit score, and the level of serum albumin.

In approximately 10-15% of cases, a definitive diagnosis of ulcerative colitis or Crohn's disease cannot be made and such cases are often referred to as "indeterminate colitis." Two antibody detection tests are available that can help the diagnosis, each of which assays for antibodies in the blood. The antibodies are "perinuclear anti-neutrophil antibody" (pANCA) and "anti-Saccharomyces cervisiae antibody" (ASCA). Most patients with ulcerative colitis have the pANCA antibody but not the ASCA antibody, while most patients with Crohn's disease have the ASCA antibody but not the pANCA antibody. However, these two tests have shortcomings as some patients have neither antibody and some Crohn's disease patients may have only the pANCA antibody.For clinical practice, a reliable test that would indicate the presence and/or progression of an IBD based on molecular markers rather than the measurement of a multitude of variables would be useful for identifying and/or treating individuals with an IBD. Hypothesis free, linkage and association studies have identified genetic loci that have been associated with UC, notably the MHC region on chromosome 6,(Rioux et al. Am J Hum Genet. 2000;66:1863-1870; Stokkers et al. Gut. 1999; 45:395-401; Van Heel et al. Hum Mol Genet. 2004;13:763-770) the IBD2 locus on chromosome 12 (Parkes et al. Am J Hum Genet. 2000;67:1605-1610; Satsangi et al. Nat Genet. 1996;14:199-202) and the IBD5 locus on chromosome 5. (Giallourakis et. al. Am J. Hum Genet. 2003;73:205-211; Palmieri et. al Aliment Pharmacol Ther. 2006;23:497-506; Russell et. al. Gut. 2006;55:1114-1123; Waller et. al. Gut. 2006;55:809-814) Following a UK wide linkage scan identifying a putative loci of association for UC on chromosome 7q, further studies have implicated variants in the ABCB1 (MDR1) gene which is involved in cellular detoxification with UC. (Satsangi et. al. Nat Genet. 1996;14:199-202; Brant et.al. Am J Hum Genet. 2003;73:1282-1292; Ho et. al. Gastroenterology. 2005;128:288-296)

A complementary approach towards the identification and understanding of the complex gene-gene and gene- environment relationships that result in the chronic intestinal inflammation observed in inflammatory bowel disease (IBD) is microarray gene expression analysis. Microarrays allow a comprehensive picture of gene expression at the tissue and cellular level, thus helping understand the underlying patho-physiological processes. (Stoughton et. al. Annu Rev Biochem. 2005;74:53-82) Microarray analysis was first applied to patients with IBD in 1997, comparing expression of 96 genes in surgical resections of patients with CD to synovial tissue of patients with rheumatoid arthritis. (Heller et. al. Proc Natl Acad Sci U S A. 1997;94:2150-2155) Further studies using microarray platforms to interrogate surgical specimens from patients with IBD identified an number of novel genes that were differentially regulated when diseased samples were compared to controls. (Dieckgraefe et.al. Physiol Genomics. 2000;4:1-11; Lawrance et. al. Hum Mol Genet. 2001;10:445-456).

Current evidence suggests that the inflammatory bowel diseases, Crohn's disease (CD) and ulcerative colitis (UC) are complex non- Mendelian polygenic disorders with important environmental interactions and stimuli. (Gaya et al. Lancet 2006;367:1271-1284) The finding that variants of the NOD2/CARD15 gene are associated with susceptibility to CD is regarded as a landmark discovery and has catalysed widespread interest in the role of the innate and adaptive immune response in the development of CD. (Hugot et al. Nature 2001;411:599-603; Ogura et al. Nature 2001;411:603-606)

Recently genome wide scans (GWS) have identified a number of genetic variants that are associated with CD. The first genome wide association study was carried out in the Japanese CD population (Yamazaki et al. Hum Mol Genet 2005;14:3499-3506), and subsequent studies have now been undertaken in CD populations in North America and Europe.

Polymorphisms in the IL-23R gene on chromosome 1p31 were observed to be associated with CD initially in a US study (Duerr et al. Science 2006;314:1461-1463), and this has now been widely replicated in Europe catalyzing interest in the IL-23/ Th17 pathway. (The Wellcome Trust Case Control Consortium, Nature 2007;447:661-678) In the past 2 years, a number of genome-wide association studies (GWAS) in populations of European descent and a subsequent meta-analysis have identified 32 confirmed CD susceptibility genes/loci. (Barrett et al. Nat Genet 2008, Aug;40(8):955-62) These include innate immune genes that are specific to CD; NOD2, originally described in 2001 (Hugot et al. *Nature* 2001;**411**(6837):599-603; Ogura et al. *Nature* 2001;**411**(6837):603-6) and the autophagy genes ATG16L1 and IRGM (The Wellcome Trust Case Control Consortium, Nature 2007;447:661-678), clearly indicating that defects in the intracellular processing of bacteria constitutes a central feature in the pathogenesis of CD. The discovery that germline variants of IL-23R were protective in CD coincided with murine experiments detailing the contribution of IL-23 (rather than IL-12 with which it shares the p40 subunit) to Th17 driven chronic intestinal inflammation. (Duerr et al. *Science* 2006;**314**(5804):1461-3; Maloy et al. *Mucosal Immunol* 2008;**1**(5):339-49) The meta-analysis and subsequent studies in UC have demonstrated that 3 other IL-23 pathway genes (IL12B, JAK2 and STAT3) are all IBD susceptibility genes. (Barrett et al. Nat Genet 2008, Aug;40(8):955-62)

At present there are no large scale intestinal genome-wide expression studies in CD. There is now an immediate need to explore in detail the function and expression of the novel genetic associations. We have previously applied the technique of genome-wide expression to examine gene profiles in colonic biopsies from patients with UC. (Noble et al. Gut 2008, Oct;57(10):1398-405) Findings included an expression gradient in the healthy adult colon and a change in expression of a number of novel genes as well as established candidate genes such as the alpha defensins 5 and 6. In the healthy adult colon cluster analysis showed differences in gene expression between the right and left colon and the developmental genes HOXA13, HOXB13, GLI1 and GLI3 primarily drove this separation. In UC expression of serum amyloid A1 (SAA1) and the alpha defensins A5&6 were increased, and the increase in DEFA5&6 expression was further characterized to Paneth cell metaplasia by immunohistochemistry and *in-situ* hybridization.

Increasingly intestinal epithelial cells (IEC) are observed to play a critical role in immune homeostasis in the gut. Indeed the discovery of the role of NOD2/CARD15 and other pathogen-associated molecular pattern (PAMP) receptors play in recognizing intestinal pathogens and responding to cellular stress signals have put IECs at the forefront of intestinal immunological defense.(Strober et al., J.Clin.Invest 2007;117(3):514-21.) The IEC response targets the nuclear transcription factor NF-κB, the central regulator of this pathway.

A number of microarray studies have now been carried out in immune cell subsets to try to understand differences in gene expression during activation and inflammation. Genome wide expression from a compendium of six immune cell types has allowed investigators to identify a collection of immune response *in silico* genes that have specific expression signatures in immune cells. (Abbas et al. Genes Immun 2005;6:319-331) These genes have allowed investigators to differentiate signaling pathways in immune cell subsets and to characterize the inflammatory response of genes known to play a role in immune response and genes of unknown function.

Endoscopic pinch mucosal biopsies have allowed investigators to microarray tissue from a larger range of patients encompassing those with less severe disease. Langmann et. al. used microarray technology to analyze 22,283 genes in biopsy specimens from macroscopically non affected areas of the colon and terminal ileum. (Langmann et. al. Gastroenterology. 2004;127:26-40) Genes which were involved in cellular detoxification and biotransformation (Pregnane X receptor and MDR1) were significantly downregulated in the colon of patients with UC, however, there was no change in the expression of these genes in the biopsies from patients with CD. Costello and colleagues (Costello et. al. PLoS Med. 2005;2:e199) looked at the expression of 33792 sequences in endoscopic sigmoid colon biopsies obtained from healthy controls, patients with CD and UC. A number of sequences representing novel proteins were differentially regulated and *in silico* analysis suggested that these proteins had putative functions related to disease pathogenesis – transcription factors, signaling molecules and cell adhesion.

In a study of patients with UC, Okahara et al. (Aliment Pharmacol Ther. 2005;21:1091-1097) observed that (migration inhibitory factor- related protein 14 (MRP14), growth- related oncogene gamma (GROγ) and serum amyloid A1 (SAA1) were upregulated where as TIMP1 and elfin were down regulated in the inflamed biopsies when compared to the non- inflamed biopsies. When observing 41 chemokines and 21 chemokine receptors, Puleston et al demonstrated that chemokines CXCLs 1-3 and 8 and CCL20 were upregulated in active colonic CD and UC. (Aliment Pharmacol Ther. 2005;21:109-120) Overall these studies illustrate the heterogeneity of early microarray platforms and tissue collection. However, despite these problems differential expression of a number of genes was consistently observed.

Despite the above identified advances in IBD research, there is a great need for additional diagnostic and therapeutic agents capable of detecting IBD in a mammal and for effectively treating this disorder.

All publications mentioned herein are incorporated herein by reference to disclose and describe the methods and/or materials in connection with which the publications are cited. Publications cited herein are cited for their disclosure prior to the filing date of the present application. Nothing here is to be construed as an admission that the inventors are not entitled to antedate the publications by virtue of an earlier priority date or prior date of invention. Further the actual publication dates may be different from those shown and require independent verification.

Summary of the Invention

The present invention provides polynucleotides and polypeptides that are overexpressed in inflammatory bowel disease (IBD) as compared to normal tissue, and methods of using those polypeptides, and their encoding nucleic acids, for to detect or diagnose the presence of IBD in mammalian subjects and subsequently to treat those subjects in which IBD is detected with suitable IBD therapeutic agents.

The present invention also provides methods for detecting the presence of and determining the progression of IBD, including Crohn's disease (CD).

The invention disclosed herein provides methods and assays examining expression of one or more gene expression markers in a mammalian tissue or cell sample, wherein the expression of one or more such biomarkers is predictive of whether the mammalian subject from which the tissue or cell sample was taken is more likely to have IBD. In various embodiments of the invention, the methods and assays examine the expression of gene expression markers such as those listed in Table 1 and determine whether expression is differentially expressed relative to a control sample.

In one aspect, the invention concerns a method of detecting or diagnosing an IBD in a mammalian subject comprising determining, in a biological sample obtained from the subject, a differential expression level of (i) one or more nucleic acids encoding one or more polypeptides selected from Table 1, or (ii) RNA transcripts or their expression products of one or more genes selected from Table 1, relative to the expression level in a control, wherein the differential level of expression is indicative of the presence of an IBD in the subject from which the test sample was obtained. In all embodiments, the expression level of a nucleic acid encoding a polypeptide shown as any one of SEQ ID NOS: 5, 6, 8, 11, 12, 2, 14, 16, 18, 20, and 22, is determined.

In one embodiment, the methods of diagnosing or detecting the presence of an IBD in a mammalian subject comprise determining that the expression level of (i) one or more nucleic acids encoding one or more polypeptides selected from Table 1; or (ii) RNA transcripts or expression products thereof of one or more genes selected from Table 1 in a test sample obtained from the subject is lower relative to the level of expression in a control, wherein the lower level of expression is indicative of the presence of IBD in the subject from which the test sample was obtained. In all embodiments, the lower expression level of a nucleic acid encoding a polypeptide shown as any one of SEQ ID NOS: 5, 6, 8, 11, 12, 2, 14, and 16, is determined.

In another embodiment, the methods of diagnosing or detecting the presence of IBD in a mammalian subject comprise determining that the expression level of (i) one or more nucleic acids encoding one or more polypeptides selected from Table 1; or (ii) RNA transcripts or expression products thereof of one or more genes selected from Table 1 in a test sample obtained from the subject is higher relative to the level of expression in a control, wherein the higher level of expression is indicative of the presence of IBD in the subject from which the test sample was obtained. In all embodiments, the higher expression level of a nucleic acid encoding a polypeptide shown as any one of SEQ ID NOS: 18, 20, and 22, is determined.

In one aspect, the methods are directed to diagnosing or detecting a flare-up of an IBD in mammalian subject that was previously diagnosed with an IBD and is currently in remission. The subject may have completed treatment for the IBD or is currently undergoing treatment for the IBD. In one embodiment, the methods comprise determining a differential expression level of (i) one or more nucleic acids encoding one or more polypeptides selected from Table 1; or (ii) RNA transcripts or expression products thereof of one or more genes selected from Table 1 in a biological sample obtained from a mammalian subject relative to the expression level of a control, wherein the difference in expression indicates the subject is more likely to have an IBD flareup. In all embodiments, the differential expression level of a nucleic acid encoding a polypeptide shown as any one of SEQ ID NOS: 5, 6, 8, 11, 12, 2, 14, 16, 18, 20, and 22, is determined. In all embodiments, the test sample may be compared to a prior test sample of the mammalian subject, if available, obtained before, after, or at the time of the intial IBD diagnosis.

In all aspects, the mammalian subject preferably is a human patient, such as a human patient diagnosed with or at risk of developing an IBD. The subject may also be an IBD patient who has received prior treatment for an IBD but is at risk of a recurrence of the IBD.

For all aspects of the method of the invention, determining the expression level of one or more genes described herein (or one or more nucleic acids encoding polypeptide(s) expressed by one or more of such genes) may be obtained, for example, by a method of gene expression profiling. The method of gene expression profiling may be, for example, a PCR-based method.

In various embodiments, the diagnosis includes quantification of the expression level of (i) one or more nucleic acids encoding one or more polypeptides selected from Table 1; or (ii) RNA transcripts or expression products thereof of one or more genes selected from Table 1, such as by immunohistochemistry (IHC) and/or fluorescence *in situ* hybridization (FISH).

For all aspects of the invention, the expression levels of the genes may be normalized relative to the expression levels of one or more reference genes, or their expression products.

For all aspects of the invention, the method may further comprise determining evidence of the expression levels of at least two, three, four, five, six, seven, eight, or nine of said genes, or their expression products.

In another aspect, the methods of present invention also contemplate the use of a "panel" of such genes (i.e. IBD markers as disclosed herein) based on the evidence of their level of expression. In some embodiments, the panel of IBD markers will include at least one, two, three, four, five, six, seven, eight, or nine IBD markers. The panel may include an IBD marker that is overexpressed in IBD relative to a control, an IBD marker that is underexpressed in IBD relative to a control, or IBD markers that are both overexpressed and underexpressed in IBD relative to a control. Such panels may be used to screen a mammalian subject for the differential expression of one or more IBD markers in order to make a determination on whether an IBD is present in the subject.

In one embodiment, the IBD markers that make up the panel are selected from Table 1. In a preferred embodiment, the methods of diagnosing or detecting the presence of an IBD in a mammalian subject comprise determining a differential expression level of RNA transcripts or expression products thereof from a panel of IBD markers in a test sample obtained from the subject relative to the level of expression in a control, wherein the differential level of expression is indicative of the presence of an

IBD in the subject from which the test sample was obtained. The differential expression in the test sample may be higher and/or lower relative to a control as discussed herein.

For all aspects of the invention, the method may further comprise the step of creating a report summarizing said prediction.

For all aspects, the IBD diagnosed or detected according to the methods of the present invention is Crohn's disease (CD), ulcerative colitis (UC), or both CD and UC.

For all aspects of the invention, the test sample obtained from a mammalian subject may be derived from a colonic tissue biopsy. In a preferred embodiment, the biopsy is a tissue selected from the group consisting of terminal ileum, the ascending colon, the descending colon, and the sigmoid colon. In other preferred embodiments, the biopsy is from an inflamed colonic area or from a non-inflamed colonic area. The inflamed colonic area may be acutely inflamed or chronically inflamed.

For all aspects, determination of expression levels may occur at more than one time. For all aspects of the invention, the determination of expression levels may occur before the patient is subjected to any therapy before and/or after any surgery. In some embodiments, the determining step is indicative of a recurrence of an IBD in the mammalian subject following surgery or indicative of a flare-up of said IBD in said mammalian subject. In a preferred embodiment, the IBD is Crohn's disease.

In another aspect, the present invention concerns methods of treating a mammalian subject in which the presence of an IBD has been detected by the methods described herein. For example, following a determination that a test sample obtained from the mammalian subject exhibits differential expression relative to a control of one or more of the RNA transcripts or the corresponding gene products of an IBD marker described herein, the mammalian subject may be administered an IBD therapeutic agent.

In one embodiment, the methods of treating an IBD in a mammalian subject in need thereof, comprise (a) determining a differential expression level of (i) one or more nucleic acids encoding one or more polypeptides selected from Table 1; or (ii) RNA transcripts or expression products thereof of one or more genes selected from Table 1 in a test sample obtained from the subject relative to the expression level of a control, wherein said differential level of expression is indicative of the presence of an IBD in the subject from which the test sample was obtained; and (b) administering to said subject an effective amount of an IBD therapeutic agent. In all embodiments, the expression level of a nucleic acid encoding a polypeptide shown as any one of SEQ ID NOS: 5, 6, 8, 11, 12, 2, 14, 16, 18, 20, and 22, is determined.

In a preferred embodiment, the methods of treating an IBD comprise (a) determining that the expression level of (i) one or more nucleic acids encoding one or more polypeptides selected from Table 1; or (ii) RNA transcripts or expression products thereof of one or more genes selected from Table 1 in a test sample obtained from the subject is lower relative to the level of expression in a control, wherein the lower level of expression is indicative of the presence of an IBD in the subject from which the test sample was obtained; and (b) administering to said subject an effective amount of an IBD therapeutic agent. In all embodiments, the lower level of expression of a nucleic acid encoding a polypeptide shown as any one of SEQ ID NOS: 5, 6, 8, 11, 12, 2, 14, and 16 is determined.

In another preferred embodiment, the methods of treating an IBD comprise (a) determining that the expression level of (i) one or more nucleic acids encoding one or more polypeptides selected from Table 1; or (ii) RNA transcripts or expression products thereof of one or more genes selected from Table 1 in a test sample obtained from the subject is higher relative to the level of expression in a control, wherein the higher level of expression is indicative of the presence of an IBD in the subject from which the test sample was obtained. In all embodiments, the higher level of expression of a nucleic acid encoding a polypeptide shown as any one of SEQ ID NOS: 18, 20, and 22, is determined.

In some preferred embodiments, the IBD therapeutic agent is one or more of an aminosalicylate, a corticosteroid, and an immunosuppressive agent.

In one aspect, the panel of IBD markers discussed above is useful in methods of treating an IBD in a mammalian subject. In one embodiment, the mammalian subject is screened against the panel of markers and if the presence of an IBD is determined, IBD therapeutic agent(s) may be administered as discussed herein.

In a different aspect the invention concerns a kit comprising one or more of (1) extraction buffer/reagents and protocol; (2) reverse transcription buffer/reagents and protocol; and (3) qPCR buffer/reagents and protocol suitable for performing the methods of this invention. The kit may comprise data retrieval and analysis software.

In one embodiment, the gene whose differential expression is indicative of an IBD is one or more of: CCL23, CXCL13, IRTA1, ATG16L1, ATG4D, ATG3, ATG12, ATG16L2, LC3B, or any combination thereof.

These and further embodiments of the present invention will be apparent to those of ordinary skill in the art.

Brief Description of Drawings

Figure 1 depicts the nucleic acid sequence (SEQ ID NO:1) encoding human IRTA1 polypeptide

Figure 2 depicts the amino acid sequence (SEQ ID NO:2) encoded by the nucleic acid sequence of Figure 1.

Figure 3 depicts the nucleic acid sequence (SEQ ID NO:3) encoding the CKbeta8-1 transcript of the human CCL23 polypeptide.

Figure 4 depicts the nucleic acid sequence (SEQ ID NO:4) encoding the CKbeta8 transcript of the human CCL23 polypeptide.

Figure 5 depicts the amino acid sequence (SEQ ID NO:5) encoded by the nucleic acid sequence of Figure 3.

Figure 6 depicts the amino acid sequence (SEQ ID NO:6) encoded by the nucleic acid sequence of Figure 4.

Figure 7 depicts the nucleic acid sequence (SEQ ID NO:7) encoding human CXCL13 polypeptide.

Figure 8 depicts the amino acid sequence (SEQ ID NO:8) encoded by the nucleic acid sequence of Figure 7.

Figure 9 depicts the nucleic acid sequence (SEQ ID NO:9) encoding human ATG16L1 polypeptide (isoform 2).

Figure 10 depicts the nucleic acid sequence (SEQ ID NO:10) encoding human ATG16L1 polypeptide (isoform 1).

Figure 11 depicts the amino acid sequence (SEQ ID NO:11) encoded by the nucleic acid sequence of Figure 9.

Figure 12 depicts the amino acid sequence (SEQ ID NO:12) encoded by the nucleic acid sequence of Figure 10.

Figure 13 depicts the nucleic acid sequence (SEQ ID NO:13) encoding human ATG4D polypeptide.

Figure 14 depicts the amino acid sequence (SEQ ID NO:14) encoded by the nucleic acid sequence of Figure 13.

Figure 15 depicts the nucleic acid sequence (SEQ ID NO:15) encoding human ATG3 polypeptide.

Figure 16 depicts the amino acid sequence (SEQ ID NO:16) encoded by the nucleic acid sequence of Figure 15.

Figure 17 depicts the nucleic acid sequence (SEQ ID NO:17) encoding human ATG12 polypeptide.

Figure 18 depicts the amino acid sequence (SEQ ID NO:18) encoded by the nucleic acid sequence of Figure 17.

Figure 19 depicts the nucleic acid sequence (SEQ ID NO:19) encoding human ATG16L2 polypeptide.

Figure 20 depicts the amino acid sequence (SEQ ID NO:20) encoded by the nucleic acid sequence of Figure 19.

Figure 21 depicts the nucleic acid sequence (SEQ ID NO:21) encoding human LC3B polypeptide.

Figure 22 depicts the amino acid sequence (SEQ ID NO:22) encoded by the nucleic acid sequence of Figure 21.

Figure 23 illustrates hierarchical clustering of terminal ileal biopsies from females with Crohn's disease and controls. The data comprises terminal ileal biopsies from 8 patients with CD, three healthy controls with normal terminal ileal pathology and one patient with UC who had normal terminal ileal pathology were clustered. The CD, UC and control patients are annotated with the inflammation status of the biopsy. The degree of upregulation measured in red and downregulation measured in blue can be quantified using the logarithmic key. Two areas appeared to be driving this separation and these have been highlighted in solid line oval- downregulated and dashed line oval - upregulated.

Figure 24 depicts fold changes in gene expression, comparing CD biopsies to controls. Gene Annotation: SAA1-serum amyloid A1, REGL- Rat regenerating islet-derivedlike human homolog, S100A8 & 9-calcium binding protein A8 and A9, TNIP3-TNFAIP3 interacting protein 3, IL-8- Interleukin 8, IF- I factor (complement), KCND3- Potassium voltage-gated channel (Shal-related subfamily) member 3, CLECSF12- C-type (calcium dependent, carbohydrate-recognition domain) lectin, regenerating islet-derived 3 gamma- Pancreatitis-associated protein 2, TFECTranscription factor EC, IGSF6- Immunoglobulin superfamily member 6, A_32_P90385- unknown, GW112- Olfactomedin-4 Precursor (OLM4), MGC27165-Protein containing four immunoglobulin (Ig) domains, MMP3- matrix metalloproteinase 3, KLK12-kallikrein 12, TZFP- testis zinc finger protein, REG4-regenerating islet-derived family, member 4, CLECSF9- C-t ype (calcium dependent, carbohydrate-recognition domain) lectin, superfamily member 9, IF- I factor (complement), AVP- Prepro-arginine vasopressin-neurophysin II, AATK- apoptosisassociated tyrosine kinase, ECT2- epithelial cell transforming sequence 2 oncogene, SLC26A2- solute carrier family 26, XRRA1- X-ray radiation resistance associated 1, RPS28- ribosomal protein S28, ISL1- Insulin gene enhancer protein 1, MGC29643-LY6/PLAUR domain containing 1, AQP8- aquaporin 8, FLJ25770- Hypothetical protein, ANKRD17- ankyrin repeat domain 17, A_32_P191066- Weakly similar to PN0099, FLJ12572- Hypothetical protein, LOC339881- similar to eukaryotic initiation factor 4B, NKD1-naked cuticle homolog 1, CA1 & 2- carbonic anhydrase 1 & 2, PRAC- Prostate, rectum and colon expressed gene protein, LOC389023-hypothetical gene, SLC14A2- solute carrier family 14.

Figure 25 depicts fold changes in gene expression, comparing CD and control biopsies of the terminal ileum. Gene annotation: UBD- Diubiquitin, TIMD4- T-cell immunoglobulin and mucin domain-containing protein 4 Precursor, FLJ25393 & FLJ27099- hypothetical proteins, SOX14- SRY (sex determining region Y)-box 14, BX108833- Soares infant brain 1NIB, HK2-Hexokinase-2, RP11-653A5.1- novel protein, TEX12- testis expressed sequence 12, III-prostate-specific membrane antigen-like protein, S100P- S100 calcium binding protein P, C1orf34- DEME-6 protein, Sprn-shadow of prion protein, FOLH1- folate hydrolase, LOC92552- similar to homologue of MJD, EYA2- Eyesabsent homolog 2, CEACAM3-carcinoembryonic antigen-related cell adhesion molecule 3, C14orf81- hypothetical protein LOC90925, MUC4- mucin 4, TNFRSF13C- Tumor necrosis factor receptor superfamily member 13C, HEBP1-Heme-binding protein, ARHGAP24- Rho GTPase-activating protein 24, LOC375180-Homo sapiens LOC388920, SUSD2- sushi domain containing 2, AGXT2-alanineglyoxylate aminotransferase 2, CYFIP2- Cytoplasmic FMR1 interacting protein 2, FNBP1- Formin binding protein 1, SLC28A2- Solute carrier family 28 member 2, OTTHUMP00000011522- hyporthetical protein MGC27169, PAX8- paired box gene 8, CXCR4- CXC chemokine receptor 4, APOA1- apolipoprotein A-I, C6orf32-chromosome 6 open reading frame 32, NPPC- C-type natriuretic peptide, CCL23-chemokine (C-C motif) ligand 23, APOC3- apolipoprotein C-III, IRTA1-immunoglobulin superfamily receptor translocation associated 1, MGC27169-hypothetical protein.

Figure 26 depicts fold changes in gene expression, comparing non- inflamed CD and control sigmoid colon biopsies.

Figure 27 depicts fold changes in gene expression, comparing inflamed and non- inflamed CD sigmoid colon biopsies.

Figure 28 illustrates expression analysis of the IL-23/ Th17 pathway in Crohn's disease and controls. The IL-23 pathway is depicted along with gene expression of constituent molecules in CD and control biopsies separated by inflammation status. Gene expression is shown as box- whisker plots. The boxes are 25th to the 75th centile. The IL-23 pathway is upregulated in CD biopsies compared to controls and in inflamed CD biopsies compared to non- inflamed CD biopsies.

Figure 29 illustrates the expression analysis of the autophagy pathway in Crohn's disease and controls. The autophagy pathway with gene expression is shown as box-whisker plots. Differential gene expression was observed in 6 of the 20 genes that were examined with ATG16LI, ATG4D and ATG3 being downregulated and ATG12, ATG16L2 and LC3B marginally upregulated. PE – Phosphatidylethanolamine, a lipid which covalently attaches to ATG8/LC3 and mediates its attachment to autophagic membranes.

Figure 30 shows sigmoid colon Crohn's Disease and control biopsies clustered by epithelial cell markers. The colonic biopsies are annotated along the top of the figure: controls (e.g., numbers 1-5, and 7-11), non- inflamed CD (numbers 6, 12, 34, 50-51, and 57), inflamed CD (numbers 15, 45, 49, 52-55, 58, and 60-61), untreated CD (numbers 42, 46-48, 56, and 59). On the right of the figure the epithelial cell cytokines are annotated. The degree of upregulation measured in red and downregulation measured in blue can be quantified using the logarithmic key.

Detailed Description of the Invention

A. Definitions

Unless defined otherwise, technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs. Singleton *et al.*, Dictionary of Microbiology and Molecular Biology 2nd ed., J. Wiley & Sons (New York, NY 1994), and

March, Advanced Organic Chemistry Reactions, Mechanisms and Structure 4th ed., John Wiley & Sons (New York, NY 1992), provide one skilled in the art with a general guide to many of the terms used in the present application.

One skilled in the art will recognize many methods and materials similar or equivalent to those described herein, which could be used in the practice of the present invention. Indeed, the present invention is in no way limited to the methods and materials described. For purposes of the present invention, the following terms are defined below.

The term "inflammatory bowel disease" or "IBD" is used as a collective term for ulcerative colitis and Crohn's disease. Although the two diseases are generally considered as two different entities, their common characteristics, such as patchy necrosis of the surface epithelium, focal accumulations of leukocytes adjacent to glandular crypts, and an increased number of intraepithelial lymphocytes (IEL) and certain macrophage subsets, justify their treatment as a single disease group.

The term "Crohn's disease" or "CD" is used herein to refer to a condition involving chronic inflammation of the gastrointestinal tract. Crohn's-related inflammation usually affects the intestines, but may occur anywhere from the mouth to the anus. CD differs from UC in that the inflammation extends through all layers of the intestinal wall and involves mesentery as well as lymph nodes. The disease is often discontinuous, i.e., severely diseased segments of bowel are separated from apparently disease-free areas. In CD, the bowel wall also thickens which can lead to obstructions, and the development of fistulas and fissures are not uncommon. As used herein, CD may be one or more of several types of CD, including without limitation, ileocolitis (affects the ileum and the large intestine); ileitis (affects the ileum); gastroduodenal CD (inflammation in the stomach and the duodenum); jejunoileitis (spotty patches of inflammation in the jejunum); and Crohn's (granulomatous) colitis (only affects the large intestine).

The term "ulcerative colitis" or "UC" is used herein to refer to a condition involving inflammation of the large intestine and rectum. In patients with UC, there is an inflammatory reaction primarily involving the colonic mucosa. The inflammation is typically uniform and continuous with no intervening areas of normal mucosa. Surface mucosal cells as well as crypt epithelium and submucosa are involved in an inflammatory reaction with neutrophil infiltration. Ultimately, this reaction typically progresses to epithelial damage and loss of epithelial cells resulting in multiple ulcerations, fibrosis, dysplasia and longitudinal retraction of the colon.

The term "inactive" IBD is used herein to mean an IBD that was previously diagnosed in an individual but is currently in remission. This is in contrast to an "active" IBD in which an individual has been diagnosed with and IBD but has not undergone treatment. In addition, the active IBD may be a recurrence of a previously diagnosed and treated IBD that had gone into remission (i.e. become an inactive IBD). Such recurrences may also be referred to herein as "flare-ups" of an IBD. Mammalian subjects having an active autoimmune disease, such as an IBD, may be subject to a flare-up, which is a period of heightened disease activity or a return of corresponding symptoms. Flare-ups may occur in response to severe infection, allegic reactions, physical stress, emotional trauma, surgery, or environmental factors.

The term "modulate" is used herein to mean that the expression of the gene, or level of RNA molecule or equivalent RNA molecules encoding one or more proteins or protein subunits, or activity of one or more proteins or protein subunits is up regulated or down regulated, such that expression, level, or activity is greater than or less than that observed in the absence of the modulator.

The terms “inhibit”, “down-regulate”, “underexpress” and “reduce” are used interchangeably and mean that the expression of a gene, or level of RNA molecules or equivalent RNA molecules encoding one or more proteins or protein subunits, or activity of one or more proteins or protein subunits, is reduced relative to one or more controls, such as, for example, one or more positive and/or negative controls.

The term “up-regulate” or “overexpress” is used to mean that the expression of a gene, or level of RNA molecules or equivalent RNA molecules encoding one or more proteins or protein subunits, or activity of one or more proteins or protein subunits, is elevated relative to one or more controls, such as, for example, one or more positive and/or negative controls.

The term "diagnosis" is used herein to refer to the identification of a molecular or pathological state, disease or condition, such as the identification of IBD.

The term "prognosis" is used herein to refer to the prediction of the likelihood of IBD development or progression, including autoimmune flare-ups and recurrences following surgery. Prognostic factors are those variables related to the natural history of IBD, which influence the recurrence rates and outcome of patients once they have developed IBD. Clinical parameters that may be associated with a worse prognosis include, for example, an abdominal mass or tenderness, skin rash, swollen joints, mouth ulcers, and borborygmus (gurgling or splashing sound over the intestine). Prognostic factors may be used to categorize patients into subgroups with different baseline recurrence risks.

The “pathology” of an IBD includes all phenomena that compromise the well-being of the patient. IBD pathology is primarily attributed to abnormal activation of the immune system in the intestines that can lead to chronic or acute inflammation in the absence of any known foreign antigen, and subsequent ulceration. Clinically, IBD is characterized by diverse manifestations often resulting in a chronic, unpredictable course. Bloody diarrhea and abdominal pain are often accompanied by fever and weight loss. Anemia is not uncommon, as is severe fatigue. Joint manifestations ranging from arthralgia to acute arthritis as well as abnormalities in liver function are commonly associated with IBD. During acute “attacks” of IBD, work and other normal activity are usually impossible, and often a patient is hospitalized.

The aetiology of these diseases is unknown and the initial lesion has not been clearly defined; however, patchy necrosis of the surface epithelium, focal accumulations of leukocytes adjacent to glandular crypts, and an increased number of intraepithelial lymphocytes and certain macrophage subsets have been described as putative early changes, especially in Crohn's disease.

The term “treatment” refers to both therapeutic treatment and prophylactic or preventative measures for IBD, wherein the object is to prevent or slow down (lessen) the targeted pathologic condition or disorder. Those in need of treatment include those already with an IBD as well as those prone to have an IBD or those in whom the IBD is to be prevented. Once the diagnosis of an IBD has been made by the methods disclosed herein, the goals of therapy are to induce and maintain a remission.

Various agents that are suitable for use as an “IBD therapeutic agent” are known to those of ordinary skill in the art. As described herein, such agents include without limitation, aminosalicylates, corticosteroids, and immunosuppressive agents.

The term “test sample” refers to a sample from a mammalian subject suspected of having an IBD, known to have an IBD, or known to be in remission from an IBD. The test sample may originate from various sources in the mammalian subject including, without limitation, blood, semen, serum, urine, feces, bone marrow, mucosa, tissue, etc. The test sample may originate from a tissue biopsy of the gastrointestinal tract including, without limitation, ascending colon tissue, descending colon tissue, sigmoid colon tissue, ileocolon, and terminal ileum tissue.

The term “control” or “control sample” refers a negative control in which a negative result is expected to help correlate a positive result in the test sample. Controls that are suitable for the present invention include, without limitation, a sample known to have normal levels of gene expression, a sample obtained from a mammalian subject known not to have an IBD, and a sample obtained from a mammalian subject known to be normal. A control may also be a sample obtained from a subject previously diagnosed and treated for an IBD who is currently in remission; and such a control is useful in determining any recurrence of an IBD in a subject who is in remission. In addition, the control may be a sample containing normal cells that have the same origin as cells contained in the test sample. Those of skill in the art will appreciate other controls suitable for use in the present invention.

The term "microarray" refers to an ordered arrangement of hybridizable array elements, preferably polynucleotide probes, on a substrate.

The term "polynucleotide," when used in singular or plural, generally refers to any polyribonucleotide or polydeoxribonucleotide, which may be unmodified RNA or DNA or modified RNA or DNA. Thus, for instance, polynucleotides as defined herein include, without limitation, single- and double-stranded DNA, DNA including single- and double-stranded regions, single- and double-stranded RNA, and RNA including single- and double-stranded regions, hybrid molecules comprising DNA and RNA that may be single-stranded or, more typically, double-stranded or include single- and double-stranded regions. In addition, the term “polynucleotide” as used herein refers to triple-stranded regions comprising RNA or DNA or both RNA and DNA. The strands in such regions may be from the same molecule or from different molecules. The regions may include all of one or more of the molecules, but more typically involve only a region of some of the molecules. One of the molecules of a triple-helical region often is an oligonucleotide. The term “polynucleotide” specifically includes cDNAs. The term includes DNAs (including cDNAs) and RNAs that contain one or more modified bases. Thus, DNAs or RNAs with backbones modified for stability or for other reasons are "polynucleotides" as that term is intended herein. Moreover, DNAs or RNAs comprising unusual bases, such as inosine, or modified bases, such as tritiated bases, are included within the term "polynucleotides" as defined herein. In general, the term "polynucleotide" embraces all chemically, enzymatically and/or metabolically modified forms of unmodified polynucleotides, as well as the chemical forms of DNA and RNA characteristic of viruses and cells, including simple and complex cells.

The term "oligonucleotide" refers to a relatively short polynucleotide, including, without limitation, single-stranded deoxyribonucleotides, single- or double-stranded ribonucleotides, RNA:DNA hybrids and double-stranded DNAs. Oligonucleotides, such as single-stranded DNA probe oligonucleotides, are often synthesized by chemical methods, for example using automated oligonucleotide synthesizers that are commercially available. However, oligonucleotides can be made by a variety of other methods, including *in vitro* recombinant DNA-mediated techniques and by expression of DNAs in cells and organisms.

The terms "differentially expressed gene," "differential gene expression" and their synonyms, which are used interchangeably, refer to a gene whose expression is activated to a higher or lower level in a subject suffering from a disease, specifically an IBD, such as UC or CD, relative to its expression in a normal or control subject. The terms also include genes whose expression is activated to a higher or lower level at different stages of the same disease. It is also understood that a differentially expressed gene may be either activated or inhibited at the nucleic acid level or protein level, or may be subject to alternative splicing to result in a different polypeptide product. Such differences may be evidenced by a change in mRNA levels, surface expression, secretion or other partitioning of a polypeptide, for example. Differential gene expression may include a comparison of expression between two or more genes or their gene products, or a comparison of the ratios of the expression between two or more genes or their gene products, or even a comparison of two differently processed products of the same gene, which differ between normal subjects and subjects suffering from a disease, specifically an IBD, or between various stages of the same disease. Differential expression includes both quantitative, as well as qualitative, differences in the temporal or cellular expression pattern in a gene or its expression products among, for example, normal and diseased cells, or among cells which have undergone different disease events or disease stages. For the purpose of this invention, "differential gene expression" is considered to be present when there is an at least about one-fold, at least about 1.5-fold, at least about 2-fold, at least about 2.5-fold, at least about 3-fold, at least about 3.5 fold, at least about 4-fold, at least about 4.5-fold, at least about 5-fold, at least about 5.5-fold, at least about 6-fold, at least about 7-fold, at least about 8-fold, at least about 9-fold, or at least about 10-fold difference between the expression of a given gene in normal and diseased subjects, or in various stages of disease development in a diseased subject.

The term "over-expression" with regard to an RNA transcript is used to refer to the level of the transcript determined by normalization to the level of reference mRNAs, which might be all transcripts detected in the specimen or a particular reference set of mRNAs.

The phrase "gene amplification" refers to a process by which multiple copies of a gene or gene fragment are formed in a particular cell or cell line. The duplicated region (a stretch of amplified DNA) is often referred to as "amplicon". Usually, the amount of the messenger RNA (mRNA) produced, *i.e.,* the level of gene expression, also increases in the proportion of the number of copies made of the particular gene expressed.

In general, the term "marker" or "biomarker" or refers to an identifiable physical location on a chromosome, such as a restriction endonuclease recognition site or a gene, whose inheritance can be monitored. The marker may be an expressed region of a gene referred to as a "gene expression marker", or some segment of DNA with no known coding function. An "IBD marker" as used herein refers those genes listed in Table 1.

"Stringency" of hybridization reactions is readily determinable by one of ordinary skill in the art, and generally is an empirical calculation dependent upon probe length, washing temperature, and salt concentration. In general, longer probes require higher temperatures for proper annealing, while shorter probes need lower temperatures. Hybridization generally depends on the ability of denatured DNA to reanneal when complementary strands are present in an environment below their melting temperature. The higher the degree of desired homology between the probe and hybridizable sequence, the higher the relative temperature which can be used. As a result, it follows that higher relative temperatures would tend to make the reaction conditions more stringent, while lower temperatures less so. For additional details and explanation of stringency of hybridization reactions, see Ausubel et al., Current Protocols in Molecular Biology, Wiley Interscience Publishers, (1995).

"Stringent conditions" or "high stringency conditions", as defined herein, typically: (1) employ low ionic strength and high temperature for washing, for example 0.015 M sodium chloride/0.0015 M sodium citrate/0.1% sodium dodecyl sulfate at 50°C; (2) employ during hybridization a denaturing agent, such as formamide, for example, 50% (v/v) formamide with 0.1% bovine serum albumin/0.1% Ficoll/0.1% polyvinylpyrrolidone/50mM sodium phosphate buffer at pH 6.5 with 750 mM sodium chloride, 75 mM sodium citrate at 42°C; or (3) employ 50% formamide, 5 x SSC (0.75 M NaCl, 0.075 M sodium citrate), 50 mM sodium phosphate (pH 6.8), 0.1% sodium pyrophosphate, 5 x Denhardt's solution, sonicated salmon sperm DNA (50 μg/ml), 0.1% SDS, and 10% dextran sulfate at 42°C, with washes at 42°C in 0.2 x SSC (sodium chloride/sodium citrate), 50% formamide, followed by a high-stringency wash consisting of 0.1 x SSC containing EDTA at 55°C.

"Moderately stringent conditions" may be identified as described by Sambrook et al., Molecular Cloning: A Laboratory Manual, New York: Cold Spring Harbor Press, 1989, and include the use of washing solution and hybridization conditions (e.g., temperature, ionic strength and %SDS) less stringent that those described above. An example of moderately stringent conditions is overnight incubation at 37°C in a solution comprising: 20% formamide, 5 x SSC (150 mM NaCl, 15 mM trisodium citrate), 50 mM sodium phosphate (pH 7.6), 5 x Denhardt's solution, 10% dextran sulfate, and 20 mg/ml denatured sheared salmon sperm DNA, followed by washing the filters in 1 x SSC at about 37-50°C. The skilled artisan will recognize how to adjust the temperature, ionic strength, etc. as necessary to accommodate factors such as probe length and the like.

In the context of the present invention, reference to "at least one," "at least two," "at least five," etc. of the genes listed in any particular gene set means any one or any and all combinations of the genes listed.

The terms “splicing” and “RNA splicing” are used interchangeably and refer to RNA processing that removes introns and joins exons to produce mature mRNA with continuous coding sequence that moves into the cytoplasm of an eukaryotic cell.

In theory, the term “exon” refers to any segment of an interrupted gene that is represented in the mature RNA product (B. Lewin. <u>Genes IV</u> Cell Press, Cambridge Mass. 1990). In theory the term “intron” refers to any segment of DNA that is transcribed but removed from within the transcript by splicing together the exons on either side of it. Operationally, exon sequences occur in the mRNA sequence of a gene as defined by Ref. SEQ ID numbers. Operationally, intron sequences are the intervening sequences within the genomic DNA of a gene, bracketed by exon sequences and having GT and AG splice consensus sequences at their 5’ and 3’ boundaries.

An “interfering RNA” or “small interfering RNA (siRNA)” is a double stranded RNA molecule usually less than about 30 nucleotides in length that reduces expression of a target gene. Interfering RNAs may be identified and synthesized using known methods (Shi Y., *Trends in Genetics* 19(1):9-12 (2003), WO/2003056012 and WO2003064621), and siRNA libraries are commercially available, for example from Dharmacon, Lafayette, Colorado.

A “native sequence” polypeptide is one which has the same amino acid sequence as a polypeptide derived from nature, including naturally occurring or allelic variants. Such native sequence polypeptides can be isolated from nature or can be produced by recombinant or synthetic means. Thus, a native sequence polypeptide can have the amino acid sequence of naturally occurring human polypeptide, murine polypeptide, or polypeptide from any other mammalian species.

The term “antibody” herein is used in the broadest sense and specifically covers monoclonal antibodies, polyclonal antibodies, multispecific antibodies (*e.g.* bispecific antibodies), and antibody fragments, so long as they exhibit the desired biological activity. The present invention particularly contemplates antibodies against one or more of the IBD markers disclosed herein. Such antibodies may be referred to as “anti-IBD marker antibodies”.

The term “monoclonal antibody” as used herein refers to an antibody from a population of substantially homogeneous antibodies, *i.e.*, the individual antibodies comprising the population are identical and/or bind the same epitope(s), except for possible variants that may arise during production of the monoclonal antibody, such variants generally being present in minor amounts. Such monoclonal antibody typically includes an antibody comprising a polypeptide sequence that binds a target, wherein the target-binding polypeptide sequence was obtained by a process that includes the selection of a single target binding polypeptide sequence from a plurality of polypeptide sequences.

The monoclonal antibodies herein specifically include “chimeric” antibodies in which a portion of the heavy and/or light chain is identical with or homologous to corresponding sequences in antibodies derived from a particular species or belonging to a particular antibody class or subclass, while the remainder of the chain(s) is identical with or homologous to corresponding sequences in antibodies derived from another species or belonging to another antibody class or subclass, as well as fragments of such antibodies, so long as they exhibit the desired biological activity (U.S. Patent No. 4,816,567; and Morrison *et al., Proc. Natl. Acad. Sci. USA*, 81:6851-6855 (1984)). Chimeric antibodies of interest herein include "primatized" antibodies comprising variable domain antigen-binding sequences derived from a non-human primate (*e.g.* Old World Monkey, Ape etc) and human constant region sequences, as well as "humanized" antibodies.

"Humanized" forms of non-human (*e.g.*, rodent) antibodies are chimeric antibodies that contain minimal sequence derived from non-human immunoglobulin. For the most part, humanized antibodies are human immunoglobulins (recipient antibody) in which residues from a hypervariable region of the recipient are replaced by residues from a hypervariable region of a non-human species (donor antibody) such as mouse, rat, rabbit or nonhuman primate having the desired specificity, affinity, and capacity.

An "intact antibody" herein is one which comprises two antigen binding regions, and an Fc region. Preferably, the intact antibody has a functional Fc region.

"Antibody fragments" comprise a portion of an intact antibody, preferably comprising the antigen binding region thereof. Examples of antibody fragments include Fab, Fab', $F(ab')_2$, and Fv fragments; diabodies; linear antibodies; single-chain antibody molecules; and multispecific antibodies formed from antibody fragment(s).

"Native antibodies" are usually heterotetrameric glycoproteins of about 150,000 daltons, composed of two identical light (L) chains and two identical heavy (H) chains. Each light chain is linked to a heavy chain by one covalent disulfide bond, while the number of disulfide linkages varies among the heavy chains of different immunoglobulin isotypes. Each heavy and light chain also has regularly spaced intrachain disulfide bridges. Each heavy chain has at one end a variable domain (V_H) followed by a number of constant domains. Each light chain has a variable domain at one end (V_L) and a constant domain at its other end. The constant domain of the light chain is aligned with the first constant domain of the heavy chain, and the light-chain variable domain is aligned with the variable domain of the heavy chain. Particular amino acid residues are believed to form an interface between the light chain and heavy chain variable domains.

The term "variable" refers to the fact that certain portions of the variable domains differ extensively in sequence among antibodies and are used in the binding and specificity of each particular antibody for its particular antigen. However, the variability is not evenly distributed throughout the variable domains of antibodies. It is concentrated in three segments called hypervariable regions both in the light chain and the heavy chain variable domains. The more highly conserved portions of variable domains are called the framework regions (FRs). The variable domains of native heavy and light chains each comprise four FRs, largely adopting a β-sheet configuration, connected by three hypervariable regions, which form loops connecting, and in some cases forming part of, the β-sheet structure. The hypervariable regions in each chain are held together in close proximity by the FRs and, with the hypervariable regions from the other chain, contribute to the formation of the antigen-binding site of antibodies (see Kabat *et al., Sequences of Proteins of Immunological Interest*, 5th Ed. Public Health Service, National Institutes of Health, Bethesda, MD. (1991)).

The term "*hypervariable region,*" "*HVR,*" or "*HV,*" when used herein refers to the regions of an antibody-variable domain that are hypervariable in sequence and/or form structurally defined loops. Generally, antibodies comprise six HVRs; three in the VH (H1, H2, H3), and three in the VL (L1, L2, L3). In native antibodies, H3 and L3 display the most diversity of the six HVRs, and H3 in particular is believed to play a unique role in conferring fine specificity to antibodies. See, *e.g.*, Xu *et al. Immunity* 13:37-45 (2000); Johnson and Wu in *Methods in Molecular Biology* 248:1-25 (Lo, ed., Human Press, Totowa, NJ, 2003)). Indeed, naturally occurring camelid antibodies consisting of a heavy chain only are functional and stable in the absence of light chain. See, *e.g.*, Hamers-Casterman *et al., Nature* 363:446-448 (1993) and Sheriff *et al., Nature Struct. Biol.* 3:733-736 (1996).

A number of HVR delineations are in use and are encompassed herein. The Kabat Complementarity Determining Regions (CDRs) are based on sequence variability and are the most commonly used (Kabat et al., Sequences of Proteins of Immunological Interest, 5th Ed. Public Health Service, National Institutes of Health, Bethesda, MD. (1991)). Chothia refers instead to the location of the structural loops (Chothia and Lesk J. Mol. Biol. 196:901-917 (1987)). The AbM HVRs represent a compromise between the Kabat HVRs and Chothia structural loops, and are used by Oxford Molecular's AbM antibody modeling software. The "contact" HVRs are based on an analysis of the available complex crystal structures. The residues from each of these HVRs are noted below.

Loop	Kabat	AbM	Chothia	Contact
L1	L24-L34	L24-L34	L26-L32	L30-L36
L2	L50-L56	L50-L56	L50-L52	L46-L55
L3	L89-L97	L89-L97	L91-L96	L89-L96
H1	H31-H35B	H26-H35B	H26-H32	H30-H35B
	(Kabat Numbering)			
H1	H31-H35	H26-H35	H26-H32	H30-H35
	(Chothia Numbering)			
H2	H50-H65	H50-H58	H53-H55	H47-H58
H3	H95-H102	H95-H102	H96-H101	H93-H101

HVRs may comprise "extended HVRs" as follows: 24-36 or 24-34 (L1), 46-56 or 50-56 (L2) and 89-97 or 89-96 (L3) in the VL and 26-35 (H1), 50-65 or 49-65 (H2) and 93-102, 94-102, or 95-102 (H3) in the VH. The variable domain residues are numbered according to Kabat et al., supra, for each of these definitions.

The expression "variable-domain residue-numbering as in Kabat" or "amino-acid-position numbering as in Kabat," and variations thereof, refers to the numbering system used for heavy-chain variable domains or light-chain variable domains of the compilation of antibodies in Kabat *et al., supra.*

Using this numbering system, the actual linear amino acid sequence may contain fewer or additional amino acids corresponding to a shortening of, or insertion into, a FR or HVR of the variable domain. For example, a heavy-chain variable domain may include a single amino acid insert (residue 52a according to Kabat) after residue 52 of H2 and inserted residues (*e.g.* residues 82a, 82b, and 82c, *etc.* according to Kabat) after heavy-chain FR residue 82. The Kabat numbering of residues may be determined for a given antibody by alignment at regions of homology of the sequence of the antibody with a "standard" Kabat numbered sequence.

Papain digestion of antibodies produces two identical antigen-binding fragments, called "Fab" fragments, each with a single antigen-binding site, and a residual "Fc" fragment, whose name reflects its ability to crystallize readily. Pepsin treatment yields an $F(ab')_2$ fragment that has two antigen-binding sites and is still capable of cross-linking antigen.

"Fv" is the minimum antibody fragment which contains a complete antigen-recognition and antigen-binding site. This region consists of a dimer of one heavy chain and one light chain variable domain in tight, non-covalent association. It is in this configuration that the three hypervariable regions of each variable domain interact to define an antigen-binding site on the surface of the V_H-V_L dimer. Collectively, the six hypervariable regions confer antigen-binding specificity to the antibody. However, even a single variable domain (or half of an Fv comprising only three hypervariable regions specific for an antigen) has the ability to recognize and bind antigen, although at a lower affinity than the entire binding site.

The Fab fragment also contains the constant domain of the light chain and the first constant domain (CH1) of the heavy chain. Fab' fragments differ from Fab fragments by the addition of a few residues at the carboxy terminus of the heavy chain CH1 domain including one or more cysteines from the antibody hinge region. Fab'-SH is the designation herein for Fab' in which the cysteine residue(s) of the constant domains bear at least one free thiol group. $F(ab')_2$ antibody fragments originally were produced as pairs of Fab' fragments which have hinge cysteines between them. Other chemical couplings of antibody fragments are also known.

The "light chains" of antibodies from any vertebrate species can be assigned to one of two clearly distinct types, called kappa (κ) and lambda (λ), based on the amino acid sequences of their constant domains.

The term "Fc region" herein is used to define a C-terminal region of an immunoglobulin heavy chain, including native sequence Fc regions and variant Fc regions. Although the boundaries of the Fc region of an immunoglobulin heavy chain might vary, the human IgG heavy chain Fc region is usually defined to stretch from an amino acid residue at position Cys226, or from Pro230, to the carboxyl-terminus thereof. The C-terminal lysine (residue 447 according to the EU numbering system) of the Fc region may be removed, for example, during production or purification of the antibody, or by recombinantly engineering the nucleic acid encoding a heavy chain of the antibody. Accordingly, a composition of intact antibodies may comprise antibody populations with all K447 residues removed, antibody populations with no K447 residues removed, and antibody populations having a mixture of antibodies with and without the K447 residue.

Unless indicated otherwise, herein the numbering of the residues in an immunoglobulin heavy chain is that of the EU index as in Kabat *et al., Sequences of Proteins of Immunological Interest*, 5th Ed. Public Health Service, National Institutes of Health, Bethesda, MD (1991), expressly incorporated herein by reference. The "EU index as in Kabat" refers to the residue numbering of the human IgG1 EU antibody.

A "native sequence Fc region" comprises an amino acid sequence identical to the amino acid sequence of an Fc region found in nature. Native sequence human Fc regions include a native sequence human IgG1 Fc region (non-A and A allotypes); native sequence human IgG2 Fc region; native sequence human IgG3 Fc region; and native sequence human IgG4 Fc region as well as naturally occurring variants thereof.

A "variant Fc region" comprises an amino acid sequence which differs from that of a native sequence Fc region by virtue of at least one amino acid modification, preferably one or more amino acid substitution(s). Preferably, the variant Fc region has at least one amino acid substitution compared to a native sequence Fc region or to the Fc region of a parent polypeptide, *e.g.* from about one to about ten amino acid substitutions, and preferably from about one to about five amino acid substitutions in a native sequence Fc region or in the Fc region of the parent polypeptide. The variant Fc region herein will preferably possess at least about 80% homology with a native sequence Fc region and/or with an Fc region of a parent polypeptide, and most preferably at least about 90% homology therewith, more preferably at least about 95% homology therewith.

Depending on the amino acid sequence of the constant domain of their heavy chains, intact antibodies can be assigned to different "classes". There are five major classes of intact antibodies: IgA, IgD, IgE, IgG, and IgM, and several of these may be further divided into "subclasses" (isotypes), *e.g.*, IgG1, IgG2, IgG3, IgG4, IgA, and IgA2. The heavy-chain constant domains that correspond to the different classes of antibodies are called α, δ, ε, γ, and μ, respectively. The subunit structures and three-dimensional configurations of different classes of immunoglobulins are well known.

"Single-chain Fv" or "scFv" antibody fragments comprise the V_H and V_L domains of antibody, wherein these domains are present in a single polypeptide chain. Preferably, the Fv polypeptide further comprises a polypeptide linker between the V_H and V_L domains which enables the scFv to form the desired structure for antigen binding. For a review of scFv see Plückthun in *The Pharmacology of Monoclonal Antibodies*, vol. 113, Rosenburg and Moore eds., Springer-Verlag, New York, pp. 269-315 (1994).

The term "diabodies" refers to small antibody fragments with two antigen-binding sites, which fragments comprise a variable heavy domain (V_H) connected to a variable light domain (V_L) in the same polypeptide chain (V_H - V_L). By using a linker that is too short to allow pairing between the two domains on the same chain, the domains are forced to pair with the complementary domains of another chain and create two antigen-binding sites. Diabodies are described more fully in, for example, EP 404,097; WO 93/11161; and Hollinger *et al., Proc. Natl. Acad. Sci. USA*, 90:6444-6448 (1993).

A "naked antibody" is an antibody that is not conjugated to a heterologous molecule, such as a small molecule or radiolabel.

An "isolated" antibody is one which has been identified and separated and/or recovered from a component of its natural environment. Contaminant components of its natural environment are materials which would interfere with diagnostic or therapeutic uses for the antibody, and may include enzymes, hormones, and other proteinaceous or nonproteinaceous solutes. In preferred embodiments, the antibody will be purified (1) to greater than 95% by weight of antibody as determined by the Lowry method, and most preferably more than 99% by weight, (2) to a degree sufficient to obtain at least 15 residues of N-terminal or internal amino acid sequence by use of a spinning cup sequenator, or (3) to homogeneity by SDS-PAGE under reducing or nonreducing conditions using Coomassie blue or, preferably, silver stain. Isolated antibody includes the antibody *in situ* within recombinant cells since at least one component of the antibody's natural environment will not be present. Ordinarily, however, isolated antibody will be prepared by at least one purification step.

An "affinity matured" antibody is one with one or more alterations in one or more hypervariable regions thereof which result an improvement in the affinity of the antibody for antigen, compared to a parent antibody which does not possess those alteration(s). Preferred affinity matured antibodies will have nanomolar or even picomolar affinities for the target antigen. Affinity matured antibodies are produced by procedures known in the art. Marks *et al. Bio/Technology* 10:779-783 (1992) describes affinity maturation by VH and VL domain shuffling. Random mutagenesis of HVR and/or framework residues is described by: Barbas *et al. Proc Nat. Acad. Sci, USA* 91:3809-3813 (1994); Schier *et al. Gene* 169:147-155 (1995); Yelton *et al. J. Immunol.* 155:1994-2004 (1995); Jackson *et al., J. Immunol.* 154(7):3310-9 (1995); and Hawkins *et al, J. Mol. Biol.* 226:889-896 (1992).

An "amino acid sequence variant" antibody herein is an antibody with an amino acid sequence which differs from a main species antibody. Ordinarily, amino acid sequence variants will possess at least about 70% homology with the main species antibody, and preferably, they will be at least about 80%, more preferably at least about 90% homologous with the main species antibody. The amino acid sequence variants possess substitutions, deletions, and/or additions at certain positions within or adjacent to the amino acid sequence of the main species antibody. Examples of amino acid sequence variants herein include an acidic variant (*e.g.* deamidated antibody variant), a basic variant, an antibody with an amino-terminal leader extension (*e.g.* VHS-) on one or two light chains thereof, an antibody with a C-terminal lysine residue on one or two heavy chains thereof, etc., and includes combinations of variations to the amino acid sequences of heavy and/or light chains. The antibody variant of particular interest herein is the antibody comprising an amino-terminal leader extension on one or two light chains thereof, optionally further comprising other amino acid sequence and/or glycosylation differences relative to the main species antibody.

A "glycosylation variant" antibody herein is an antibody with one or more carbohydrate moieities attached thereto which differ from one or more carbohydrate moieties attached to a main species antibody. Examples of glycosylation variants herein include antibody with a G1 or G2 oligosaccharide structure, instead a G0 oligosaccharide structure, attached to an Fc region thereof, antibody with one or two carbohydrate moieties attached to one or two light chains thereof, antibody with no carbohydrate attached to one or two heavy chains of the antibody, etc., and combinations of glycosylation alterations.

Where the antibody has an Fc region, an oligosaccharide structure may be attached to one or two heavy chains of the antibody, *e.g.* at residue 299 (298, Eu numbering of residues). For pertuzumab, G0 was the predominant oligosaccharide structure, with other oligosaccharide structures such as G0-F, G-1, Man5, Man6, G1-1, G1(1-6), G1(1-3) and G2 being found in lesser amounts in the pertuzumab composition.

Unless indicated otherwise, a "G1 oligosaccharide structure" herein includes G-1, G1-1, G1(1-6) and G1(1-3) structures.

An "amino-terminal leader extension" herein refers to one or more amino acid residues of the amino-terminal leader sequence that are present at the amino-terminus of any one or more heavy or light chains of an antibody. An exemplary amino-terminal leader extension comprises or consists of three amino acid residues, VHS, present on one or both light chains of an antibody variant.

A "deamidated" antibody is one in which one or more asparagine residues thereof has been derivatized, *e.g.* to an aspartic acid, a succinimide, or an iso-aspartic acid.

B.1 <u>General Description of the Invention</u>

The practice of the present invention will employ, unless otherwise indicated, conventional techniques of molecular biology (including recombinant techniques), microbiology, cell biology, and biochemistry, which are within the skill of the art. Such techniques are explained fully in the literature, such as, "Molecular Cloning: A Laboratory Manual", 2nd edition (Sambrook et al., 1989); "Oligonucleotide Synthesis" (M.J. Gait, ed., 1984); "Animal Cell Culture" (R.I. Freshney, ed., 1987); "Methods in Enzymology" (Academic Press, Inc.); "Handbook of Experimental Immunology", 4th edition (D.M. Weir & C.C. Blackwell, eds., Blackwell Science Inc., 1987); "Gene Transfer Vectors for Mammalian Cells" (J.M. Miller & M.P. Calos, eds., 1987); "Current Protocols in Molecular Biology" (F.M. Ausubel et al., eds., 1987); and "PCR: The Polymerase Chain Reaction", (Mullis et al., eds., 1994).

As discussed above, the detection or diagnosis of IBD is currently obtained by various classification systems that rely on a number of variables observed in a patient. The present invention is based on the identification of genes that are associated with IBD. Accordingly, the expression levels of such genes can serve as diagnostic markers to identify patients with IBD. As described in the Examples, the differential expression of a number of genes in IBD patients has been observed. Thus, according to the present invention, the genes listed in Table 1 have been identified as differentially expressed in IBD.

Table 1

Gene	Indication(s)	Change in expression	SEQ ID NO nucleic acid	SEQ ID NO amino acid	Figure(s)
IRTA1	CD	Decrease	1	2	1, 2
CCL23 (CKbeta8-1)	CD	Decrease	3	5	3, 5
CCL23 (CKbeta8)			4	6	4,6
CXCL13	CD	Decrease	7	8	7,8
ATG16L1 (isoform 2)	CD	Decrease	9	11	9,11
ATG16L1 (isoform 1)			10	12	10,12
ATG4D	CD	Decrease	13	14	13,14
ATG3	CD	Decrease	15	16	15,16
ATG12	CD	Increase	17	18	17,18
ATG16L2	CD	Increase	19	20	19,20
LC3B	CD	Increase	21	22	21,22

a. *Biomarkers of the Invention*

The present invention provides numerous gene expression markers or biomarkers for IBD listed in Table 1. In one embodiment of the present invention, the biomarkers are suitable for use in a panel of markers (as described herein). Such panels may include one or more markers from Table 1. Those of ordinary skill in the art will appreciate the various combinations of biomarkers from Table 1 that are suitable for use in the panels described herein.

The genes of Table 1 are considered to be differentially expressed when there is an at least about one-fold, at least about 1.5-fold, at least about 2-fold, at least about 2.5-fold, at least about 3-fold, at least about 3.5 fold, at least about 4-fold, at least about 4.5-fold, at least about 5-fold, at least about 5.5-fold, at least about 6-fold, at least about 7-fold, at least about 8-fold, at least about 9-fold, or at least about 10-fold difference between the expression of a given gene in normal and diseased subjects, or in various stages of disease development in a diseased subject.

In one embodiment of the present invention, a preferred set of IBD markers identified by microarray analysis, includes markers that are upregulated in an IBD. Preferably, the set of upregulated markers includes ATG12, ATG16L2, and LC3B (regulators of the autophagy pathway).

A preferred set of downregulated markers includes immune associated genes IRTA1- a novel surface B-cell receptor, CCL23, CXCL13, and regulators of the autophagy pathway including ATG16L1, ATG4D; and ATG3. IRTA1 is also known as FCRH4; IGFP2; IRTA1; MGC150522; MGC150523; dJ801G22.1; FCRL4. CCL23 is also known as CKb8; MIP3; Ckb-8; MIP-3; MPIF-1; SCYA23; Ckb-8-1; CK-BETA-8; CCL23. CXCL13 is also known as BLC; BCA1; ANGIE; BCA-1; BLR1L; ANGIE2; SCYB13; CXCL13. ATG16L1 is also known as IBD10; WDR30; APG16L; ATG16L; FLJ00045; FLJ10035; FLJ10828; FLJ22677; ATG16L1. ATG4D is also known as APG4D; AUTL4; APG4-D; ATG4D. ATG3 is also known as APG3; APG3L; PC3-96; FLJ22125; MGC15201; APG3-LIKE;

DKFZp564M1178; ATG3. ATG12 is also known as APG12; FBR93; APG12L; HAPG12; ATG12. ATG16L2 is also known as WDR80; FLJ00012; ATG16L2. LC3B is also known as LC3B; MAP1A/1BLC3; MAP1LC3B. A panel of biomarkers as described herein may include one of, more than one of, or all of these markers. The panel may include CCL23. Alternatively, the panel may include at least one marker corresponding to a regulator of the autophagy pathway. The panel may further include one or more of IRTA1, CCL23, and CXCL13.

A panel of biomarkers may include one or more of, or all of the markers of Table 1 plus at least one marker from Figure 24, 25, 26, or 27. The panel may include at least one marker from Figure 24, 25, 26, or 27.

Members of lists provided above, as single markers or in any combination, are preferred for use in prognostic and diagnostic assays of the present invention. The IBD markers of the present invention are differentially expressed genes or regions of genes. A differential level of expression of one or more markers in a test sample from a mammalian subject relative to a control can determined from the level of RNA transcripts or expression products detected by one or more of the methods described in further detail below.

Based on evidence of differential expression of RNA transcripts in normal cells and cells from a mammalian subject having IBD, the present invention provides gene markers for IBD. The IBD markers and associated information provided by the present invention allow physicians to make more intelligent treatment decisions, and to customize the treatment of IBD to the needs of individual patients, thereby maximizing the benefit of treatment and minimizing the exposure of patients to unnecessary treatments, which do not provide any significant benefits and often carry serious risks due to toxic side-effects.

Multi-analyte gene expression tests can measure the expression level of one or more genes involved in each of several relevant physiologic processes or component cellular characteristics. In some instances the predictive power of the test, and therefore its utility, can be improved by using the expression values obtained for individual genes to calculate a score which is more highly correlated with outcome than is the expression value of the individual genes. For example, the calculation of a quantitative score (recurrence score) that predicts the likelihood of recurrence in estrogen receptor-positive, node-negative breast cancer is describe in U.S. Published Patent Application No. 20050048542. The equation used to calculate such a recurrence score may group genes in order to maximize the predictive value of the recurrence score. The grouping of genes may be performed at least in part based on knowledge of their contribution to physiologic functions or component cellular characteristics such as discussed above. The formation of groups, in addition, can facilitate the mathematical weighting of the contribution of various expression values to the recurrence score. The weighting of a gene group representing a physiological process or component cellular characteristic can reflect the contribution of that process or characteristic to the pathology of the IBD and clinical outcome. Accordingly, in an important aspect, the present invention also provides specific groups of the genes identified herein, that together are more reliable and powerful predictors of outcome than the individual genes or random combinations of the genes identified.

In addition, based on the determination of a recurrence score, one can choose to partition patients into subgroups at any particular value(s) of the recurrence score, where all patients with values in a given range can be classified as belonging to a particular risk group. Thus, the values chosen will define subgroups of patients with respectively greater or lesser risk.

The utility of a gene marker in predicting the development or progression of an IBD may not be unique to that marker. An alternative marker having a expression pattern that is closely similar to a particular test marker may be substituted for or used in addition to a test marker and have little impact on the overall predictive utility of the test. The closely similar expression patterns of two genes may result from involvement of both genes in a particular process and/or being under common regulatory control. The present invention specifically includes and contemplates the use of such substitute genes or gene sets in the methods of the present invention.

The markers and associated information provided by the present invention predicting the development and/or progression of an IBD also have utility in screening patients for inclusion in clinical trials that test the efficacy of drug compounds for the treatment of patients with IBD.

The markers and associated information provided by the present invention predicting the presence, development and/or progression of an IBD are useful as criterion for determing whether IBD treatment is appropriate. For example, IBD treatment may be appropriate where the results of the test indicate that an IBD marker is differentially expressed in a test sample from an individual relative to a control sample. The individual may be an individual not known to have an IBD, an individual known to have an IBD, an individual previously diagnosed with an IBD undergoing treatment for the IBD, or an individual previously diagnosed with an IBD and having had surgery to address the IBD. In addition, the present invention contemplates methods of treating an IBD. As described below, the diagnostic methods of the present invention may further comprise the step of administering an IBD therapeutic agent to the mammalian subject that provided the test sample in which the differential expression of one or more IBD markers was observed relative to a control. Such methods of treatment would therefore comprise (a) determining the presence of an IBD in a mammalian subject, and (b) administering an IBD therapeutic agent to the mammalian subject.

In another embodiment, the IBD markers and associated information are used to design or produce a reagent that modulates the level or activity of the gene's transcript or its expression product. Said reagents may include but are not limited to an antisense RNA, a small inhibitory RNA (siRNA), a ribozyme, a monoclonal or polyclonal antibody. In a further embodiment, said gene or its transcript, or more particularly, an expression product of said transcript is used in an (screening) assay to identify a drug compound, wherein said drug compounds is used in the development of a drug to treat an IBD.

In various embodiments of the inventions, various technological approaches described below are available for determination of expression levels of the disclosed genes. In particular embodiments, the expression level of each gene may be determined in relation to various features of the expression products of the gene including exons, introns, protein epitopes and protein activity. In other embodiments, the expression level of a gene may be inferred from analysis of the structure of the gene, for example from the analysis of the methylation pattern of gene's promoter(s).

b. *Diagnostic Methods of the Invention*

The present invention provides methods of detecting or diagnosing an IBD in a mammalian subject based on differential expression of an IBD marker. In a one embodiment, the methods comprise the use of a panel of IBD markers as discussed above. The panels may include one or more IBD markers selected from Table 1. In one other embodiment, the panel includes ATG16L1 and at least one additional IBD marker selected Table 1.

In some embodiments, the panel of IBD markers will include at least 1 IBD marker, at least two IBD markers, at least three IBD markers, at least 4 IBD markers, at least five IBD markers, at least 6 IBD markers, at least 7 IBD marker, at least 8 IBD markers, or at least 9 IBD markers. In one embodiment, the panel includes markers in increments of five. In another embodiment, the panel includes markers in increments of ten. The panel may include an IBD marker that is overexpressed in IBD relative to a control, an IBD marker that is underexpressed in IBD relative to a control, or IBD markers that are both overexpressed and underexpressed in IBD relative to a control. In a preferred embodiment, the panel includes one or more markers that are upregulated in CD and one or more markers that are downregulated in CD.

In another embodiment, the panels of the present invention may include an IBD marker that is overexpressed in an active IBD relative to a control, underexpressed in an active IBD relative to a control, or IBD markers that are both overexpressed and underexpressed in an active IBD relative to a control. In another embodiment, the panels of the present invention may include an IBD marker that is overexpressed in an inactive IBD relative to a control, underexpressed in an inactive IBD relative to a control, or IBD markers that are both overexpressed and underexpressed in an inactive IBD relative to a control. In a preferred embodiment, the active IBD is CD. In another preferred embodiment, the inactive IBD is CD.

In a preferred embodiment, the methods of diagnosing or detecting the presence of an IBD in a mammalian subject comprise determining a differential expression level of RNA transcripts or expression products thereof from a panel of IBD markers in a test sample obtained from the subject relative to the level of expression in a control, wherein the differential level of expression is indicative of the presence of an IBD in the subject from which the test sample was obtained. The differential expression in the test sample may be higher and/or lower relative to a control as discussed herein.

Differential expression or activity of one or more of the genes provided in the lists above, or the corresponding RNA molecules or encoded proteins in a biological sample obtained from the patient, relative to control, indicates the presence of an IBD in the patient. The control can, for example, be a gene, present in the same cell, which is known to be up-regulated (or down-regulated) in an IBD patient (positive control). Alternatively, or in addition, the control can be the expression level of the same gene in a normal cell of the same cell type (negative control). Expression levels can also be normalized, for example, to the expression levels of housekeeping genes, such as glyceraldehyde-3-phosphate-dehydrogenase (GAPDH) and/or β-actin, or to the expression levels of all genes in the sample tested. In one embodiment, expression of one or more of the above noted genes is deemed positive expression if it is at the median or above, *e.g.* compared to other samples of the same type. The median expression level can be determined essentially contemporaneously with measuring gene expression, or may have been determined previously. These and other methods are well known in the art, and are apparent to those skilled in the art.

Methods for identifying IBD patients are provided herein. Of this patient population, patients with an IBD can be identified by determining the expression level of one or more of the genes, the corresponding RNA molecules or encoded proteins in a biological sample comprising cells obtained from the patient. The biological sample can, for example, be a tissue biopsy as described herein.

The methods of the present invention concern IBD diagnostic assays, and imaging methodologies. In one embodiment, the assays are performed using antibodies as described herein. The invention also provides various immunological assays useful for the detection and quantification of proteins. These assays are performed within various immunological assay formats well known in the art, including but not limited to various types of radioimmunoassays, enzyme-linked immunosorbent assays (ELISA), enzyme-linked immunofluorescent assays (ELIFA), and the like. In addition, immunological imaging methods capable of detecting an IBD characterized by expression of a molecule described herein are also provided by the invention, including but not limited to radioscintigraphic imaging methods using labeled antibodies. Such assays are clinically useful in the detection, monitoring, diagnosis and prognosis of IBD characterized by expression of one or more molecules described herein.

Another aspect of the present invention relates to methods for identifying a cell that expresses a molecule described herein. The expression profile of a molecule(s) described herein make it a diagnostic marker for IBD. Accordingly, the status of the expression of the molecule(s) provides information useful for predicting a variety of factors including susceptibility to advanced stages of disease, rate of progression, and/or sudden and severe onset of symptoms in an active IBD or an inactive IBD, i.e. flare-ups.

In one embodiment, the present invention provides methods of detecting an IBD. A test sample from a mammalian subject and a control sample from a known normal mammal are each contacted with an anti-IBD marker antibody or a fragment thereof. The level of IBD marker expression is measured and a differential level of expression in the test sample relative to the control sample is indicative of an IBD in the mammalian subject from which the test sample was obtained. In some embodiments, the level of IBD marker expression in the test sample is determined to be higher than the level of expression in the control, wherein the higher level of expression indicates the presence of an IBD in the subject from which the test sample was obtained. In another embodiments, the level of IBD marker expression in the test sample is determined to be lower than the level of expression in the control, wherein the lower level of expression indicates the presence of an IBD in the subject from which the test sample was obtained.

In another embodiment, the IBD detected by the methods of the present invention is the recurrence or flareup of an IBD in the mammalian subject.

In preferred embodiments, the methods are employed to detect the flare-up of an IBD or a recurrence of an IBD in a mammalian subject previously determined to have an IBD who underwent treatment for the IBD, such as drug therapy or a surgical procedure. Following initial detection of an IBD, additional test samples may be obtained from the mammalian subject found to have an IBD. The additional sample may be obtained hours, days, weeks, or months after the initial sample was taken. Those of skill in the art will appreciate the appropriate schedule for obtaining such additional samples, which may include second, third, fourth, fifth, sixth, etc. test samples. The intial test sample and the additional sample (and alternately a control sample as described herein) are contacted with an anti-IBD marker antibody. The level of IBD marker expression is measured and a differential level of expression in the additional test sample as compared to the initial test sample is indicative of a flare-up in or a recurrence of an IBD in the mammalian subject from which the test sample was obtained.

In one aspect, the methods of the present invention are directed to a determining step. In one embodiment, the determining step comprises measuring the level of expression of one or more IBD markers in a test sample relative to a control. Typically, measuring the level of IBD marker expression, as described herein, involves analyzing a test sample for differential expression of an IBD marker relative to a control by performing one or more of the techniques described herein. The expression level data obtained from a test sample and a control are compared for differential levels of expression. In another embodiment, the determining step further comprises an examination of the test sample and control expression data to assess whether an IBD is present in the subject from which the test sample was obtained.

The methods of the present invention are valuable tools for detecting and IBD marker. Measurement of biomarker expression or protein levels may be performed by using a software program executed by a suitable processor. Suitable software and processors are well known in the art and are commercially available. The program may be embodied in software stored on a tangible medium such as CD-ROM, a floppy disk, a hard drive, a DVD, or a memory associated with the processor, but persons of ordinary skill in the art will readily appreciate that the entire program or parts thereof could alternatively be executed by a device other than a processor, and/or embodied in firmware and/or dedicated hardware in a well known manner.

Following the measurement of one or more IBD markers, the assay results, findings, diagnoses, predictions and/or treatment recommendations are typically recorded and communicated to technicians, physicians and/or patients, for example. In certain embodiments, computers will be used to communicate such information to interested parties, such as, patients and/or the attending physicians. In some embodiments, the assays will be performed or the assay results analyzed in a country or jurisdiction which differs from the country or jurisdiction to which the results or diagnoses are communicated.

To facilitate diagnosis, the level of one or more IBD markers can be displayed on a display device, contained electronically, or in a machine-readable medium, such as but not limited to, analog tapes like those readable by a VCR, CD-ROM, DVD-ROM, USB flash media, among others. Such machine-readable media can also contain additional test results, such as, without limitation, measurements of clinical parameters and traditional laboratory risk factors. Alternatively or additionally, the machine-readable media can also comprise subject information such as medical history and any relevant family history.

The methods of this invention, when practiced for commercial diagnostic purposes generally produce a report or summary of the normalized levels of one or more of the biomarkers described herein. The methods of this invention will produce a report comprising one or more predictions concerning a patient and an IBD.

The methods and reports of this invention can further include storing the report in a database. Alternatively, the method can further create a record in a database for the subject and populate the record with data. In one embodiment the report is a paper report, in another embodiment the report is an auditory report, in another embodiment the report is an electronic record. It is contemplated that the report is provided to a physician and/or the patient. The receiving of the report can further include establishing a network connection to a server computer that includes the data and report and requesting the data and report from the server computer. The methods provided by the present invention may also be automated in whole or in part.

In some embodiments, the determining step comprises the use of a software program executed by a suitable processor for the purpose of (i) measuring the differential level of IBD marker expression in a test sample and a control; and/or (ii) analyzing the data obtained from measuring differential level of IBD marker expression in a test sample and a control. Suitable software and processors are well known in the art and are commercially available. The program may be embodied in software stored on a tangible medium such as CD-ROM, a floppy disk, a hard drive, a DVD, or a memory associated with the processor, but persons of ordinary skill in the art will readily appreciate that the entire program or parts thereof could alternatively be executed by a device other than a processor, and/or embodied in firmware and/or dedicated hardware in a well known manner.

Following the determining step, the measurement results, findings, diagnoses, predictions and/or treatment recommendations are typically recorded and communicated to technicians, physicians and/or patients, for example. In certain embodiments, computers will be used to communicate such information to interested parties, such as, patients and/or the attending physicians. In some embodiments, the assays will be performed or the assay results analyzed in a country or jurisdiction which differs from the country or jurisdiction to which the results or diagnoses are communicated.

In a preferred embodiment, a diagnosis, prediction and/or treatment recommendation based on the level of expression of one or more IBD markers disclosed herein measured in a test subject of having one or more of the IBD markers herein is communicated to the subject as soon as possible after the assay is completed and the diagnosis and/or prediction is generated. The results and/or related information may be communicated to the subject by the subject's treating physician. Alternatively, the results may be communicated directly to a test subject by any means of communication, including writing, electronic forms of communication, such as email, or telephone. Communication may be facilitated by use of a computer, such as in case of email communications. In certain embodiments, the communication containing results of a diagnostic test and/or conclusions drawn from and/or treatment recommendations based on the test, may be generated and delivered automatically to the subject using a combination of computer hardware and software which will be familiar to artisans skilled in telecommunications. One example of a healthcare-oriented communications system is described in U.S. Pat. No. 6,283,761; however, the present invention is not limited to methods which utilize this particular communications system. In certain embodiments of the methods of the invention, all or some of the method steps, including the assaying of samples, diagnosing of diseases, and communicating of assay results or diagnoses, may be carried out in diverse (e.g., foreign) jurisdictions.

The invention provides assays for detecting the differential expression of an IBD marker in tissues associated with the gastrointestinal tract including, without limitation, ascending colon tissue, descending colon tissue, sigmoid colon tissue, and terminal ileum tissue; as well expression in other biological samples such as serum, semen, bone, prostate, urine, cell preparations, and the like. Methods for detecting differential expression of an IBD marker are also well known and include, for example, immunoprecipitation, immunohistochemical analysis, Western blot analysis, molecular binding assays, ELISA, ELIFA and the like. For example, a method of detecting the differential expression of an IBD marker in a biological sample comprises first contacting the sample with an anti-IBD marker antibody, an IBD marker-reactive fragment thereof, or a recombinant protein containing an antigen-binding region of an anit-IBD marker antibody; and then detecting the binding of an IBD marker protein in the sample.

In various embodiments of the inventions, various technological approaches are available for determination of expression levels of the disclosed genes, including, without limitation, RT-PCR, microarrays, serial analysis of gene expression (SAGE) and Gene Expression Analysis by Massively Parallel Signature Sequencing (MPSS), which will be discussed in detail below. In particular embodiments, the expression level of each gene may be determined in relation to various features of the expression products of the gene including exons, introns, protein epitopes and protein activity. In other embodiments, the expression level of a gene may be inferred from analysis of the structure of the gene, for example from the analysis of the methylation pattern of gene's promoter(s).

In one embodiment, the present invention provides a method of diagnosing the presence of an IBD in a mammalian subject by determining that the level of expression of a nucleic acid encoding a polypeptide of Table 1 in a test sample obtained from the subject is different relative to the level of expression in a control, wherein the different level of expression is indicative of the presence of an IBD in the subject from which the test sample was obtained.

In the methods described herein, the determining step may be preceded by the step of obtaining a test sample from the mammalian subject. The determining step may also be preceded by the step of contacting a test sample from the mammalian subject with an agent for the detection of the differential level of expression.

In another embodiment, the present invention provides a method of diagnosing the degree of IBD-associated inflammation in a mammalian subject by determining that the level of expression of a nucleic acid encoding a polypeptide of Table 1 in a test sample obtained from the subject is different relative to the level of expression in a control, wherein the different level of expression is indicative of the degree of IBD-associated inflammation in the the subject from which the test sample was obtained. In another embodiment, the determining step is preceded by the step of obtaining a test sample from the mammalian subject. In one other embodiment, the determining step is preceded by the step of contacting a test sample from the mammalian subject with an agent for the detection of the differential level of expression.

c. *Therapeutic Methods of the Invention*

The present invention provides therapeutic methods of treating an IBD in a subject in need that comprise detecting the presence of an IBD in a mammalian subject by the diagnostic methods described herein and then administering to the mammalian subject an IBD therapeutic agent. Those of ordinary skill in the art will appreciate the various IBD therapeutic agents that may be suitable for use in the present invention (see St Clair Jones, Hospital Pharmacist, May 2006, Vol. 13; pages 161-166, hereby incorporated by reference in its entirety). The present invention contemplates methods of IBD treatment in which one or more IBD therapeutic agents are administered to a subject in need. In one embodiment, the IBD therapeutic agent is one or more of an aminosalicylate, a corticosteroid, and an immunosuppressive agent. In a preferred embodiment, the aminosalicylate is one of sulfasalazine, olsalazine, mesalamine, balsalazide, and asacol. In another preferred embodiment, multiple aminosalicylates are co-administered, such as a combination of sulfasalazine and olsalazine. In other preferred embodiments, the corticosteroid may be budesonide, prednisone, prednisolone, methylprednisolone, 6-mercaptopurine (6-MP), azathioprine, methotrexate, and cyclosporin. In other preferred embodiments, the IBD therapeutic agent may an antibiotic, such as ciprofloxacin and/or metronidazole; or an antibody-based agent such as infliximab (Remicade®).

The least toxic IBD therapeutic agents which patients are typically treated with are the aminosalicylates. Sulfasalazine (Azulfidine), typically administered four times a day, consists of an active molecule of aminosalicylate (5-ASA) which is linked by an azo bond to a sulfapyridine. Anaerobic bacteria in the colon split the azo bond to release active 5-ASA. However, at least 20% of patients cannot tolerate sulfapyridine because it is associated with significant side-effects such as reversible sperm abnormalities, dyspepsia or allergic reactions to the sulpha component. These side effects are reduced in patients taking olsalazine. However, neither sulfasalazine nor olsalazine are effective for the treatment of small bowel inflammation. Other formulations of 5-ASA have been developed which are released in the small intestine (e.g. mesalamine and asacol). Normally it takes 6-8 weeks for 5-ASA therapy to show full efficacy. Patients who do not respond to 5-ASA therapy, or who have a more severe disease, are prescribed corticosteroids. However, this is a short term therapy and cannot be used as a maintenance therapy. Clinical remission is achieved with corticosteroids within 2-4 weeks, however the side effects are significant and include Cushing goldface, facial hair, severe mood swings and sleeplessness. The response to sulfasalazine and 5-aminosalicylate preparations is poor in CD, fair to mild in early ulcerative colitis and poor in severe UC. If these agents fail, powerful immunosuppressive agents such as cyclosporine, prednisone, 6-mercaptopurine or azathioprine (converted in the liver to 6-mercaptopurine) are typically tried. For CD patients, the use of corticosteroids and other immunosuppressives must be carefully monitored because of the high risk of intra-abdominal sepsis originating in the fistulas and abscesses common in this disease. Approximately 25% of IBD patients will require surgery (colectomy) during the course of the disease.

Treatment of an IBD may include a surgical procedure, including without limitation, a bowel resection, anastomosis, a colectomy, a proctocolectomy, and an ostomy, or any combination thereof.

In addition to pharmaceutical medicine and surgery, nonconventional treatments for IBD such as nutritional therapy have also been attempted. For example, Flexical®, a semi-elemental formula, has been shown to be as effective as the steroid prednisolone. Sanderson *et al.*, *Arch. Dis. Child.* 51:123-7 (1987). However, semi-elemental formulas are relatively expensive and are typically unpalatable- thus their use has been restricted. Nutritional therapy incorporating whole proteins has also been attempted to alleviate the symptoms of IBD. Giafer *et al.*, *Lancet* 335: 816-9 (1990). U.S. Patent No. 5,461,033 describes the use of acidic casein isolated from bovine milk and TGF-2. Beattie *et al.*, *Aliment. Pharmacol. Ther.* 8: 1-6 (1994) describes the use of casein in infant formula in children with IBD. U.S.P. 5,952,295 describes the use of casein in an enteric formulation for the treatment of IBD. However, while nutrional therapy is non-toxic, it is a palliative treatment and does not treat the underlying cause of the disease.

The present invention contemplates methods of IBD treatment, including for example, in vitro, ex vivo and in vivo therapeutic methods. The invention provides methods useful for treating an IBD in a subject in need upon the detection of an IBD disease state in the subject associated with the expression of one or more IBD markers disclosed herein, such as increased and/or decreased IBD marker expression. In one preferred embodiment, the method comprises (a) determining that the level of expression of (i) one or more nucleic acids encoding one or more polypeptides selected from Table 1; or (ii) RNA transcripts or expression products thereof of one or more genes listed in Table 1 in a test sample obtained from said subject is higher and/or lower relative to the level of expression in a control, wherein said higher and/or lower level of expression is indicative of the presence of an IBD in the subject from which the test sample was obtained; and (b) administering to said subject an effective amount of an IBD therapeutic agent. The determining step (a) may comprise the measurement of the expression of multiple IBD marker

The method of treatment comprises detecting the IBD and administering an effective amount of an IBD therapeutic agent to a subject in need of such treatment. In some embodiments, the IBD disease state is associated with an increased and/or decrease in expression of one or more IBD markers.

In one aspect, the invention provides methods for treating or preventing an IBD, the methods comprising detecting the presence of an IBD in a subject and administering an effective amount of an

IBD therapeutic agent to the subject. It is understood that any suitable IBD therapeutic agent may be used in the methods of treatment, including aminosalicylates, corticosteroids, and immunosuppressive agents as discussed herein.

In any of the methods herein, one may administer to the subject or patient along with a single IBD therapeutic agent discussed herein an effective amount of a second medicament (where the single IBD therapeutic agent herein is a first medicament), which is another active agent that can treat the condition in the subject that requires treatment. For instance, an aminosalicylate may be co-administered with a corticosteroid, an immunsuppressive agent, or another aminosalicylate. The type of such second medicament depends on various factors, including the type of IBD, its severity, the condition and age of the patient, the type and dose of first medicament employed, etc.

Such treatments using first and second medicaments include combined administration (where the two or more agents are included in the same or separate formulations), and separate administration, in which case, administration of the first medicament can occur prior to, and/or following, administration of the second medicament. In general, such second medicaments may be administered within 48 hours after the first medicaments are administered, or within 24 hours, or within 12 hours, or within 3-12 hours after the first medicament, or may be administered over a pre-selected period of time, which is preferably about 1 to 2 days, about 2 to 3 days, about 3 to 4 days, about 4 to 5 days, about 5 to 6 days, or about 6 to 7 days.

The first and second medicaments can be administered concurrently, sequentially, or alternating with the first and second medicament or upon non-responsiveness with other therapy. Thus, the combined administration of a second medicament includes co-administration (concurrent administration), using separate formulations or a single pharmaceutical formulation, and consecutive administration in either order, wherein preferably there is a time period while both (or all) medicaments simultaneously exert their biological activities. All these second medicaments may be used in combination with each other or by themselves with the first medicament, so that the express "second medicament" as used herein does not mean it is the only medicament besides the first medicament, respectively. Thus, the second medicament need not be one medicament, but may constitute or comprise more than one such drug. These second medicaments as set forth herein are generally used in the same dosages and with administration routes as the first medicaments, or about from 1 to 99% of the dosages of the first medicaments. If such second medicaments are used at all, preferably, they are used in lower amounts than if the first medicament were not present, especially in subsequent dosings beyond the initial dosing with the first medicament, so as to eliminate or reduce side effects caused thereby.

Where the methods of the present invention comprise administering one or more IBD therapeutic agent to treat or prevent an IBD, it may be particularly desirable to combine the administering step with a surgical procedure that is also performed to treat or prevent the IBD. The IBD surgical procedures contemplated by the present invention include, without limitation, a bowel resection, anastomosis, a colectomy, a proctocolectomy, and an ostomy, or any combination thereof. For instance, an IBD therapeutic agent described herein may be combined with a colectomy in a treatment scheme, e.g. in treating an IBD. Such combined therapies include and separate administration, in which case, administration of the IBD therapeutic agent can occur prior to, and/or following, the surgical procedure.

Treatment with a combination of one or more IBD therapeutic agents; or a combination of one or more IBD therapeutic agents and a surgical procedure described herein preferably results in an improvement in the signs or symptoms of an IBD. For instance, such therapy may result in an improvement in the subject receiving the IBD therapeutic agent treatment regimen and a surgical procedure, as evidenced by a reduction in the severity of the pathology of the IBD.

The IBD therapeutic agent(s) is/are administered by any suitable means, including parenteral, subcutaneous, intraperitoneal, intrapulmonary, and intranasal, and, if desired for local treatment, intralesional administration. Parenteral infusions include intramuscular, intravenous, intraarterial, intraperitoneal, or subcutaneous administration. Dosing can be by any suitable route, e.g. by injections, such as intravenous or subcutaneous injections, depending in part on whether the administration is brief or chronic.

The IBD therapeutic agent(s) compositions administered according to the methods of the invention will be formulated, dosed, and administered in a fashion consistent with good medical practice. Factors for consideration in this context include the particular disorder being treated, the particular mammal being treated, the clinical condition of the individual patient, the cause of the disorder, the site of delivery of the agent, the method of administration, the scheduling of administration, and other factors known to medical practitioners. The first medicament(s) need not be, but is optionally formulated with one or more additional medicament(s) (e.g. second, third, fourth, etc. medicaments) described herein. The effective amount of such additional medicaments depends on the amount of the first medicament present in the formulation, the type of disorder or treatment, and other factors discussed above. These are generally used in the same dosages and with administration routes as used hereinbefore or about from 1 to 99% of the heretofore employed dosages.

For the prevention or treatment of an IBD, the appropriate dosage of an IBD therapeutic agent (when used alone or in combination with other agents) will depend on the type of disease to be treated, the type of IBD therapeutic agent(s), the severity and course of the disease, whether the IBD therapeutic agent is administered for preventive or therapeutic purposes, previous therapy, the patient's clinical history and response to the IBD therapeutic agent, and the discretion of the attending physician. The IBD therapeutic agent is suitably administered to the patient at one time or over a series of treatments. Depending on the type and severity of the disease, about 1 ug/kg to 15 mg/kg (e.g. 0.1 mg/kg-10 mg/kg) of IBD therapeutic agent is an initial candidate dosage for administration to the patient, whether, for example, by one or more separate administrations, or by continuous infusion. One typical daily dosage might range from about 1 ug/kg to 100 mg/kg or more, depending on the factors mentioned above. For repeated administrations over several days or longer, depending on the condition, the treatment is sustained until a desired suppression of disease symptoms occurs. One exemplary dosage of the IBD therapeutic agent would be in the range from about 0.05 mg/kg to about 10 mg/kg. Thus, one or more doses of about 0.5 mg/kg, 2.0 mg/kg, 4.0 mg/kg or 10 mg/kg (or any combination thereof) may be administered to the patient. Such doses may be administered intermittently, e.g. every week or every three weeks (e.g. such that the patient receives from about two to about twenty, e.g. about six doses of the IBD therapeutic agent). An initial higher loading dose, followed by one or more lower doses may be administered. An exemplary dosing regimen comprises administering an initial loading dose of about 4 mg/kg, followed by a weekly maintenance dose of about 2 mg/kg of the IBD therapeutic agent. However, other dosage regimens may be useful. The progress of this therapy is easily monitored by conventional techniques and assays.

B.2. Gene Expression Profiling

In general, methods of gene expression profiling can be divided into two large groups: methods based on hybridization analysis of polynucleotides, and other methods based on biochemical detection or sequencing of polynucleotides. The most commonly used methods known in the art for the quantification of mRNA expression in a sample include northern blotting and in situ hybridization (Parker & Barnes, Methods in Molecular Biology 106:247-283 (1999)); RNAse protection assays (Hod, Biotechniques 13:852-854 (1992)); and reverse transcription polymerase chain reaction (RT-PCR) (Weis et al., Trends in Genetics 8:263-264 (1992)). Alternatively, antibodies may be employed that can recognize specific duplexes, including DNA duplexes, RNA duplexes, and DNA-RNA hybrid duplexes or DNA-protein duplexes. Various methods for determining expression of mRNA or protein include, but are not limited to, gene expression profiling, polymerase chain reaction (PCR) including quantitative real time PCR (qRT-PCR), microarray analysis that can be performed by commercially available equipment, following manufacturer's protocols, such as by using the Affymetrix GenChip technology, serial analysis of gene expression (SAGE) (Velculescu et al., Science 270:484-487 (1995); and Velculescu et al., Cell 88:243-51 (1997)), MassARRAY, Gene Expression Analysis by Massively Parallel Signature Sequencing (MPSS) (Brenner et al., Nature Biotechnology 18:630-634 (2000)), proteomics, immunohistochemistry (IHC), etc. Preferably mRNA is quantified. Such mRNA analysis is preferably performed using the technique of polymerase chain reaction (PCR), or by microarray analysis. Where PCR is employed, a preferred form of PCR is quantitative real time PCR (qRT-PCR).

a. *Reverse Transcriptase PCR (RT-PCR)*

Of the techniques listed above, the most sensitive and most flexible quantitative method is RT-PCR, which can be used to compare mRNA levels in different sample populations, in normal and test sample tissues, to characterize patterns of gene expression, to discriminate between closely related mRNAs, and to analyze RNA structure.

The first step is the isolation of mRNA from a target sample. The starting material is typically total RNA isolated from colonic tissue biopsies. Thus, RNA can be isolated from a variety of tissues, including without limitation, the terminal ileum, the ascending colon, the descending colon, and the sigmoid colon. In addition, the colonic tissue from which a biopsy is obtained may be from an inflamed and/or a non-inflamed colonic area.

In one embodiment, the mRNA is obtained from a biopsy as defined above wherein the biopsy is obtained from the left colon or from the right colon. As used herein, the "left colon" refers to the sigmoideum and rectosigmoideum and the "right colon" refers to the cecum.

General methods for mRNA extraction are well known in the art and are disclosed in standard textbooks of molecular biology, including Ausubel et al., Current Protocols of Molecular Biology, John Wiley and Sons (1997). In particular, RNA isolation can be performed using purification kit, buffer set and protease from commercial manufacturers, such as Qiagen, according to the manufacturer's instructions. Total RNA from tissue samples can be isolated using RNA Stat-60 (Tel-Test). RNA prepared from a biopsy can be isolated, for example, by cesium chloride density gradient centrifugation.

As RNA cannot serve as a template for PCR, the first step in gene expression profiling by RT-PCR is the reverse transcription of the RNA template into cDNA, followed by its exponential amplification in a PCR reaction. The two most commonly used reverse transcriptases are avilo myeloblastosis virus reverse transcriptase (AMV-RT) and Moloney murine leukemia virus reverse transcriptase (MMLV-RT). The reverse transcription step is typically primed using specific primers, random hexamers, or oligo-dT primers, depending on the circumstances and the goal of expression profiling. For example, extracted RNA can be reverse-transcribed using a GeneAmp RNA PCR kit (Perkin Elmer, CA, USA), following the manufacturer's instructions. The derived cDNA can then be used as a template in the subsequent PCR reaction.

Although the PCR step can use a variety of thermostable DNA-dependent DNA polymerases, it typically employs the Taq DNA polymerase, which has a 5'-3' nuclease activity but lacks a 3'-5' proofreading endonuclease activity. Thus, TaqMan® PCR typically utilizes the 5'-nuclease activity of Taq or Tth polymerase to hydrolyze a hybridization probe bound to its target amplicon, but any enzyme with equivalent 5' nuclease activity can be used. Two oligonucleotide primers are used to generate an amplicon typical of a PCR reaction. A third oligonucleotide, or probe, is designed to detect nucleotide sequence located between the two PCR primers. The probe is non-extendible by Taq DNA polymerase enzyme, and is labeled with a reporter fluorescent dye and a quencher fluorescent dye. Any laser-induced emission from the reporter dye is quenched by the quenching dye when the two dyes are located close together as they are on the probe. During the amplification reaction, the Taq DNA polymerase enzyme cleaves the probe in a template-dependent manner. The resultant probe fragments disassociate in solution, and signal from the released reporter dye is free from the quenching effect of the second fluorophore. One molecule of reporter dye is liberated for each new molecule synthesized, and detection of the unquenched reporter dye provides the basis for quantitative interpretation of the data.

TaqMan® RT-PCR can be performed using commercially available equipment, such as, for example, ABI PRISM 7700TM Sequence Detection SystemTM (Perkin-Elmer-Applied Biosystems, Foster City, CA, USA), or Lightcycler (Roche Molecular Biochemicals, Mannheim, Germany). In a preferred embodiment, the 5' nuclease procedure is run on a real-time quantitative PCR device such as the ABI PRISM 7700TM Sequence Detection SystemTM. The system consists of a thermocycler, laser, charge-coupled device (CCD), camera and computer. The system amplifies samples in a 96-well format on a thermocycler. During amplification, laser-induced fluorescent signal is collected in real-time through fiber optics cables for all 96 wells, and detected at the CCD. The system includes software for running the instrument and for analyzing the data.

5'-Nuclease assay data are initially expressed as Ct, or the threshold cycle. As discussed above, fluorescence values are recorded during every cycle and represent the amount of product amplified to that point in the amplification reaction. The point when the fluorescent signal is first recorded as statistically significant is the threshold cycle (Ct).

To minimize errors and the effect of sample-to-sample variation, RT-PCR is usually performed using an internal standard. The ideal internal standard is expressed at a constant level among different tissues, and is unaffected by the experimental treatment. RNAs most frequently used to normalize patterns of gene expression are mRNAs for the housekeeping genes glyceraldehyde-3-phosphate-dehydrogenase (GAPDH) and β-actin.

A more recent variation of the RT-PCR technique is the real time quantitative PCR, which measures PCR product accumulation through a dual-labeled fluorigenic probe (i.e., TaqMan® probe). Real time PCR is compatible both with quantitative competitive PCR, where internal competitor for each target sequence is used for normalization, and with quantitative comparative PCR using a normalization gene contained within the sample, or a housekeeping gene for RT-PCR. For further details see, e.g. Held et al., Genome Research 6:986-994 (1996).

According to one aspect of the present invention, PCR primers and probes are designed based upon intron sequences present in the gene to be amplified. In this embodiment, the first step in the primer/probe design is the delineation of intron sequences within the genes. This can be done by publicly available software, such as the DNA BLAT software developed by Kent, W.J., Genome Res. 12(4):656-64 (2002), or by the BLAST software including its variations. Subsequent steps follow well established methods of PCR primer and probe design.

In order to avoid non-specific signals, it is important to mask repetitive sequences within the introns when designing the primers and probes. This can be easily accomplished by using the Repeat Masker program available on-line through the Baylor College of Medicine, which screens DNA sequences against a library of repetitive elements and returns a query sequence in which the repetitive elements are masked. The masked intron sequences can then be used to design primer and probe sequences using any commercially or otherwise publicly available primer/probe design packages, such as Primer Express (Applied Biosystems); MGB assay-by–design (Applied Biosystems); Primer3 (Steve Rozen and Helen J. Skaletsky (2000) Primer3 on the WWW for general users and for biologist programmers. In: Krawetz S, Misener S (eds) Bioinformatics Methods and Protocols: Methods in Molecular Biology. Humana Press, Totowa, NJ, pp 365-386).

The most important factors considered in PCR primer design include primer length, melting temperature (Tm), and G/C content, specificity, complementary primer sequences, and 3'-end sequence. In general, optimal PCR primers are generally 17-30 bases in length, and contain about 20-80%, such as, for example, about 50-60% G+C bases. Tm's between 50 and 80 °C, e.g. about 50 to 70 °C are typically preferred.

For further guidelines for PCR primer and probe design see, e.g. Dieffenbach, C.W. et al., "General Concepts for PCR Primer Design" in: PCR Primer, A Laboratory Manual, Cold Spring Harbor Laboratory Press, New York, 1995, pp. 133-155; Innis and Gelfand, "Optimization of PCRs" in: PCR Protocols, A Guide to Methods and Applications, CRC Press, London, 1994, pp. 5-11; and Plasterer, T.N. Primerselect: Primer and probe design. Methods Mol. Biol. 70:520-527 (1997), the entire disclosures of which are hereby expressly incorporated by reference.

Further PCR-based techniques include, for example, differential display (Liang and Pardee, Science 257:967-971 (1992)); amplified fragment length polymorphism (iAFLP) (Kawamoto et al., Genome Res. 12:1305-1312 (1999)); BeadArray™ technology (Illumina, San Diego, CA; Oliphant et al., Discovery of Markers for Disease (Supplement to Biotechniques), June 2002; Ferguson et al., Analytical Chemistry 72:5618 (2000)); BeadsArray for Detection of Gene Expression (BADGE), using the commercially available Luminex100 LabMAP system and multiple color-coded microspheres (Luminex Corp., Austin, TX) in a rapid assay for gene expression (Yang et al., Genome Res. 11:1888-1898 (2001)); and high coverage expression profiling (HiCEP) analysis (Fukumura et al., Nucl. Acids. Res. 31(16) e94 (2003)).

b. ***Microarrays***

Differential gene expression can also be identified, or confirmed using the microarray technique. Thus, the expression profile of IBD-associated genes can be measured in either fresh or paraffin-embedded tissue, using microarray technology. In this method, polynucleotide sequences of interest (including cDNAs and oligonucleotides) are plated, or arrayed, on a microchip substrate. The arrayed sequences are then hybridized with specific DNA probes from cells or tissues of interest. Just as in the RT-PCR method, the source of mRNA typically is total RNA isolated from biopsy tissue or cell lines derived from cells obtained from a subject having an IBD, and corresponding normal tissues or cell lines. Thus RNA can be isolated from a variety of colonic tissues or colonic tissue-based cell lines.

In a specific embodiment of the microarray technique, PCR amplified inserts of cDNA clones are applied to a substrate in a dense array. Preferably at least 10,000 nucleotide sequences are applied to the substrate. The microarrayed genes, immobilized on the microchip at 10,000 elements each, are suitable for hybridization under stringent conditions. Fluorescently labeled cDNA probes may be generated through incorporation of fluorescent nucleotides by reverse transcription of RNA extracted from tissues of interest. Labeled cDNA probes applied to the chip hybridize with specificity to each spot of DNA on the array. After stringent washing to remove non-specifically bound probes, the chip is scanned by confocal laser microscopy or by another detection method, such as a CCD camera. Quantitation of hybridization of each arrayed element allows for assessment of corresponding mRNA abundance. With dual color fluorescence, separately labeled cDNA probes generated from two sources of RNA are hybridized pairwise to the array. The relative abundance of the transcripts from the two sources corresponding to each specified gene is thus determined simultaneously. The miniaturized scale of the hybridization affords a convenient and rapid evaluation of the expression pattern for large numbers of genes. Such methods have been shown to have the sensitivity required to detect rare transcripts, which are expressed at a few copies per cell, and to reproducibly detect at least approximately two-fold differences in the expression levels (Schena et al., Proc. Natl. Acad. Sci. USA 93(2):106-149 (1996)). Microarray analysis can be performed by commercially available equipment, following manufacturer's protocols, such as by using the Affymetrix GenChip technology, or Incyte's microarray technology, or Agilent's Whole Human Genome microarray technology.

c. *Serial Analysis of Gene Expression (SAGE)*

Serial analysis of gene expression (SAGE) is a method that allows the simultaneous and quantitative analysis of a large number of gene transcripts, without the need of providing an individual hybridization probe for each transcript. First, a short sequence tag (about 10-14 bp) is generated that contains sufficient information to uniquely identify a transcript, provided that the tag is obtained from a unique position within each transcript. Then, many transcripts are linked together to form long serial molecules, that can be sequenced, revealing the identity of the multiple tags simultaneously. The expression pattern of any population of transcripts can be quantitatively evaluated by determining the abundance of individual tags, and identifying the gene corresponding to each tag. For more details see, e.g. Velculescu *et al., Science* 270:484-487 (1995); and Velculescu *et al., Cell* 88:243-51 (1997).

d. *MassARRAY Technology*

In the MassARRAY®-based gene expression profiling method, developed by Sequenom, Inc. (San Diego, CA) following the isolation of RNA and reverse transcription, the obtained cDNA is spiked with a synthetic DNA molecule (competitor), which matches the targeted cDNA region in all positions, except a single base, and serves as an internal standard. The cDNA/competitor mixture is PCR amplified and is subjected to a post-PCR shrimp alkaline phosphatase (SAP) enzyme treatment, which results in the dephosphorylation of the remaining nucleotides. After inactivation of the alkaline phosphatase, the PCR products from the competitor and cDNA are subjected to primer extension, which generates distinct mass signals for the competitor- and cDNA-derives PCR products. After purification, these products are dispensed on a chip array, which is pre-loaded with components needed for analysis with matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF MS) analysis. The cDNA present in the reaction is then quantified by analyzing the ratios of the peak areas in the mass spectrum generated. For further details see, e.g. Ding and Cantor, Proc. Natl. Acad. Sci. USA 100:3059-3064 (2003).

e. *Gene Expression Analysis by Massively Parallel Signature Sequencing (MPSS)*

This method, described by Brenner *et al., Nature Biotechnology* 18:630-634 (2000), is a sequencing approach that combines non-gel-based signature sequencing with *in vitro* cloning of millions of templates on separate 5 μm diameter microbeads. First, a microbead library of DNA templates is constructed by *in vitro* cloning. This is followed by the assembly of a planar array of the template-containing microbeads in a flow cell at a high density (typically greater than 3 x 10^6 microbeads/cm^2). The free ends of the cloned templates on each microbead are analyzed simultaneously, using a fluorescence-based signature sequencing method that does not require DNA fragment separation. This method has been shown to simultaneously and accurately provide, in a single operation, hundreds of thousands of gene signature sequences from a yeast cDNA library.

The steps of a representative protocol for profiling gene expression using fixed, paraffin-embedded tissues as the RNA source, including mRNA isolation, purification, primer extension and amplification are given in various published journal articles (for example: Godfrey *et al. J. Molec. Diagnostics* 2: 84-91 (2000); Specht *et al., Am. J. Pathol.* 158: 419-29 (2001)). Briefly, a representative process starts with cutting about 10 microgram thick sections of paraffin-embedded tissue samples. The mRNA is then extracted, and protein and DNA are removed. General methods for mRNA extraction are well known in the art and are disclosed in standard textbooks of molecular biology, including Ausubel *et al.*, Current Protocols of Molecular Biology, John Wiley and Sons (1997). Methods for RNA extraction from paraffin embedded tissues are disclosed, for example, in Rupp and Locker, *Lab Invest.* 56:A67 (1987), and De Andrés *et al., BioTechniques* 18:42044 (1995). In particular, RNA isolation can be performed using purification kit, buffer set and protease from commercial manufacturers, such as Qiagen, according to the manufacturer's instructions. For example, total RNA from cells in culture can be isolated using Qiagen RNeasy mini-columns. Other commercially available RNA isolation kits include MasterPure™ Complete DNA and RNA Purification Kit (EPICENTRE®, Madison, WI), and Paraffin Block RNA Isolation Kit (Ambion, Inc.). Total RNA from tissue samples can be isolated using RNA Stat-60 (Tel-Test). RNA prepared from tissues can be isolated, for example, by cesium chloride density gradient centrifugation. After analysis of the RNA concentration, RNA repair and/or amplification steps may be included, if necessary, and RNA is reverse transcribed using gene specific promoters followed by PCR. Peferably, real time PCR is used, which is compatible both with quantitative competitive PCR, where internal competitor for each target sequence is used for normalization, and with quantitative comparative PCR using a normalization gene contained within the sample, or a housekeeping gene for RT-PCR. For further details see, e.g. "PCR: The Polymerase Chain Reaction", Mullis et al., eds., 1994; and Held *et al., Genome Research* 6:986-994 (1996). Finally, the data are analyzed to identify the best treatment option(s) available to the patient on the basis of the characteristic gene expression pattern identified in the sample examined.

f. ***Immunohistochemistry***

Immunohistochemistry methods are also suitable for detecting the expression levels of the IBD markers of the present invention. Thus, antibodies or antisera, preferably polyclonal antisera, and most preferably monoclonal antibodies specific for each marker are used to detect expression. The antibodies can be detected by direct labeling of the antibodies themselves, for example, with radioactive labels, fluorescent labels, hapten labels such as, biotin, or an enzyme such as horse radish peroxidase or alkaline phosphatase. Alternatively, unlabeled primary antibody is used in conjunction with a labeled secondary antibody, comprising antisera, polyclonal antisera or a monoclonal antibody specific for the primary antibody. Immunohistochemistry protocols and kits are well known in the art and are commercially available.

Expression levels can also be determined at the protein level, for example, using various types of immunoassays or proteomics techniques.

In immunoassays, the target diagnostic protein marker is detected by using an antibody specifically binding to the markes. The antibody typically will be labeled with a detectable moiety. Numerous labels are available which can be generally grouped into the following categories:

Radioisotopes, such as 35S, 14C, 125I, 3H, and 131I. The antibody can be labeled with the radioisotope using the techniques described in Current Protocols in Immunology, Volumes 1 and 2, Coligen et al. (1991) Ed. Wiley-Interscience, New York, New York, Pubs. for example and radioactivity can be measured using scintillation counting.

Fluorescent labels such as rare earth chelates (europium chelates) or fluorescein and its derivatives, rhodamine and its derivatives, dansyl, Lissamine, phycoerythrin and Texas Red are available. The fluorescent labels can be conjugated to the antibody using the techniques disclosed in Current Protocols in Immunology, supra, for example. Fluorescence can be quantified using a fluorimeter.

Various enzyme-substrate labels are available and U.S. Patent No. 4,275,149 provides a review of some of these. The enzyme generally catalyzes a chemical alteration of the chromogenic substrate which can be measured using various techniques. For example, the enzyme may catalyze a color change in a substrate, which can be measured spectrophotometrically. Alternatively, the enzyme may alter the fluorescence or chemiluminescence of the substrate. Techniques for quantifying a change in fluorescence are described above. The chemiluminescent substrate becomes electronically excited by a chemical reaction and may then emit light which can be measured (using a chemiluminometer, for example) or donates energy to a fluorescent acceptor. Examples of enzymatic labels include luciferases (e.g., firefly luciferase and bacterial luciferase; U.S. Patent No. 4,737,456), luciferin, 2,3-dihydrophthalazinediones, malate dehydrogenase, urease, peroxidase such as horseradish peroxidase (HRPO), alkaline phosphatase, β-galactosidase, glucoamylase, lysozyme, saccharide oxidases (e.g., glucose oxidase, galactose oxidase, and glucose-6-phosphate dehydrogenase), heterocyclic oxidases (such as uricase and xanthine oxidase), lactoperoxidase, microperoxidase, and the like. Techniques for conjugating enzymes to antibodies are described in O'Sullivan et al. (1981) Methods for the Preparation of Enzyme-Antibody Conjugates for use in Enzyme Immunoassay, in Methods in Enzym. (ed J. Langone & H. Van Vunakis), Academic press, New York 73:147-166.

Examples of enzyme-substrate combinations include, for example: horseradish peroxidase (HRPO) with hydrogen peroxidase as a substrate, wherein the hydrogen peroxidase oxidizes a dye precursor (e.g.,orthophenylene diamine (OPD) or 3,3',5,5'-tetramethyl benzidine hydrochloride (TMB)); alkaline phosphatase (AP) with para-Nitrophenyl phosphate as chromogenic substrate; and β-D-galactosidase (β-D-Gal) with a chromogenic substrate (e.g., p-nitrophenyl-β-D-galactosidase) or fluorogenic substrate 4-methylumbelliferyl-β-D-galactosidase.

Numerous other enzyme-substrate combinations are available to those skilled in the art. For a general review of these, see U.S. Patent Nos. 4,275,149 and 4,318,980.

Sometimes, the label is indirectly conjugated with the antibody. The skilled artisan will be aware of various techniques for achieving this. For example, the antibody can be conjugated with biotin and any of the three broad categories of labels mentioned above can be conjugated with avidin, or vice versa. Biotin binds selectively to avidin and thus, the label can be conjugated with the antibody in this indirect manner. Alternatively, to achieve indirect conjugation of the label with the antibody, the antibody is conjugated with a small hapten (e.g., digoxin) and one of the different types of labels mentioned above is conjugated with an anti-hapten antibody (e.g., anti-digoxin antibody). Thus, indirect conjugation of the label with the antibody can be achieved.

In other versions of immunoassay techniques, the antibody need not be labeled, and the presence thereof can be detected using a labeled antibody which binds to the antibody.

Thus, the diagnostic immunoassays herein may be in any assay format, including, for example, competitive binding assays, direct and indirect sandwich assays, and immunoprecipitation assays. Zola, Monoclonal Antibodies: A Manual of Techniques, pp.147-158 (CRC Press, Inc. 1987).

Competitive binding assays rely on the ability of a labeled standard to compete with the test sample analyze for binding with a limited amount of antibody. The amount of antigen in the test sample is inversely proportional to the amount of standard that becomes bound to the antibodies. To facilitate determining the amount of standard that becomes bound, the antibodies generally are insolubilized before or after the competition, so that the standard and analyze that are bound to the antibodies may conveniently be separated from the standard and analyze which remain unbound.

Sandwich assays involve the use of two antibodies, each capable of binding to a different immunogenic portion, or epitope, of the protein to be detected. In a sandwich assay, the test sample analyze is bound by a first antibody which is immobilized on a solid support, and thereafter a second antibody binds to the analyze, thus forming an insoluble three-part complex. See, e.g.,U.S. Pat No. 4,376,110. The second antibody may itself be labeled with a detectable moiety (direct sandwich assays) or may be measured using an anti-immunoglobulin antibody that is labeled with a detectable moiety (indirect sandwich assay). For example, one type of sandwich assay is an ELISA assay, in which case the detectable moiety is an enzyme.

g. ***Proteomics***

The term “proteome” is defined as the totality of the proteins present in a sample (e.g. tissue, organism, or cell culture) at a certain point of time. Proteomics includes, among other things, study of the global changes of protein expression in a sample (also referred to as “expression proteomics”). Proteomics typically includes the following steps: (1) separation of individual proteins in a sample by 2-D gel electrophoresis (2-D PAGE); (2) identification of the individual proteins recovered from the gel, e.g. my mass spectrometry or N-terminal sequencing, and (3) analysis of the data using bioinformatics. Proteomics methods are valuable supplements to other methods of gene expression profiling, and can be used, alone or in combination with other methods, to detect the products of the markers of the present invention.

h. *5'-multiplexed Gene Specific Priming of Reverse Transcription*

RT-PCR requires reverse transcription of the test RNA population as a first step. The most commonly used primer for reverse transcription is oligo-dT, which works well when RNA is intact. However, this primer will not be effective when RNA is highly fragmented.

The present invention includes the use of gene specific primers, which are roughly 20 bases in length with a Tm optimum between about 58 °C and 60 °C. These primers will also serve as the reverse primers that drive PCR DNA amplification.

An alternative approach is based on the use of random hexamers as primers for cDNA synthesis. However, we have experimentally demonstrated that the method of using a multiplicity of gene-specific primers is superior over the known approach using random hexamers.

i. *Promoter Methylation Analysis*

A number of methods for quantization of RNA transcripts (gene expression analysis) or their protein translation products are discussed herein. The expression level of genes may also be inferred from information regarding chromatin structure, such as for example the methylation status of gene promoters and other regulatory elements and the acetylation status of histones.

In particular, the methylation status of a promoter influences the level of expression of the gene regulated by that promoter. Aberrant methylation of particular gene promoters has been implicated in expression regulation, such as for example silencing of tumor suppressor genes. Thus, examination of the methylation status of a gene's promoter can be utilized as a surrogate for direct quantization of RNA levels.

Several approaches for measuring the methylation status of particular DNA elements have been devised, including methylation-specific PCR (Herman J.G. et al. (1996) Methylation-specific PCR: a novel PCR assay for methylation status of CpG islands. Proc. Natl Acad. Sci. USA. **93**, 9821–9826.) and bisulfite DNA sequencing (Frommer M. et al. (1992) A genomic sequencing protocol that yields a positive display of 5-methylcytosine residues in individual DNA strands. Proc. Natl Acad. Sci. USA. **89**, 1827–1831.). More recently, microarray-based technologies have been used to characterize promoter methylation status (Chen C.M. (2003) Methylation target array for rapid analysis of CpG island hypermethylation in multiple tissue genomes. Am. J. Pathol. 163, 37–45.).

j. *Coexpression of Genes*

A further aspect of the invention is the identification of gene expression clusters. Gene expression clusters can be identified by analysis of expression data using statistical analyses known in the art, including pairwise analysis of correlation based on Pearson correlation coefficients (Pearson K. and Lee A. (1902) Biometrika 2, 357).

In one embodiment, an expression cluster identified herein includes genes upregulated in the left colon.

In another embodiment, an expression cluster identified herein includes genes upregulated in the right colon.

In one other embodiment, an expression cluster identified herein includes genes upregulated in the terminal ileum.

In other embodiments, the expression cluster identified herein includes genes in the

In some embodiments, the expression cluster identified herein includes genes classified under an immune response.

In other embodiments, the expression cluster identified herein includes genes classified under a response to wounding.

k. *Design of Intron-Based PCR Primers and Probes*

According to one aspect of the present invention, PCR primers and probes are designed based upon intron sequences present in the gene to be amplified. Accordingly, the first step in the primer/probe design is the delineation of intron sequences within the genes. This can be done by publicly available software, such as the DNA BLAT software developed by Kent, W.J., Genome Res. 12(4):656-64 (2002), or by the BLAST software including its variations. Subsequent steps follow well established methods of PCR primer and probe design.

In order to avoid non-specific signals, it is important to mask repetitive sequences within the introns when designing the primers and probes. This can be easily accomplished by using the Repeat Masker program available on-line through the Baylor College of Medicine, which screens DNA sequences against a library of repetitive elements and returns a query sequence in which the repetitive elements are masked. The masked intron sequences can then be used to design primer and probe sequences using any commercially or otherwise publicly available primer/probe design packages, such as Primer Express (Applied Biosystems); MGB assay-by–design (Applied Biosystems); Primer3 (Steve Rozen and Helen J. Skaletsky (2000) Primer3 on the WWW for general users and for biologist programmers. In: Krawetz S, Misener S (eds) Bioinformatics Methods and Protocols: Methods in Molecular Biology. Humana Press, Totowa, NJ, pp 365-386).

The most important factors considered in PCR primer design include primer length, melting temperature (Tm), and G/C content, specificity, complementary primer sequences, and 3'-end sequence. In general, optimal PCR primers are generally 17-30 bases in length, and contain about 20-80%, such as, for example, about 50-60% G+C bases. Tm's between 50 and 80 °C, e.g. about 50 to 70 °C are typically preferred.

For further guidelines for PCR primer and probe design see, e.g. Dieffenbach, C.W. et al., "General Concepts for PCR Primer Design" in: PCR Primer, A Laboratory Manual, Cold Spring Harbor

Laboratory Press, New York, 1995, pp. 133-155; Innis and Gelfand, "Optimization of PCRs" in: PCR Protocols, A Guide to Methods and Applications, CRC Press, London, 1994, pp. 5-11; and Plasterer, T.N. Primerselect: Primer and probe design. Methods Mol. Biol. 70:520-527 (1997), the entire disclosures of which are hereby expressly incorporated by reference.

l. *IBD Gene Set, Assayed Gene Subsequences, and Clinical Application of Gene Expression Data*

An important aspect of the present invention is to use the measured expression of certain genes by colonic issue to provide diagnostic information. For this purpose it is necessary to correct for (normalize away) both differences in the amount of RNA assayed and variability in the quality of the RNA used. Therefore, the assay typically measures and incorporates the expression of certain normalizing genes, including well known housekeeping genes, such as GAPDH and Cyp1. Alternatively, normalization can be based on the mean or median signal (Ct) of all of the assayed genes or a large subset thereof (global normalization approach). On a gene-by-gene basis, measured normalized amount of a patient colonic tissue mRNA is compared to the amount found in an appropriate tissue reference set. The number (N) of tissues in this reference set should be sufficiently high to ensure that different reference sets (as a whole) behave essentially the same way. If this condition is met, the identity of the individual colonic tissues present in a particular set will have no significant impact on the relative amounts of the genes assayed. Usually, the tissue reference set consists of at least about 30, preferably at least about 40 different IBD tissue specimens. Unless noted otherwise, normalized expression levels for each mRNA/tested tissue/patient will be expressed as a percentage of the expression level measured in the reference set. More specifically, the reference set of a sufficiently high number (e.g. 40) of IBD samples yields a distribution of normalized levels of each mRNA species. The level measured in a particular sample to be analyzed falls at some percentile within this range, which can be determined by methods well known in the art. Below, unless noted otherwise, reference to expression levels of a gene assume normalized expression relative to the reference set although this is not always explicitly stated.

m. *Production of antibodies*

The present invention further provides anti-IBD marker antibodies. Exemplary antibodies include polyclonal, monoclonal, humanized, bispecific, and heteroconjugate antibodies. As discussed herein, the antibodies may be used in the diagnostic methods for IBD, and in some cases in methods of treatment of IBD.

(1) Polyclonal antibodies

Polyclonal antibodies are preferably raised in animals by multiple subcutaneous (sc) or intraperitoneal (ip) injections of the relevant antigen and an adjuvant. It may be useful to conjugate the relevant antigen to a protein that is immunogenic in the species to be immunized, e.g., keyhole limpet hemocyanin, serum albumin, bovine thyroglobulin, or soybean trypsin inhibitor using a bifunctional or derivatizing agent, for example, maleimidobenzoyl sulfosuccinimide ester (conjugation through cysteine residues), N-hydroxysuccinimide (through lysine residues), glutaraldehyde, succinic anhydride, SOCl2, or R1N=C=NR, where R and R1 are different alkyl groups.

Animals are immunized against the antigen, immunogenic conjugates, or derivatives by combining, e.g., 100 μg or 5 μg of the protein or conjugate (for rabbits or mice, respectively) with 3 volumes of Freund's complete adjuvant and injecting the solution intradermally at multiple sites. One month later the animals are boosted with 1/5 to 1/10 the original amount of peptide or conjugate in Freund's complete adjuvant by subcutaneous injection at multiple sites. Seven to 14 days later the animals are bled and the serum is assayed for antibody titer. Animals are boosted until the titer plateaus. Preferably, the animal is boosted with the conjugate of the same antigen, but conjugated to a different protein and/or through a different cross-linking reagent. Conjugates also can be made in recombinant cell culture as protein fusions. Also, aggregating agents such as alum are suitably used to enhance the immune response.

(2) Monoclonal antibodies

Various methods for making monoclonal antibodies herein are available in the art. For example, the monoclonal antibodies may be made using the hybridoma method first described by Kohler et al., Nature, 256:495 (1975), by recombinant DNA methods (U.S. Patent No. 4,816,567).

In the hybridoma method, a mouse or other appropriate host animal, such as a hamster, is immunized as hereinabove described to elicit lymphocytes that produce or are capable of producing antibodies that will specifically bind to the protein used for immunization. Alternatively, lymphocytes may be immunized *in vitro*. Lymphocytes then are fused with myeloma cells using a suitable fusing agent, such as polyethylene glycol, to form a hybridoma cell (Goding, *Monoclonal Antibodies: Principles and Practice*, pp.59-103 (Academic Press, 1986)).

The hybridoma cells thus prepared are seeded and grown in a suitable culture medium that preferably contains one or more substances that inhibit the growth or survival of the unfused, parental myeloma cells. For example, if the parental myeloma cells lack the enzyme hypoxanthine guanine phosphoribosyl transferase (HGPRT or HPRT), the culture medium for the hybridomas typically will include hypoxanthine, aminopterin, and thymidine (HAT medium), which substances prevent the growth of HGPRT-deficient cells.

Preferred myeloma cells are those that fuse efficiently, support stable high-level production of antibody by the selected antibody-producing cells, and are sensitive to a medium such as HAT medium. Among these, preferred myeloma cell lines are murine myeloma lines, such as those derived from MOPC-21 and MPC-11 mouse tumors available from the Salk Institute Cell Distribution Center, San Diego, California USA, and SP-2 or X63-Ag8-653 cells available from the American Type Culture Collection, Rockville, Maryland USA. Human myeloma and mouse-human heteromyeloma cell lines also have been described for the production of human monoclonal antibodies (Kozbor, J. Immunol., 133:3001 (1984); and Brodeur et al., Monoclonal Antibody Production Techniques and Applications, pp. 51-63 (Marcel Dekker, Inc., New York, 1987)).

Culture medium in which hybridoma cells are growing is assayed for production of monoclonal antibodies directed against the antigen. Preferably, the binding specificity of monoclonal antibodies produced by hybridoma cells is determined by immunoprecipitation or by an in vitro binding assay, such as radioimmunoassay (RIA) or enzyme-linked immunoabsorbent assay (ELISA).

The binding affinity of the monoclonal antibody can, for example, be determined by the Scatchard analysis of Munson et al., Anal. Biochem., 107:220 (1980).

After hybridoma cells are identified that produce antibodies of the desired specificity, affinity, and/or activity, the clones may be subcloned by limiting dilution procedures and grown by standard methods (Goding, Monoclonal Antibodies: Principles and Practice, pp.59-103 (Academic Press, 1986)). Suitable culture media for this purpose include, for example, D-MEM or RPMI-1640 medium. In addition, the hybridoma cells may be grown in vivo as ascites tumors in an animal.

The monoclonal antibodies secreted by the subclones are suitably separated from the culture medium, ascites fluid, or serum by conventional antibody purification procedures such as, for example, protein A-Sepharose, hydroxylapatite chromatography, gel electrophoresis, dialysis, or affinity chromatography.

DNA encoding the monoclonal antibodies is readily isolated and sequenced using conventional procedures (e.g., by using oligonucleotide probes that are capable of binding specifically to genes encoding the heavy and light chains of murine antibodies). The hybridoma cells serve as a preferred source of such DNA. Once isolated, the DNA may be placed into expression vectors, which are then transfected into host cells such as E. coli cells, simian COS cells, Chinese Hamster Ovary (CHO) cells, or myeloma cells that do not otherwise produce antibody protein, to obtain the synthesis of monoclonal antibodies in the recombinant host cells. Review articles on recombinant expression in bacteria of DNA encoding the antibody include Skerra et al., Curr. Opinion in Immunol., 5:256-262 (1993) and Plückthun, Immunol. Revs., 130:151-188 (1992).

In a further embodiment, monoclonal antibodies or antibody fragments can be isolated from antibody phage libraries generated using the techniques described in McCafferty et al., Nature, 348:552-554 (1990). Clackson et al., Nature, 352:624-628 (1991) and Marks et al., J. Mol. Biol., 222:581-597 (1991) describe the isolation of murine and human antibodies, respectively, using phage libraries. Subsequent publications describe the production of high affinity (nM range) human antibodies by chain shuffling (Marks et al., Bio/Technology, 10:779-783 (1992)), as well as combinatorial infection and in vivo recombination as a strategy for constructing very large phage libraries (Waterhouse et al., Nuc. Acids. Res., 21:2265-2266 (1993)). Thus, these techniques are viable alternatives to traditional monoclonal antibody hybridoma techniques for isolation of monoclonal antibodies.

The DNA also may be modified, for example, by substituting the coding sequence for human heavy chain and light chain constant domains in place of the homologous murine sequences (U.S. Patent No. 4,816,567; and Morrison, et al., Proc. Natl Acad. Sci. USA, 81:6851 (1984)), or by covalently joining to the immunoglobulin coding sequence all or part of the coding sequence for a non-immunoglobulin polypeptide.

Typically such non-immunoglobulin polypeptides are substituted for the constant domains of an antibody, or they are substituted for the variable domains of one antigen-combining site of an antibody to create a chimeric bivalent antibody comprising one antigen-combining site having specificity for an antigen and another antigen-combining site having specificity for a different antigen.

(3) Humanized antibodies

Methods for humanizing non-human antibodies have been described in the art. Preferably, a humanized antibody has one or more amino acid residues introduced into it from a source which is non-human. These non-human amino acid residues are often referred to as "import" residues, which are typically taken from an "import" variable domain. Humanization can be essentially performed following the method of Winter and co-workers (Jones et al., Nature, 321:522-525 (1986); Riechmann et al., Nature, 332:323-327 (1988); Verhoeyen et al., Science, 239:1534-1536 (1988)), by substituting hypervariable region sequences for the corresponding sequences of a human antibody. Accordingly, such "humanized" antibodies are chimeric antibodies (U.S. Patent No. 4,816,567) wherein substantially less than an intact human variable domain has been substituted by the corresponding sequence from a non-human species. In practice, humanized antibodies are typically human antibodies in which some hypervariable region residues and possibly some FR residues are substituted by residues from analogous sites in rodent antibodies. An example of a humanized antibody used to treat IBD is infliximab (Remicade®), an engineered murine-human chimeric monoclonal antibody. The antibody binds the cytokine TNF-alpha and prevents it from binding its receptors to trigger and sustain an inflammatory response. Infliximab is used to treat both CD and UC.

The choice of human variable domains, both light and heavy, to be used in making the humanized antibodies is very important to reduce antigenicity. According to the so-called "best-fit" method, the sequence of the variable domain of a rodent antibody is screened against the entire library of known human variable-domain sequences. The human sequence which is closest to that of the rodent is then accepted as the human framework region (FR) for the humanized antibody (Sims et al., J. Immunol., 151:2296 (1993); Chothia et al., J. Mol. Biol., 196:901 (1987)). Another method uses a particular framework region derived from the consensus sequence of all human antibodies of a particular subgroup of light or heavy chains. The same framework may be used for several different humanized antibodies (Carter et al., Proc. Natl. Acad. Sci. USA, 89:4285 (1992); Presta et al., J. Immunol., 151:2623 (1993)).

It is further important that antibodies be humanized with retention of high affinity for the antigen and other favorable biological properties. To achieve this goal, according to a preferred method, humanized antibodies are prepared by a process of analysis of the parental sequences and various conceptual humanized products using three-dimensional models of the parental and humanized sequences. Three-dimensional immunoglobulin models are commonly available and are familiar to those skilled in the art. Computer programs are available which illustrate and display probable three-dimensional conformational structures of selected candidate immunoglobulin sequences. Inspection of these displays permits analysis of the likely role of the residues in the functioning of the candidate immunoglobulin sequence, i.e., the analysis of residues that influence the ability of the candidate immunoglobulin to bind its antigen. In this way, FR residues can be selected and combined from the recipient and import sequences so that the desired antibody characteristic, such as increased affinity for the target antigen(s), is achieved. In general, the hypervariable region residues are directly and most substantially involved in influencing antigen binding.

Various forms of the humanized antibody are contemplated. For example, the humanized antibody may be an antibody fragment, such as a Fab, which is optionally conjugated with one or more cytotoxic agent(s) in order to generate an immunoconjugate. Alternatively, the humanized antibody may be an intact antibody, such as an intact IgG1 antibody.

(4) Human antibodies

As an alternative to humanization, human antibodies can be generated. For example, it is now possible to produce transgenic animals (e.g., mice) that are capable, upon immunization, of producing a full repertoire of human antibodies in the absence of endogenous immunoglobulin production. For example, it has been described that the homozygous deletion of the antibody heavy-chain joining region (JH) gene in chimeric and germ-line mutant mice results in complete inhibition of endogenous antibody production. Transfer of the human germ-line immunoglobulin gene array in such germ-line mutant mice will result in the production of human antibodies upon antigen challenge. See, e.g., Jakobovits et al., Proc. Natl. Acad. Sci. USA, 90:2551 (1993); Jakobovits et al., Nature, 362:255-258 (1993); Bruggermann et al., Year in Immuno., 7:33 (1993); and U.S. Patent Nos. 5,591,669, 5,589,369 and 5,545,807. Alternatively, phage display technology (McCafferty et al., Nature 348:552-553 (1990)) can be used to produce human antibodies and antibody fragments in vitro, from immunoglobulin variable (V) domain gene repertoires from unimmunized donors. According to this technique, antibody V domain genes are cloned in-frame into either a major or minor coat protein gene of a filamentous bacteriophage, such as M13 or fd, and displayed as functional antibody fragments on the surface of the phage particle. Because the filamentous particle contains a single-stranded DNA copy of the phage genome, selections based on the functional properties of the antibody also result in selection of the gene encoding the antibody exhibiting those properties. Thus, the phage mimics some of the properties of the B-cell. Phage display can be performed in a variety of formats; for their review see, e.g., Johnson, Kevin S. and Chiswell, David J., Current Opinion in Structural Biology 3:564-571 (1993). Several sources of V-gene segments can be used for phage display. Clackson et al., Nature, 352:624-628 (1991) isolated a diverse array of anti-oxazolone antibodies from a small random combinatorial library of V genes derived from the spleens of immunized mice. A repertoire of V genes from unimmunized human donors can be constructed and antibodies to a diverse array of antigens (including self-antigens) can be isolated essentially following the techniques described by Marks et al., J. Mol. Biol. 222:581-597 (1991), or Griffith et al., EMBO J. 12:725-734 (1993). See, also, U.S. Patent Nos. 5,565,332 and 5,573,905.

As discussed above, human antibodies may also be generated by *in vitro* activated B cells (see U.S. Patents 5,567,610 and 5,229,275).

(5) Antibody fragments

Various techniques have been developed for the production of antibody fragments comprising one or more antigen binding regions. Traditionally, these fragments were derived via proteolytic digestion of intact antibodies (see, e.g., Morimoto et al., Journal of Biochemical and Biophysical Methods 24:107-117 (1992); and Brennan et al., Science, 229:81 (1985)). However, these fragments can now be produced directly by recombinant host cells. For example, the antibody fragments can be isolated from the antibody phage libraries discussed above. Alternatively, Fab'-SH fragments can be directly recovered from E. coli and chemically coupled to form F(ab')2 fragments (Carter et al., Bio/Technology 10:163-167 (1992)). According to another approach, F(ab')2 fragments can be isolated directly from recombinant host cell culture. Other techniques for the production of antibody fragments will be apparent to the skilled practitioner. In other embodiments, the antibody of choice is a single chain Fv fragment (scFv). See WO 93/16185; U.S. Patent No. 5,571,894; and U.S. Patent No. 5,587,458. The antibody fragment may also be a Alinear antibody@, *e.g.*, as described in U.S. Patent 5,641,870 for example. Such linear antibody fragments may be monospecific or bispecific.

(6) Bispecific antibodies

Bispecific antibodies are antibodies that have binding specificities for at least two different epitopes. Exemplary bispecific antibodies may bind to two different epitopes of an IBD marker protein. Bispecific antibodies may also be used to localize agents to cells which express an IBD marker protein.

These antibodies possess an IBD marker-binding arm and an arm which binds an agent (e.g. an aminosalicylate). Bispecific antibodies can be prepared as full length antibodies or antibody fragments (e.g. F(ab')2 bispecific antibodies).

Methods for making bispecific antibodies are known in the art. . Traditional production of full length bispecific antibodies is based on the coexpression of two immunoglobulin heavy chain-light chain pairs, where the two chains have different specificities (Millstein *et al., Nature*, 305:537-539 (1983)). Because of the random assortment of immunoglobulin heavy and light chains, these hybridomas (quadromas) produce a potential mixture of 10 different antibody molecules, of which only one has the correct bispecific structure. Purification of the correct molecule, which is usually done by affinity chromatography steps, is rather cumbersome, and the product yields are low. Similar procedures are disclosed in WO 93/08829, and in Traunecker *et al., EMBO J.*, 10:3655-3659 (1991).

According to a different approach, antibody variable domains with the desired binding specificities (antibody-antigen combining sites) are fused to immunoglobulin constant domain sequences. The fusion preferably is with an immunoglobulin heavy chain constant domain, comprising at least part of the hinge, CH2, and CH3 regions. It is preferred to have the first heavy-chain constant region (CH1) containing the site necessary for light chain binding, present in at least one of the fusions. DNAs encoding the immunoglobulin heavy chain fusions and, if desired, the immunoglobulin light chain, are inserted into separate expression vectors, and are co-transfected into a suitable host organism. This provides for great flexibility in adjusting the mutual proportions of the three polypeptide fragments in embodiments when unequal ratios of the three polypeptide chains used in the construction provide the optimum yields. It is, however, possible to insert the coding sequences for two or all three polypeptide chains in one expression vector when the expression of at least two polypeptide chains in equal ratios results in high yields or when the ratios are of no particular significance.

In a preferred embodiment of this approach, the bispecific antibodies are composed of a hybrid immunoglobulin heavy chain with a first binding specificity in one arm, and a hybrid immunoglobulin heavy chain-light chain pair (providing a second binding specificity) in the other arm. It was found that this asymmetric structure facilitates the separation of the desired bispecific compound from unwanted immunoglobulin chain combinations, as the presence of an immunoglobulin light chain in only one half of the bispecific molecule provides for a facile way of separation. This approach is disclosed in WO 94/04690. For further details of generating bispecific antibodies see, for example, Suresh *et al., Methods in Enzymology*, 121:210 (1986).

According to another approach described in U.S. Patent No. 5,731,168, the interface between a pair of antibody molecules can be engineered to maximize the percentage of heterodimers which are recovered from recombinant cell culture. The preferred interface comprises at least a part of the C_H3 domain of an antibody constant domain. In this method, one or more small amino acid side chains from the interface of the first antibody molecule are replaced with larger side chains (*e.g.* tyrosine or tryptophan). Compensatory "cavities" of identical or similar size to the large side chain(s) are created on the interface of the second antibody molecule by replacing large amino acid side chains with smaller ones (*e.g.* alanine or threonine). This provides a mechanism for increasing the yield of the heterodimer over other unwanted end-products such as homodimers.

Bispecific antibodies include cross-linked or "heteroconjugate" antibodies. For example, one of the antibodies in the heteroconjugate can be coupled to avidin, the other to biotin. Such antibodies have, for example, been proposed to target immune system cells to unwanted cells (U.S. Patent No. 4,676,980), and for treatment of HIV infection (WO 91/00360, WO 92/200373, and EP 03089). Heteroconjugate antibodies may be made using any convenient cross-linking methods. Suitable cross-linking agents are well known in the art, and are disclosed in U.S. Patent No. 4,676,980, along with a number of cross-linking techniques.

Techniques for generating bispecific antibodies from antibody fragments have also been described in the literature. For example, bispecific antibodies can be prepared using chemical linkage. Brennan *et al., Science*, 229: 81 (1985) describe a procedure wherein intact antibodies are proteolytically cleaved to generate $F(ab')_2$ fragments. These fragments are reduced in the presence of the dithiol complexing agent sodium arsenite to stabilize vicinal dithiols and prevent intermolecular disulfide formation. The Fab' fragments generated are then converted to thionitrobenzoate (TNB) derivatives. One of the Fab'-TNB derivatives is then reconverted to the Fab'-thiol by reduction with mercaptoethylamine and is mixed with an equimolar amount of the other Fab'-TNB derivative to form the bispecific antibody. The bispecific antibodies produced can be used as agents for the selective immobilization of enzymes.

Various techniques for making and isolating bispecific antibody fragments directly from recombinant cell culture have also been described. For example, bispecific antibodies have been produced using leucine zippers. Kostelny *et al.*, *J. Immunol.*, 148(5):1547-1553 (1992). The leucine zipper peptides from the Fos and Jun proteins were linked to the Fab' portions of two different antibodies by gene fusion. The antibody homodimers were reduced at the hinge region to form monomers and then re-oxidized to form the antibody heterodimers. This method can also be utilized for the production of antibody homodimers. The "diabody" technology described by Hollinger *et al., Proc. Natl. Acad. Sci. USA*, 90:6444-6448 (1993) has provided an alternative mechanism for making bispecific antibody fragments. The fragments comprise a heavy-chain variable domain (V_H) connected to a light-chain variable domain (V_L) by a linker which is too short to allow pairing between the two domains on the same chain. Accordingly, the V_H and V_L domains of one fragment are forced to pair with the complementary V_L and V_H domains of another fragment, thereby forming two antigen-binding sites. Another strategy for making bispecific antibody fragments by the use of single-chain Fv (sFv) dimers has also been reported. See Gruber *et al., J. Immunol.*, 152:5368 (1994).

Antibodies with more than two valencies are contemplated. For example, trispecific antibodies can be prepared. Tutt *et al. J. Immunol.* 147: 60 (1991).

(7) Other amino acid sequence modifications

Amino acid sequence modification(s) of the antibodies described herein are contemplated. For example, it may be desirable to improve the binding affinity and/or other biological properties of the antibody. Amino acid sequence variants of the antibody are prepared by introducing appropriate nucleotide changes into the antibody nucleic acid, or by peptide synthesis. Such modifications include, for example, deletions from, and/or insertions into and/or substitutions of, residues within the amino acid sequences of the antibody. Any combination of deletion, insertion, and substitution is made to arrive at the final construct, provided that the final construct possesses the desired characteristics. The amino acid changes also may alter post-translational processes of the antibody, such as changing the number or position of glycosylation sites.

A useful method for identification of certain residues or regions of the antibody that are preferred locations for mutagenesis is called "alanine scanning mutagenesis" as described by Cunningham and Wells *Science*, 244:1081-1085 (1989). Here, a residue or group of target residues are identified (*e.g.*, charged residues such as arg, asp, his, lys, and glu) and replaced by a neutral or negatively charged amino acid (most preferably alanine or polyalanine) to affect the interaction of the amino acids with antigen. Those amino acid locations demonstrating functional sensitivity to the substitutions then are refined by introducing further or other variants at, or for, the sites of substitution. Thus, while the site for introducing an amino acid sequence variation is predetermined, the nature of the mutation *per se* need not be predetermined. For example, to analyze the performance of a mutation at a given site, ala scanning or random mutagenesis is conducted at the target codon or region and the expressed antibody variants are screened for the desired activity.

Amino acid sequence insertions include amino- and/or carboxyl-terminal fusions ranging in length from one residue to polypeptides containing a hundred or more residues, as well as intrasequence insertions of single or multiple amino acid residues. Examples of terminal insertions include antibody with an N-terminal methionyl residue or the antibody fused to a cytotoxic polypeptide. Other insertional variants of the antibody molecule include the fusion to the N- or C-terminus of the antibody to an enzyme (*e.g.* for ADEPT) or a polypeptide which increases the serum half-life of the antibody.

Another type of variant is an amino acid substitution variant. These variants have at least one amino acid residue in the antibody molecule replaced by a different residue. The sites of greatest interest for substitutional mutagenesis include the hypervariable regions, but FR alterations are also contemplated. Conservative substitutions are shown in Table 1 under the heading of "preferred substitutions". If such substitutions result in a change in biological activity, then more substantial changes, denominated "exemplary substitutions" in the following table, or as further described below in reference to amino acid classes, may be introduced and the products screened.

Original Residue	Exemplary Substitutions	Preferred Substitutions
Ala (A)	val; leu; ile	val
Arg (R)	lys; gln; asn	lys
Asn (N)	gln; his; lys; arg	gln
Asp (D)	glu	glu
Cys (C)	ser	ser
Gln (Q)	asn	asn
Glu (E)	asp	asp
Gly (G)	pro; ala	ala
His (H)	asn; gln; lys; arg	arg
Ile (I)	leu; val; met; ala; phe; norleucine	leu
Leu (L)	norleucine; ile; val; met; ala; phe	ile
Lys (K)	arg; gln; asn	arg
Met (M)	leu; phe; ile	leu
Phe (F)	leu; val; ile; ala; tyr	leu
Pro (P)	ala	ala
Ser (S)	thr	thr
Thr (T)	ser	ser
Trp (W)	tyr; phe	tyr
Tyr (Y)	trp; phe; thr; ser	phe

Val (V)	ile; leu; met; phe; ala; norleucine	leu

Substantial modifications in the biological properties of the antibody are accomplished by selecting substitutions that differ significantly in their effect on maintaining (a) the structure of the polypeptide backbone in the area of the substitution, for example, as a sheet or helical conformation, (b) the charge or hydrophobicity of the molecule at the target site, or (c) the bulk of the side chain. Amino acids may be grouped according to similarities in the properties of their side chains (in A. L. Lehninger, in *Biochemistry*, second ed., pp. 73-75, Worth Publishers, New York (1975)): non-polar: Ala (A), Val (V), Leu (L), Ile (I), Pro (P), Phe (F), Trp (W), Met (M); uncharged polar: Gly (G), Ser (S), Thr (T), Cys (C), Tyr (Y), Asn (N), Gln (Q); acidic: Asp (D), Glu (E); and basic: Lys (K), Arg (R), His(H).

Alternatively, naturally occurring residues may be divided into groups based on common side-chain properties: hydrophobic : Norleucine, Met, Ala, Val, Leu, Ile; neutral hydrophilic: Cys, Ser, Thr, Asn, Gln; acidic: Asp, Glu; basic: His, Lys, Arg; residues that influence chain orientation: Gly, Pro; and aromatic: Trp, Tyr, Phe.

Non-conservative substitutions will entail exchanging a member of one of these classes for another class.

Any cysteine residue not involved in maintaining the proper conformation of the antibody also may be substituted, generally with serine, to improve the oxidative stability of the molecule and prevent aberrant crosslinking. Conversely, cysteine bond(s) may be added to the antibody to improve its stability (particularly where the antibody is an antibody fragment such as an Fv fragment).

A particularly preferred type of substitutional variant involves substituting one or more hypervariable region residues of a parent antibody (*e.g.* a humanized or human antibody). Generally, the resulting variant(s) selected for further development will have improved biological properties relative to the parent antibody from which they are generated. A convenient way for generating such substitutional variants involves affinity maturation using phage display. Briefly, several hypervariable region sites (*e.g.* 6-7 sites) are mutated to generate all possible amino substitutions at each site. The antibody variants thus generated are displayed in a monovalent fashion from filamentous phage particles as fusions to the gene III product of M13 packaged within each particle. The phage-displayed variants are then screened for their biological activity (*e.g.* binding affinity) as herein disclosed. In order to identify candidate hypervariable region sites for modification, alanine scanning mutagenesis can be performed to identify hypervariable region residues contributing significantly to antigen binding. Alternatively, or additionally, it may be beneficial to analyze a crystal structure of the antigen-antibody complex to identify contact points between the antibody and an IBD marker protein. Such contact residues and neighboring residues are candidates for substitution according to the techniques elaborated herein. Once such variants are generated, the panel of variants is subjected to screening as described herein and antibodies with superior properties in one or more relevant assays may be selected for further development.

Engineered antibodies with three or more (preferably four) functional antigen binding sites are also contemplated (U.S. Published Patent Application No. US2002/0004587 A1, Miller *et al.*).

Nucleic acid molecules encoding amino acid sequence variants of the antibody are prepared by a variety of methods known in the art. These methods include, but are not limited to, isolation from a natural source (in the case of naturally occurring amino acid sequence variants) or preparation by oligonucleotide-mediated (or site-directed) mutagenesis, PCR mutagenesis, and cassette mutagenesis of an earlier prepared variant or a non-variant version of the antibody.

B.3 Determination of inflammation

In one aspect, the identification in a subject of a differentially expressed biomarker described herein may be correlated to a determination of inflammation in the subject. In one embodiment, the expression of a biomarker may be used as a surrogate for inflammation (Sands et al. (2005) Inflamm Bowel Dis. 11(1):S22-S28). In another embodiment, the expression of a biomarker is validated against a determination of inflammation by other techniques. In one other embodiment, the methods of diagnosis and/or treatment of the present invention comprise the step of determinining inflammation in a subject. In another embodiment, the determining step comprises histological evaluation of a test sample obtained from the subject for inflammatory cell infiltrate. In one embodiment, the test sample is a tissue biopsy obtained from the subject.

In another embodiment, the determining step comprises evaluation of a non-tissue biopsy as a test sample from the subject. In one embodiment, the test sample is a biopsy obtained from the fecal material of the subject. In another embodiment, the test sample is blood. In one other embodiment, the determining step comprises a fecal calprotectin or fecal lactoferrin test (Joishy et al. (2008) J Pediatr Gastroenterol Nutr. 48(1):48-54) or a C reactive protein (CRP) blood test (Henriksen et al. (2008) Gut. 57:1518-1523).

B.4 Kits of the invention

The materials for use in the methods of the present invention are suited for preparation of kits produced in accordance with well known procedures. The invention thus provides kits comprising agents, which may include gene-specific or gene-selective probes and/or primers, for quantitating the expression of the disclosed genes for IBD. Such kits may optionally contain reagents for the extraction of RNA from samples, in particular fixed paraffin-embedded tissue samples and/or reagents for RNA amplification. In addition, the kits may optionally comprise the reagent(s) with an identifying description or label or instructions relating to their use in the methods of the present invention. The kits may comprise containers (including microtiter plates suitable for use in an automated implementation of the method), each with one or more of the various reagents (typically in concentrated form) utilized in the methods, including, for example, pre-fabricated microarrays, buffers, the appropriate nucleotide triphosphates (e.g., dATP, dCTP, dGTP and dTTP; or rATP, rCTP, rGTP and UTP), reverse transcriptase, DNA polymerase, RNA polymerase, and one or more probes and primers of the present invention (e.g., appropriate length poly(T) or random primers linked to a promoter reactive with the RNA polymerase).

B.5 Reports of the invention

The methods of this invention, when practiced for commercial diagnostic purposes generally produce a report or summary of the normalized expression levels of one or more of the selected genes. The methods of this invention will produce a report comprising a prediction of the clinical outcome of a subject diagnosed with an IBD before and after any surgical procedure to treat the IBD. The methods and reports of this invention can further include storing the report in a database. Alternatively, the method can further create a record in a database for the subject and populate the record with data. In one embodiment the report is a paper report, in another embodiment the report is an auditory report, in another embodiment the report is an electronic record. It is contemplated that the report is provided to a physician and/or the patient. The receiving of the report can further include establishing a network connection to a server computer that includes the data and report and requesting the data and report from the server computer.

The methods provided by the present invention may also be automated in whole or in part.

All aspects of the present invention may also be practiced such that a limited number of additional genes that are co-expressed with the disclosed genes, for example as evidenced by high Pearson correlation coefficients, are included in a prognostic or predictive test in addition to and/or in place of disclosed genes.

Having described the invention, the same will be more readily understood through reference to the following Examples, which is provided by way of illustration, and is not intended to limit the invention in any way.

Example

Example 1 - Characterisation of Intestinal Gene Expression Profiles in Crohn's Disease by Genome- wide Microarray Analysis

Genome-wide microarray expression analysis creates a comprehensive picture of gene expression at the cellular level. The aim of this study was to investigate differential intestinal gene expression in patients with Crohn's disease (CD) and controls with sub-analysis of confirmed CD susceptibility genes, associated pathways and cell lineages.

53 CD and 31 control subjects- 23 normal and 8 inflamed non-inflammatory bowel disease patients were studied. Paired endoscopic biopsies were taken from 5 specific anatomical locations for RNA extraction and histology. 41058 expression sequence tags were analyzed using the Agilent platform.

Clustering analysis separated CD and control terminal ileal (TI) biopsies from colonic biopsies and CD and control TI biopsies. In the CD TI biopsies diubiquitin (FC+11.3, p<1x10-45), MMP3 (FC+7.4, p=1.3x10-11), IRTA1 (FC-11.4, p=4.7x10-12) and CCL23 (FC-7.1, p=1.6x10-10) were differentially expressed compared to controls. In the colon SAA1 (FC+6.3, p=5.3x10-8) was upregulated and TSLP (FC-2.3, p=2.7x10-6) was downregulated comparing non-inflamed CD and control biopsies, and the colonic inflammatory CD signature was characterised by downregulated organic solute carriers-SLC38A4, SLC26A2 and OST alpha. Analysis of the IL-23 pathway revealed IL-23A, JAK2 and STAT3 were upregulated in the CD group compared to controls and in the inflamed compared to non-inflamed CD biopsies. Differential expression was also observed in a number of the autophagy genes, notably ATG16L1.

Methods

Patient recruitment

53 patients with CD (Table 2) and 31 control patients who were undergoing colonoscopy were recruited. All CD patients attended the clinic at the Western General Hospital, Edinburgh and the diagnosis of CD adhered to the criteria of Lennard-Jones. (Lennard-Jones JE. Scand J Gastroenterol Suppl 1989;170:2-6) Quiescent CD was classified as Harvey-Bradshaw score of < 3 prior to bowel preparation and normal histology or histology showing only mild chronic inflammation. Active CD was classified as a Harvey-Bradshaw score of 4 or greater prior to bowel preparation and histology showing chronic active inflammation or acute on chronic inflammation.

Table 2: The Demographics of the Crohn's disease and control patients.

	Crohn's disease	Controls
Number of patients	53	31
Male/ Female	26/27	11/20
Median age at diagnosis (years)	28.6	43 at time of endoscopy
Median duration of follow up (years)	8.1	
Surgery*	20 (38%)	
Current Smoker	11 (21%)	
Family history of IBD	12 (23%)	
Extra-articular symptoms	13 (25%)	
5 ASA Therapy	21 (40%)	
Corticosteroid therapy	4 (8%)	
Immunosuppressant therapy (AZA, 6MP, MTX, MMF)	13 (25%)	
Disease Group		
New Diagnosis (1)	7 (13%)	
Quiescent disease (2)	30 (57%)	
Active disease (3)	16 (30%)	
Vienna Classification of disease location at endoscopy		
Ileal disease (L1)	6 (11%)	
Colonic disease (L2)	28 (53%)	
Ileo-colonic disease (L3)	19 (36%)	
Vienna Classification of disease behavoiur at endoscopy		
Inflammatory (B1)	32 (60%)	
Stricturing (B2)	8 (16%)	
Penetrating (B3)	12 (23%)	

* Includes patients who had surgery for luminal complications of Crohn's disease. AZA-azathioprine, 6MP-6 mercaptopurine, MTX-methotrexate, MMFmycophenolate Full phenotypic data were available on 94% of patients at the time of diagnosis and 100% of patients at the time of endoscopy.

Phenotypic data were collected by interview and case-note review. Eleven of the controls were male, 20 were female and they had a median age of 43 at the time of endoscopy. (Noble et al. Gut 2008, Oct;57(10):1398-405) Six of the controls had normal colonoscopies for colon cancer screening, 10 controls had symptoms consistent with irritable bowel syndrome and had a normal colonoscopic investigation and 7 patients had a colonoscopy for an other indication and histologically normal biopsies were obtained. Eight control patients had abnormal inflamed colonic biopsies (1 pseudomembranous colitis, 1 diverticulitis, 1 amoebiasis, 2 microscopic colitis, 1 eosoinophilic infiltrate, 2 scattered lymphoid aggregates and a history of gastroenteritis). For the female TI clustering analysis, one female UC patient with a non-inflamed terminal ileal biopsy was included. Phenotypic data were collected by interview and case-note review. Lothian Local Research Ethics Committee approved the study protocol: REC 04/S1103/22.

Biopsy Collection

Paired biopsies were taken from the terminal ileum (TI) and 4 sites in the colon (Table 3). One biopsy was sent for histological examination and the other was snap frozen in liquid nitrogen for RNA extraction. Each biopsy was graded histologically into those with no evidence of inflammation, biopsies with evidence of chronic inflammation and a chronic inflammatory cell infiltrate and those with acute inflammation and an acute inflammatory cell infiltrate.

Table 3: The location and number of biopsies in Crohn's disease patients and controls

	Crohn's disease		**Controls**	
Total number of paired biopsies	**106**		**76**	
Terminal Ileum	16		6	
Ascending colon	25		17	
Descending colon	32		23	
Sigmoid colon biopsies.	33		27	
Removed from analysis	7		3	
	Inflamed	**Non-inflamed**	**Inflamed**	**Non-inflamed**
Terminal Ileum	10	6	1	5
Ascending colon	12	8	3	14
Descending colon	14	16	6	17
Sigmoid colon biopsies.	16	17	8	19

The distribution of log intensities for each sample was plotted and outlier samples (i.e. greater than 2 standard deviations from the mean) were excluded from analysis.

Microarray Analysis

Nucleic acid microarrays, often containing thousands of gene sequences, are useful for identifying differentially expressed genes in diseased tissues as compared to their normal counterparts. Using nucleic acid microarrays, test and control mRNA samples from test and control tissue samples are reverse transcribed and labeled to generate cDNA probes. The cDNA probes are then hybridized to an array of nucleic acids immobilized on a solid support. The array is configured such that the sequence and position of each member of the array is known. For example, a selection of genes known to be expressed in certain disease states may be arrayed on a solid support. Hybridization of a labeled probe with a particular array member indicates that the sample from which the probe was derived expresses that gene. If the hybridization signal of a probe from a test (for example, disease tissue) sample is greater than hybridization signal of a probe from a control, normal tissue sample, the gene or genes overexpressed in the disease tissue are identified. The implication of this result is that an overexpressed protein in a disease tissue is useful not only as a diagnostic marker for the presence of the disease condition, but also as a therapeutic target for treatment of the disease condition.

The methodology of hybridization of nucleic acids and microarray technology is well known in the art. In one example, the specific preparation of nucleic acids for hybridization and probes, slides, and hybridization conditions are all detailed in PCT Patent Application Serial No. PCT/US01/10482, filed on

March 30, 2001 and which is herein incorporated by reference. The detailed microarray methodology has also previously been reported by Noble et al. (Gut 2008, Oct;57(10):1398-405)

Total RNA was extracted from each biopsy using the micro total RNA isolation from animal tissues protocol (*Qiagen, Valencia, CA*). 1µg of total RNA was amplified using the Low RNA Input Fluorescent Linear Amplification protocol (*Agilent Technologies, Palo Alto, CA*). A T7 RNA polymerase single round of linear amplification was carried out to incorporate Cyanine-3 and Cyanine-5 label into cRNA. The cRNA was purified using the RNeasy Mini Kit (*Qiagen*). 1 µl of cRNA was quantified using the NanoDrop ND-1000 spectrophotometer (*NanoDrop Technologies, Delaware*). 750ng of Universal Human Reference (*Stratagene, La Jolla, CA*) cRNA labeled with Cyanine-3 and 750ng of the test sample cRNA labeled with Cyanine-5 were fragmented for 30 minutes at 60°C before loading onto the *Agilent* Whole Human Genome microarrays (Agilent Technologies, Palo Alto, CA) which are annotated to represent 33296 genes. The samples were hybridized for 18 hours at 60°C with constant rotation. Microarrays were washed, dried and scanned on the Agilent scanner according to the manufacturer's protocol. Microarray image files were analysed using Agilent's Feature Extraction software version 7.5. The genes were normalized using the *Stratagene* Universal Human Reference. The distribution of log intensities for each sample was plotted and outlier samples (i.e. greater than 2 standard deviations from the mean) were excluded from analysis. The whole data set are available online under the Gene Expression Omnibus of the National Center for Biotechnology Information website.

Real Time PCR

Real time PCR analysis was undertaken in 5 genes-IL-8, SAA1, DEFA5 & 6 and MMP3 on RNA from 15 CD and 6 control TI biopsies. IL-8 and SAA1 were chosen as robust markers of epithelial inflammation and DEFA5 & 6 were selected as there has been considerable interest in their expression in TI CD. Prior to real time PCR analysis 1 RNA amplification cycle was carried out using the MessageAmp™ II aRNA Amplification Kit protocol *(Applied Biosystems, Foster City, CA).* Reverse transcription PCR was then performed on 50ng of RNA using Stratagene model MX4000. TaqMan primers and probes were manufactured in house. **(Table 4)** PRC conditions comprised of 48°C for 30 minutes, 95°C hold for 10 minutes, followed by 40 cycles of 30 second 95°C melt and 1 minute 60°C anneal/extend. Absolute quantification of product was calculated by normalizing to RPL19.

Table 4: TaqMan primers used for real- time PCR

Gene		**Sequence**	**SEQ ID NO:**
SAA1	forward	agcgatgccagagagaata	23
	reverse	ggaagtgattggggtctttg	24
	Taq	ctttggccatggtgcggagg	25
IL8	forward	actcccagtcttgtcattgc	26
	reverse	caagtttcaaccagcaagaa	27
	Taq	tgtgttggtagtgctgtgttgaattacgg,	28
DEFA5	forward	gctacccgtgagtccctct	29
	reverse	tcttgcactgctttggtttc	30

	Taq	tgtgtgaaatcagtggccgcct	31
DEFA6	forward	agagctttgggctcaacaag	32
	reverse	atgacagtgcaggtcccata	33
	Taq	cacttgccattgcagaaggtcctg	34
MMP3	forward	aagggaacttgagcgtgaat	35
	reverse	gagtgcttccccttctcttg	36
	Taq	ggcattcaaatgggctgctgc	37

Data Analysis

Microarray data were analysed using the Rosetta Resolver® software (*Rosetta Inpharmatics, Seattle*). Statistical significance of the microarray data was determined by Student's unpaired *t* test. $p < 0.01$. Fold change data were calculated using the Rosetta Resolver software. To correct for multiple hypothesis testing a q-value was calculated for each tested feature to estimate significance in terms of the false discovery rate (FDR) rather than the false positive rate. For every differential expression analysis the q-value was calculated and a FDR was calculated using the method proposed by Storey et al. (Proc Natl Acad Sci U S A 2003;100:9440-9445) A FDR of less than 5% was calculated for each of the presented analysis. Hierarchical clustering analysis was undertaken using Pearson correlation method. Gene ontology was analyzed using Ingenuity software (*Ingenuity Systems, Mountain View, CA)* The Mann-Whitney U test was used to analyze the real time PCR data. $p < 0.05$ was considered significant.

Gene ontology was analysed using Ingenuity software (*Ingenuity Systems, Mountain View, CA*). Hierarchical clustering analysis using a collection of immune response *in silico* genes from a compendium of six immune cell types was undertaken. (Abbas et al. *Genes Immun* 2005;**6**(4):319-31) Hierarchical clustering analysis was also undertaken using a set of 14 epithelial cell cytokines-CXCL1, CXCL2 CXCL5, CXCL9, CXCL10, CXCL11, CCL2, CCL4, CCL7, CCL20, IL-8, IL-12A, IL-23A and MDK. (Dwinell et al. *Gastroenterology* 2001;**120**(1):49-59; Lee et al. *J Immunol* 2008;**181**(9):6536-45; Yang et al. *Gastroenterology* 1997;**113**(4):1214-23)

Results

The aim of the present study was to use microarray expression analysis to describe the transcriptional profiles in the colon and the terminal ileum in patients with CD and controls. In additional to this hypothesis-free scanning, expression of germ line variants identified by GWAS and cell specific lineage analysis were also investigated.

Unsupervised Hierarchical Clustering Analysis

When all of the CD (n=99) and control biopsies (n=73) were clustered together using unsupervised hierarchical clustering analysis, no separation of the biopsies by either disease status or by the degree of inflammation was observed. When the anatomical location that the biopsies were taken from was considered, 18 TI biopsies clustered together (6 control and 12 CD)($p<0.001$).

Figure 23 shows an unsupervised clustering analysis of the TI biopsies initially was confounded by the sex of patients, however when a degree of supervision was introduced and only TI biopsies from female patients and controls were clustered, clustering by disease status was observed.

Gene ontology of the 593 downregulated sequences grouped by biological process revealed a preponderance of genes associated with carboxylitic acid metabolic processes (39 of a total of 464 genes classified by the ontology software to this biological group; OR 3.4, $p=7x10^{-13}$), organic acid metabolic processes (38/464; OR 3.1 $p=1x10^{-12}$) and lipid metabolic processes (46/620; OR 3.0, $p=6.6x10^{-12}$). When the downregulated sequences were grouped by biological function genes grouped under solute/ cation transporter activity (11/50; OR 10.3, $p=6.9x10^{-15}$), electrochemical potential- driven transporter activity (23/188; OR 5.16, $p=2.7x10^{-14}$) and solute/ sodium transporter activity (10/46; OR 10.1, $p=2.4x10^{-13}$) were disproportionately downregulated. When these groups of genes were combined to encompass all genes involved in transporter activity, there was a significant over representation of this group in the downregulated genes (64/1138; OR 2.3, $p=3.6x10^{-9}$).

367 sequences were upregulated in a subset of the CD samples compared to the controls. Ontology of these genes grouping by biological processes showed that genes that grouped into structural molecule activity (22/603; OR 2.62, $p=4.5x10^{-5}$) and extracellular matrix structural constituents (6/87; OR 5.5, $p=0.0003$) were overrepresented. When the genes were grouped by biological function upregulated genes grouped into sequence specific DNA binding (11/430; OR 2.28, $p=0.007$) and transcription factor activity (20/810; OR 1.7, $p=0.043$).

Gene Expression in Crohn's Disease and Controls

When 99 CD biopsies were compared to 73 control biopsies, 259 sequences were upregulated and 87 sequences were downregulated **(Figure 24).** Notably upregulated genes in the CD biopsies included the acute phase proteins serum amyloid A1, (SAA1; FC +7.5, $p=1.47x10^{-41}$), the regenerating C-type lectin family member (REGL; FC +7.3, $p=2.3x10^{-16}$), the acute phase proteins (S100A9; FC +4.4, $p=2.4x10^{-22}$) and (S100A8; FC +4.0, $p= 3.5x10^{-18}$). IL-8 a robust marker of mucosal inflammation was the sixth most upregulated gene (FC +3.6, $p=5.6x10^{-19}$). Among the most downregulated genes were genes involved in cellular detoxification- (SLC14A2; FC -2.49, $p=0.00002$), (carbonic anhydrase 2; FC -2.4, $p=8.4x10^{-10}$) and (carbonic anhydrase 1; FC -2.3, $p=7.5x10^{-6}$).

Gene Expression in the Terminal Ileum

TI biopsies from 16 patients with CD- 6 non-inflamed biopsies, 7 chronically inflamed biopsies and 3 acutely inflamed biopsies were compared to 6 healthy control TI biopsies. When all of the CD terminal ileal (TI) biopsies were compared to control TI biopsies 1045 sequences had a fold change of greater than 1.5 and 1044 sequences had a fold change of less than -1.5 ($p<0.01$).

(Figure 25). Interesting upregulated genes in the CD biopsies included diubiquitin (UBD) which is involved in synaptic transmission; FC +11.3, $p<1x10^{-45}$, (MMP3; FC +7.4, $p=1.3x10^{-11}$), (IL-8; FC +4.9, $p=2.3x10^{-8}$), (trefoil factor 1 (TFF1) which acts in the GI tract to maintain the mucosal surface barrier; FC +4.3, $p=1.3x10^{-7}$) and the cytokeratin (keratin 5β; FC +4.2, p=0.005) **(Table 5)**. Downregulated genes included immune associated genes (IRTA1- a novel surface B-cell receptor; FC -11.1, $p=4.7x10^{-12}$), (CCL23; FC -7.1, $p=1.6x10^{-10}$), (CXCR4; FC -6.0, $p=8.2x10^{-18}$), and genes involved in cholesterol metabolism (APOC3; FC -8.2, $p=7.0x10^{-8}$) and (APOA1; FC -6.9, p=0.0031).

Table 5: Expression changes in genes of interest in biopsies from the terminal ileum.

Gene	Sequence Code/ Genbank cluster code	All CD samples (16) v controls (6). Fold change (FC)	p value	CD Non-inflamed (6) v non-inflamed controls (6) (FC)	p value	CD Inflamed (10) v non-inflamed (6) (FC)	p value
CXCR4	A_23_P102000	-6.02	$8.2x10^{-18}$	-2.1	$5.23x10^{-10}$	+1.73	0.0033
IL-8	A_32_P87013	+4.85	$2.30x10^{-8}$	+1.63	0.0017	+16.9	$1.26x10^{-13}$
APOA1	A_23_P203191	-6.86	0.0031	-1.032	0.91	-12.22	0.00003
APOC3	A_23_P203183	-8.18	$7.02x10^{-8}$	+1.36	0.10	-12.36	$9.70x10^{-14}$
TFF3	A_23_P257296	+2.40	$<10^{-45}$	+2.0	$1.47x10^{-16}$	+1.72	$6.1x10^{-22}$
CD28	A_23_P91015	-3.76	$1.77x10^{-17}$	-4.52	$1.32x10^{-22}$	+1.30	0.12
UBD	A_23_P81898	+11.3	$<10^{-45}$	+8.48	$1.32x10^{-34}$	+2.50	0.00009
IRTA1	A_23_P115201	-11.43	$4.72x10^{-12}$	-1.57	0.0001	-2.93	0.0032
CCL23	A_24_P133905	-7.14857	1.62E-10				
DefA5	A_23_P112086	-1.16	0.034	-1.07	0.41	-1.14	0.22
DefA6	A_23_P363711	-1.085	0.11	-1.11	0.34	+1.04	0.70

Fold changes and p values are shown in a number of different genes in three different experiments. The number of biopsies analyzed in each experiment is shown in brackets. Candidate genes were included in this table if significant consistent changes in expression were observed across more than one experiment. Analysis of DefA5 and DefA6 expression showed no significant changes across the different groups that were examined.

Colonic Gene Expression Analysis

To minimize the effect of differential gene expression related to the anatomical location of the biopsy, sigmoid colon biopsies were used for analysis. (Noble et al. Gut 2008, Oct;57(10):1398-405) To also remove the acute inflammatory expression signature non-inflamed CD biopsies (n=17) were compared to non-inflamed control biopsies (n=18) **(Figure 26)**. SAA1 remained the most upregulated gene; FC +6.3, $p=5.3x10^{-8}$ and in total 279 sequences were upregulated. 349 sequences were downregulated and the most downregulated genes included (MMP1; FC -3.6, $p=2.4x10^{-15}$), (CXCL13; FC –2.7, p=0.005) and TSLP -thymic stromal lymphoprotein; FC -2.3, $p=2.7x10^{-6}$**(Table 6).**

When the acute inflammatory signal was examined in the sigmoid colon and 16 inflamed CD biopsies were compared to 17 non- inflamed CD biopsies, 279 sequences were upregulated and 148 sequences were down regulated **(Figure 27).** The most upregulated gene in the inflamed biopsies was OLFM4- an anti-apoptotic molecule that inhibits the capsase cascade and also binds to GRIM19; FC +6.2, $p=2.9x10^{-14}$. Downregulated genes included organic solute carriers (SLC38A4; FC -2.7, p=0.005), (SLC26A2; FC -2.5, p=0.00001) and (OST alpha; FC -2.5, p=0.008).

Expression of Genes implicated by GWAS Meta-analysis

Expression of susceptibility genes identified by GWAS meta- analysis by *Barrett et al* (Nat Genet 2008, Aug;40(8):955-62) were investigated along with further detailed analysis of the IL-23 and autophagy pathways. **(Table 7)** Upregulated genes in the CD biopsies compared to the controls included (NOD2/CARD15; FC +1.23, p=0.000243) (PTGER4- prostaglandin E receptor 4; FC +1.1, p=0.00010) and NKX2.3, a 3 exon homeobox gene; FC +1.37, p=0.001. The cell cycle control gene (CDKAL1; FC -1.1, p=0.0096) was downregulated in the CD biopsies compared to the controls. No expression data was present for on the *Agilent* chip for IGRM and no differences were observed between disease groups when expression of TNFSF15, PTPN22, ICOSLG, ITLN1, ZNF365, LRRK2 and PTPN2 were examined.

When inflamed and non-inflamed CD sigmoid colon biopsies were compared MST1-Macrophage stimulatory protein; FC -1.58, p=0.0037 and (C11orf30; FC -1.22, p=0.0078) were downregulated in the inflamed biopsies.

Table 6: Expression changes in genes of interest in biopsies from the colon.

Gene	Sequence code	All CD (99) v controls (73) All CD Fold change (FC)	p value	Inflamed (16) v non-inflamed (17) CD sigmoid (FC)	p value	Inflamed CD sigmoid (16) v inflamed control sigmoid (9) (FC)	p value	Non-inflamed CD sigmoid (17) v non-inflamed control (18) sigmoid Fold change	p value
SAA1	A_24_P335092	+7.5	1.5×10^{-41}	+3.6	5.6×10^{-15}	+8.1	1.4×10^{-7}	+6.3	5.3×10^{-8}
IL-8	A_32_P87013	+7.5	1.5×10^{-41}	+2.5	0.0088	+3.35	0.0030	+1.06	0.59
IFNG	A_23_P151294	+2.1	2.3×10^{-9}	+2.0	0.0080	+1.29	0.50	+1.37	0.18
TSLP	A_23_P121987	-1.52	0.00021	-1.19	0.34	-1.42	0.49	-2.34	2.7×10^{-6}
MMP3	A_23_P52761	+2.63	3.9×10^{-10}	+2.3	0.0029	+7.6	3.14×10^{-10}	-1.50	0.015.
TNIP3	A_23_P386478	+3.84	4.2×10^{-6}	+3.63	2.9×10^{-10}	+4.41	0.00008	-1.27	0.27.
TNF	A_23_P376488	-1.079	0.0031	+1.26	0.0044	-1.13	0.15	-1.10	0.13
CXCL13	A_23_P121695	-2.76064	0.00528						

Fold changes and p values are shown in a number of different genes in four different experiments. The number of biopsies analyzed in each experiment is shown in brackets. Novel genes identified by analysis of the microarray data set and genes with an established role in the pathogenesis of inflammatory bowel disease were investigated.

Table 7: Expression of genes identified by *Barrett et al* (Nat Genet 2008, Aug;40(8):955-62) as being associated with Crohn's disease.

Entrez Gene			All CD (99) v controls (73)		Inflamed CD sigmoid (16) v non-inflamed CD sigmoid (17)	
ID	**Symbol**	**Agilent ID**	**Fold Change**	**p value**	**Fold Change**	**p value**
3717	JAK2	A_23_P123608	+1.90	9.43E-07	+1.58	0.000031
55054	ATG16L1	A_32_P113508	-1.16	1.96E-05	+1.06	0.549
3593	IL-23A/ p19	A_23_P425197	+2.32	0.000099	+2.11	0.000031
5734	PTGER4	A_23_P435394	+1.11	0.000104	-1.04	0.55
64127	NOD2	A_23_P420863	+1.23	0.000243	+1.24	0.1092
6774	STAT3	A_24_P116805	+2.23	0.000353	+1.66	0.0002
159296	NKX2-3	A_23_P52425	+1.37	0.000994	-1.17	0.456
54901	CDKAL1	A_23_P44781	-1.1	0.00964	-1.14	0.0919
94103	ORMDL3	A_23_P38190	+1.13	0.0140	+1.07	0.656
56946	C11orf30	A_23_P380839	+1.1	0.0156	-1.22	0.0077
9966	TNFSF15	A_23_P94754	+1.08	0.0447	+1.09	0.5281
26191	PTPN22	A_23_P201181	+1.07	0.107	+1.03	0.6849
1235	CCR6	A_24_P234921	+1.21	0.144	+1.84	0.0566
23308	ICOSLG	A_23_P317667	+1.1	0.161	-1.10	0.857
55600	ITLN1	A_23_P95790	-1.1	0.162	-1.02	0.905
22891	ZNF365	A_23_P86610	+1.17	0.244	-1.22	0.423
120892	LRRK2	A_23_P128447	+1.25	0.413	+1.37	0.135
5771	PTPN2	A_23_P309701	-1.04	0.483	+1.07	0.545
4485	MST1	A_24_P148796	-1.04	0.709	-1.58	0.0036
149233	IL-23R	A_23_P7560	-1.02	0.823	+1.05	0.4271

For each experiment the fold change and p values have been calculated. The number of biopsies analysed in each experiment are shown in brackets. Gene annotation- JAK2-Tyrosine-protein kinase JAK2, ATG16L1-Prostaglandin E2 receptor EP4, NOD2-Nucleotide-binding oligomerization domain-containing protein 2, STAT3-Signal transducer and activator of transcription, NKX2-3- Homeobox protein Nkx-2.3, CDKAL1- CDK5 regulatory subunit-associated protein 1-like 1, ORMDL3- ORM1-like protein 3, C11orf30- Protein EMSY, TNFSF15- Tumor necrosis factor ligand superfamily member 15, PTPN22 & PTPN22- Tyrosine-protein phosphatase non-receptor type 22 and 2, CCR6- C-C chemokine receptor type 6, ICOSLG- ICOS ligand Precursor, ITLN1- Intelectin-1 Precursor, ZNF365- zinc finger protein 365, LRRK2- Leucine-rich repeat serine/threonine-protein kinase 2, MST1-Macrophage stimulatory protein.

The IL-23 Pathway

Figure 28 shows that when CD samples were compared to controls (IL-23A/p19; FC +2.32, p=0.000099), (TYK2; FC +1.18, p=0.0052), (JAK2; FC +1.90, p=9.4x10^{-7}), (STAT3; FC +2.23, p=0.0004), (INFγ; FC +2.31, p=0.0019) and (IL17F; FC +1.11, p<0.0001) were significantly upregulated in the CD biopsies. When inflamed CD biopsies were compared to non-inflamed CD biopsies (IL-23A/p19; FC +2.11, p=0.000031), (TYK2; FC +1.14, p=0.0052), (JAK2; FC +1.90, p=0.00003), (STAT3; FC +1.66, p=0.0002) and (INFγ; FC +2.33, p<0.0001) had increased expression in the inflamed biopsies. No significant changes were observed in IL-23R expression.

Autophagy Pathway

Figure 29 shows the analysis for ATG16LI and 19 other genes and key regulators of the autophagy pathway. ATG16LI was downregulated in the CD biopsies regardless of inflammation status compared to controls; FC -1.16, p=1.96x10^{-5} as was (ATG4D; FC -1.14, p=0.0007) and (ATG3; FC -1.06, p=0.0052). (ATG12; FC +1.1, p=0.041), (ATG16L2; FC +1.1, p=0.045) and (LC3B; FC +1.18, p=0.0003) were marginally upregulated in the CD biopsies compared to the controls.

Hierarchical Clustering by Specific Probe Subsets: *Immune Response in Silico (IRIS)* Probes

Using the previously defined *IRIS* probes to detect differential expression, CD and control biopsies from the ascending and descending colon were compared. (Abbas et al. *Genes Immun* 2005;**6**(4):319-31) Using the B cell, monocyte and T cell probes we were able to observe separation of the biopsies into CD and control biopsies by unsupervised clustering- B cell probes (p=0.0006, OR 2.74), the monocyte probes (p<0.0001 OR 5.22) and the T cell probes (p=0.0047 OR 2.4) using Chi squared analysis. In the monocyte cluster 2 genes CXCL1 and MMP1 were markedly differentially regulated in the CD biopsies and controls. No TI clustering was observed for any of the examined probes.

Hierarchical Clustering by Epithelial Cell Markers

Figure 30 shows an unsupervised clustering analysis using a panel of 14 epithelial cell cytokines, CXCL1, CXCL2 CXCL5, CXCL9, CXCL10, CXCL11, CCL2, CCL4, CCL7, CCL20, IL-8, IL-12A, IL-23A and MDK (Dwinell et al., Gastroenterology 2001; 120(1):49-59; Lee et al., J. Immunol. 2008; 181(9):6536-45; Yang et al., Gastroenteroloty 1997;113 (4):1214-23) showed clear separation between colonic biopsies from CD patients and controls p<0.00001. When TI biopsies were considered this separation was not observed (p=0.052).

Real Time PCR Confirmation of Microarray Results

In line with the histological classification of the biopsies, and the microarray results significantly higher IL-8 levels were observed in the CD TI biopsies compared to the control TI biopsies (p=0.0045) and in the inflamed CD TI biopsies compared to the non- inflamed CD TI biopsies (p=0.0046)**(Table 8)**. Trends were also observed towards SAA1 being more highly expressed in the CD biopsies compared to the controls and in the inflamed compared to the non-inflamed CD TI biopsies. No difference in DEFA5 & 6 expression was observed in the CD TI biopsies compared to the control TI biopsies (p=0.73 and p=0.97 respectively), nor when the inflamed CD TI biopsies were compared to non-inflamed CD TI biopsies (p=0.39 and p=0.69 respectively).

Table 8: Real time PCR expression in terminal ileal biopsies of patients with Crohn's disease and controls

Genes	Median Relative Expression in control TI biopsies (6)	Median Relative Expression in CD TI biopsies (15)	Median Relative Expression in non- inflamed CD TI biopsies (7)	Median Relative Expression v inflamed CD TI biopsies (8)	Median Relative Expression in inflamed (8) v non-inflamed (7) CD TI biopsies
IL-8	8.4	65.7 (0.0045)	20.1 (0.054)	307 (0.0037)	307 v 20.1 (0.0046)
Def A5	1.26	0.70 (0.73)	0.51 (0.43)	0.96 (0.95)	0.98 v 0.51 (0.39)
Def A6	0.87	1.07 (0.97)	1.1 (0.74)	1.04 (0.85)	1.04 v 1.1 (0.69)
SAA1	1.7	3.52 (0.20)	2.0 (0.52)	20.7 (0.14)	20.7 v 2.0 (0.18)
MMP3	1.0	1.0 (1.0)	1.0 (1.0)	1.0 (1.0)	1.0 v 1.0 (1.0)

The median relative expression of each gene is shown in disease groups along with the p value in brackets. The p values are calculated compared to the control group for each gene analysed. The number of biopsy samples used in each analysis is also shown in brackets.

DISCUSSION

In this accurately phenotyped data set we have used clustering analysis to interrogate the genome wide expression profiles of patients with CD and controls. For the large number of novel CD susceptibility genes from GWAS where little data are presently available, we have been able to investigate expression profiles in the human colon and TI.

Given current concerns with respect to the reproducibility of microarray expression data it is firstly reassuring that our results are consistent with the findings from a previous microarray study in CD patients where increased expression of the S100 and the REG gene families were observed. (Lawrance et al. *Hum Mol Genet* 2001;**10**(5):445-56) Furthermore, in parallel with the results of Costello et al we observed a number of sequences representing novel proteins that were differentially expressed and using ontology and *in silico* analysis we were able characterise genes into functions related to CD pathogenesis. (Costello et al. *PLoS Med* 2005;**2**(8):e199)

This is the first study where genome wide expression has been investigated in unpooled TI endoscopic biopsies from CD patients and controls. Clustering analysis allowed us to differentiate between biopsies from CD patients and controls and the observed separation was driven by a cluster of downregulated genes involved in the normal homeostasis of the TI- organic acid and lipid metabolic processes, and solute/ cation transporter activity, and a cluster of genes that were upregulated which grouped into structural molecule activity. The most upregulated gene in the CD compared to the control TI biopsies was diubiquitin or ubiquitin-like protein FAT10. The family of ubiquitin-like proteins function as part of the ubiquitin proteasome system which is a crucial pathway for protein degradation in eukaryotic cells.(Madsen et al., BMC.Biochem. 2007;8 Suppl 1:S1) The gene is located at the major histocompatibility complex locus in on chromosome 6 (Fan et al., Immunogenetics 1996;44(2):97-103), an established CD susceptibility loci and its expression has been observed to be increased in 90% of hepatocellular carcinomas and in 80% of colon cancers.(Lee et al., Oncogene 1-5-2003;22(17):2592-603) Diubiquitin is a downstream target of p53 and in p53-defective cells its expression is increased resulting in chromosomal instability.(Ren et al., J.Biol.Chem. 21-4-2006;281(16):11413-21; Zhang et al., Oncogene 2006;25(16):2318-27) Overall in this data set diubiquitin was upregulated when all CD biopsies were compared controls by a fold change of 1.5. Furthermore, diubiquitin expression in hepatocellular cancer and colon cancer correlates with increased expression of IFN-gamma and TNFα suggesting a mechanism for carcinogenesis in this pro-inflammatory environment.(Lukasiak et al., Oncogene 9-10-2008;27(46):6068-74)

The differing expression signature observed in the TI biopsies appeared to be primarily inflammation driven, rather than disease specific as the changes were less obvious in the non- inflamed analysis than when the inflamed and non-inflamed CD biopsies were compared. These dysregulated probes could form the basis of a diagnostic expression chip to help diagnose ileal CD and grade its severity.

Another of the notable observations in the TI analysis were data showing no difference in expression of the alpha defensins 5 and 6 (DEFA5&6) in the CD patients and controls regardless of the degree of inflammation in the biopsies. These results were confirmed by real time PCR and are contrary to previous data where reduced DEFA5&6 expression was observed in the TI of CD patients regardless of the degree of inflammation. (Wehkamp et al. *Proc Natl Acad Sci U S A* 2005;**102**(50):18129-34)

More recently, Simms et al also showed that expression of DEFA5&6 was down regulated in TI CD biopsies. (Simms et al. *Gut* 2008;**57**(7):903-10) However, this downregulation was inflammation specific, probably reflecting a loss of the epithelial layer and a reduction of epithelial and Paneth cells as a consequence of persistent inflammation. In our data set increased expression of DEFA5&6 was observed in the sigmoid colon biopsies of CD patients and this correlated with the degree of inflammation of the biopsies. Previously we have shown that the increase in colonic expression of DEFA5&6 in UC patients is largely mediated by Paneth cell metaplasia and that in the colon unregulated Paneth cell differentiation, and the consequent increase in DEFA5&6 expression, may perpetuate mucosal inflammation. (Noble et al. Gut 2008, Oct;57(10):1398-405)

When the colonic analysis was compared to our previous expression studies in UC there was a 23% homology between the differentially regulated genes in the respective CD and UC analysis compared to controls. (Noble et al. Gut 2008, Oct;57(10):1398-405) The colonic inflammatory expression signature observed in the CD biopsies was also similar to that observed in the UC biopsies and one of the most differentially regulated genes in both of the data sets was serum amyloid A1 (SAA1).

SAA1 is a HLA- associated apolipoprotein acute phase reactant and levels can be elevated in inflammation, trauma and neoplasia. Its transcription is induced by the pro- inflammatory cytokines IL-2, IL-6, TNFα and bacterial LPS, and it is the major factor responsible for the development of secondary AA amyloidosis in chronic immune mediated diseases such as Rheumatoid arthritis or CD. (Gutfeld et al. *J Histochem Cytochem* 2006;**54**(1):63-73) In CD reactive AA amyloidosis is rare and a much more attractive role for SAA1 would be as a marker of disease activity, severity, and potentially because of its induction by TNFα a predictor of response to anti-TNF therapy.

A further interesting change in expression in the colonic CD biopsies reflecting the traditional Th1 and novel Th17 paradigm in CD was the downregulation of thymic stromal lymphopoietin (TSLP) in non-inflamed colonic CD samples compared to non- inflamed controls. TSLP is a cytokine that mediates its effect through dendritic cells to promote the Th2 differentiation of $CD4^+$ T cells. (Al Shami et al. *J Exp Med* 2005;**202**(6):829-39) Moreover, mice with an intestinal epithelial cell (IEC) deletion of intrinsic IκB kinase, have reduced TSLP expression and as a consequence have a poor Th2 immune response resulting in a inability to eradicate infection. (Zaph et al. *Nature* 2007;**446**(7135):552-6) These mice also develop severe intestinal inflammation as a result of dendritic cell derived Th1 and Th17 pathway activation and it is intriguing to speculate that in the non- inflamed human CD colon decreased levels of TSLP may perpetuate the subsequent persistent and excessive inflammation.

The identification of IL-23R as a CD susceptibility gene has focused investigation towards the distinct Th17 lineage. (Cho et al. *Gastroenterology* 2007;**133**(4):1327-39) We observed that expression of a number of components of this pro-inflammatory pathway- IL-23A, TYK2, STAT3, JAK2, IFNγ and IL-17 were increased in CD compared to controls and that this change was driven by active as opposed to quiescent disease. These convincing genetic and expression data emphasize the importance of this pro-inflammatory pathway in the pathogenesis of CD. Multiple therapeutic targets have been identified in this pathway and clinical trials of a monoclonal antibody against the p40 subunit of IL-23 have produced promising early clinical data. (Sandborn et al. *Gastroenterology* 2008;**135**(4):1130-41)

The discovery of ATG16L1 as a CD specific susceptibility gene has strongly implicated the autophagy pathway in the pathogenesis of CD. Autophagy is a highly conserved cellular process where the cell digests part of its own cytoplasm and it functions as a normal physiological response to remove toxic material or intracellular bacteria from the cell. The pathway has also been implicated in the pathogenesis of neurodegenerative diseases such as Alzheimer's and Parkinson's disease. (Lees et al. *Inflammatory Bowl Disease Monitor* 2009;**Vol 9**(No 2))

In our data set, 6 of the 20 autophagy genes that we examined were dysregulated emphasizing the importance of this pathway in CD. Recent data have linked the innate immune response and autophagy via Toll-like-receptor (TLR) engagement. (Sanjuan et al. *Nature* 2007;**450**(7173):1253-7) TLR induced phagosomes within macrophages triggered ATG5 and ATG7 mediated acidification and enhanced killing of the ingested organisms. These interactions between the innate immune system and the autophagy pathway have provoked investigators to speculate about specific interaction between NOD2/CARD15 and autophagy and this is an area of active investigation. For example, NOD1 and NOD2 have been shown to recruit ATG16L1 to the plasma membrane at site of bacterial entry into the cell and that in cells with NOD2 mutations this response is impaired. (Travassos et al., Nat.Immunol. 8-11-2009)

An alternative method for interpreting genome wide expression data is to cluster samples using a subset of genes related to cell lineage. (Abbas et al. *Genes Immun* 2005;**6**(4):319-31) We have undertaken this analysis in our samples by separating by genes from key immune cell types and observed clustering of the colonic biopsies. From this we can clearly identify immune cell infiltration in the biopsies and characterize the most differentially expressed genes. These expression signatures can also be used to gain insight into genes of unknown function and provide a resource to investigate immune cell differentiation in health and in different immune mediated diseases.

A final area of interest was in the role of the intestinal epithelial cell (IEC) in the inflammatory process. The fourteen IEC markers we investigated showed good ability to segregate CD patients and controls by clustering analysis with the majority of the chemokines being upregulated in the colonic CD biopsies in an inflammation dependant manner. These results are consistent with previous data from Puleston and colleagues who observed a subset of chemokines-CXCLs 1-3 and CCL20 were upregulated in colonic IBD along with their receptors in a coordinated IEC inflammatory response. (Puleston et al.

Aliment Pharmacol Ther 2005;**21**(2):109-20) The upregulation of these chemokines was significantly more than known leukocyte chemokines emphasizing the central role of the IEC in colonic inflammation.

Further studies carried out in human colonic IBD biopsies, in human colonic cell lines and in human fetal intestinal xenografts have all confirmed the central role of the IEC in mediating, coordinating and perpetuating the pathogenic inflammatory response observed in the colon in both CD and UC. (Dwinell et al. *Gastroenterology* 2001;**120**(1):49-59; Banks et al. *J Pathol* 2003;**199**(1):28-35; Kwon et al. *Gut* 2002;**51**(6):818-26)

The strengths of this data are the number of biopsies we analyzed, the lack of pooling of the samples and the rigorous attention to the inflammation status of the biopsies, and their anatomical location. Our data are also consistent with previous expression studies in inflammatory bowel disease and add considerably to the recent genome wide association studies in providing complimentary human colonic and ileal expression data along with detailed analysis of the IL-23 and autophagy pathways.

In conclusion this valuable data set has allowed us to gain novel insight into the pathogenesis of CD at the mucosal level. The data add considerably to the recent genome wide association studies in providing complimentary human colonic and ileal expression data along with detailed analysis of the IL-23 and autophagy pathways. In depth analysis of these exciting new candidate genes along with IEC specific analysis have generated a number of potential therapeutic targets worthy of further investigation.

WHAT IS CLAIMED:

1. A method of diagnosing the presence of an inflammatory bowel disease (IBD) in a mammalian subject, comprising determining a differential expression level of a nucleic acid encoding a polypeptide shown as any one of SEQ ID NOS: 5, 6, 8, 11, 12, 2, 14, 16, 18, 20, and 22 in a test sample obtained from the subject relative to the expression level of a control, wherein said differential level of expression is indicative of the presence of an IBD in the subject from which the test sample was obtained.

2. The method of claim 1, wherein the differential level of expression is a lower level of expression for a nucleic acid encoding a polypeptide shown as any one of SEQ ID NOS: 5, 6, 8, 11, 12, 2, 14, and 16, wherein the lower level of expression is indicative of the presence of an IBD in the subject from which the test sample was obtained.

3. The method of claim 1, wherein the differential level of expression is a higher level of expression for a nucleic acid encoding a polypeptide shown as any one of SEQ ID NOS: 18, 20, and 22, wherein the higher level of expression is indicative of the presence of an IBD in the subject from which the test sample was obtained.

4. The method of claim 1, 2, or 3 wherein said mammalian subject is a human patient.

5. The method of claim 4 wherein evidence of said expression level is obtained by a method of gene expression profiling.

6. The method of claim 4 wherein said method is a PCR-based method.

7. The method of claim 5 wherein said expression levels are normalized relative to the expression levels of one or more reference genes, or their expression products.

8. The method of claim 1, 2 or 3 comprising determining evidence of the expression levels of at least two of said genes, or their expression products.

9. The method of claim 1, 2 or 3 comprising determining evidence of the expression levels of at least three of said genes, or their expression products.

10. The method of claim 1 or 2 comprising determining evidence of the expression levels of at least four of said genes, or their expression products.

11. The method of claim 1 or 2 comprising determining evidence of the expression levels of at least five of said genes, or their expression products.

12. The method of claim 1, 2, or 3 further comprising the step of creating a report summarizing said IBD detection.

13. The method of claim 1, 2, or 3, wherein said IBD is Crohn's disease.

14. The method of claim 1, 2, or 3, wherein said test sample is from a colonic tissue biopsy.

15. The method of claim 14, wherein said biopsy is from a tissue selected from the group consisting of the terminal ileum, the ascending colon, the descending colon, and the sigmoid colon.

16. The method of claim 14, wherein said biopsy is from an inflamed colonic area.

17. The method of claim 14, wherein said biopsy is from a non-inflamed colonic area.

18. The method of claim 1, 2, or 3, wherein said determining step is indicative of a recurrence of an IBD in said mammalian subject, and wherein said mammalian subject was previously diagnosed with an IBD and treated for said previously diagnosed IBD.

19. The method of claim 18, wherein said treatment comprised surgery.

20. The method of claim 1, 2, or 3, wherein said determining step is indicative of a flare-up of said IBD in said mammalian subject.

21. A method of treating an inflammatory bowel disorder (IBD) in a mammalian subject in need thereof, the method comprising the steps of

(a) determining a differential expression level of a nucleic acid encoding a polypeptide shown as any one of SEQ ID NOS: 5, 6, 8, 11, 12, 2, 14, 16, and 18, in a test sample obtained from said subject relative to the expression level of a control, wherein said differential level of expression is indicative of the presence of an IBD in the subject from which the test sample was obtained; and

(b) administering to said subject an effective amount of an IBD therapeutic agent.

22. The method of claim 21, wherein the differential level of expression is a lower level of expression for a nucleic acid encoding a polypeptide shown as any one of SEQ ID NOS: 5, 6, 8, 11, 12, 2, 14, and 16, wherein the lower level of expression is indicative of the presence of an IBD in the subject from which the test sample was obtained.

23. The method of claim 21, wherein the differential level of expression is a higher level of expression for a nucleic acid encoding a polypeptide shown as any one of SEQ ID NOS: 18, 20, and 22, wherein the higher level of expression is indicative of the presence of an IBD in the subject from which the test sample was obtained.

24. The method of claim 21, 22, or 23 wherein said mammalian subject is a human patient.

25. The method of claim 24 wherein evidence of said expression level is obtained by a method of gene expression profiling.

26. The method of claim 24 wherein said method is a PCR-based method.

27. The method of claim 26 wherein said expression levels are normalized relative to the expression levels of one or more reference genes, or their expression products.

28. The method of claim 21, 22, or 23 comprising determining evidence of the expression levels of at least two of said genes, or their expression products.

29. The method of claim 21, 22, or 23 comprising determining evidence of the expression levels of at least three of said genes, or their expression products.

30. The method of claim 21 or 22 comprising determining evidence of the expression levels of at least four of said genes, or their expression products.

31. The method of claim 21 or 22 comprising determining evidence of the expression levels of at least five of said genes, or their expression products.

32. The method of claim 21, 22, or 23 further comprising the step of creating a report summarizing said IBD detection.

33. The method of claim 21, 22, or 23, wherein said IBD is Crohn's disease.

34. The method of claim 21, 22, or 23, wherein said test sample is from a colonic tissue biopsy.

35. The method of claim 34, wherein said biopsy is from a tissue selected from the group consisting of the terminal ileum, the ascending colon, the descending colon, and the sigmoid colon.

36. The method of claim 34, wherein said biopsy is from an inflamed colonic area.

37. The method of claim 34, wherein said biopsy is from a non-inflamed colonic area.

38. The method of claim 21, 22, or 23, wherein said determining step is indicative of a recurrence of an IBD in said mammalian subject, and wherein said mammalian subject was previously diagnosed with an IBD and treated for said previously diagnosed IBD.

39. The method of claim 38, wherein said treatment comprised surgery.

40. The method of claim 21, 22, or 23, wherein said determining step is indicative of a flare-up of said IBD in said mammalian subject.

41. The method of claim 21, 22, or 23, wherein said IBD therapeutic agent is an aminosalicylate.

42. The method of claim 21, 22, or 23, wherein said IBD therapeutic agent is a corticosteroid.

43. The method of claim 21, 22, or 23, wherein said IBD therapeutic agent is an immunosuppressive agent.

```
   1 ctcaatcagc tttatgcaga gaagaagctt actgagctca ctgctggtgc tggtgtaggc
  61 aagtgctgct ttggcaatct gggctgacct ggcttgtctc ctcagaactc cttctccaac
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2581 ctcaaaggaa ataaggttgc ttttcttgta ggaactgtgt ctttgagtta ctaattagtt
2641 tatatgagaa taattcttgc aataaatgaa gaaggaataa aagaaatagg aagccacaaa
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2761 aatattagag gtctcctgat ggaagtgtac aataccacct acaaattatc catgccccaa
2821 gtgttaaaac tgaatccatt caagtctttc taactgaata cttgttttat agaaaatgca
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Figure 1A

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3001 aaataaaaag aagagaggga ggaagaaagg gagagagaag aaaagaaaaa tgaagaaaag
3061 taattagaat attttcaaca taaagaaaag acgaatattt aaggtgacag atatcccaac
3121 tacgctgatt tgatctttac aaattatatg agtgtatgaa tttgtcacat gtatcacccc
3181 caaaaaaaga gaaaaagaaa aatagaagac atataaatta aatgagacga gacatgtcga
3241 ccaaaaggaa tgtgtgggtc ttgtttggat cctgactcaa attaagaaaa aataaaacta
3301 cctacgaaat actaagaaaa atttgtatac taatattaag aaattgttgt gtgttttgga
3361 tataagtgat agtttattgt agtgatgttt ttataaaagc aaaaggatat tcactttcag
3421 cgcttatact gaagtattag attaaagctt attaacgta
```

Figure 1B

```
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121 lrchrrrkek ltavkytwng nilsisnksw dllipqassn nngnyrcigy gdendvfrsn
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241 stypelqlpt vwrensgsyw cgaetvrgni hkhspslqih vqripvsgvl letqpsggqa
301 vegemlvlvc svaegtgdtt fswhredmqe slgrktqrsl raelelpair qshaggyyct
361 adnsygpvqs mvlnvtvret pgnrdglvaa gatggllsal llavallfhc wrrrksgvgf
421 lgdetrlppa pgpgesshsi cpaqvelqsl yvdvhpkkgd lvyseiqttq lgeeeeants
481 rtlledkdvs vvysevktqh pdnsagkiss kdees
```

Figure 2

```
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121 ttggatccca ggcccgggtc acaaaagatg cagagacaga gttcatgatg tcaaagcttc
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481 attgaacttg tcaaggtgaa gggacacaag ttgccagcca ccaactttct tgcctcaact
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601 catctaataa acagtttctc actttaaaaa aaaaaaaaaa a
```

Figure 3

```
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481 gcctcaacta ccttcctgaa ttattttta aagaagcatt tattcttgtg ttctggattt
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601 aaa
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Figure 4

```
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121 vcvrmlkldt riktrkn
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Figure 5

```
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```

Figure 6

```
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1201 taaaaaaaaa aaaaaaaaa
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Figure 7

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Figure 8

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Figure 9A

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Figure 9B

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1861 ctgactggac cagagttgtc ttcagccctg atggcagtta cgtggcggca ggctctgctg
1921 agggctctct gtatatctgg agtgtgctca cagggaaagt ggaaaaggtt ctttcaaagc
1981 agcacagctc atccatcaat gcggtggcgt ggtcgccctc tggctcgcac gttgtcagtg
2041 tggacaaagg atgcaaagct gtgctgtggg cacagtactg acggggctct caggctgggg
2101 aggaccccag tgccctcctc agaagaagca catgggctcc tgcagccctg tcctggcagg
2161 tgatgtgctg ggtatagcat ggacctccca gagaagctca agctatgtgg cactgtagct
2221 ttgccgtgaa tgggatttct gaagatttga ctgaggtctc tcttggcctg gaagaataac
2281 actgaaaaaa cctgacgctg cggtcactta gcagaggctc aggttcttgc cttgggaaac
2341 actactagct ctgaccttcc atacctcact tgggggagca cagggccccg ctgggcctcc
2401 tcaccaacgg cagtgccaaa atcagccccc acatcaaggt ggtgttctct gtgctttctc
2461 tcgtccttcc aaagtcggtt ctggcctaac gcatgtccca acaccttggg ttcatttgcc
2521 cggtgaactc actttaagca ttggattaac ggaaactccc gaactacaga cccctccctg
2581 gtgggttgca tgaatgtgtc tcattactgc tgaaatgtcc tcacatctct ttcactgttc
2641 ttcagagctt tctggctctc tttcccccac aaaattcgac atatttaaaa atctccgtgt
2701 ggctttaaaa aatggttttt tgtttttttg tttttttgag gtgggagagg atgtgtgaaa
```

Figure 10A

```
2761 atcttttcca gggaaatggg ttcgctgcag aggtaaggat gtgttcctgt atcgatctgc
2821 agacacccag aaggtgggtg cacactgcat gcttgggggt gccaagggat tcgagacctc
2881 caacatactt gtctgaaggt ggtgattctg gccatggccc ctctgccaag cctgtgtgcg
2941 atgcccttgg tgctttagtg caagaagcct aggctcagaa gcacagcagc gccatctttc
3001 cgtttcaggg gttgtgatga aggccaagga aaaacattta tctttactat tttacctacg
3061 tataaagttt tagttcattg ggtgtgcgaa acaccctttt tatcactttt aaatttgcac
3121 tttatttttt ttcttccatg cttgttctct ggacatttgg ggatgtgagt gttagagctg
3181 gtgagagagg agtcaggtgg ccttcccacc gatggtcctg gcctccacct gccctctctt
3241 ccctgcctga tcaccgcttt ccaatttgcc cttcagagaa cttaagtcaa ggagagttga
3301 aattcacagg ccagggcaca tcttttattt atttcattat gttggccaac agaacttgat
3361 tgtaaataat aataaagaaa tctgttatat acttttcaaa ctccaaaaaa a
```

Figure 10B

```
  1 mssglraadf prwkrhiseq lrrrdrlqrq afeeiilqyn klleksdlhs vlaqklqaek
 61 hdvpnrheis pghdgtwndn qlqemaqlri khqeeltelh kkrgelaqlv idlnnqmqrk
121 dremqmneak iaeclqtisd letecldlrt klcdleranq tlkdeydalq itftalegkl
181 rktteenqel vtrwmaekaq eanrlnaene kdsrrrqarl qkelaeaake plpveqdddi
241 evivdetsdh teetspvrai sraatrrsvs sfpvpqdnvd thpgsgkevr vpatalcvfd
301 ahdgevnavq fspgsrllat ggmdrrvklw evfgekcefk gslsgsnagi tsiefdsags
361 yllaasndfa sriwtvddyr lrhtltghsg kvlsakflld narivsgshd rtlklwdlrs
421 kvciktvfag sscndivcte qcvmsghfdk kirfwdirse sivremellg kitaldlnpe
481 rtellscsrd dllkvidlrt naikqtfsap gfkcgsdwtr vvfspdgsyv aagsaegsly
541 iwsvltgkve kvlskqhsss inavawspsg shvvsvdkgc kavlwaqy
```

Figure 11

```
  1 mssglraadf prwkrhiseq lrrrdrlqrq afeeiilqyn klleksdlhs vlaqklqaek
 61 hdvpnrheis pghdgtwndn qlqemaqlri khqeeltelh kkrgelaqlv idlnnqmqrk
121 dremqmneak iaeclqtisd letecldlrt klcdleranq tlkdeydalq itftalegkl
181 rktteenqel vtrwmaekaq eanrlnaene kdsrrrqarl qkelaeaake plpveqdddi
241 evivdetsdh teetspvrai sraatkrlsq pagglldsit nifgrrsvss fpvpqdnvdt
301 hpgsgkevrv patalcvfda hdgevnavqf spgsrllatg gmdrrvklwe vfgekcefkg
361 slsgsnagit siefdsagsy llaasndfas riwtvddyrl rhtltghsgk vlsakflldn
421 arivsgshdr tlklwdlrsk vciktvfags scndivcteq cvmsghfdkk irfwdirses
481 ivremellgk italdlnper tellscsrdd llkvidlrtn aikqtfsapg fkcgsdwtrv
541 vfspdgsyva agsaegslyi wsvltgkvek vlskqhsssi navawspsgs hvvsvdkgck
601 avlwaqy
```

Figure 12

```
   1 ctggggacgg gggccgagta gcgccttccc cgggccccgt gaaccggctg cgggtcgccc
  61 ttggggggca gcggccgcag ccccccacct gggccctcgg tccgccctcc cggcgcgtcc
 121 atgaactcag tgtcgccggc cgccgcgcag taccggagca gcagcccgga ggacgcgcgc
 181 cgccggcccg aggcccgcag gccgcggggt cccagaggcc cagaccccaa cggcctgggg
 241 ccttccggag ccagcggccc cgctcttggc tctcccgggg ctggcccgag tgagccggac
 301 gaagtggaca agttcaaggc caagttcctg acagcctgga acaacgtcaa gtacggttgg
 361 gtggttaaaa gccggaccag ctttagcaag atctccagca tccacctctg tggccgccgc
 421 taccgtttcg agggcgaggg tgacatacag cgtttccagc gggactttgt gtcccgcctg
 481 tggctcacat accgccggga cttcccgccc cttcctgggg gctgcctgac ctcggactgt
 541 ggctgggggt gcatgttacg cagcggccag atgatgctgg cacagggcct tctgctgcat
 601 ttcctgccca gagactggac atgggccgag ggcatgggcc tgggcccccc tgagctgtca
 661 gggtcagcct ctcccagccg gtaccatggg cctgcccgct ggatgccccc acgctgggcc
 721 cagggtgccc ctgagctgga gcaggaacgc cggcaccggc agattgtgtc ctggttcgcc
 781 gaccaccccc gggccccctt tggcctacac cggctggtgg agcttgggca gagctcaggc
 841 aagaaggcag gtgactggta tgggccatcg ctagtggcac acatcctcag gaaagccgtg
 901 gagagctgct ccgacgtcac ccgcctggtg gtgtacgttt ctcaggactg cacagtgtac
 961 aaggcggatg tggcacgcct ggtggccagg ccagacccca cagccgagtg gaagtctgtg
1021 gtcatcctgg tgcccgtgcg actgggtggc gagactctca accccgtgta tgtgccctgc
1081 gtgaaggaac tcctgcgttg cgagctgtgc ctgggcatca tgggtgggaa accgcgacac
1141 tcactgtact tcattggcta ccaagatgac ttcctgctgt acctggaccc tcactactgc
1201 cagcccactg tggatgtcag ccaggccgac ttccccctgg agtccttcca ctgcacctcg
1261 ccccgcaaga tggcctttgc caagatggac ccaagctgta ccgtgggctt ctatgctgga
1321 gacaggaagg agtttgagac actctgctca gagctgacca gggtcctcag ctcctcctca
1381 gccacagagc ggtaccccat gttcaccctg gccgagggcc atgctcagga ccacagcctg
1441 gacgacctct gctcccagct cgcccagccc acactccggc tccctcgcac agggcggctc
1501 ctcagggcca aacgccccag ctctgaggac tttgtgtttt tataaaggga ggggatgagg
1561 ggaaagatac aacactattt atttttttat ttatgtcatg tcgggtgtgg gatcttgagc
1621 tctggcagtg atgatggtac ttcctgttgt cagcccctca agcccagctg caaccagtct
1681 ggggccattc agccagggac agagcccaca gagcccatac acctgtctcc caccagcggg
1741 gccctcctgg cagggtaggg aaggaggacc ccgggcaccc ccctcagggc ctgactcacg
1801 tactgtagtt tgcactggac gcccgggccc tccctgtccc aaagccccct tgggggaact
1861 gtggctgctg gggccaata aagctgtgta acttgaaaaa aaaaaaaaaa aaaaaaaaaa
1921 aaaaaaaaa
```

Figure 13

```
  1 mnsvspaaaq yrssspedar rrpearrprg prgpdpnglg psgasgpalg spgagpsepd
 61 evdkfkakfl tawnnvkygw vvksrtsfsk issihlcgrr yrfegegdiq rfqrdfvsrl
121 wltyrrdfpp lpggcltsdc gwgcmlrsgq mmlaqglllh flprdwtwae gmglgppels
181 gsaspsryhg parwmpprwa qgapeleqer rhrqivswfa dhprapfglh rlvelgqssg
241 kkagdwygps lvahilrkav escsdvtrlv vyvsqdctvy kadvarlvar pdptaewksv
301 vilvpvrlgg etlnpvyvpc vkellrcelc lgimggkprh slyfigyqdd fllyldphyc
361 qptvdvsqad fplesfhcts prkmafakmd psctvgfyag drkefetlcs eltrvlssss
421 aterypmftl aeghaqdhsl ddlcsqlaqp tlrlprtgrl lrakrpssed fvfl
```

Figure 14

```
   1 cgggtgctga tgcgagtcgg tggcagcgag gacattttct gactccctgg cccctgacac
  61 ggctgcactt tccatcccgt cgcggggccg gccgctactc cggccccagg atgcagaatg
 121 tgattaatac tgtgaaggga aaggcactgg aagtggctga gtacctgacc ccggtcctca
 181 aggaatcaaa gtttaaggaa acaggtgtaa ttaccccaga agagtttgtg gcagctggag
 241 atcacctagt ccaccactgt ccaacatggc aatgggctac aggggaagaa ttgaaagtga
 301 aggcatacct accaacaggc aaacaatttt tggtaaccaa aaatgtgccg tgctataagc
 361 ggtgcaaaca gatggaatat tcagatgaat tggaagctat cattgaagaa gatgatggtg
 421 atggcggatg ggtagataca tatcacaaca caggtattac aggaataacg gaagccgtta
 481 aagagatcac actggaaaat aaggacaata taaggcttca agattgctca gcactatgtg
 541 aagaggaaga agatgaagat gaaggagaag ctgcagatat ggaagaatat gaagagagtg
 601 gattgttgga aacagatgag gctaccctag atacaaggaa aatagtagaa gcttgtaaag
 661 ccaaaactga tgctggcggt gaagatgcta ttttgcaaac cagaacttat gacctttaca
 721 tcacttatga taaatattac cagactccac gattatggtt gtttggctat gatgagcaac
 781 ggcagccttt aacagttgag cacatgtatg aagacatcag tcaggatcat gtgaagaaaa
 841 cagtgaccat tgaaaatcac cctcatctgc caccacctcc catgtgttca gttcacccat
 901 gcaggcatgc tgaggtgatg aagaaaatca ttgagactgt tgcagaagga gggggagaac
 961 ttggagttca tatgtatctt cttattttct tgaaatttgt acaagctgtc attccaacaa
1021 tagaatatga ctacacaaga cacttcacaa tgtaatgaag agagcataaa atctatccta
1081 attattggtt ctgattttta aagaattaac ccatagatgt gaccattgac catattcatc
1141 aatatataca gtttctctaa taagggactt atatgtttat gcattaaata aaaatatgtt
1201 ccactaccag ccttacttgt ttaataaaaa tcagtgcaaa gaaaaaaaaa aaaaaaaaaa
1261 aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa
1321 aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aa
```

Figure 15

```
  1 mqnvintvkg kalevaeylt pvlkeskfke tgvitpeefv aagdhlvhhc ptwqwatgee
 61 lkvkaylptg kqflvtknvp cykrckqmey sdeleaiiee ddgdggwvdt yhntgitgit
121 eavkeitlen kdnirlqdcs alceeeeded egeaadmeey eesglletde atldtrkive
181 ackaktdagg edailqtrty dlyitydkyy qtprlwlfgy deqrqpltve hmyedisqdh
241 vkktvtienh phlppppmcs vhpcrhaevm kkiietvaeg ggelgvhmyl liflkfvqav
301 iptieydytr hftm
```

Figure 16

```
   1 cgaccgagca cagacacgtt gcccaccgct cctctcccga ggtctgtagt cgcggagaaa
  61 cacatgttgc gttactaacg ttcagaggtc tgcgacagct tcgatttgaa tgactagccg
 121 ggaacaccaa gtttcactgt gtaattgcgt ccccctactc cggcgcctcc tttgcgacgc
 181 tccctggaga aaagcacgcc cactgcacgc gctcagtcgc tacttccgct ctcgagtgtc
 241 tccaagcaag atggcggagg agccgcagtc tgtgttgcag cttcctactt caattgctgc
 301 tggaggggaa ggacttacgg atgtctcccc agaaacaacc accccggagc cccegtcttc
 361 cgctgcagtt tccccgggaa cagaggaacc tgctggcgac accaagaaaa aaattgacat
 421 tttgctaaag gctgtgggag acactcctat tatgaaaaca aagaagtggg cagtagagcg
 481 aacacgaacc atccaaggac tcattgactt catcaaaaag tttcttaaac ttgtggcctc
 541 agaacagttg tttatttatg tgaatcagtc ctttgctcct tccccagacc aagaagttgg
 601 aactctctat gagtgttttg gcagtgatgg taaactggtt ttacattact gcaagtctca
 661 ggcgtgggga tgaaccacaa agaaaatcaa cttgctacta catgaaatgg attttcacgg
 721 aagagacagc tctgaaaagt tttgatgctt gtggcaagag acttaacaga tgtgatctat
 781 ttagtatgtg tctactctat gtttatgcat aagaaaacat ccatagcatg aatggactca
 841 gaaaaatgtg atttgtatta atgcaccagt catcataaaa gatggtcatg atagtacacc
 901 cattgctcct acttgttact attattgctg cagatctgcc tccaaggttg aaaaggagac
 961 taagactgta taaacatctt cattgtcagt tctcaaaatg actgaaattg ttttcatggt
1021 aaaagttaat atactaaagg gttccttttt ttttaatgtt tacatttatc tctatgttta
1081 cctttttagt cacattgacc tgctggctga atacctcaaa tagtccagta gagggcagtc
1141 caccaggcag aaaaggttag gcgttttggt ttcacatctt tgctggggaa taatagggga
1201 aatggctgtt tttgctaatt tttagctaat atctagccag gagagcaagc acataggaca
1261 gactgaaaga ctgtaatttt acacaataca catggcttaa ttattttatt gggatacaga
1321 aaaatataaa ttctggacaa ataagtcata tacctgtttt cagtcctaac atttaaggat
1381 tcttgagtcc caatcacata actgtggtgt tactctgtca tttatatggt gtcaaaagca
1441 cttgatgagt aaacccagta gcatcttttt gagtgtttca taatgcattt tccaacttga
1501 aaacaataat tgaaaaatag ccttattgta tattttatgc catgactaaa agtgccattt
1561 ttactgatgc tattagactg ataatttctt gaagtgaaat ttaacctttt tttctcttta
1621 gtattatgtt tataatgcca tatttttaga aagcattcca gatcaggcat ggtggcttac
1681 acctgtaatc ccagcacttt ggaaggctga ggtgtgggga ttgcgtgaag ccacaagttt
1741 gagaccagcc tggttagcaa ggcaagatcc ccaactctac aaaaaaataa aaattaaaaa
1801 aaaattatta ggctgcagag gcaagaggat cccctgagcc cagaagttca agggtatagt
1861 gagtcgtgat tgtaccactg cattcctgct gagcaacaga gtgagacccc atctcaaaaa
1921 agaaaaaaaa aggcattcta gtaaatcgaa tgtaatgtga atggaatttc aaaacaggat
1981 ctaagatggt atgtagtaga attcaaagta atatcatttt aaagttaaat gagtatggaa
2041 aaggtctgtt ctctagtttt gtccagttca gtttactgaa ggaatatatt taattatatt
2101 catatattta acaaataaaa atatgttgaa ttttcgtatt gtttgccact gagggttcag
2161 atgatagacc tcaaaaaatc gaaaatactg gttgaaattt gtagcatcca tttagttatt
2221 ctttttgacc taaataactt aatagtttat taaatctaag gttagctaaa tatgtagcta
2281 accttatttg ttttctttcc taacaactct gaagaataca taggactttg cacttttttt
2341 tttttttttt tttttaaa
```

Figure 17

```
  1 mtsrehqvsl cncvpllrrl lcdapwrkar plhalsryfr srvspskmae epqsvlqlpt
 61 siaaggeglt dvspetttpe ppssaavspg teepagdtkk kidillkavg dtpimktkkw
121 avertrtiqg lidfikkflk lvaseqlfiy vnqsfapspd qevgtlyecf gsdgklvlhy
181 cksqawg
```

Figure 18

```
   1 tgggcgggag gaacgcgccg ctaggcggga gagcgcggcc atggcggggc cgggcgtccc
  61 cggtgccccc gcagcgcgct ggaaacgcca catcgtgcgg cagctgcggc ttcgggaccg
 121 tacgcaaaag gcgcttttcc tggagctggt gccggcctat aaccatctct tagagaaggc
 181 tgagctgctg gacaagttct caaagaagct gcagccggag ccaaacagtg tcactcccac
 241 cacccaccag ggcccctggg aggagtcaga gcttgactca gaccaagtcc catcactggt
 301 cgcactgagg gtgaagtggc aggaggagga ggaggggctc cggctggtct gtggtgagat
 361 ggcctaccag gtggtggaga agggcgcggc cctgggcacg ctggagtcgg agctgcagca
 421 gaggcaaagc aggctggcag ccctggaggc ccgcgtggcg cagctgcgag aggcgcgggc
 481 gcagcaggcc cagcaggtgg aggagtggcg ggcgcagaat gcggtgcagc gggcagccta
 541 cgaggcgctg cgcgcgcacg tcgggctccg ggaggcggca ctgcgcaggc tccaggaaga
 601 ggcgcgcgac ctgctggaga ggctcgtgca gcgcaaggcg cgcgccgcgg ccgagcgcaa
 661 cctgcgcaac gagcgccggg agcgggccaa gcaggcgcgg gtgtcccagg agctgaagaa
 721 ggctgccaag cggaccgtga gcatcagcga gggcccggac accctaggcg atgggatgag
 781 ggagagaagg gagactctgg ctctggcccc tgagccagag cccctggaga aggaagcttg
 841 tgagaagtgg aagaggccct tcaggtctgc ctcagccacc tccctgacgc tgtcccactg
 901 tgtggatgtg gtgaaggggc ttctggattt taagaagagg agaggtcact caattggggg
 961 agcccctgag cagcgatacc agatcatccc tgtgtgtgtg gctgcccgac ttcctacccg
1021 ggctcaggat gtgctggatg cccacctctc tgaggtcaat gctgttcgtt ttggccccaa
1081 cagcagcctc ctggccactg gaggggctga ccgcctgatc cacctctgga atgttgtggg
1141 aagtcgcctg gaggccaacc agaccctgga gggagctggt ggcagcatca ccagtgtgga
1201 ctttgacccc tcgggctacc aggttttagc agcaacttac aaccaggctg cccagctctg
1261 gaaggtgggg gaggcacagt ccaaggagac actgtctgga cacaaggata aggtgacagc
1321 tgccaaattc aagctaacga ggcaccaggc agtgactggg agccgcgacc ggacagtgaa
1381 ggagtgggac ctcggccgtg cctattgctc caggaccatc aatgtccttt cctactgtaa
1441 tgacgtggtg tgtggggacc atatcatcat tagtggccac aatgaccaga agatccggtt
1501 ctgggacagc aggggggccc actgcaccca ggtcatccct gtgcagggcc gggtcacctc
1561 cctgagcctc agccacgacc aactgcacct gctcagctgt tcccgagaca acacactcaa
1621 ggtcatcgac ctgcgtgtca gcaacatccg ccaggtgttc agggccgatg gcttcaagtg
1681 tggttctgac tggaccaaag ctgtgttcag cccggacaga agctatgcac tggcaggctc
1741 ctgtgatggg gccctttaca tctgggatgt ggacaccggg aaactggaga gcagactaca
1801 gggaccccat tgcgctgccg tcaacgccgt ggcctggtgc tactccggga gccacatggt
1861 gagcgtggac cagggcagga aggttgtgct ctggcagtag ggccacgacc tgcctgcctg
1921 ggctggagct cttgcccgaa gcctgaagct tccttcggcg ccatgcaggg gttggggttg
1981 ggactggagc tggccttggg atttaatggg gaagaaggcc tggcaggacc tggcctgttt
2041 gtttaaaaat gaagtatggg ttgggggatt acgctagttt ttctttgtat ttttatctct
2101 atctcctcac tttttctccc aaagtagaaa aaaatgatat ctgaaaaaaa aaaaaaaaaa
```

Figure 19

```
  1 magpgvpgap aarwkrhivr qlrlrdrtqk alflelvpay nhllekaell dkfskklqpe
 61 pnsvtptthq gpweeselds dqvpslvalr vkwqeeeegl rlvcgemayq vvekgaalgt
121 leselqqrqs rlaalearva qlrearaqqa qqveewraqn avqraayeal rahvglreaa
181 lrrlqeeard llerlvqrka raaaernlrn errerakqar vsqelkkaak rtvsisegpd
241 tlgdgmrerr etlalapepe plekeacekw krpfrsasat sltlshcvdv vkglldfkkr
301 rghsiggape qryqiipvcv aarlptraqd vldahlsevn avrfgpnssl latggadrli
361 hlwnvvgsrl eanqtlegag gsitsvdfdp sgyqvlaaty nqaaqlwkvg eaqsketlsg
421 hkdkvtaakf kltrhqavtg srdrtvkewd lgraycsrti nvlsycndvv cgdhiiisgh
481 ndqkirfwds rgphctqvip vqgrvtslsl shdqlhllsc srdntlkvid lrvsnirqvf
541 radgfkcgsd wtkavfspdr syalagscdg alyiwdvdtg klesrlqgph caavnavawc
601 ysgshmvsvd qgrkvvlwq
```

Figure 20

```
   1 acgctgcgtg ccgctgctgg gttccgccac gcccgtcatg gcggcggccc cggccggctc
  61 tggccccgcc cctcggtgac gcgtcgcgag tcacctgacc aggctgcggg ctgaggagat
 121 acaagggaag tggctatcgc cagagtcgga ttcgccgccg cagcagccgc cgcccccggg
 181 agccgccggg accctcgcgt cgtcgccgcc gccgccgccc agatccctgc accatgccgt
 241 cggagaagac cttcaagcag cgccgcacct tcgaacaaag agtagaagat gtccgactta
 301 ttcgagagca gcatccaacc aaaatcccgg tgataataga acgatacaag ggtgagaagc
 361 agcttcctgt tctggataaa acaaagttcc ttgtacctga ccatgtcaac atgagtgagc
 421 tcatcaagat aattagaagg cgcttacagc tcaatgctaa tcaggccttc ttcctgttgg
 481 tgaacggaca cagcatggtc agcgtctcca caccaatctc agaggtgtat gagagtgaga
 541 aagatgaaga tggattcctg tacatggtct atgcctccca ggagacgttc gggatgaaat
 601 tgtcagtgta aaaccagaaa aaatgcagct cttctagaat tgtttaaacc cttaccaagg
 661 aaaaaaaagg gatgttacca actgagatcg atcagttcat ccaatcacag atcatgaaac
 721 agtagtgttc ccacctagga gtgttaggaa gttgtgtttg tgtttcaagc agaaaaactg
 781 agctccaagt gagcacattc agctttggaa actatattat ttaatgtagg ctagcttgtt
 841 ttcaaatttt aaaagtttaa aaataaaata ctttgcattc taagttgcca ataaaataga
 901 ccttcaagtt attttaatgc tcttttctca ctaataggaa cttgtaattc cagcagtaat
 961 ttaaaggctt tcagagagac cctgagtctt ctcttcaggt tcacagaacc cgccgccttt
1021 ttgggtagaa gttttctact cagctagaga gatctcccta agaggatctt taggcctgag
1081 ttgtgaagcg caacccccgc aaaacgcatt tgccatcaca gttggcacaa acgcagggta
1141 aacgggctgt gtgagaaaac ggccctgact gtaaactgct gaaggtccct gactcctaag
1201 agaaccacac ccaaagtcct cactcttgca ggggtagaca tttctggttt ggtttgttct
1261 ctagatagtt acacacataa agacaccact caaaaggaaa cttgaataat ttataatttt
1321 gatcgagttt cttaaaagac cctggagaaa gagtggcatt tcttctgttt caggttttgt
1381 ctgagttcaa actagtgcct gtgttgttac ggaaagcagc agtgtaccag tgtcactctg
1441 gagtacagcg ggagaaacac aaaatagtat aactgaaaac attaacattc agacacactc
1501 ccttctgcct tccggcttaa agctgtggat gatccacgtt tttgtttttt taatgttaaa
1561 tgtgtaactc agtattactg aaaaggtacc cacattttga atagtagtta tcactcttag
1621 gtcagacagc catcagaatt ctcccacacc aagtgcatgt cagttgtgga gaaaacatag
1681 caaaaagagc cgtacgctct ttacagatac taatgtcaag agttaaacct cctcaggttc
1741 aacctgtgat aaaagactag tgcttcccag tacttgcatg gggttcacta tttatagttt
1801 tcttgggagt atcacaggaa aatcacaatt acaccacttt agaccctatg tgtagcaggt
1861 cacaacttac ccttgtgtgt ttagatgtgt atgaaatacc tgtatacgtt agtgaaagct
1921 gtttactgta acggggaaaa ccagattctt tgcatctggg ccctctactg attgttaaag
1981 gagttcctgt cacctgctcc ccccaccccc gcatgcgtct gtccacttgg ctaactttta
2041 atatgtgtat ttttacatta tgtatattct taactggact gtctcgttta gactgtatac
2101 atcatatctg acattattgt aactaccgtg tgatcagtaa gattcctgta agaaatactg
2161 ctttttaaga aaaaaaataa catgctgagg ggtgacctat atcccatgtg agtggtcact
2221 ttatttatag gatctttaaa acatttttaa tgaactaagt tgaataaagg cacaattaaa
2281 aactgtcaaa aaaaaaaaaa aaaa
```

Figure 21

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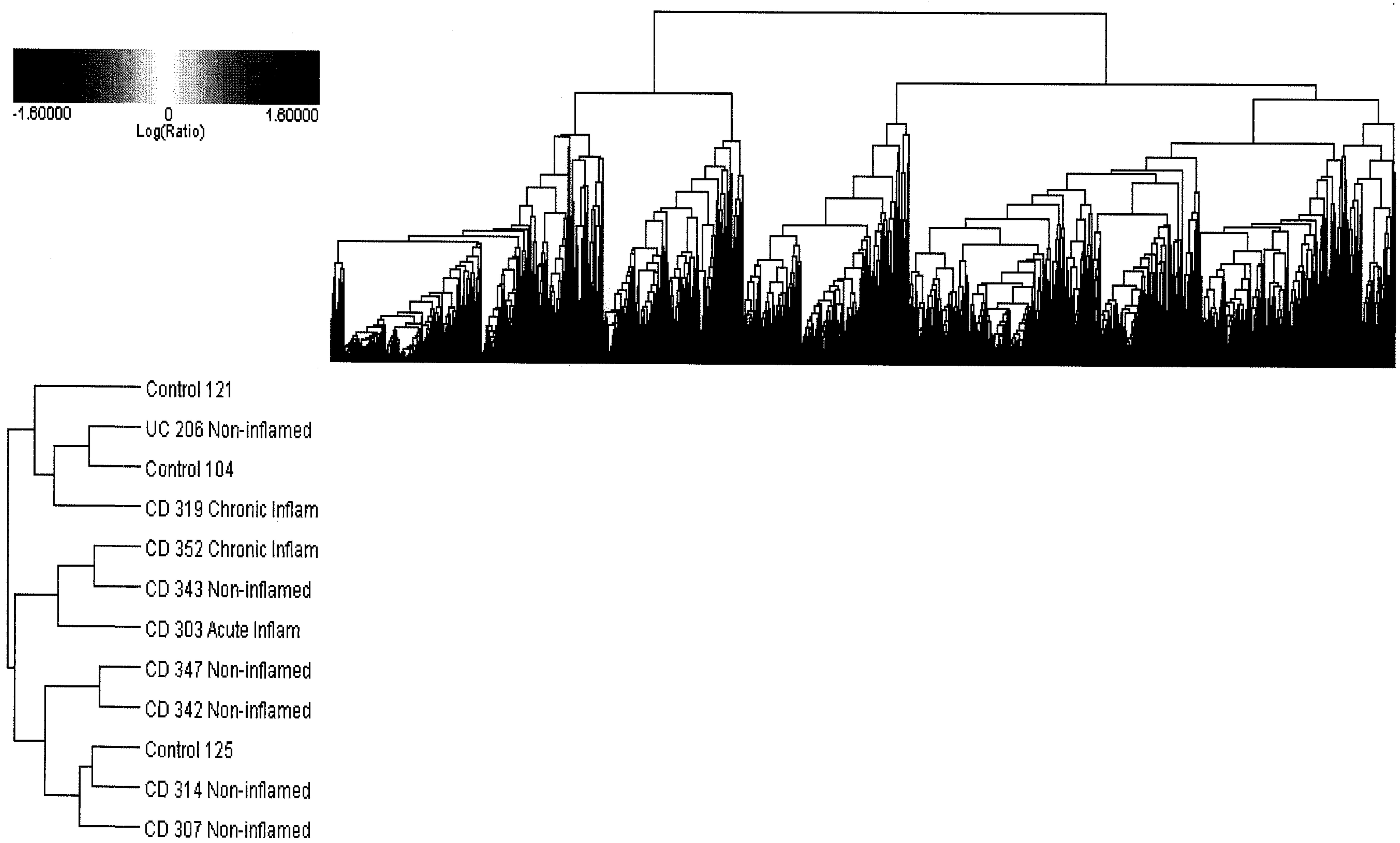
  1 mpsektfkqr rtfeqrvedv rlireqhptk ipviierykg ekqlpvldkt kflvpdhvnm
 61 selikiirrr lqlnanqaff llvnghsmvs vstpisevye sekdedgfly mvyasqetfg
121 mklsv
```

Figure 22

Figure 23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0
1.60000
Log(Ratio)
Control 121
UC 206 Non-inflamed
Control 104
CD 319 Chronic Inflam
CD 352 Chronic Inflam
CD 343 Non-inflamed
CD 303 Acute Inflam
CD 347 Non-inflamed
CD 342 Non-inflamed
Control 125
CD 314 Non-inflamed
CD 307 Non-inflamed

Figure 24

Gene Name	Sequence Code	Entrez Gene	Fold Change	P-value
SAA1	A_24_P335092	6288	7.47764	1.47E-41
REGL	A_23_P108546	5969	7.26194	2.25E-16
S100A9	A_23_P23048	94195	4.37037	2.37E-22
S100A8	A_23_P434809	6279	4.00494	3.48E-18
FLJ21162/ TNIP3	A_23_P386478	79931	3.83902	4.17E-06
IL8	A_32_P87013	3576	3.60471	5.60E-15
IF	A_24_P92472	79126	3.52236	6.18E-13
KCND3	A_32_P140268	56543	3.38296	2.37E-18
CLECSF12	A_24_P235988	502902	3.28581	6.65E-10
chromosome 10 open reading frame 81	A_23_P23980	499377	3.19877	6.76E-13
regenerating islet-derived 3 gamma	A_32_P65628	24618	3.15414	6.74E-07
TFEC	A_32_P184394	26296	3.10908	5.09E-12
IGSF6	A_23_P106629	10261	2.99982	1.28E-12
A_32_P90385	A_32_P90385		2.99826	5.10E-14
GW112	A_23_P2789	290409	2.84338	5.99E-19
MGC27165	A_24_P315941		2.63927	2.00E-06
MMP3	A_23_P161698	171045	2.62676	3.91E-10
KLK12	A_23_P500010	43849	2.60484	2.40E-11
TZFP	A_23_P131024	58206	2.57661	1.09E-08
REG4	A_24_P58673	445583	2.56805	1.39E-12
CLECSF9	A_24_P78531	56619	2.56703	2.91E-06
IF	A_23_P7212	79126	2.55712	1.58E-17
K5B	A_23_P331098	332131	2.54589	7.70E-12
MGC27165	A_23_P259763		2.52785	1.12E-07
BC031882	A_24_P928176		2.50166	4.11E-08
SEPP1	A_23_P121926	29360	2.4221	4.12E-21
THC1946344	A_32_P157124		2.38008	1.24E-06
GPCR	A_23_P214267	301266	2.29623	1.74E-16
C10orf81	A_24_P286951	499377	2.265	3.63E-11
MGC27165	A_24_P100684	28396	2.25742	1.17E-15
GPR86	A_23_P211948	310444	2.25571	1.11E-08
GPR91	A_23_P69171	84112	2.24741	4.29E-13
similar to RIKEN cDNA A630077B13 gene	A_23_P7827	215900	2.23841	8.24E-22
C14orf81	A_24_P323298		2.2301	4.22E-18
SELL	A_23_P103522	20343	2.21998	0.00009
CXCL10	A_24_P303091	3627	2.20177	4.54E-07
OAS2	A_24_P343929	363938	2.20011	5.09E-13
LOC129026	A_23_P435390		2.19506	4.06E-19
GPNMB	A_23_P134426	10457	2.18278	1.57E-23
KDR	A_32_P82650		2.18082	8.42E-07
DMBT1	A_23_P86599	170568	2.15398	1.02E-18
SEC6L1	A_24_P419300		2.1492	4.55E-12
AF267875	A_24_P179107		2.14271	9.23E-09
MGC27165	A_24_P488083	28396	2.11246	3.30E-18
IgH	A_24_P24053		2.10524	1.89E-10
TRHDE	A_23_P366983	237553	2.09908	2.66E-07

IFIT4	A_23_P35412	309526	2.09755	1.68E-32
OTTHUMP00000028776	A_24_P239076	91353	2.09112	2.72E-23
ZBP1	A_23_P259141	81030	2.0683	9.68E-29
C14orf81	A_24_P608268		2.04648	0.00005
IFNG	A_23_P151294	3458	2.03635	3.27E-09
CXCL11	A_23_P125278	56066	2.03494	4.47E-08
LOC169355	A_24_P12690	169355	2.03447	3.91E-07
C14orf54	A_23_P328145	161142	2.02637	6.48E-06
Ig V<kappa}	A_23_P361654		2.01562	1.31E-10
hypothetical protein MGC27165	A_24_P590547		2.00797	2.20E-17
IL2RA	A_23_P127288	25704	1.98937	1.15E-09
IGLL1	A_24_P83102	3543	1.98934	7.28E-19
SLC8A1	A_32_P108277		1.98247	8.15E-06
IGHG1	A_24_P604784		1.97918	2.22E-10
CHRDL2	A_23_P13548	69121	1.96837	1.36E-06
immunoglobulin kappa constant	A_24_P263786	651751	1.96372	7.65E-07
MGC27165	A_24_P860662		1.94854	7.66E-10
PLEK	A_23_P209678	5341	1.94585	3.93E-12
BCL2A1	A_23_P152002	12044	1.9372	8.40E-09
DEFA5	A_23_P112086	1670	1.93514	0.02416
LIMK1	A_23_P215461	65172	1.9311	2.60E-20
LCN2	A_23_P169437	16819	1.92183	3.46E-09
IGHM	A_24_P813550		1.91931	9.54E-12
C10orf63	A_24_P115651	291354	1.91497	0.00002
ARP10	A_32_P347617	164668	1.91488	4.79E-16
UNG2	A_23_P92860	499528	1.91387	4.61E-15
LOC204777	A_24_P204374		1.90904	1.08E-17
immunoglobulin lambda constant 1	A_24_P605563	28815	1.90902	5.36E-15
NCF2	A_23_P138194	17970	1.89691	4.08E-07
BTN3A3	A_24_P311917	10384	1.88782	2.78E-20
LPL	A_23_P146233	24539	1.8841	1.75E-07
FLJ31842	A_32_P19539		1.88017	0.00121
MDK	A_23_P116235	4192	1.87533	1.61E-34
UNC5CL	A_23_P428298	301225	1.86538	1.52E-07
IGKV	A_24_P16004		1.85532	0.00002
IGLJ3	A_24_P510357		1.84708	2.26E-22
HLA-DQB2	A_23_P8108	3120	1.83952	4.17E-07
BLVRA	A_23_P71148	644	1.83279	5.78E-21
A_23_P84791	A_23_P84791		1.8298	1.42E-20
AIF1	A_23_P214627	29427	1.82732	6.18E-21
MAS1	A_23_P168339	17171	1.82572	0.00012
similar to Ig heavy chain V-III region VH26	A_24_P33341		1.82528	2.94E-11
CYP2C19	A_23_P158484	1557	1.82169	0.00159
TDO2	A_23_P80974	56720	1.82051	0.00008
LAX	A_24_P370952	54900	1.81993	1.11E-06
FLJ30469	A_24_P323148	502308	1.81697	1.14E-08
LILRB1	A_23_P343221	10859	1.81079	0.00382
ETV7	A_23_P42353	51513	1.80731	3.25E-11
XIST	A_24_P500584		1.80134	0.15183
similar to KIAA1501 protein	A_24_P110487		1.78347	1.82E-06
OLFM4	A_24_P181254	290409	1.77867	0.00002
CHI3L1	A_23_P137665	89824	1.77741	1.26E-15

AB063751	A_23_P21249		1.76454	1.25E-10
IFIT2	A_24_P304071	15958	1.75461	2.09E-07
LOC401119	A_32_P208328		1.75343	0.00065
IgH	A_24_P15388		1.75309	5.82E-10
IGLJ3	A_24_P519504		1.75244	1.44E-16
PLA2G7	A_23_P145096	27226	1.75039	2.77E-08
MGC52019	A_24_P934387	241612	1.7467	1.60E-06
ROBO1	A_24_P77432	58946	1.74457	5.47E-09
APP	A_24_P314159	351	1.73781	1.56E-16
VIM	A_23_P161194	22352	1.73515	4.43E-17
BHLHB5	A_32_P75581	27319	1.73277	0.00019
KIAA0802	A_23_P360605	68617	1.72532	1.35E-09
similar to Ig kappa light chain variable region	A_24_P384604		1.72175	8.69E-09
FLJ21308	A_23_P121898	294762	1.71746	1.73E-12
A_32_P165504	A_32_P165504		1.71677	3.43E-07
CALCRL	A_23_P39898	10203	1.71489	0.00008
serum amyloid A3 pseudogene	A_24_P556318		1.71419	1.57E-06
HLA-DMA	A_23_P42306	3108	1.71207	1.21E-09
APOB	A_23_P79591	238055	1.7114	1.03E-06
LOC285189	A_32_P197825	100134363	1.71118	0.00118
similar to bA110H4.2	A_23_P395705		1.7069	1.34E-06
TPM1	A_24_P179244		1.7048	1.06E-09
BF	A_23_P156687	294257	1.70254	8.27E-15
PSMB9	A_23_P111000	16912	1.70251	2.93E-31
PCDH17	A_24_P911906	306055	1.70107	0.00008
GBP1	A_23_P62890	304266	1.69986	4.21E-08
FHL5	A_32_P88587		1.69418	0.01214
APOC1	A_24_P109214	11812	1.69242	4.37E-13
immunoglobulin lambda constant 1	A_24_P318990		1.68835	2.60E-22
HLA-DRA	A_32_P115555		1.68766	1.53E-11
GCG	A_23_P254664	24952	1.6857	4.53E-06
RAB8B	A_23_P317465	235442	1.68534	1.88E-21
LOC256021	A_32_P437735		1.6806	4.21E-09
immunoglobulin kappa constant	A_23_P61068		1.67197	9.67E-12
LAIR2	A_23_P209129	3904	1.67103	0.0005
CXCL3	A_24_P183150	20310	1.66718	0.00002
immunoglobulin lambda constant 1	A_23_P72252	28793	1.66538	6.27E-06
P5-1	A_32_P220770		1.66523	1.65E-09
HLA-G	A_23_P300112	14991	1.66287	5.56E-29
CNGA1	A_24_P256722	1259	1.65504	0.00001
LOC286207	A_24_P229638	286207	1.65441	0.0001
DEFB114	A_24_P931533	245928	1.65314	0.0002
LUM	A_23_P99063	81682	1.64985	1.45E-08
TSPAN-2	A_24_P62659	10100	1.64836	0.00583
XBP1	A_24_P100228	22433	1.6463	1.09E-14
CD74	A_23_P70095	972	1.64322	2.51E-06
ALDH1A2	A_24_P73577	116676	1.63966	2.72E-12
INHBA	A_24_P535256		1.63772	3.59E-06
MMP7	A_23_P52761	25335	1.63242	0.00017
HLA-G histocompatibility antigen, class I, G	A_23_P370707	3136	1.63063	3.33E-21
TFF1	A_24_P322771	21784	1.6303	9.94E-12
guanylate binding protein 4	A_23_P103496	310917	1.62876	4.05E-06

MGC16664	A_24_P190873	329274	1.62592	0.01392
LTB	A_23_P93348	361795	1.62323	9.59E-07
HLA-DRB1	A_24_P169013	731247	1.62309	0.01877
similar to KIAA1501 protein	A_24_P101226		1.62278	0.0067
A_24_P926354	A_24_P926354		1.62193	0.00107
MGC27165	A_32_P51988		1.62132	1.26E-09
MGC27165	A_23_P390209		1.61688	0.0134
EPSTI1	A_23_P105794	108670	1.61509	1.94E-08
HLA-F	A_23_P314024	3134	1.61502	9.90E-17
IGLJ3	A_24_P76868		1.61398	5.83E-20
BAL	A_23_P69383	80285	1.61314	4.64E-23
HLA-DPB2	A_24_P288836	3116	1.61229	3.51E-10
A_32_P64263	A_32_P64263		1.61059	6.31E-09
TFF1	A_23_P68759	21784	1.60329	1.19E-20
C14orf161	A_23_P77043	79820	1.60248	6.98E-06
CLEC-6	A_23_P25235	362432	1.59674	3.05E-08
ATCV32560	A_23_P373126		1.59386	4.94E-19
SST	A_23_P252817	6750	1.5935	0.00054
ACPP	A_24_P37589	55	1.5903	0.00022
CCL20	A_23_P17065	29538	1.58789	3.13E-12
NYD-SP26	A_24_P388662	64029	1.58651	0.00002
TRIM22	A_23_P203498	10346	1.58545	9.17E-09
IGLV8S1	A_23_P159435		1.58463	5.26E-11
IFIT2	A_23_P24004		1.58415	1.60E-27
VSNL1	A_23_P209978	26950	1.58261	8.81E-07
GNB4	A_32_P184916	294962	1.58156	5.57E-08
HLA-DQB2	A_23_P19510	3120	1.57933	5.48E-11
TAGAP	A_24_P354724	308097	1.57865	1.04E-06
IGLJ3	A_24_P169713		1.57322	4.44E-07
HLA-A	A_23_P408353	3105	1.57306	2.76E-18
STE	A_23_P155786	20860	1.57303	0.00026
CXCR6	A_23_P109913	80901	1.57223	0.00601
immunoglobulin lambda constant 1	A_23_P43979		1.57106	2.27E-10
TREM1	A_23_P19333	54210	1.56992	9.91E-07
THC1873675	A_32_P17343		1.56975	3.36E-07
CSTA	A_23_P41114	1475	1.56884	0.00006
DKFZp686N02209	A_23_P124632	3493	1.56795	9.97E-09
PARP8	A_32_P34495		1.56739	5.04E-25
FLJ32334	A_24_P44453	213696	1.5658	0.0001
guanylate binding protein 2,	A_24_P36898		1.56307	4.57E-24
hypothetical protein FLJ33318	A_23_P38388	544806	1.56266	1.15E-09
DEFA6	A_24_P363711	1671	1.56089	0.03134
BST2	A_23_P39465	69550	1.56081	4.47E-20
CD72	A_23_P250245	313498	1.55969	0.01101
GALNT8	A_23_P65100	26290	1.55678	6.37E-11
major histocompatibility complex, class I, B	A_23_P125109	3107	1.5561	1.85E-16
FKBP10	A_23_P15727	14230	1.55561	6.86E-13
MAP3K8	A_23_P23947	116596	1.55297	1.42E-10
major histocompatibility complex, class I, B	A_24_P101771	3107	1.55225	6.49E-18
PRO1073	A_24_P829261		1.55224	3.12E-10
CYP2U1	A_24_P913156		1.54915	0.00305
A_24_P788772	A_24_P788772		1.54854	1.13E-09

HLA-DMB	A_32_P351968	3109	1.54844	0.00004
VIM	A_23_P161190	22352	1.54813	4.02E-11
HOXB4	A_24_P305067	3214	1.54744	1.19E-06
BTN3A2	A_23_P391264	294268	1.5462	5.15E-34
Sprn	A_24_P930415	503542	1.54571	0.01182
CCL11	A_23_P66635	20292	1.54193	3.09E-17
MGC27165	A_24_P702749	28396	1.54162	1.06E-06
APOL3	A_24_P416997	278679	1.54118	4.42E-11
HLA-DPA1	A_24_P243528	3113	1.54109	5.44E-10
MGC27165	A_24_P204727		1.53986	2.68E-16
SLC6A6	A_24_P46093	29464	1.53957	5.11E-14
SAMHD1	A_24_P267592	25939	1.53838	3.14E-07
ATM	A_24_P103944	651610	1.53663	0.00015
PIK3R3	A_23_P22970	8503	1.53506	1.00E-07
DPYD	A_24_P514678		1.53457	4.91E-08
RIS1	A_23_P369899	72309	1.53451	8.71E-09
DPLK24430	A_23_P338113		1.53348	3.85E-14
ATCV32560	A_24_P860781		1.53214	1.78E-19
C7orf6	A_23_P145874	500015	1.53212	7.82E-15
GALNAC4S-6ST	A_32_P94176		1.53123	3.32E-11
BRCA2	A_24_P917810		1.53094	0.00162
TAP1	A_23_P59005	24811	1.53036	1.70E-18
SLC5A7	A_32_P114502	63993	1.53026	8.79E-06
COL3A1	A_24_P503729		1.53004	0.0371
EGLN3	A_23_P360379	54702	1.53004	9.21E-18
THC1906127	A_32_P183598	645904	1.52853	0.01176
LOC440361	A_24_P144346	100132941	1.52837	7.43E-08
C6orf32	A_23_P358394	306934	1.52609	0.0032
similar to MHC HLA-SX-alpha	A_24_P246626		1.52243	2.03E-07
PBX2	A_32_P164225		1.51907	0.00138
LST1	A_24_P103469	7940	1.51811	1.25E-08
AIG1	A_24_P740692		1.51792	0.00022
C6orf194	A_23_P133854	66707	1.51646	7.47E-07
HF1	A_24_P273972	12628	1.51562	0.00285
chromosome 10 open reading frame 63	A_24_P215240	291354	1.51429	2.08E-07
HLA-E	A_24_P326082	3133	1.51349	1.68E-16
C2	A_32_P162183	12263	1.51143	2.41E-16
BTN2A2	A_24_P337592	238555	1.51031	3.03E-21
PF4V1	A_24_P63347	5197	1.51017	7.69E-06
LYZ	A_24_P42264	17110	1.51005	0.00006
AFP	A_23_P58205	11576	1.50709	3.80E-08
LOC441158	A_32_P112263		1.50708	8.54E-06
immunoglobulin lambda variable 6-57	A_24_P361816		1.50702	3.09E-22
HLA-F	A_23_P145264	3134	1.50693	1.05E-17
BC034913	A_32_P217128		1.50658	0.04922
HLA-DMB	A_24_P481844		1.50617	2.70E-06
ITGB2	A_23_P329573	3689	1.50542	4.60E-06
LOC124411	A_24_P764690		1.50503	8.70E-06
BC039414	A_32_P179138	2982	1.50436	2.16E-06
HLA-B	A_24_P161933	3107	1.50428	9.13E-17
UBD	A_23_P81898	54393	1.50418	0.00003
IKIP	A_23_P53467	121457	1.50388	2.79E-16

SNX10	A_24_P98109	297096	1.50234	7.73E-10
S100P	A_23_P58266	6286	1.50181	6.91E-07
KIAA1268	A_32_P92415		1.50079	4.84E-10
FLJ22761	A_23_P202427	216019	1.50062	2.26E-10
multiple coiled-coil GABABR1-binding protein	A_23_P144274	152789	1.50007	2.62E-12
A_24_P780709	A_24_P780709		-1.50313	1.61E-15
solute carrier family 25	A_23_P9435	227731	-1.50456	2.75E-07
NIN	A_24_P928361	18080	-1.50612	0.0003
GTPBP2	A_24_P77826		-1.5075	0.00055
GRIN2D	A_23_P153549	24412	-1.51017	1.20E-15
similar to protein phosphatase 1, regulator	A_24_P110101		-1.5112	7.51E-19
PCSK7	A_23_P203095	18554	-1.51157	6.97E-12
SP5	A_32_P74615	296510	-1.51206	1.70E-23
LGALS2	A_23_P120902	171134	-1.51236	7.66E-06
IER5	A_24_P379223	15939	-1.5134	1.43E-15
SNIP1	A_23_P23175	313588	-1.5135	0.00006
AK094323	A_24_P315500		-1.51379	9.83E-22
LOC440345	A_32_P11359		-1.51414	3.46E-10
FLJ34218	A_24_P348083	494470	-1.51567	1.05E-14
A_24_P942036	A_24_P942036		-1.51819	0.00533
ZNF575	A_24_P416595	101544	-1.52002	2.86E-17
SLC4A4	A_32_P358887	54403	-1.52149	1.57E-07
PCK1	A_23_P408249	362282	-1.52405	0.00004
TSLP	A_23_P121987	85480	-1.52502	0.00021
INSL5	A_23_P51479	23919	-1.52523	0.0001
TTID	A_23_P110764	9499	-1.53428	0.00078
DATF1	A_32_P19917		-1.53541	1.06E-17
C9orf62	A_24_P303874	157927	-1.53697	8.17E-20
C8FW	A_32_P38821		-1.53983	0.00226
POLK	A_24_P919863		-1.54053	0.00011
SCARF2	A_24_P108738	224024	-1.54857	2.79E-28
LOC441207	A_24_P911310		-1.54908	0.00008
RKHD1	A_24_P923765	299613	-1.54923	1.54E-16
C21orf88	A_32_P34826	114041	-1.55181	0.00191
HSPB3	A_23_P92730	56534	-1.55802	3.74E-08
KIAA0828	A_24_P72518	312192	-1.56735	4.48E-07
FLJ11342	A_24_P268662	303953	-1.56803	0.00124
GPR7	A_23_P20458	297795	-1.57075	1.99E-28
FABP5	A_23_P59877	728641	-1.57113	2.79E-11
GDNF	A_24_P376451	2668	-1.57189	8.11E-25
MGC5347	A_24_P922252		-1.58106	0.00014
A_32_P161327	A_32_P161327		-1.58259	5.39E-07
RNF150	A_24_P350589	330812	-1.58266	0.00007
FLJ38359	A_24_P11737	100132017	-1.58439	1.04E-31
NLN	A_32_P891680		-1.5847	2.43E-06
GSTA2	A_24_P300394	2939	-1.58675	1.59E-08
POU3F3	A_24_P34575	5455	-1.58739	1.05E-22
LOC92552	A_23_P361744		-1.58754	0.01092
FABP5	A_32_P204676	2171	-1.58923	1.22E-16
HOXB13	A_24_P365015	303480	-1.59522	0.00412
KIAA1524	A_24_P351466	360711	-1.59584	0.00003
PRO1073	A_24_P873659		-1.59703	4.48E-11

FLJ21195	A_24_P40626	64388	-1.60841	1.26E-10
ND4	A_23_P360213		-1.60919	3.33E-22
MGC39571	A_23_P423462	221241	-1.60927	2.49E-07
MT1K	A_23_P66241	4499	-1.6186	1.86E-06
SLC7A11	A_24_P200420	26570	-1.62113	0.00065
ZNF262	A_32_P233278		-1.62205	1.33E-21
RC1	A_24_P924185		-1.62363	8.71E-14
HIST1H1B	A_23_P250385	3009	-1.62459	4.05E-09
CANP	A_24_P332314	374393	-1.62691	0.00001
FLJ22774	A_23_P65307	239250	-1.6272	1.80E-26
WDR33	A_32_P328023	55339	-1.63029	0.00003
ZNF206	A_23_P15135	332221	-1.63594	6.06E-23
similar to Hypothetical protein CBG17606	A_24_P846988	393078	-1.64001	8.96E-34
RP11-653A5.1	A_32_P84237	295528	-1.64034	0.01055
LOC51270	A_23_P10518	51270	-1.64985	1.55E-07
KIAA1804	A_24_P130959	84451	-1.65844	0.00016
ZNF205	A_24_P56689	287095	-1.66234	6.21E-37
ADH1C	A_23_P81158	24172	-1.66486	1.33E-11
FRMD1	A_32_P174285		-1.67103	2.66E-08
AVP	A_23_P109133	24221	-1.70781	2.31E-18
AATK	A_23_P10559	690853	-1.71307	1.55E-13
ECT2	A_24_P366033	1894	-1.72142	2.52E-06
SLC26A2	A_23_P250951	13521	-1.72588	0.00003
XRRA1	A_23_P370162	143570	-1.73618	6.37E-07
RPS28	A_24_P40010		-1.77456	3.88E-17
ISL1	A_23_P81529	3670	-1.79059	5.87E-07
MGC29643	A_23_P419696	360838	-1.79074	4.43E-09
AQP8	A_23_P26522	343	-1.79996	0.00004
FLJ25770	A_24_P401185	289502	-1.85266	0.00031
IL1R2	A_23_P79398	7850	-1.86364	5.39E-11
ANKRD17	A_24_P220771	289521	-1.87438	1.63E-06
A_32_P191066	A_32_P191066		-1.89029	1.62E-06
FLJ12572	A_24_P65121	67009	-1.90062	0.00052
LOC339881	A_24_P846810		-1.94299	1.28E-10
NKD1	A_24_P304881		-2.10407	1.48E-17
CA1	A_23_P168916	759	-2.26411	7.46E-06
PRAC	A_23_P15619	84366	-2.42192	4.16E-11
CA2	A_23_P8913	54231	-2.44317	8.36E-10
LOC389023	A_32_P86578	389023	-2.48381	2.18E-28
SLC14A2	A_24_P136471	54302	-2.49075	0.00002

Figure 25

Gene Name	Sequence Code	Entrez Gene	Fold Change	P-value
UBD	A_23_P81898	54393	11.30144	<10E-45
TIMD4	A_32_P69616		10.1666	1.21E-08
FLJ25393	A_24_P305993	315438	9.5289	0.00061
FLJ27099	A_32_P200144		9.09174	2.98E-32
SOX14	A_32_P183652		8.89445	2.28E-14
BX108833	A_24_P460405		8.28796	4.11E-08
HK2	A_32_P175739		7.76749	5.97E-19
MMP3	A_23_P161698	171045	7.42185	1.29E-11
RP11-653A5.1	A_32_P84237	295528	7.41899	2.75E-07
TEX12	A_23_P150362	56158	7.1498	7.01E-09
III	A_32_P157391	219595	7.06942	2.35E-10
S100P	A_23_P58266	6286	6.37114	3.88E-28
C1orf34	A_23_P160214	298366	6.28438	4.85E-18
Sprn	A_24_P930415	503542	5.92864	0.00002
FOLH1	A_23_P47616	2346	5.8971	1.55E-20
LOC92552	A_23_P361744		5.3328	6.97E-06
EYA2	A_23_P500421	14049	5.32674	0.00091
CEACAM3	A_23_P130515	361516	5.29423	1.44E-06
C14orf81	A_24_P323298		5.29169	8.53E-08
MUC4	A_24_P208825	140474	5.2894	2.62E-07
MGC27165	A_23_P259763		5.26036	0.00012
Ig V<kappa}	A_23_P361654		5.08707	1.64E-07
S100A9	A_23_P23048	94195	5.04077	9.60E-09
IL8	A_32_P87013	3576	4.85129	2.30E-08
HIST1H2BA	A_23_P323823	24829	4.80955	5.25E-06
MGC27165	A_24_P100684	28396	4.75028	1.37E-10
APP	A_24_P314159	351	4.63652	1.01E-11
MMP1	A_23_P1691	4312	4.61477	0.00002
CTSZ	A_23_P40240	1522	4.45679	1.33E-09
S100A8	A_23_P434809	6279	4.43724	3.89E-11
HLA-DPB1	A_23_P258769	3115	4.37801	0.00002
ZCCHC13	A_32_P11096	389874	4.34044	2.73E-07
TFF1	A_24_P322771	21784	4.28597	1.26E-17
K5B	A_23_P331098	332131	4.2102	0.00541
C14orf54	A_23_P328145	161142	4.11293	7.49E-06
C14orf81	A_24_P608268		4.01367	0.00074
ASHG31000	A_32_P203046		3.97446	2.44E-07
IgH	A_24_P24053		3.95346	3.70E-08
KCND3	A_32_P140268	56543	3.94555	0.00719
MGC27165	A_24_P488083	28396	3.90693	3.91E-06
MUC1	A_23_P137856	4582	3.90295	0.00002
ATPase, H+ transportin	A_24_P923415	296981	3.82098	3.49E-06
KIAA2002	A_24_P933802	79834	3.74854	9.12E-09
PGNT12817	A_24_P548966		3.67339	4.27E-06
SST	A_23_P252817	6750	3.60772	5.89E-08
BI826226	A_32_P233911		3.59653	4.72E-06
NOS2A	A_23_P502464	18126	3.57082	1.43E-10
BC034913	A_32_P217128		3.55599	0.00461
LOC387630	A_24_P461001		3.54088	0.00022

THC1892477	A_32_P171427		3.52216	0.00006
CXCL6	A_23_P155755	20311	3.4496	4.11E-06
REG4	A_24_P58673	445583	3.44795	9.80E-08
MLLT2	A_24_P170613		3.43138	8.96E-07
FLJ25770	A_24_P401185	289502	3.42673	1.33E-06
THC1896134	A_32_P135469		3.40686	1.78E-08
PROZ	A_23_P140074	66901	3.35043	0.00645
CXCL11	A_23_P125278	56066	3.31233	0.00001
FLJ21616	A_24_P932736	79618	3.3115	8.48E-07
similar to KIAA1501 protein	A_24_P110487		3.30026	2.57E-07
P101-PI3K	A_23_P66543	320207	3.29258	4.23E-08
KIAA1115	A_23_P119448	361502	3.27878	3.52E-06
DKFZp686O04253	A_24_P913819	242594	3.26939	0.00006
C14orf129	A_24_P292710	66787	3.2643	2.10E-09
WDR33	A_32_P328023	55339	3.2528	5.82E-07
HSGP25L2G	A_23_P70127	361207	3.2432	1.51E-38
AREG	A_23_P259071	374	3.23267	6.09E-13
KIAA1126	A_23_P384816	315054	3.22584	0.00003
CABP7	A_24_P177236	360970	3.20817	2.40E-06
FLJ10290	A_24_P46484	66810	3.17213	0.00007
12MelaCE5B3CD	A_24_P920573		3.14633	5.07E-06
LTB	A_23_P93348	361795	3.13757	2.83E-09
A_24_P926354	A_24_P926354		3.13377	0.00507
C1S	A_23_P2492	716	3.1175	0.00163
Immunoglobulin	A_24_P263786	651751	3.1169	0.00002
LOC285189	A_32_P197825	100134363	3.11449	0.0017
TPSB2	A_23_P37702	64499	3.09515	1.99E-10
BX119435	A_32_P73903		3.09208	0.00001
CGB1	A_23_P39095	114335	3.08549	0.00032
NUCB2	A_23_P13364	53322	3.07764	1.85E-07
VH4	A_23_P158817	3492	3.07257	0.00063
GPCR	A_23_P214267	301266	3.03444	0.00002
RAP1GA1	A_24_P36890	5909	3.02124	0.00003
ITLN1	A_23_P95790	16429	3.01288	6.82E-25
SCRG1	A_23_P167159	64458	3.00367	0.00678
polymeric immunoglobulin	A_23_P149517	25046	3.00237	3.03E-11
VSNL1	A_23_P209978	26950	2.98363	0.00017
BC031882	A_24_P928176		2.98246	0.00083
WNT5A	A_23_P211926	64566	2.9704	5.41E-10
DMBT1	A_23_P86599	170568	2.95354	0.00629
DMD	A_24_P925615		2.94977	0.00003
THC1923453	A_32_P35668		2.92493	2.82E-06
SYTL5	A_24_P14776	236643	2.88392	2.32E-07
S100A6	A_23_P201711	85247	2.87938	0
FLJ35773	A_23_P340218	162387	2.87553	3.93E-09
ALEK31460	A_32_P222474		2.86673	3.57E-07
FOLH1	A_32_P178513	2346	2.84466	0.00084
AW939148	A_32_P199824		2.84432	0.0001
LIPH	A_23_P84219	200879	2.82078	1.64E-09
CXCL14	A_23_P213745	306748	2.81255	1.28E-08
HLA-DPB1	A_24_P166443	3115	2.80803	0.00262
FLJ12572	A_24_P65121	67009	2.79644	0.00099

IGFBP2	A_23_P119943	16008	2.79178	6.80E-14
KCNIP1	A_23_P30554	70357	2.77552	3.26E-07
FLRT3	A_23_P166109	71436	2.75316	1.07E-10
CCL28	A_23_P503072	56477	2.74974	1.40E-06
LOC388962	A_24_P719081		2.74256	0.00001
DKFZP434B044	A_24_P136619		2.74214	3.68E-06
GW112	A_23_P2789	290409	2.74134	0.0001
AGR2	A_23_P31407	298961	2.74061	8.76E-10
NPY1R	A_23_P69699	4886	2.73866	0.00212
BX119852	A_24_P640617		2.7242	0.00014
A_23_P370408	A_23_P370408		2.72326	0.00001
LOC124220	A_23_P118203	124220	2.70434	1.74E-14
SCGB2A1	A_23_P312300	4246	2.68503	7.64E-07
ATP10B	A_23_P311901	319767	2.6824	8.21E-10
IDH2	A_23_P129209	3418	2.67254	2.18E-29
IF	A_23_P7212	79126	2.65082	1.63E-09
IGLJ3	A_24_P519504		2.64667	1.78E-07
A_32_P234405	A_32_P234405		2.64212	7.87E-08
GCNT3	A_23_P151915	286976	2.64086	0.00002
PLA2G2A	A_23_P321949	29692	2.63498	3.59E-09
EMP2	A_23_P106682	13731	2.60466	1.67E-25
immunoglobulin lambda	A_24_P318990		2.59751	1.56E-11
IER3	A_23_P42257	8870	2.58917	1.08E-10
EP400	A_24_P298939	75560	2.58026	0.00442
CPEB3	A_32_P140153		2.57989	0.00265
IGKV	A_24_P16004		2.56259	0.00784
TORC3	A_32_P80016		2.55893	0.00015
HLA-DPA1	A_23_P30913	3113	2.55655	0.00119
COX17 homolog,	A_23_P144244	12856	2.5466	0.00001
SLC12A2	A_32_P25437	83629	2.54219	6.93E-11
PLCB2	A_24_P287664	85240	2.54058	0.00106
DIAPH2	A_23_P254212	29935	2.53087	5.62E-06
LOC389043	A_24_P786357	389043	2.52117	0.00186
MAP17	A_23_P394304	10158	2.51718	5.86E-08
IF	A_24_P92472	79126	2.51529	3.33E-06
EPN3	A_23_P130027	71889	2.5107	8.83E-07
MGC27165	A_24_P392414		2.50998	9.03E-09
IRX5	A_23_P9779	54352	2.50474	0.00067
TFF3	A_24_P289208	7033	2.50197	5.98E-12
LOC286207	A_24_P229638	286207	2.49619	0.00029
A_23_P84791	A_23_P84791		2.48958	0.00041
FLJ32940	A_23_P356425	126859	2.48671	0.00002
LU	A_23_P55716	57278	2.48363	5.20E-12
IGHM	A_24_P813550		2.48054	0.00043
BCR	A_24_P127235		2.47733	0.00009
STARD13	A_23_P342727	90627	2.47261	0.00011
SPON2	A_23_P121533	10417	2.46774	1.47E-06
GCNT3	A_23_P420209	286976	2.45765	0.0006
DKFZp686N02209	A_23_P124632	3493	2.45369	4.41E-06
NAVL30649	A_24_P145019	100129858	2.44919	1.76E-07
CD74	A_23_P70095	972	2.44632	0.00046
LOC285331	A_23_P396981	320234	2.44563	0.00099

CEACAM6	A_23_P421483	4680	2.44554	0.00003
LOC390205	A_24_P460419		2.44365	0.0011
LOC204777	A_24_P204374		2.44157	0.00016
S100A11	A_23_P126593	445415	2.4415	2.17E-13
PLN	A_24_P414803	5350	2.44068	0.00138
OTTHUMP00000028776	A_24_P239076	91353	2.43229	0.00011
TFF1	A_23_P68759	21784	2.43216	1.23E-10
BQ013066	A_32_P107994		2.43062	0.00048
immunoglobulin lambda	A_24_P605563	28815	2.41824	0.00099
HBB	A_23_P203558	3043	2.41458	4.25E-06
EVI1	A_23_P317324	2122	2.41166	3.18E-13
MGC29643	A_32_P101031	360838	2.40755	0.00003
KCNK1	A_23_P126075	16525	2.3972	5.09E-25
PCDH7	A_23_P310921	54216	2.38089	0.00196
SLC2A1	A_23_P571	24778	2.37536	0.00123
KRT18	A_24_P161809		2.36748	1.52E-16
pseudoTPMT	A_24_P67375		2.36209	1.56E-11
FLJ32940	A_32_P39855	126859	2.36003	0.00005
SLPI	A_24_P190472	6590	2.35588	2.47E-11
SSR2	A_32_P82515		2.35369	5.53E-09
TEF	A_24_P151582	21685	2.35307	0.0004
C20orf56	A_32_P23125		2.34088	2.91E-09
CD86	A_24_P131589	56822	2.34074	0.00121
TFF3	A_23_P257296	7033	2.33669	3.33E-07
PYGL	A_23_P48676	110095	2.33612	1.45E-07
ZNF501	A_24_P248741	115560	2.33547	0.00512
BU587941	A_32_P201292		2.33486	1.10E-06
TIMP1	A_23_P62115	21857	2.33362	0.00117
C6orf117	A_23_P357207	112609	2.3313	7.97E-11
CCL11	A_23_P66635	20292	2.3255	4.60E-17
TFF3	A_23_P393099	7033	2.31462	1.12E-07
LOC129026	A_23_P435390		2.31191	0.00015
L-threonine	A_23_P256965	157739	2.30975	2.23E-11
MIG-6	A_23_P46470	74155	2.30041	5.68E-10
EMR2	A_23_P502336	30817	2.29665	7.56E-06
RIMS3	A_23_P319583	242662	2.29508	0.00001
C4BPB	A_23_P319598	725	2.29452	1.83E-06
ANKTM1	A_23_P94255	312896	2.29292	3.68E-08
TMPRSS3	A_23_P211273	140765	2.28892	4.09E-06
ENST00000305824	A_24_P315014		2.28438	1.08E-06
ADM	A_23_P127948	25026	2.28047	1.59E-10
CTGF	A_23_P19663	64032	2.27387	4.89E-08
IGLL1	A_24_P83102	3543	2.26252	0.0011
IGLJ3	A_24_P510357		2.26249	1.26E-07
EDN3	A_23_P17438	1908	2.26028	0.00023
ABCA4	A_23_P160940	310836	2.25637	0.00556
PRO1073	A_24_P829261		2.25481	4.25E-14
kielin/chordin-like protein 1	A_24_P246278		2.25431	2.36E-06
A_32_P183656	A_32_P183656		2.25257	5.55E-06
ATPase, (Na+)/K+	A_23_P217430	23439	2.25119	0.00259
LRRC2	A_23_P155463	74249	2.24843	0.00166
FLJ40919	A_32_P332551	144809	2.24411	0.0008

CKAP4	A_23_P48056	362859	2.24182	0.00005
INHBA	A_24_P535256		2.23414	0.00328
PDE6C	A_23_P98070	361752	2.23398	0.00261
ENMV29985	A_32_P216369	100134159	2.22531	5.59E-17
HS3ST1	A_23_P121657	15476	2.22304	6.55E-06
RPL10	A_32_P108636		2.20838	0.00486
PYCR1	A_23_P130194	209027	2.20716	5.97E-11
LILRB2	A_23_P4773	690955	2.20413	6.17E-08
TPMT	A_23_P214108	22017	2.20072	1.58E-14
POPDC3	A_23_P358597	64208	2.19914	6.38E-11
similar to elongation factor	A_24_P754817	727963	2.19394	4.41E-06
ITGA2	A_32_P178800	170921	2.19266	0.00018
AKAP12	A_23_P111311	83425	2.19174	0.00309
DCDC1	A_24_P272073		2.19034	6.58E-20
RAB31	A_23_P141688	106572	2.18792	8.64E-13
COPE	A_24_P399622	59042	2.18412	0.00002
GNAT1	A_24_P320036	363143	2.18355	3.84E-07
C2	A_32_P162183	12263	2.18328	0.0001
PODXL	A_23_P215060	192181	2.17951	0.00116
TIMP3	A_23_P211468		2.17407	4.71E-12
ACAT2	A_23_P383835	224530	2.17359	5.32E-16
VWF	A_23_P105562	7450	2.16794	0.00105
UNG2	A_23_P92860	499528	2.16785	8.80E-06
RGN	A_23_P114423	25106	2.16347	3.46E-07
VPS18	A_24_P18802	57617	2.16229	0.00315
CCL13	A_23_P26965	24770	2.16098	2.49E-07
KIAA1931	A_23_P427472	212483	2.15693	0.00369
LOC220856	A_24_P290314		2.15689	1.28E-15
AB063751	A_23_P21249		2.1562	0.00011
ring finger protein 186	A_23_P126248	690433	2.15392	0.00674
D2S448	A_24_P944570	100134134	2.14834	9.70E-06
MLPH	A_23_P165783	79083	2.14739	2.03E-11
ZNF252	A_24_P800629		2.14733	1.61E-08
GCG	A_23_P254664	24952	2.1464	0.0088
A_32_P77416	A_32_P77416		2.14199	0.00123
SLC5A10	A_23_P328022	109342	2.14022	0.00995
immunoglobulin kappa constant	A_23_P61068		2.13975	0.00007
TSSC3	A_23_P47614	293637	2.13652	1.33E-19
similar to Keratin, type I cytoskeletal 18 (Cytokeratin 18) (K18) (CK 18)	A_24_P24645		2.1336	1.82E-12
RASSF6	A_23_P302404	73246	2.12871	0.00109
DCLRE1B	A_24_P54131	310745	2.12836	6.14E-07
STE	A_23_P155786	20860	2.12824	0.00189
GALNT8	A_23_P65100	26290	2.12615	0.0001
NID67	A_23_P414273	85027	2.12522	0.00053
HF1	A_24_P273972	12628	2.12273	0.00013
hypothetical protein MGC27165	A_24_P590547		2.11998	0.00305
ACVRL1	A_24_P945113	11482	2.11513	0.00953
ANXA3	A_23_P121716	25291	2.1117	1.78E-10
XBP1	A_24_P100228	22433	2.1116	2.03E-08
PLS3	A_23_P250607	81748	2.11131	0.00137

ERP70	A_23_P42802	116598	2.10816	2.42E-09
BAP29	A_23_P412526	55973	2.10751	3.82E-12
HCP19	A_24_P187094		2.1045	7.53E-20
POF1B	A_24_P250815	69693	2.10426	2.15E-08
RAB18	A_23_P138376	19330	2.10243	2.98E-06
BTC	A_23_P135722	12223	2.10158	3.45E-07
FLJ10156	A_32_P182683		2.10087	0.00014
A_24_P161827	A_24_P161827		2.09943	9.18E-17
IFITM2	A_24_P287043	114709	2.09862	0.00002
MAD	A_23_P408094	362391	2.09518	0.00782
THC1925468	A_32_P58606	9480	2.09513	2.17E-06
AK1	A_23_P217088	11636	2.0905	1.72E-10
CX62	A_23_P416666	14610	2.08197	0.00779
IFNK	A_32_P54128		2.08135	0.00418
CLCA4	A_23_P45751	99709	2.07579	1.95E-06
CYCS	A_24_P376556	54205	2.07402	2.85E-13
UBCH7N	A_32_P91250		2.06936	7.43E-30
tripartite motif-containing 26	A_24_P377394	309586	2.06682	0.00002
LOC285016	A_24_P561341	285016	2.06575	0.00817
DKFZp434G0522	A_24_P264978		2.06313	0.00576
LCMR1	A_23_P150510	311165	2.06286	6.37E-07
GATA4	A_23_P384761	54254	2.0614	0.00019
LOC246737	A_24_P541482		2.05994	3.50E-11
GPR91	A_23_P69171	84112	2.05558	0.00203
LOC86123	A_24_P492562		2.05452	1.51E-07
PGM3	A_23_P19592	109785	2.05299	3.25E-21
similar to Destrin (Actin-depolymerizing factor) (ADF)	A_32_P64928		2.04896	8.58E-12
HCP29	A_23_P64184		2.04521	1.43E-17
A_24_P15803	A_24_P15803		2.04374	3.50E-11
SPUVE	A_23_P150789	76453	2.04358	9.86E-13
CPNE6	A_23_P151598	12891	2.04332	0.00036
ANXA2P3	A_24_P323114		2.03986	2.39E-13
REG1B	A_23_P389500	5968	2.03693	0.00008
ZNF7	A_24_P141168	245974	2.03537	0.00065
DUSP6	A_23_P139704	116663	2.02743	2.09E-07
ATF3	A_23_P34915	11910	2.01737	0.00006
XRRA1	A_23_P370162	143570	2.0103	0.00005
BZW1	A_24_P924389	9689	2.00851	0.00243
MYCNOS	A_24_P914711		2.00762	0.00034
HTRA3	A_23_P395438	94031	2.0059	1.98E-13
THC1862126	A_24_P732106		2.00486	8.90E-07
ENST00000330311	A_24_P273014		1.99168	1.11E-09
ICA1	A_24_P372012	3382	1.99032	4.50E-09
FER1L3	A_23_P354387	26509	1.9902	0.00028
RPL39L	A_23_P29594	116832	1.99018	2.74E-06
CTEN	A_23_P207850	84951	1.98672	1.86E-10
QSCN6	A_23_P12463	84491	1.98089	3.37E-14
PRRX1	A_23_P502731	266813	1.97939	0.00003
COL17A1	A_23_P52323	294027	1.97842	1.97E-07
ARMET	A_23_P132793	7873	1.97363	8.48E-19
LOC150554	A_32_P233860		1.97133	1.20E-09
immunoglobulin lambda	A_23_P72252	28793	1.9711	0.00012

constant 1 (Mcg marker)				
CGREF1	A_23_P403445	10669	1.97051	2.21E-06
GMDS	A_23_P72068	2762	1.97041	4.41E-12
IFITM3	A_23_P87545	361673	1.96825	0.00123
SESTD1	A_23_P367610	295678	1.96579	3.11E-06
RAB27A	A_24_P373174	11891	1.96444	0.00009
AK124173	A_32_P235358		1.96358	0.00058
caveolin 1, caveolae protein, 22kDa	A_24_P12626	12389	1.96354	0.00037
FLJ20401	A_23_P119353	292912	1.96259	0.00002
STEAP	A_23_P31453	297738	1.96104	0.00004
CDON	A_23_P98335	50938	1.95866	0.00237
P5	A_24_P319715	71853	1.95767	1.70E-10
FBLN1	A_23_P211631	14114	1.95675	9.01E-09
PTN	A_23_P303087	24924	1.95543	5.07E-06
DKFZp667J0810	A_24_P538459		1.95526	0.00003
UNQ305	A_32_P118397	253012	1.95389	6.95E-10
ARF4	A_23_P84016		1.95347	1.78E-13
MGC14161	A_32_P188193		1.95296	3.00E-06
VMP1	A_23_P129935	75909	1.95102	7.26E-19
SLC12A2	A_23_P133606	83629	1.95092	0.00317
PTP4A1	A_23_P81770	7803	1.94798	3.87E-08
similar to Six transmembrane epithelial antigen of prostate	A_32_P69149	256227	1.94722	2.06E-13
GBP1	A_23_P62890	304266	1.94563	1.49E-18
RAB43	A_32_P205859	339122	1.94365	7.42E-07
A_24_P332595	A_24_P332595		1.94007	1.75E-08
HK2	A_23_P398460	3099	1.93901	2.40E-06
CCND2	A_23_P139881	12444	1.9388	1.72E-06
dJ474I12.2	A_24_P306704		1.93848	2.45E-08
POLD3	A_32_P182439	67967	1.93814	1.93E-27
LOC199964	A_23_P11629	688864	1.93747	7.39E-21
guanylate binding protein 4	A_23_P103496	310917	1.93509	0.00349
C7orf6	A_23_P145874	500015	1.93383	0.00008
COP	A_23_P64173	114769	1.93289	1.35E-07
ACAT2	A_23_P31135	224530	1.93213	2.00E-16
GOLPH2	A_23_P146512	105348	1.9313	9.20E-08
A_24_P238377	A_24_P238377		1.92824	0.00232
KIAA0672	A_23_P26854	9912	1.92755	3.12E-14
PRO1496	A_23_P146172		1.92233	0.00009
DHCR24	A_23_P379475	74754	1.92211	1.93E-18
F3	A_23_P126782	2152	1.92163	7.91E-09
XBP1	A_23_P120845	22433	1.92065	1.26E-13
GPR56	A_23_P206280	260326	1.91717	1.94E-08
TAZ	A_24_P944383	25937	1.91494	3.50E-22
A_24_P127362	A_24_P127362		1.914	2.02E-08
CCL8	A_23_P207456	6355	1.91377	0.00023
FOS	A_23_P106194	2353	1.9119	0.00928
PDIR	A_23_P167040	10954	1.91117	0.00002
TCN1	A_23_P64372	6947	1.9039	0.00188
A_24_P349648	A_24_P349648		1.90016	0.00082
VANGL1	A_24_P199655	690366	1.89913	7.97E-23

FGA	A_23_P375372	2243	1.89603	0.00355
INPP1	A_32_P44453	16329	1.89576	2.61E-08
OR52L1	A_24_P264293		1.89395	1.14E-08
RAB1A	A_24_P251351		1.89126	2.19E-11
SFTPA2	A_24_P928306		1.89113	0.00055
PLA2G10	A_23_P88767	26565	1.89071	7.03E-07
A_24_P272653	A_24_P272653		1.88943	2.75E-07
DAF	A_23_P103951	1604	1.88803	0.00001
LOC145788	A_32_P447001	691849	1.88772	0.0007
DUSP7	A_23_P155425	1849	1.88249	2.34E-07
RAB25	A_23_P115091	57111	1.88065	9.02E-06
KLF2	A_23_P119196	10365	1.8788	0.00206
TNFRSF12A	A_23_P49338	302965	1.87776	0.00001
EIF4B	A_32_P34186		1.87588	2.52E-06
GTF2IRD1	A_23_P111621	246770	1.87404	1.13E-16
ANGPTL1	A_23_P126706	679942	1.87404	0.00171
CD97	A_23_P502312	26364	1.87255	9.42E-11
A_24_P928235	A_24_P928235		1.87064	0.00001
A_32_P174978	A_32_P174978		1.86895	6.27E-06
cytochrome c, somatic	A_24_P573978	54205	1.86711	2.14E-23
FCGR1A	A_23_P63390	2210	1.86682	0.00527
CLDN4	A_24_P115183	12740	1.86423	0.00015
CYP2C19	A_23_P158481	1557	1.86353	0.00579
FLJ30469	A_24_P323148	502308	1.86289	0.00012
DHRS9	A_23_P56559	170635	1.85925	1.07E-07
G1P2	A_23_P819	9636	1.85678	1.22E-18
RHPN2	A_23_P119464	308516	1.85621	9.61E-07
CD9	A_23_P76364	12527	1.85529	3.90E-06
PRO1855	A_24_P181585	287633	1.8543	3.57E-09
GPR105	A_24_P165864	9934	1.85376	0.00195
PIM2	A_24_P379104	18715	1.85355	0.0002
ENST00000327852	A_24_P281374		1.84881	2.84E-10
VMP1	A_32_P9753		1.84847	0.00087
S100A11	A_23_P145863		1.84836	1.36E-13
PRSS7	A_23_P102864	19146	1.84835	0.00014
UGT8	A_23_P72747	22239	1.84828	0.00092
TNRC9	A_23_P54681	27324	1.84754	0.00522
FLJ11149	A_23_P216708	55312	1.84706	6.56E-06
A_24_P315405	A_24_P315405		1.84668	1.11E-16
CACNA1D	A_23_P365767	12289	1.84668	0.00002
ARG99	A_23_P371495	362465	1.84611	0.00016
THC1826594	A_32_P147865		1.84568	3.02E-09
similar to Keratin, type I cytoskeletal 18 (Cytokeratin 18) (K18) (CK 18)	A_24_P264644		1.84491	3.46E-08
THC1963074	A_32_P24685		1.84407	0.00202
LOC346113	A_24_P58647		1.84381	4.46E-07
C20orf24	A_23_P102582	296315	1.84239	6.80E-19
ENST00000321482	A_24_P127063		1.84004	1.55E-16
A_24_P247303	A_24_P247303		1.83999	3.31E-08
LOC116166	A_32_P127153		1.83668	0.00008
ALDH1A2	A_24_P73577	116676	1.83586	0.00028
similar to UNR-interacting	A_24_P135579	344382	1.83516	1.68E-10

protein (WD-40 repeat protein PT-WD) (MAP activator with WD repeats)				
A_24_P153002	A_24_P153002		1.83487	3.39E-10
IGLV8S1	A_23_P159435		1.83419	0.00001
ARL1	A_32_P36101	64187	1.83289	3.82E-22
HES1	A_23_P17998	15205	1.83271	9.27E-06
GARS	A_24_P154948	297113	1.83255	2.51E-12
LOC246737	A_24_P541483		1.83121	1.64E-07
GIPC2	A_23_P34478	365960	1.83069	0.00267
CRK	A_24_P270814	54245	1.83046	9.21E-09
ENST00000305049	A_24_P195164		1.83042	5.10E-07
A_32_P171984	A_32_P171984		1.82943	0.00005
ANXA2P1	A_24_P204244		1.82821	2.60E-11
TFRC	A_23_P212617	64678	1.82815	3.18E-10
PTPRN2	A_32_P79434	29714	1.8266	7.33E-07
PCSK9	A_32_P142440	298296	1.82593	8.24E-06
NANS	A_23_P9214	298071	1.8258	1.40E-17
suppressor of cytokine signaling 6	A_23_P207981	307200	1.8233	0.00078
CASKIN2	A_23_P44363	57513	1.823	0.00277
FLJ10055	A_23_P141394	303630	1.82249	7.85E-13
transmembrane and coiled-coil domains 3	A_23_P87853	314751	1.82243	0.00032
C1QR1	A_32_P56001	84398	1.82216	0.00064
RIPK3	A_23_P14559	11035	1.82183	7.20E-12
RIS1	A_23_P369899	72309	1.82151	0.00009
MGC33510	A_24_P29859	76982	1.82133	0.00246
PDZRN3	A_23_P21618	55983	1.82122	0.00157
RNF31	A_23_P354547	268749	1.82088	4.86E-07
INCA	A_24_P192805	440068	1.82053	2.57E-10
APACD	A_24_P362646	98258	1.81965	3.62E-15
ENST00000331037	A_24_P16230		1.81795	5.17E-07
LAP3	A_23_P18604	51056	1.8179	6.73E-07
THC1881984	A_32_P213948		1.81651	5.44E-08
SAP30	A_23_P121602	8819	1.81612	7.23E-09
SPINK4	A_23_P71880	408233	1.81543	0.00003
DDX6	A_32_P80255		1.81539	7.36E-24
PRPS2	A_24_P531074		1.81273	1.27E-19
HES2	A_23_P304716	29567	1.81273	9.32E-07
THC1872260	A_32_P59792		1.81169	0.00398
EIF3S3	A_24_P488649		1.81124	0.00033
TUWD12	A_23_P413576	14426	1.81071	0.00173
C6orf51	A_23_P400465	361858	1.81063	3.94E-23
C13orf18	A_24_P914348		1.81046	0.00558
BRUNOL4	A_24_P661695		1.80975	0.00002
RPS2	A_32_P14544		1.80711	5.39E-15
LOC339781	A_24_P247454		1.80422	0.00001
CMIP	A_23_P377935		1.80379	0.00236
STK39	A_24_P19544	54348	1.80161	1.20E-22
LOC151825	A_24_P153003		1.80144	8.50E-09
BC029255	A_24_P901986	100133019	1.80107	0.00024
SLC8A1	A_32_P108277		1.79903	0.00002

LOC121906	A_24_P324506	121906	1.799	5.45E-35
ADORA2B	A_23_P55477	29316	1.7973	0.00004
TM4SF6	A_23_P171143	302313	1.7959	2.12E-24
RAB11A	A_24_P124957	53869	1.79342	2.76E-18
ENST00000331598	A_24_P264597		1.79108	2.12E-06
KIAA0802	A_23_P360605	68617	1.78952	0.00011
immunoglobulin lambda variable 6-57	A_24_P361816		1.7889	2.92E-08
FER1L3	A_23_P86682	26509	1.78861	1.18E-06
YWHAZ	A_32_P97489		1.78715	3.83E-20
RALGPS2	A_24_P173746	304887	1.78677	0.0001
FHL2	A_23_P108751	2274	1.7863	7.15E-09
THC1806323	A_32_P96124		1.78494	0.00011
BACE2	A_23_P154875	25825	1.78442	0.00019
MCF2L	A_24_P390172	17207	1.78436	0.00963
FMR1NB	A_32_P99019	158521	1.78392	0.00627
KIAA1155 protein	A_24_P860797	232164	1.7837	0.00229
FLJ40504	A_23_P373708	284085	1.78326	1.35E-06
THC1826185	A_32_P8234		1.78285	9.76E-09
motilin	A_23_P19523	4295	1.78235	0.00043
ZFP36	A_23_P39237	7538	1.78066	2.41E-06
SSR3	A_23_P155229		1.77969	1.16E-09
ACSL3	A_24_P37319	2181	1.77862	1.52E-13
A_32_P193952	A_32_P193952		1.77764	0.00015
KRT18	A_23_P99320	294853	1.77607	2.25E-07
TZFP	A_23_P131024	58206	1.77606	0.00455
IL1R2	A_23_P79398	7850	1.77451	0.00187
LOC389023	A_32_P86578	389023	1.77382	7.22E-06
FKBP10	A_23_P15727	14230	1.77242	0.0062
CCRL1	A_23_P6909	252837	1.7717	2.01E-12
ASPN	A_23_P216429	306805	1.77064	0.00866
RNASE4	A_23_P205531	305843	1.77036	0
IL18R1	A_24_P208567	301365	1.76813	0.00174
A_23_P61191	A_23_P61191		1.76809	2.11E-07
GPA33	A_23_P51538	59290	1.76744	3.47E-08
CENTA1	A_23_P145865	171097	1.76679	0.00061
LDLR	A_24_P117029	300438	1.76677	3.34E-13
MYH6	A_23_P37167	29556	1.76546	0.00105
PDCL2	A_23_P363301	79455	1.76463	0.00467
DAF	A_24_P188377	1604	1.76418	2.52E-09
HBA2	A_23_P26457	3039	1.76361	3.63E-09
PPP1R14A	A_24_P296772	68458	1.76212	2.74E-06
VQFL30008	A_32_P926007		1.76156	0.002
CTSL2	A_23_P146456	1515	1.76075	0.00085
SYNGR2	A_24_P347854	20973	1.76059	4.56E-12
CDC42	A_24_P42633	998	1.76002	4.98E-16
BAG3	A_23_P47077	29810	1.75861	0.00004
similar to T-complex protein 1, eta subunit (TCP-1-eta) (CCT-eta) (HIV-1 Nef interacting protein)	A_24_P118813		1.75777	0.00002
FEM1A	A_24_P219920	14154	1.75591	0.00002

MCP	A_23_P201758	4179	1.75584	0.00007
IL17F	A_23_P167882	112744	1.75581	0.00007
A_32_P109666	A_32_P109666		1.75532	0.00011
SCOC	A_23_P167293	60592	1.75483	0.00085
similar to Keratin, type I cytoskeletal 18 (Cytokeratin 18) (K18) (CK 18)	A_24_P350060		1.75473	8.58E-09
WNT2B	A_23_P138352	22414	1.7538	0.00293
PTST32656	A_32_P167592		1.75286	0.00097
F2RL2	A_32_P60065	29636	1.75174	1.02E-07
GALNT3	A_24_P114249	14425	1.75108	2.70E-09
PTK9	A_23_P48166	5756	1.7504	5.96E-10
DKFZp434C189	A_32_P319880	314061	1.74648	5.42E-07
HSPA5	A_24_P18190	25617	1.74604	1.38E-06
LOC343259	A_24_P401090		1.7448	7.81E-07
FLJ20073	A_24_P175187	54809	1.74384	0.00003
LAPTM4B	A_24_P180680	55353	1.74369	1.68E-21
LOC139060	A_24_P584463		1.74348	4.04E-08
MAIL	A_23_P212089	64332	1.74277	6.10E-09
LOC286272	A_32_P128857		1.74198	0.00207
IFITM4P	A_24_P16124		1.73999	0.00025
CASP1	A_23_P202978	834	1.73905	1.31E-06
A_32_P74680	A_32_P74680		1.73862	0.00449
ANXA2P3	A_32_P148345		1.73849	3.97E-06
H3F3B	A_23_P152516	3021	1.73739	1.24E-15
HIG1	A_24_P200162	56295	1.73716	3.61E-06
JDP1	A_23_P127220	619393	1.73573	8.47E-06
similar to rhophilin-like protein; RhoB effector; rhophilin-2; rhophilin 2	A_24_P767725		1.73543	3.92E-07
STAT1	A_23_P56630	6772	1.7354	0.00001
MRPL12	A_23_P170352	303746	1.73478	1.58E-08
HBD	A_24_P75190	3045	1.73383	4.63E-06
PTRF	A_23_P394064	19285	1.73307	4.44E-10
hypothetical protein FLJ11348	A_24_P84752		1.73269	0.00217
LMNA	A_23_P34835	4000	1.72814	1.59E-17
SERPINB5	A_24_P589301		1.72783	0.00106
SGK2	A_23_P131801	171497	1.72704	0.00868
TM4SF1	A_32_P231617	4071	1.72599	5.20E-08
similar to Histone H2B.n (H2B/n) (H2B.2)	A_24_P152345		1.72573	0.0012
HNRPAB	A_23_P19084	15384	1.72504	1.69E-06
C14orf150	A_24_P560431		1.72325	0.00871
BIGM103	A_23_P41424	295455	1.72304	0.00568
HMGCS1	A_23_P133263	3157	1.72217	0.00011
RAB43	A_32_P86318	339122	1.72118	0.00009
C14orf130	A_23_P205393	55148	1.72114	0.00003
transcription elongation factor A (SII), 3	A_23_P34376	298559	1.71957	1.16E-06
SYNJ2	A_23_P344719	8871	1.71951	0.00082
MAP2K1IP1	A_23_P110362	8649	1.71938	8.88E-09
NDUFA9	A_24_P361006	66108	1.71895	4.35E-13

ZFP67	A_24_P19884	51043	1.71855	1.26E-07
SLC38A2	A_24_P295963	54407	1.71843	1.27E-10
FLJ16124	A_24_P255954		1.71801	1.31E-06
LOC123862	A_24_P7040		1.71678	0.00151
LOC345884	A_24_P256063		1.71619	3.90E-07
EFNA2	A_32_P9368		1.71594	2.92E-23
RHOBTB3	A_23_P92710	22836	1.71451	0.00411
CRYBB2	A_23_P425066	12961	1.71302	4.44E-08
LOC343326	A_24_P169843		1.71294	3.78E-10
ENTH	A_23_P133345	9685	1.71255	1.41E-20
MGC3178	A_23_P168229	105245	1.71235	7.35E-10
similar to Keratin, type I cytoskeletal 18 (Cytokeratin 18) (K18) (CK 18)	A_24_P247233		1.71164	1.33E-08
PSMB8	A_23_P250629	16913	1.71087	3.21E-08
EHF	A_23_P203540	13661	1.71023	0.00601
NQO1	A_23_P206661	24314	1.70988	1.85E-06
hypothetical protein MGC14801	A_23_P1014	84791	1.70879	7.54E-09
ABHD2	A_23_P395172	54608	1.70853	0.00001
HBG2	A_23_P53137	502359	1.70626	4.32E-07
MGC4266	A_32_P462013		1.70578	6.53E-10
similar to SMT3 suppressor of mif two 3 homolog 2	A_24_P213228		1.70464	3.22E-12
RPL22	A_24_P849801	19934	1.70381	9.70E-11
ANXA2	A_32_P94798	56611	1.70298	5.41E-10
PPP1R1A	A_23_P53417	58200	1.70297	4.31E-08
RPS2	A_23_P106708	83789	1.70267	0.00029
protein containing single MORN motif in testis	A_32_P69465	729967	1.70124	3.41E-10
PRDM16	A_32_P225816	70673	1.70077	0.0047
CNK2	A_23_P428887	302703	1.70062	0.00129
EPHB3	A_23_P95060	13845	1.70041	9.93E-06
PHLDA1	A_23_P76450	22822	1.69949	9.79E-06
RAPH1	A_24_P924862	65059	1.6992	0.00039
PLAB	A_23_P16523	29455	1.69833	6.32E-06
PKP3	A_23_P95810	11187	1.69758	0.00249
ALAS1	A_23_P57877	11655	1.69681	0.00039
FKBP11	A_23_P25121	66120	1.69649	0.00004
RDH11	A_23_P25684	51109	1.69423	0.00003
NR0B2	A_23_P160800	8431	1.69373	0.00084
RAB43	A_24_P277295	339122	1.69317	2.96E-08
B4GalNac-T3	A_32_P49748		1.69312	0.00167
MYCBP	A_23_P201655	56309	1.69299	4.83E-24
RP11-223E19.1-001	A_32_P100428		1.69248	0
SLCO4A1	A_23_P5903		1.69226	0.00712
TAGLN2	A_32_P194848		1.69191	0.00001
NR4A1	A_23_P128230	15370	1.69118	3.20E-09
PRDX3	A_23_P63751	64371	1.69109	8.72E-11
similar to Interferon-induced transmembrane protein 3 (Interferon-inducible protein 1-8U)	A_24_P868905		1.69096	0.00203
C6orf166	A_23_P428827	297968	1.69059	3.69E-12

FLJ40873	A_32_P50943		1.68992	0.00086
C14orf129	A_23_P205336	66787	1.68947	2.67E-06
CPSF2	A_23_P99837	299256	1.68896	4.94E-12
RAB15	A_24_P193295	376267	1.6879	0.00007
SEC61B	A_23_P135342	298068	1.6865	0
MUC2	A_24_P84657	4583	1.6863	0.00024
hypothetical protein FLJ12057	A_23_P166566	79825	1.68583	3.66E-10
STN2	A_32_P103558		1.68568	3.20E-08
LOC57228	A_23_P318115	207818	1.68432	9.48E-09
ELL2	A_23_P41645		1.68424	9.39E-30
LOC125242	A_24_P471242		1.68381	2.55E-08
A_24_P186746	A_24_P186746		1.68375	3.57E-10
MUC13	A_23_P155236	207126	1.68353	0.00359
BE275835	A_32_P70027		1.68343	0.0026
NDUFS1	A_23_P131363	4719	1.68204	1.37E-09
ANXA2	A_23_P146644	56611	1.68141	2.59E-08
LOC344572	A_24_P195528		1.68105	0.00052
SLC7A11	A_32_P165477	23657	1.68091	0.00393
A_24_P341408	A_24_P341408		1.68072	3.69E-17
ENST00000330567	A_24_P221724		1.68043	8.07E-08
SPEC2	A_23_P167767	56990	1.67998	2.55E-10
SLC7A1	A_24_P253251	25648	1.67967	8.97E-13
SPARCL1	A_23_P113351	25434	1.6784	0.00766
SLC16A3	A_23_P158725	80878	1.67828	0.00005
HBA2	A_23_P37856	3039	1.67807	1.02E-08
PCDHB9	A_24_P380284	56127	1.67732	0.00002
ARHGAP4	A_23_P159927	171207	1.677	0.00232
DUOX1	A_24_P316586		1.67656	0.00331
TPM4	A_23_P141974		1.67654	3.98E-08
CGI-119	A_23_P13701	51643	1.67645	7.70E-12
SRP9	A_24_P66528	6726	1.67552	9.21E-15
ARL1	A_32_P68586	64187	1.67536	1.65E-13
CTHRC1	A_23_P111888	68588	1.67493	0.0023
A_24_P375586	A_24_P375586		1.67307	0.00011
SMARCA4	A_23_P39034	171379	1.67304	0.00107
ZNF552	A_24_P693448		1.67276	0.00103
A_24_P255303	A_24_P255303		1.67273	0.00004
FLJ20344	A_24_P168822	55634	1.6726	0.00044
MDS1	A_23_P212688	2122	1.6716	1.98E-09
C14orf47	A_23_P88439	500707	1.67028	6.01E-11
MGC21654	A_23_P334218	210544	1.66901	0.0001
G3BP	A_23_P336479	27041	1.66786	2.35E-07
PTPRO	A_24_P280953		1.66741	2.73E-09
LOC401101	A_32_P167111		1.66665	0.00272
similar to tripartite motif-containing 43	A_23_P12972	642446	1.6663	0.00144
THC1821126	A_32_P84728	100131727	1.66331	0.00087
A_24_P349547	A_24_P349547		1.66287	0.00006
THC1815179	A_24_P763655		1.6626	1.96E-08
LOC158433	A_24_P67258		1.6626	3.92E-06
FLJ11588	A_23_P12303	362562	1.66154	0.0034
MSCP	A_24_P201089	306000	1.66153	2.43E-07

PSMD1	A_24_P128205	83806	1.66135	2.48E-23
PSMB9	A_23_P111000	16912	1.66105	0.00009
A_24_P6850	A_24_P6850		1.66078	1.30E-06
IGHV4-4	A_24_P750327		1.66023	0.0001
BX374774	A_32_P162709		1.6589	6.53E-10
PREI3	A_23_P210274	19070	1.65864	5.16E-10
TIRP	A_32_P123088	225471	1.65829	0.00046
ISG20	A_23_P32404	293052	1.65739	0.0003
FLJ36046	A_23_P342108	287936	1.65662	0.0029
ITGA2	A_24_P243329	170921	1.65556	0.00291
CGI-141	A_23_P162425	362460	1.65322	0.00037
cytochrome P450, family 51, subfamily A, polypeptide 1	A_24_P130041	13121	1.65213	5.97E-10
ATP5C1	A_23_P63655	11949	1.65195	1.02E-06
NEBL	A_24_P398147	307189	1.65175	0.00415
RAD54B	A_23_P94141	100128414	1.65128	0.00255
DLC1	A_23_P252721	10395	1.65015	2.85E-16
A_24_P563068	A_24_P563068		1.65006	0.00275
PACAP	A_23_P84596	69816	1.6495	0.00063
LOC202459	A_23_P304395	202459	1.64892	4.56E-13
C2orf6	A_24_P379765	297387	1.64789	3.02E-10
LOC401233	A_32_P135890		1.64788	1.07E-14
JAG1	A_23_P210763	16449	1.64778	8.08E-14
similar to Keratin, type I cytoskeletal 18 (Cytokeratin 18) (K18) (CK 18)	A_24_P84970		1.64752	1.48E-11
FBXW7	A_23_P81153	50754	1.6472	0.00311
GNPNAT1	A_24_P943040	64841	1.64654	0.00804
DKFZp434C0328	A_24_P915095	360717	1.646	0.00336
SLPI	A_23_P91230	6590	1.64578	0.00001
MCFD2	A_23_P120270	246117	1.64558	2.04E-18
BX106694	A_24_P527274	8503	1.64522	0.00011
A_24_P272403	A_24_P272403		1.64485	3.44E-09
A_24_P792988	A_24_P792988		1.64478	1.10E-07
guanylate binding protein 2, interferon-inducible	A_24_P36898		1.64474	2.07E-06
SRP9	A_23_P45934	653226	1.64282	8.70E-10
UBR1	A_24_P102203	22222	1.64258	0.00021
FLJ39441	A_23_P429082	500144	1.64193	3.63E-07
SOD2	A_23_P134176	6648	1.64185	6.26E-06
ADAMTS4	A_23_P360754	66015	1.64168	0.00303
BC029452	A_24_P677712		1.64145	0.00002
similar to Activated RNA polymerase II transcriptional coactivator p15 (Positive cofactor 4) (PC4) (p14)	A_24_P409650		1.64036	2.01E-09
ATF7	A_24_P922475		1.64022	0.00001
GMDS	A_24_P830406		1.63981	7.33E-07
LOC285507	A_24_P417757		1.63974	0.00013
similar to Interferon-induced guanylate-binding	A_32_P107372		1.63932	1.56E-11

protein 1 (GTP-binding protein 1) (Guanine nucleotide-binding protein 1) (HuGBP-1)				
SDCBP	A_23_P157580	53378	1.6393	0.0001
EPS8L1	A_23_P208779	361503	1.63901	0.00002
solute carrier family 4, sodium bicarbonate cotransporter, member 7	A_24_P362931	218756	1.63732	1.19E-11
LAMC2	A_23_P160968	3918	1.63701	0.00154
PPIC	A_23_P84018	291463	1.63669	3.17E-32
UCHL3	A_23_P76690	498560	1.63646	5.10E-16
similar to Cu/Zn-superoxide dismutase	A_24_P15906		1.63561	1.26E-10
DC2	A_23_P411814	58505	1.63482	2.95E-15
GNMT	A_23_P7957	27232	1.6343	0.00115
THC1933014	A_32_P183442		1.63408	0.00671
ENST00000331842	A_32_P6274		1.63393	2.03E-17
Rho guanine nucleotide exchange factor (GEF) 12	A_24_P152315	69632	1.63374	0.00427
GSTP1	A_23_P202658	2950	1.63354	0.00002
PLAC8	A_23_P81219	360914	1.6335	0.0001
DELGEF	A_24_P364087	26297	1.63331	8.98E-10
FLJ00056	A_23_P99661	361034	1.633	0.00277
selenophosphate synthetase pseudogene	A_24_P118452		1.63222	0.00641
C9orf3	A_24_P89887	290963	1.63187	4.03E-10
THC1975338	A_24_P681218		1.6315	1.67E-10
KIAA0232	A_23_P327069	680039	1.63083	5.60E-22
KARS	A_23_P152487	3735	1.63	2.57E-06
ETFA	A_24_P53080	110842	1.6299	6.95E-08
MORF4L1	A_23_P37579		1.62982	1.82E-10
C14orf147	A_23_P311150	104725	1.62975	8.40E-17
C15orf25	A_32_P144220		1.62929	1.43E-08
MGC14376	A_23_P49610	84981	1.62922	0.00144
RAB1	A_23_P382148	19324	1.62896	2.78E-07
ADAM9	A_23_P72643	290834	1.62825	1.06E-08
STX1A	A_23_P82420	6804	1.62791	1.91E-09
TRA1	A_23_P2601	22027	1.62745	8.16E-09
NETO2	A_32_P77989	307757	1.62698	0.00722
MCAM	A_24_P326660	84004	1.62683	0.00007
SSR4	A_23_P259172	6748	1.62666	8.99E-20
ETS2	A_24_P314179	2114	1.62652	3.04E-09
MtFMT	A_23_P117727	123263	1.62531	3.58E-13
similar to Keratin, type I cytoskeletal 18 (Cytokeratin 18) (K18) (CK 18)	A_24_P358406		1.62512	0.00046
KRT18	A_24_P42136		1.62474	4.36E-12
hemoglobin, gamma A	A_23_P64539	94164	1.62423	8.53E-06
FUT1	A_23_P107963	81919	1.62408	0.00282
ENST00000332472	A_24_P298894		1.6237	8.54E-06
FLJ20420	A_32_P159150		1.62344	8.03E-11
CDX1	A_23_P58788	12590	1.62289	0.00548

THC1855422	A_32_P121483		1.62203	9.51E-10
RNF138	A_24_P202512	56515	1.62199	0.00433
A_24_P161733	A_24_P161733		1.62191	0.00011
NUDT15	A_24_P244699	290365	1.62154	1.02E-10
C20orf115	A_24_P913847		1.62114	0.00129
TRA1	A_24_P150361	22027	1.62087	1.17E-07
KLF15	A_24_P20327	28999	1.62053	0.00429
EHF	A_24_P64442		1.62	0.00656
MCL1	A_24_P319635	17210	1.61963	0.00101
APOL3	A_24_P416997	278679	1.61919	0.00002
RBM7	A_23_P138975	10179	1.61907	3.68E-11
A_24_P230466	A_24_P230466		1.61889	1.36E-09
A_24_P127121	A_24_P127121		1.61872	3.03E-15
REG-IV	A_23_P400310	445583	1.61795	0.00004
A_24_P792748	A_24_P792748		1.61691	0.00831
PCDH17	A_23_P205057	306055	1.61683	4.29E-06
NAG14	A_23_P8625	641521	1.61667	0.0001
PPAT	A_23_P80940	117544	1.61633	0.00207
LRRC1	A_23_P377350	367113	1.61613	0.00925
HYA22	A_23_P212436	10217	1.61543	5.52E-07
IGF1	A_24_P304419	24482	1.61534	0.00296
PBX2	A_23_P214658	18515	1.61531	4.18E-08
HBA2	A_24_P142305	3039	1.615	0.00001
CCNC	A_23_P145397	114839	1.61473	5.24E-07
HSPC009	A_24_P356453	498000	1.61282	1.18E-25
C18orf56	A_24_P238499	494514	1.61248	0.00369
UNQ6077	A_24_P323421	338366	1.61196	0.00014
PAK2	A_23_P327307	224105	1.6104	0.00108
LITAF	A_23_P3532	56722	1.61009	4.11E-08
similar to Chloride intracellular channel protein 1 (Nuclear chloride ion channel 27) (NCC27) (p64 CLCP) (Chloride channel ABP)	A_24_P263803		1.60969	9.99E-15
SEC61B	A_24_P8494	298068	1.60964	1.91E-27
CA425979	A_24_P927072		1.60865	0.00047
multiple coiled-coil GABABR1-binding protein	A_23_P144274	152789	1.60824	0.00199
SPC18	A_23_P124823	56529	1.60542	1.99E-11
YWHAH	A_23_P103070	7533	1.60506	1.51E-10
DZIP1L	A_24_P93111		1.60363	2.64E-08
DNCL1	A_24_P124672	8655	1.60354	1.77E-15
A_24_P803246	A_24_P803246		1.60332	0.00042
SYNCRIP	A_24_P791515	363113	1.60272	3.10E-11
LOC55829	A_23_P26084	109815	1.60201	1.14E-13
C1GALT2	A_23_P159839	29071	1.60191	1.42E-15
similar to heterogeneous nuclear ribonucleoprotein A3	A_32_P159347		1.60158	2.10E-07
LOC440765	A_32_P69136		1.60116	4.21E-06
similar to KRT8 protein	A_24_P67395		1.60076	0.00011
CDC45L	A_23_P57379	287961	1.6007	8.05E-06
PPP2R2B	A_24_P7750		1.60008	8.85E-06

PEPP3	A_23_P148753	360842	1.60006	0.00006
PTK9	A_24_P178273		1.60002	0.00027
MMRP19	A_23_P2066	51074	1.59911	1.84E-07
CCND2	A_24_P270235	12444	1.59881	2.19E-08
A_23_P96191	A_23_P96191		1.59868	0.00732
AY358257	A_24_P937107		1.59823	0.001
PLXNA2	A_24_P242076		1.59798	5.14E-10
NP	A_23_P140256	290029	1.59783	1.18E-07
EPSTI1	A_23_P105794	108670	1.59657	0.00006
SLC10A1	A_23_P25698	24777	1.5965	0.00541
A_24_P790361	A_24_P790361		1.59615	6.86E-06
AVIL	A_23_P390157	11567	1.59606	0.00486
LOC220959	A_24_P247074		1.59604	0.00016
VBP1	A_23_P256223	7411	1.59547	0.00005
LOC91942	A_23_P345942	361894	1.59442	2.02E-09
SLC6A14	A_24_P365721	298340	1.59411	0.00322
RAD54L	A_23_P74115	19366	1.59323	0.00358
TMOD3	A_23_P65674	29766	1.59121	3.86E-16
C22orf5	A_23_P17870	362959	1.59082	2.04E-10
PLAUR	A_23_P16469	18793	1.59023	0.00105
SEC11-like 2 (S. cerevisiae)	A_24_P83808	157708	1.59016	2.69E-09
PDCD10	A_23_P18325	494345	1.58976	8.49E-09
THC1815206	A_32_P161836		1.58962	0.00036
LOC344318	A_24_P418687		1.58939	0.00022
RALA	A_23_P168479	5898	1.58925	1.21E-09
C20orf139	A_23_P320113	296271	1.58758	2.89E-09
FLJ21019	A_32_P172188	360634	1.5874	0.00024
HNRPA2B1	A_24_P3973	362361	1.58733	8.40E-09
IL11	A_23_P67169	3589	1.58611	2.56E-06
PLAC8	A_24_P183128	360914	1.58604	0.00105
ENO1B	A_23_P259892		1.58601	8.56E-12
HLA-C	A_23_P70539	3107	1.5859	0.00141
MARVEL domain containing 1	A_23_P138725	83742	1.58557	0.00003
ME1	A_23_P422026	17436	1.58407	1.24E-10
A_24_P279760	A_24_P279760		1.58373	3.61E-12
KPNB1	A_32_P184727		1.58365	3.65E-14
DKFZp761C169	A_24_P784478		1.58358	0.00484
PSMD11	A_23_P207600	303353	1.58295	1.90E-25
C1GALT1	A_24_P911259		1.58285	1.25E-06
FLJ23091	A_24_P256380	79971	1.58264	0.0001
STRA13	A_24_P65507	201254	1.58239	3.05E-19
MGST1	A_23_P36658	4257	1.58238	2.94E-06
CEBPB	A_23_P411296	24253	1.58235	0.00004
FBXO2	A_23_P45999	26232	1.58215	5.46E-08
BC058160	A_24_P340491	554234	1.58209	4.12E-07
NDUFS4	A_23_P257198	499529	1.5818	8.45E-27
LOC92689	A_24_P941572		1.58142	1.70E-08
COPEB	A_24_P69654	58954	1.581	2.15E-07
PPIB	A_24_P304723	19035	1.58082	1.11E-09
PHB	A_24_P854199		1.57998	5.58E-11
TGIF	A_23_P153197	316742	1.57878	0.00004

ELF3	A_23_P104188	13710	1.57853	0.00524
ITM1	A_23_P104734	3703	1.57817	3.67E-20
DD96	A_23_P160920	10158	1.57799	1.09E-06
CDKN3	A_23_P48669	72391	1.57787	0.00006
RQCD1	A_23_P5464		1.5769	0.00002
MGC35048	A_23_P324523	434232	1.57645	7.38E-10
SDC1	A_23_P16944	25216	1.57642	6.76E-06
CAPZA2	A_23_P307940	830	1.57628	4.74E-06
CYB5-M	A_23_P206697	80773	1.57556	5.21E-07
S100A16	A_23_P147918	67860	1.57502	6.92E-14
GPT2	A_23_P37892	307759	1.57372	0.00017
PSMA3	A_23_P140301	408248	1.57313	4.10E-14
LOC339834	A_24_P134765	434438	1.57276	0.00062
HIF1A	A_23_P48637	15251	1.57267	0.00082
SPA17	A_23_P104876	20686	1.5724	8.82E-08
GALE	A_23_P160154	74246	1.57204	2.09E-07
SDCBP	A_23_P168974		1.57172	0.00002
BM039	A_23_P355075	72155	1.57168	0.00266
BTBD14B	A_24_P915007	66830	1.57162	4.34E-27
SH3KBP1	A_23_P374782	30011	1.5712	9.93E-08
OTTHUMP00000021724	A_24_P169343	66129	1.57105	0.00189
HCP1	A_24_P392833		1.57068	3.28E-10
TRIM7	A_23_P30315	94089	1.57041	0.00277
STAT3	A_24_P116805	25125	1.57025	0.00408
ICA1	A_23_P215419	3382	1.56984	2.49E-20
chromosome 15 open reading frame 16	A_24_P318400	161725	1.56977	1.01E-12
LOC130576	A_23_P79302	130576	1.56966	0.00507
FOXA3	A_23_P208737	15377	1.56922	2.95E-13
GMPPA	A_24_P396800	29926	1.56909	0.00098
UBE2V2	A_24_P406514	70620	1.56895	1.36E-11
GNPNAT1	A_23_P429184	64841	1.56881	0.00065
hypothetical protein FLJ10970	A_23_P15450	55273	1.56779	0.00008
FAAH_2	A_23_P49448	79152	1.56775	1.54E-06
B4GALT1	A_24_P103803	2683	1.56737	1.91E-07
PHB	A_23_P130040	688815	1.56709	2.42E-12
CCL26	A_23_P215484	10344	1.56691	0.00527
uncharacterized bone marrow protein BM039	A_23_P88740	72155	1.56629	0.00015
PDE4D	A_32_P211026		1.56605	0.00005
LOC122592	A_24_P375360		1.56551	2.64E-07
PSMB3	A_23_P100576	5691	1.56315	1.48E-20
A_24_P118336	A_24_P118336		1.56292	8.65E-06
SARA1	A_24_P158421	56681	1.56257	2.52E-14
mucin 2, intestinal/tracheal	A_23_P256784	4583	1.5624	0.00007
CGI-69	A_23_P100764	51629	1.56232	0.00002
GJB2	A_23_P204941	14619	1.55997	0.00274
FLJ22729	A_24_P365048	79736	1.55875	3.79E-13
TRIM31	A_23_P122493	294208	1.55832	0.00914
GOV	A_24_P236956		1.55827	0.00003
A_24_P383660	A_24_P383660		1.55816	0.00106
ARPC1B	A_23_P20196	11867	1.55815	0.00125

GORASP2	A_23_P165494	26003	1.55804	3.87E-13
LOC388610	A_24_P693986	69539	1.55745	0.00133
SORD	A_23_P77103		1.5565	0.00457
CBR3	A_23_P40453	874	1.55596	1.74E-06
EIF4A1	A_32_P149432		1.55586	6.48E-15
LRRN4	A_23_P111506	360779	1.55564	0.00409
UBE2B	A_23_P362415		1.55455	0.00007
CYP39A1	A_23_P133712	56050	1.55393	0.00197
ST6GalNAcI	A_23_P54968	55808	1.55291	1.88E-09
KIAA1952	A_23_P43679	114991	1.5529	0.00146
FPR1	A_23_P38795	14293	1.55244	0.00007
RNP24	A_23_P36445	65165	1.55235	3.98E-07
OAS3	A_23_P47955	246727	1.55224	0.00015
MGC23909	A_23_P351903	100129118	1.55185	2.66E-27
ARF1	A_23_P201086	375	1.55168	0.00004
MED8	A_24_P233915	362575	1.55067	0.00007
MGC23909	A_32_P81768	100129118	1.55063	4.17E-13
TRAP2	A_24_P75948		1.55054	0.00032
SCD	A_32_P163858		1.54975	7.52E-06
A_24_P255965	A_24_P255965		1.54941	0.0035
GNG5	A_23_P148513		1.54924	1.56E-09
NSAP1	A_32_P8402		1.54923	1.07E-06
A_24_P110591	A_24_P110591		1.54897	0.00002
A_24_P929650	A_24_P929650		1.54891	1.07E-08
ITGA2	A_32_P208076	170921	1.54882	0.00014
LAT1-3TM	A_24_P164388		1.54837	1.19E-15
C14orf142	A_23_P99579	84520	1.54762	0.00038
SERTAD1	A_23_P218463	361526	1.54701	8.66E-15
MGC27165	A_24_P315854		1.54694	0.00289
SC5DL	A_23_P98446	114100	1.54673	1.07E-07
DECR1	A_24_P269619	117543	1.54671	0.00026
NRG1	A_23_P360777	3084	1.5466	0.00224
KCNK6	A_23_P50591	52150	1.54559	4.51E-07
PYY2	A_24_P233078	23615	1.54556	0.00738
IBTK	A_24_P929724	25998	1.54546	0.00084
BACE2	A_24_P14584	25825	1.54528	0.00362
CYBA	A_23_P163506	79129	1.54523	1.96E-06
LOC130402	A_24_P324538		1.54504	1.70E-12
SMP1	A_24_P864777	71817	1.54496	1.40E-13
CAPN2	A_23_P23924	29154	1.5446	0.00025
ISRE32658	A_24_P400729		1.54337	8.56E-08
LOC341862	A_24_P409410		1.54283	1.44E-08
PHF20	A_23_P120644		1.54279	0.00006
FER1L4	A_23_P80048	80307	1.54103	5.62E-09
LOC377075	A_24_P229756	644950	1.54061	5.16E-10
G10	A_23_P31602	8896	1.54019	1.03E-09
TM4SF6	A_24_P83262	302313	1.53988	2.16E-07
KIAA0790	A_23_P93442	23328	1.53953	0.00034
VPS29	A_24_P175989	51699	1.53923	1.14E-07
ENST00000334026	A_24_P927474	100133477	1.53921	5.91E-21
LANO	A_23_P215024	367113	1.5388	0.00001
LIAS	A_23_P41267		1.53872	0.0015

DCTN6	A_24_P278008	290798	1.53825	1.80E-07
NUDT4	A_23_P2366	71207	1.53748	1.15E-07
FLJ16124	A_24_P350136		1.53739	2.32E-09
RNF168	A_32_P195291		1.53735	0.00019
PCDH11Y	A_32_P151544		1.53687	4.35E-18
U96394	A_24_P472081		1.53652	0.00013
A_23_P122650	A_23_P122650		1.53633	2.69E-09
TXNL5	A_23_P380848	287474	1.53628	1.96E-11
DKNE32053	A_32_P198923		1.53628	0.00014
LOC341473	A_32_P456537		1.5346	0.00004
DDEF2	A_24_P362540	8853	1.53395	8.73E-06
NDUFA9	A_23_P76499	66108	1.53343	2.28E-14
STMN2	A_23_P146274	11075	1.53292	0.00633
STX1A	A_23_P168556	6804	1.53284	1.46E-11
GARP	A_24_P389916	434215	1.53241	6.73E-08
KIAA0152	A_24_P304449	304543	1.53186	1.21E-14
DNCL1	A_23_P65031	8655	1.53169	7.64E-28
ECM1	A_23_P160559	13601	1.53168	2.07E-06
GNE	A_23_P216489	114711	1.53094	0.00225
SUMO1 pseudogene 1	A_32_P223189		1.53006	2.65E-12
similar to ribosomal protein S2; 40S ribosomal protein S2	A_24_P281504		1.53	7.26E-07
HMGCS1	A_24_P63522	3157	1.52975	0.00002
ARF4	A_23_P431789	79120	1.52959	2.99E-12
ACTBP2	A_24_P49800		1.52875	4.83E-07
FLJ10462	A_23_P150903	330450	1.52853	3.32E-06
FLJ46111 protein	A_24_P489690	283102	1.52807	0.00015
MGC11034	A_23_P149975	83641	1.52763	0.00002
TSTA3	A_23_P94301	22122	1.52742	2.04E-06
TBC1D5	A_24_P289029	72238	1.52724	0.00003
FLJ43842	A_23_P6362	690315	1.52686	0.00273
SRA1	A_23_P257578	24068	1.5268	1.55E-13
A_24_P718223	A_24_P718223		1.52669	0.00062
TFPI	A_23_P17095	7035	1.5266	1.20E-09
CDKN1C	A_23_P428129	12577	1.52617	0.00022
CD59	A_23_P75523	966	1.52597	0.0003
SRP19	A_23_P81612	66384	1.52573	6.81E-11
PP	A_23_P161338	5464	1.52565	4.91E-09
KIAA1271	A_24_P127954		1.52561	0.00008
PPIL5	A_24_P13533	122769	1.52552	4.02E-13
MGC19780	A_23_P257423	362031	1.52514	0.00002
C6orf129	A_23_P133770	154467	1.524	0.00037
A_24_P692030	A_24_P692030		1.52375	1.21E-07
A_24_P375550	A_24_P375550		1.52334	0.00006
UNQ8200	A_23_P165778	79083	1.52269	0.00145
RIPK1	A_23_P370005	19766	1.52264	0.0092
FLJ20186	A_23_P88893	54849	1.52259	3.31E-09
A_24_P254933	A_24_P254933		1.52196	0.00002
RRBP1	A_23_P120566	311483	1.52135	1.38E-11
KHSRP	A_24_P134235	8570	1.52133	4.60E-07
C12orf5	A_23_P128486	319801	1.52119	1.58E-12
ATP-binding cassette, sub-	A_24_P289265	19	1.52094	0.00231

family A (ABC1), member 1				
CSNK1A1	A_24_P183292		1.51947	7.48E-12
LOC124199	A_24_P714620		1.51906	0.00002
THC1871546	A_24_P786025		1.51897	0.00475
TTDA	A_24_P196117	66467	1.5181	1.54E-07
A_23_P347100	A_23_P347100		1.51808	1.97E-07
LOC400368	A_24_P50543		1.51782	2.50E-08
HSPC039	A_32_P429872	66191	1.51768	0.00001
CASP10	A_23_P209408	843	1.51742	2.51E-08
GGH	A_23_P134910	25455	1.51712	0.00198
CAV2	A_24_P925040	12390	1.51707	0.00802
MGC14480	A_23_P253774	201254	1.51661	1.64E-15
NASP	A_32_P28365	4678	1.51528	0.00081
PC4	A_24_P320328	10923	1.51489	6.35E-10
EPAS1	A_23_P210210	13819	1.51465	2.05E-17
C10orf42	A_23_P346405	294560	1.51428	0.00006
LNX	A_23_P213137	16924	1.51426	0.00026
CSNK1E	A_23_P40664	1454	1.51413	1.83E-06
similar to TXNDC9 protein	A_24_P263524		1.51402	2.94E-06
solute carrier family 25 (mitochondrial carrier; phosphate carrier), member 24	A_23_P74799	310791	1.5138	4.15E-09
LOC391538	A_24_P771278		1.5137	0.00038
CISH	A_23_P144096	1154	1.51309	0.00041
GPR20	A_24_P589028		1.51237	0.00484
MAP1LC3B	A_24_P108005	81631	1.51209	6.35E-08
CEACAM5	A_23_P153301	1048	1.51195	0.00175
NDUFV2	A_23_P130418	4729	1.51176	8.54E-10
PFKFB2	A_24_P413669	24640	1.51169	1.91E-06
THC1987389	A_32_P184509		1.51057	0.00004
RAB3GAP	A_23_P50942	22930	1.50957	0.00003
PCYT2	A_23_P152984	21681	1.50938	0.0001
MGC4730	A_32_P134846	66928	1.50931	2.22E-08
SIMP	A_23_P434473	68292	1.50905	7.72E-08
LOC441333	A_23_P84475		1.50878	6.25E-08
DKFZp434I1020	A_24_P110141	196968	1.50865	0.00295
ZNF354A	A_23_P60565	6940	1.5081	0.00009
ASPH	A_24_P18105	65973	1.50759	0.00007
FAD104	A_24_P919304		1.50742	0.00261
MGC10911	A_24_P21044	84262	1.50718	1.01E-06
A_24_P341546	A_24_P341546		1.50684	0.0025
A_24_P417996	A_24_P417996		1.50655	1.16E-16
CALM2P2	A_32_P100338		1.50622	0.00001
RYBP	A_23_P29365	56353	1.50598	3.61E-06
THC1952994	A_32_P189034		1.50582	1.66E-10
MMP25	A_23_P376557	240047	1.50531	0.00009
KLF6	A_24_P932981		1.50498	0.00133
PARVA	A_24_P124370	57341	1.50488	0.00009
HOMER3	A_23_P39364	26558	1.50474	0.00699
ATP1B1	A_23_P146943		1.50462	0.00023
MGC3794	A_32_P229065	360869	1.50448	1.77E-10
MGC39584	A_32_P111996	727739	1.50371	0.00771

C6orf83	A_23_P321959	292305	1.50312	2.03E-17
BCKDHB	A_24_P239664	29711	1.50305	0.00067
F2RL1	A_23_P58835	14063	1.50279	0.0067
PPP2R5C	A_24_P369694	691318	1.50248	1.52E-06
LOC148595	A_32_P164314		1.50229	8.95E-11
PRKY	A_24_P186030	5616	1.50208	0.00669
A_24_P230486	A_24_P230486		1.50202	3.34E-06
CDC42	A_32_P115015		1.50172	7.53E-14
NOS1	A_32_P332320		1.5015	0.00071
KIAA0703	A_23_P117992	69047	1.50119	5.85E-06
RPE	A_32_P220938		1.50097	0.0004
FLJ10134	A_23_P113212	56277	1.50083	2.79E-08
Novel	A_24_P341089		1.50042	0.00081
A_24_P213336	A_24_P213336		1.50031	1.63E-06
golgi autoantigen, golgin subfamily a, 2-like, Y-linked, telomeric	A_24_P733345	648795	-1.50014	0.00173
GLTSCR2	A_23_P39125	292624	-1.50036	3.82E-10
ADAMTS2	A_24_P251866	9509	-1.50069	4.46E-06
PGRMC1	A_23_P114275	291948	-1.50117	0.00121
NAIA32048	A_24_P419017		-1.50139	0.00622
SSB3	A_23_P3496	302981	-1.50205	2.58E-09
A_32_P69653	A_32_P69653		-1.50209	0.00004
CATSPER2	A_23_P88489	117155	-1.50242	0.00299
BC011998	A_32_P42104		-1.50259	8.24E-09
TAGLN	A_23_P98402	51092	-1.50298	0.00148
CCL18	A_23_P55270	6362	-1.50301	0.00565
CRYZ	A_23_P114662	362061	-1.50345	3.42E-10
LOC391403	A_24_P375322	100130440	-1.50395	0.00259
PHF15	A_23_P416434	23338	-1.50397	0.00035
TEGT	A_23_P204702	7009	-1.50419	0.00002
CDH17	A_23_P111947	117048	-1.50422	0.00034
MGC16202	A_24_P880043	76073	-1.50446	8.69E-07
SFRS2IP	A_24_P393605	72193	-1.50493	0.00001
ARNTL	A_23_P162037	11865	-1.5051	0.00342
MMP23B	A_23_P74088	94339	-1.50655	0.00005
CD97	A_23_P208579		-1.50684	1.71E-06
NAGS	A_32_P32739	303563	-1.5069	0.00974
LOC83693	A_23_P206324	72552	-1.50694	0.00113
MSN	A_32_P151102		-1.50723	0.00206
HOOK3	A_32_P103726		-1.50738	0.00088
MTND6	A_24_P614579		-1.50742	0.00592
POLDIP3	A_23_P211603		-1.50795	4.33E-11
LR8	A_23_P157007	65963	-1.50948	5.71E-06
MYO1C	A_23_P164022	4641	-1.50993	5.74E-06
GALNT3	A_23_P209459	14425	-1.51004	0.00018
KIAA0563	A_23_P89680		-1.51006	5.29E-06
ABCB4	A_23_P123112	24891	-1.51008	0.00079
KIAA1271	A_23_P68539	228607	-1.51085	2.60E-06
PRKAB2	A_23_P350704	5565	-1.51167	0.00062
VPS35	A_24_P270769	25479	-1.51242	0.00003
SESN3	A_32_P146635		-1.5125	0.00064
LOC440666	A_32_P154956		-1.51274	0.00136

PP2447	A_23_P166548	67976	-1.51287	0.00318
MAML2	A_32_P164573		-1.51327	0.00964
ZP3	A_24_P95059	114639	-1.51369	7.04E-09
C10orf10	A_24_P329795	11067	-1.51411	0.00007
CARKL	A_23_P375281	7442	-1.51411	0.00347
ZNF429	A_23_P95736	353088	-1.51445	1.71E-12
SFPQ	A_24_P520241		-1.51507	0.00004
AL049390	A_32_P208039		-1.5157	4.12E-07
AK129982	A_32_P102428		-1.5158	1.59E-06
THC1910570	A_32_P161554		-1.51662	0.00001
FTH1	A_32_P98966		-1.51682	0.00841
EPC1	A_24_P252718	307042	-1.5171	7.79E-12
A_32_P100076	A_32_P100076		-1.51727	1.16E-11
CMKLR1	A_24_P766716		-1.51837	0.00383
GGA2	A_32_P106117	293455	-1.51857	0.00586
AQP1	A_23_P19894	25240	-1.51916	0.00036
A_24_P771880	A_24_P771880		-1.51956	0.00207
SMA3	A_32_P51518		-1.52028	0.00012
OVN9-3	A_23_P84246		-1.52033	0.00046
OTTHUMP00000039781	A_32_P64200	316218	-1.52046	0.00056
PBF	A_24_P128001	55893	-1.52083	1.51E-09
LISI13253	A_32_P177685		-1.52093	0.00003
CHES1	A_32_P163443		-1.52241	0.00222
THC1871361	A_32_P37592		-1.52256	1.34E-06
A_24_P755169	A_24_P755169		-1.52259	2.84E-06
APCL	A_24_P76844	23805	-1.52294	0.00284
MAFB	A_23_P17345	16658	-1.52352	3.28E-10
ALS2CR2	A_23_P90679	227154	-1.52372	0.00053
MGAT2	A_23_P203698		-1.52424	0.00014
AF086536	A_24_P915361		-1.52469	0.00141
NR3C2	A_23_P392470	110784	-1.52554	0.00547
PKD1	A_24_P477127	5310	-1.52606	1.69E-06
LOC56920	A_23_P6818	218877	-1.52654	0.00102
hypothetical protein LOC339778	A_32_P50603	339778	-1.52732	0.0005
similar to PI-3-kinase-related kinase SMG-1 isoform 1; lambda/iota protein kinase C-interacting protein; phosphatidylinositol 3-kinase-related protein kinase	A_24_P204675		-1.52735	1.01E-07
GALNT14	A_23_P67847	71685	-1.52796	1.06E-09
QRSL1	A_24_P163477	309911	-1.52813	1.83E-08
A_24_P821693	A_24_P821693		-1.52828	1.18E-06
LOC143158	A_24_P729905		-1.5283	1.24E-08
ARID1B	A_24_P675731		-1.5285	3.30E-08
GPR154	A_23_P136013		-1.52862	0.00048
mitogen-activated protein kinase kinase kinase kinase 4	A_23_P90804	26921	-1.52867	3.00E-06
FLJ10707	A_23_P212204		-1.52951	2.09E-12
DKFZp686A20267	A_23_P61674	57396	-1.53007	0.00158

BM726442	A_32_P405942		-1.53066	0.0011
FLJ90165	A_23_P66774	71522	-1.53116	0.0009
AK098638	A_24_P700052		-1.53125	3.21E-06
THC1928980	A_32_P98940		-1.53131	7.11E-08
TNFSF10	A_23_P121253	22035	-1.53137	9.94E-08
RPS26	A_23_P116694	689919	-1.53183	3.29E-06
hypothetical protein FLJ14640	A_23_P130856	72140	-1.5321	9.12E-07
PLDN	A_23_P205801	26258	-1.53245	0.00598
OTTHUMP00000044920	A_32_P95082	54875	-1.53262	0.0006
HS3ST3B1	A_24_P23625	54710	-1.53268	0.00018
BX090412	A_32_P46495		-1.53275	0.00364
KIAA1936	A_24_P359145		-1.53295	2.51E-07
RP4-657E11.5	A_23_P201521		-1.53305	0.00153
FANCC	A_23_P71680		-1.53316	2.40E-11
LDHB	A_23_P53476	24534	-1.53318	0.00015
FLJ37874	A_24_P754999		-1.53342	9.46E-08
HS2ST1	A_24_P242357	292155	-1.53353	4.01E-08
CAPN12	A_23_P16409	308476	-1.53393	0.00039
A_32_P221641	A_32_P221641		-1.53487	0.00055
LOC441419	A_23_P348979	100132439	-1.53627	2.61E-06
A_32_P200429	A_32_P200429		-1.53654	1.10E-15
AMY1A	A_23_P23611	109959	-1.53656	1.29E-06
IGFBP3	A_24_P320699	16009	-1.53676	4.62E-24
HspB9	A_23_P416212	363681	-1.53683	1.86E-07
FLJ11259	A_24_P355816	71712	-1.53706	0.00061
A_24_P75558	A_24_P75558		-1.53849	0.00008
GALT	A_24_P12865	14430	-1.53875	0.00002
MKNK2	A_23_P142310	299618	-1.54044	0.00002
ABCB1	A_23_P82523	170913	-1.54065	0.00218
zinc finger protein 292	A_23_P428468	23036	-1.54247	0.00001
similar to FRG1 protein (FSHD region gene 1 protein)	A_24_P417526		-1.54299	5.12E-07
OCIA domain containing 2	A_23_P121702	132299	-1.54417	0.00002
ZFP90	A_24_P176404	22751	-1.54427	0.0002
KIAA1533	A_23_P56213	57655	-1.54437	0.00019
MGC34079	A_23_P404595	147687	-1.54502	0.00112
DAPK1	A_24_P602168		-1.54514	3.28E-06
MUC17	A_24_P169507	140453	-1.5452	0.00657
LCE2C	A_23_P427768	353140	-1.54525	8.78E-11
KCTD9	A_32_P216004		-1.54535	0.0018
BI497361	A_32_P220161		-1.54539	3.38E-08
similar to BC004636 protein	A_24_P901084		-1.54545	0.00024
FLJ10830	A_23_P89812	291394	-1.54566	1.75E-10
AE2	A_24_P566932		-1.54583	1.14E-06
RPL21	A_32_P194821	433387	-1.5461	0.00002
similar to MGC9515 protein	A_32_P140823	729978	-1.54674	9.06E-10
A_32_P22989	A_32_P22989		-1.54676	4.01E-10
E2F3	A_23_P32684		-1.54702	1.63E-06
RELB	A_23_P55706	5971	-1.54708	2.40E-06
A_32_P78285	A_32_P78285		-1.54726	0.00898

ATP8A2	A_24_P944714	51761	-1.54734	0.00266
AKAP9	A_23_P309261	100986	-1.5474	0.0002
ACAS2L	A_23_P120594	68738	-1.54793	0.00048
MGC42174	A_32_P232192	208718	-1.54836	0.00361
LOC389607	A_24_P660811		-1.54855	0.00036
PAG	A_32_P61684	55824	-1.54961	0.00003
LOC116238	A_32_P132337		-1.54999	4.02E-14
SFRS7	A_24_P222911	6432	-1.55148	1.10E-06
thyrotropin beta subunit, TSH beta subunit,thyrotropin beta subunit, TSH beta subu>	A_24_P912490		-1.55229	0.00518
OGT	A_32_P201020		-1.55233	0.00375
IRA1	A_24_P114604	365755	-1.55239	0.00153
GLS	A_24_P294233	2744	-1.5524	5.99E-06
cytochrome P450, family 1, subfamily A, polypeptide 2	A_23_P206110	13077	-1.55259	1.53E-11
UNC119	A_23_P49842	9094	-1.55285	0.00174
PDE4C	A_23_P119583	290646	-1.55362	1.90E-20
AMN	A_24_P313210		-1.55413	0.00037
MYH11	A_24_P70183	24582	-1.55439	0.0002
TMEM41B	A_24_P668572		-1.55467	0.00478
TCF7	A_23_P7582	21414	-1.55541	0.00695
FLJ13848	A_23_P35782	79829	-1.55543	9.74E-06
LRRC19	A_23_P364625	100061	-1.55557	0.00073
LOC220466	A_32_P124493		-1.55611	2.07E-08
SWAP70	A_23_P116533	20947	-1.55617	2.94E-07
A_24_P281853	A_24_P281853		-1.55632	0.00122
LTB4DH	A_23_P157809	192227	-1.55636	0.00176
FBXL17	A_32_P20288		-1.55649	0.00383
MEP1A	A_23_P93122	17287	-1.55651	0.00167
TRF4-2	A_24_P940197	307745	-1.55765	0.00305
FLJ23516	A_23_P148345	66889	-1.55848	0.00129
embigin	A_24_P684186		-1.55869	0.00007
IMAP1	A_23_P427023	312312	-1.55919	0.00012
PACS1	A_23_P47220		-1.55932	7.95E-15
LOC55565	A_23_P77669	307834	-1.55937	1.56E-13
MGC61716	A_24_P817066	363289	-1.56039	1.55E-12
A_32_P80587	A_32_P80587		-1.56039	5.05E-08
FABP7	A_23_P134139	80841	-1.56052	1.49E-08
pp9099	A_23_P129246	80301	-1.56076	0.00014
CGI-14	A_24_P287785		-1.56179	2.13E-10
GPR20	A_24_P266466	239530	-1.56211	1.85E-11
ISAH21588	A_23_P354609		-1.56214	0.00031
AK098134	A_23_P93709		-1.56219	7.65E-08
KIAA1002 protein	A_24_P207907	22864	-1.56229	0.0086
TGOLN2	A_24_P413988	192152	-1.5628	3.13E-11
MGC4728	A_23_P153256	374928	-1.56337	0.00016
DOCK10	A_24_P391811		-1.56341	0.00146
ODZ3	A_24_P911420	23965	-1.56404	0.0088
FABP2	A_23_P391711	14079	-1.56414	0.00859
DKFZP586A0522	A_23_P415021	25840	-1.56437	7.95E-09
SLC1A1	A_23_P216468	6505	-1.56478	0.00347

hypothetical protein FLJ25102	A_24_P6764	348738	-1.56534	0.00741
SMA3	A_32_P146898		-1.56584	0.00002
ISFL13026	A_32_P31123		-1.56596	0.00027
SOX12	A_23_P131887	689988	-1.56603	3.22E-06
similar to Immunoglobulin-binding protein 1 (CD79a-binding protein 1) (B cell signal transduction molecule alpha 4) (Alpha 4 protein)	A_24_P238868		-1.56611	1.74E-06
LHPP	A_23_P75299	76429	-1.56686	2.25E-09
SP5	A_32_P183718	296510	-1.56687	0.00045
MGC33867	A_23_P51346		-1.56691	0.00008
SH2D1A	A_24_P203103	501502	-1.56693	1.75E-06
UNQ338	A_23_P94434	646962	-1.56701	0.00366
RORA	A_23_P26124	19883	-1.56746	0.0038
LOC440546	A_24_P222054		-1.56785	0.00041
inactivation escape 1	A_23_P148602		-1.56816	2.37E-09
SSR1	A_32_P128588		-1.56846	0.00226
AK095945	A_24_P221385		-1.56864	0.00013
GK	A_24_P100387	79223	-1.56895	0.00657
CBX7	A_23_P250735	23492	-1.57027	1.64E-07
DPYSL4	A_23_P331049	25417	-1.57112	0.00115
POMT1	A_23_P146354	10585	-1.57293	3.75E-12
WBSCR23	A_23_P123018		-1.57334	2.99E-15
PRKAG2	A_24_P384779		-1.57346	0.00001
GPR150	A_24_P37887	238725	-1.57486	0.00006
KCNH6	A_23_P83558	192775	-1.57606	0.00717
MGC24047	A_32_P232455	298602	-1.57671	0.00001
KIAA1936	A_24_P75344	114826	-1.57712	4.73E-08
UBE2D3	A_24_P630916		-1.57795	1.32E-15
PRO2133	A_23_P110655		-1.57868	0.0001
HT036-ISO	A_23_P200976	81888	-1.57891	0.0003
USP22	A_24_P94034	23326	-1.57914	0.00095
BM662290	A_32_P60076		-1.58012	1.27E-15
NTN1	A_32_P53524	18208	-1.58021	0.00019
H63 breast cancer expressed gene	A_23_P140469	113201	-1.58035	0.00781
RSBN1L	A_32_P230465		-1.58091	5.52E-09
UGT2B17	A_24_P17691	29623	-1.58112	0.0057
LAMP2	A_23_P217447	24944	-1.58165	8.35E-06
VIPR1	A_24_P105933	22354	-1.58208	0.00538
HSPC088	A_24_P324396		-1.58213	0.00046
LOC392465	A_23_P95619		-1.58229	1.09E-08
LOC401504	A_24_P661593		-1.58232	5.91E-08
NMNAT1	A_24_P139742	298653	-1.58263	0.00016
DKFZP434A0131	A_23_P93818		-1.58304	3.94E-14
MC1R	A_23_P329271	4157	-1.58322	4.50E-08
PRDX2	A_32_P227525		-1.58341	0.00694
MAGI1	A_23_P134085	154043	-1.58386	0.0021
SLC22A5	A_24_P174755	29726	-1.58431	0.00681
ZDHHC21	A_24_P933492	298184	-1.58432	7.75E-07
SLC2A5	A_23_P160159	65197	-1.58474	0.00187

AK023660	A_32_P217261		-1.58492	4.48E-06
MGC15631	A_23_P56150	84839	-1.58509	0.00017
RANBP9	A_32_P106523		-1.58606	4.39E-09
LOC51240	A_24_P371053	94101	-1.58702	1.41E-06
LOC440444	A_23_P207680	51326	-1.58708	0.00016
FLJ45645	A_32_P116660		-1.58714	0.00256
OTTHUMP00000021414	A_24_P145035	728013	-1.58749	0.00047
LOC51014	A_32_P18147		-1.58757	0.00118
Z25424	A_24_P938135		-1.5878	2.34E-15
SEC15L2	A_32_P16258		-1.59095	0.00203
SYNPO	A_23_P213798	11346	-1.59129	1.74E-07
FLJ10579	A_23_P152087	55177	-1.59149	0.00013
LOC346245	A_24_P67748		-1.5922	2.58E-10
FLJ20373	A_24_P157165	26921	-1.59222	4.20E-07
THC1812997	A_32_P190682		-1.59256	0.00061
CLN5	A_24_P270357	306128	-1.59276	0.00857
KIAA0577	A_32_P64688		-1.59312	0.00545
LPP	A_32_P70519		-1.59314	6.01E-09
OTTHUMP00000035566	A_24_P289447		-1.5938	1.58E-13
PFKFB4	A_24_P362904	5210	-1.5941	0.00021
THC1933362	A_32_P115446		-1.59446	0.00001
similar to hypothetical protein	A_24_P204690	391003	-1.59485	1.74E-08
C7orf32	A_23_P61960	76252	-1.596	8.55E-08
MGC24039	A_32_P19561		-1.5973	0.00026
FLJ23235	A_23_P92334	243025	-1.59756	0.00107
MUC17	A_24_P913828		-1.59791	1.04E-06
PLAG1	A_23_P411723	5324	-1.59805	0.00024
GAEV4856	A_24_P930088		-1.59871	2.55E-06
BM726576	A_32_P90685		-1.59938	0.00765
FFFF31786	A_24_P936282		-1.59956	0.00007
CNOT2	A_24_P741023		-1.5997	0.00004
KDR	A_23_P58419	16542	-1.59983	0.00437
FLJ00312	A_32_P134825		-1.60024	0.00285
LOC116236	A_23_P363034	67477	-1.60036	0.00415
GPR160	A_23_P167005	71862	-1.6004	7.30E-07
LOC374654	A_24_P203689	374654	-1.60075	0.00056
A_32_P44932	A_32_P44932		-1.60226	0.00018
FXYD5	A_24_P194081	18301	-1.60244	0.00062
ATP5F1	A_32_P181183		-1.60266	0.00928
MME	A_23_P212061	17380	-1.60323	0.00039
ENST00000296879	A_23_P361085		-1.60517	3.32E-20
LOC441419	A_32_P100475		-1.60581	4.98E-06
ZNF505	A_23_P135826		-1.60581	0.00615
NCR3	A_23_P251881	259197	-1.60585	0.00027
RUNX3	A_23_P51231	12399	-1.60597	0.00006
CD8B1	A_23_P159335	24931	-1.60605	1.59E-08
MGC8902	A_24_P16541	55672	-1.6063	0.00552
GLS	A_23_P308800		-1.60679	2.65E-06
GGTLA4	A_23_P57199	92086	-1.60806	0.00331
OTTHUMP00000021401	A_24_P886197		-1.60811	6.63E-07
C7orf19	A_24_P329353	269717	-1.60918	1.18E-06
ZFPM1	A_23_P54573	161882	-1.61022	0.00546

PGRMC2	A_24_P405850	361940	-1.61046	0.00007
DKFZp667I133	A_23_P168388	243374	-1.61061	0.00002
C6orf96	A_24_P343271	66084	-1.61172	0.00057
CDH11	A_23_P152305	84407	-1.61336	0.00791
UGT2B10	A_23_P7342	305264	-1.6137	0.00934
MICAL3	A_23_P403195	685601	-1.61409	0.00588
CRA	A_23_P51986	689613	-1.61449	0.00784
PRPS2	A_23_P96641	110639	-1.61503	0.00005
KCNJ13	A_24_P307896		-1.61523	0.00537
UBCE7IP5	A_23_P218717		-1.61571	0.00039
LOC51170	A_23_P408271	114664	-1.6159	0.0003
RKHD3	A_23_P163440	108797	-1.61673	5.75E-06
ANGPTL4	A_23_P159325	362850	-1.61691	0.00007
embigin homolog (mouse)	A_32_P206541	13723	-1.61733	4.75E-11
A_32_P103776	A_32_P103776		-1.61766	0.00071
FLJ11588	A_23_P904	362564	-1.61786	0.00872
ANKRD9	A_24_P599496		-1.61875	0.00022
BS69	A_23_P75083	66505	-1.61916	7.87E-08
PRKAR2A	A_24_P943335		-1.62013	0.00783
PTPN1	A_32_P108033		-1.62024	0.0051
A_24_P84268	A_24_P84268		-1.62035	4.83E-07
TNFRSF13B	A_23_P84705	691719	-1.62055	0.00463
A_23_P141785	A_23_P141785		-1.62101	0.00001
CILP	A_23_P151895	8483	-1.62124	0.002
ARHGAP11A	A_32_P147090	89839	-1.62205	0.00013
LOC283767	A_32_P42236	283796	-1.62261	5.88E-10
MGC13057	A_23_P17130	84281	-1.62302	0.00012
PAM	A_24_P323815	290447	-1.62312	0.00178
PS1TP4	A_24_P772330		-1.62414	0.00028
polycomb group ring finger 4	A_24_P303989	648	-1.62441	0.00083
DNASE1L2	A_23_P3643	1775	-1.62443	0.00667
F7	A_23_P117298	2155	-1.62494	1.87E-25
AI140519	A_24_P740022		-1.62527	0.00002
TCF1	A_24_P372913	21405	-1.62573	0.00097
EVI2A	A_23_P78092	685433	-1.62578	0.00074
LOC285440	A_32_P23838	266761	-1.62585	6.64E-15
FLVCR	A_23_P12113	226844	-1.62726	0.00186
transcription factor EC	A_24_P98210	26296	-1.6273	0.00018
SLY	A_24_P237443	317578	-1.62805	0.00397
ABCA3	A_23_P140876	21	-1.62856	0.00615
SIPA1L3	A_32_P225301		-1.62884	0.00005
STATIP1	A_23_P78438	55250	-1.62955	2.09E-12
DKFZp434F222	A_23_P159355	304573	-1.62984	0.00093
PLEKHF1	A_24_P194068	79156	-1.62992	0.00006
THC1878025	A_32_P40611		-1.63008	0.00001
ZNF345	A_23_P39154	25850	-1.63044	0.00002
TRIM4	A_24_P68247	89122	-1.63049	0.00777
MGAT3	A_24_P128361		-1.63103	0.00045
CYP3A5	A_24_P915256		-1.6312	0.00218
MGC10334	A_24_P234105	79554	-1.63169	4.07E-07
NECL1	A_23_P201156	57863	-1.63173	0.00008
DKFZp686E15222	A_23_P128447	120892	-1.63201	0.00116

LOC133374	A_24_P811954		-1.63202	0.00415
PDIP	A_23_P325642	69191	-1.6323	0.00675
FLJ12768	A_23_P143935	239827	-1.63235	1.65E-06
SPANXE	A_23_P73501	171489	-1.63309	0.00284
TMEFF2	A_24_P239364		-1.63317	0.00011
FMR1	A_24_P93967	14265	-1.63366	0.00033
IGBP1	A_23_P171255	645545	-1.63417	3.97E-08
RNU47	A_24_P545200		-1.6343	0.00013
THC1857568	A_32_P40424		-1.63507	0.00007
ZNF25	A_23_P381577	219749	-1.63599	0.00163
ABLIM2	A_23_P255672	84448	-1.63629	1.14E-08
QGRL32255	A_32_P122907		-1.63663	0.00004
A_23_P78975	A_23_P78975		-1.63809	1.09E-13
SFRS16	A_23_P78509	499390	-1.63869	1.81E-34
THC1932558	A_32_P118325		-1.63995	0.00953
deformed epidermal autoregulatory factor 1 (Drosophila)	A_32_P35375	83632	-1.64026	0.00876
THEA	A_23_P417415	26027	-1.64038	1.06E-08
MGC10500	A_23_P15108	66090	-1.64154	3.34E-07
CHES1	A_32_P167631		-1.64177	0.00499
FLJ11722	A_23_P14649		-1.64225	1.88E-08
EIF3S3	A_24_P501698		-1.64293	0.0015
LOC388240	A_24_P167877		-1.64303	0.0037
ZFP36L1	A_23_P99540	12192	-1.64309	1.84E-06
THC1815377	A_32_P67680		-1.6433	0.00764
MGC1842	A_23_P17773	68778	-1.64554	0.00672
ABCA1	A_24_P235429	19	-1.64555	0.00508
THC1954314	A_32_P162076		-1.64699	0.00001
MGC40107	A_23_P3994	287442	-1.64786	0.00673
KLHDC2	A_24_P116242	23588	-1.64819	2.87E-19
LOC400551	A_32_P101884		-1.64834	0.00334
TRIAD3	A_23_P42724	304294	-1.64908	0.00089
FLJ20060	A_24_P644742		-1.64912	0.00437
LOC441433	A_24_P890536		-1.64938	0.00757
similar to bA476I15.3 (novel protein similar to septin)	A_32_P27698		-1.6498	0.00592
FLJ10520	A_24_P287826	361409	-1.65089	0.005
THC1924978	A_32_P162443		-1.65103	0.00272
STK17B	A_24_P476081		-1.65118	0.00326
PRO0478 protein	A_23_P430140	29048	-1.65179	6.64E-23
C6orf209	A_23_P81660	246046	-1.65329	5.23E-23
IMMP2L	A_32_P113007		-1.65387	0.00003
MRE11A	A_23_P150189	17535	-1.6539	0.00014
NOTCH2	A_32_P5040		-1.65639	0.00029
FLJ12895	A_24_P920880		-1.65643	0.00005
ND4	A_23_P431853		-1.65677	0.00088
HDAC10	A_23_P211673		-1.65764	5.51E-13
LOC153222	A_23_P404606	303016	-1.65789	0.0024
KLRB1	A_23_P99275	689817	-1.65951	0.00028
KIRREL2	A_23_P315451	243911	-1.66018	0.00073
ZHX2	A_32_P216122		-1.66021	0.00034

MAML2	A_32_P88987		-1.66025	0.0002
LOC400509	A_32_P10557		-1.66041	0.00039
FIBP	A_23_P1615	9158	-1.66047	4.03E-06
LOC221442	A_24_P303420		-1.6605	4.99E-06
CHFR	A_24_P921103		-1.66064	2.34E-07
MBNL1	A_24_P925361		-1.66086	1.54E-09
THC1874006	A_32_P24877		-1.66191	3.10E-10
B3GALT4	A_24_P845082		-1.66383	3.32E-06
TAC3	A_23_P2283	21334	-1.66499	1.63E-07
GPR7	A_23_P20458	297795	-1.66573	0.00082
ASRGL1	A_23_P203391	246307	-1.66603	1.18E-08
VEGFB	A_24_P55971	22340	-1.66605	0.00165
ZNF205	A_24_P56689	287095	-1.66739	0.00093
KCNG1	A_23_P210581	296395	-1.66743	6.94E-14
BAT4	A_23_P133923	81845	-1.66774	5.98E-21
MUCDHL	A_23_P202683	53841	-1.6678	0.0041
LOC391124	A_24_P828496		-1.6679	0.00411
TNFSF5	A_23_P62220	21947	-1.66813	0.00776
ALDOB	A_23_P32143	229	-1.66956	0.00015
A_24_P711477	A_24_P711477		-1.66998	3.64E-34
cysteine sulfinic acid decarboxylase	A_23_P105732	51380	-1.67074	2.34E-20
THC1902516	A_32_P137299		-1.67099	0.00372
LOC388221	A_32_P182458		-1.67104	1.28E-11
MSH6	A_23_P102202	2956	-1.67266	3.36E-08
CD37	A_24_P82749	29185	-1.67496	0.00012
LOC389289	A_23_P431591	389289	-1.67577	0.00095
FLJ33977	A_32_P147189		-1.67711	0.00005
MAOB	A_23_P85008	109731	-1.67743	0.00372
DKFZP434C131	A_23_P206103	25989	-1.67835	0.00605
KIAA0882	A_23_P41487	304645	-1.67842	0.0003
MGC45438	A_23_P26640	146556	-1.67924	0.00766
TSGA10	A_23_P17103	211484	-1.67925	0.00388
EPHX2	A_23_P8834	13850	-1.681	7.10E-06
CBS	A_23_P166306	24250	-1.68306	0.00105
RPS6KB1	A_24_P521409	6198	-1.68549	0.00407
THC1807481	A_32_P139391		-1.68657	0.00057
FYN	A_32_P224888		-1.68719	0.00428
SMA4	A_23_P121869	653188	-1.68789	1.28E-08
PHLDB3	A_32_P170879		-1.68795	0.00001
ZCCHC11	A_23_P34433	230594	-1.6882	0.00095
FLJ32818	A_23_P50320		-1.69054	1.40E-07
A_32_P187458	A_32_P187458		-1.69184	0.00003
ENST00000323012	A_24_P367282		-1.69273	3.31E-06
A_32_P166540	A_32_P166540		-1.69317	7.05E-25
ADD3	A_24_P90097	27360	-1.69439	2.14E-16
NEU4	A_23_P218626	241159	-1.6948	0.00231
NUP210L	A_32_P69379		-1.69512	1.00E-10
LIV-1	A_23_P50167	25800	-1.69565	0.0015
chromosome 10 open reading frame 116	A_23_P161439	10974	-1.69647	0.00155
PPT1	A_23_P62659	19063	-1.69663	0.00081
PRO1073	A_24_P25698		-1.6973	4.64E-06

CMRF-35H	A_24_P159434	217303	-1.69736	6.76E-06
similar to CDNA sequence BC012256	A_32_P218707		-1.69762	0.00354
JAZF1	A_32_P36694	221895	-1.69764	4.11E-07
THC1955861	A_32_P36292		-1.69826	2.11E-06
centromere protein B, 80kDa	A_24_P213912	362217	-1.6989	0.00097
MAML2	A_32_P43878		-1.69918	0.00211
ADRA1B	A_23_P33326	24173	-1.69946	6.98E-10
GGA1	A_24_P926400	26088	-1.70051	0.00237
AADAC	A_23_P80570	13	-1.70204	0.00457
NPL4	A_24_P136551	217365	-1.70208	0.00205
AW511222	A_24_P506680		-1.704	0.00029
RPN2	A_32_P63643		-1.70426	1.89E-06
RECK	A_23_P83028	53614	-1.70449	0.00006
NGGA30351	A_24_P886336		-1.70631	3.92E-12
SLC20A2	A_24_P649829		-1.70644	0.00098
THC1948634	A_32_P142802		-1.70646	0.00045
trophoblast-derived	A_24_P290999		-1.70698	0.00038
LICR2	A_23_P74112	163702	-1.70723	0.00003
SSH2	A_32_P211048		-1.70791	1.28E-07
ENO1	A_32_P229365		-1.70803	2.36E-09
LOC440444	A_24_P579826		-1.70873	0.00382
FOXP1	A_24_P460763		-1.7104	1.38E-07
CBX7	A_24_P19410	23492	-1.71067	2.53E-09
PECI	A_23_P156852	10455	-1.71196	2.81E-18
FLJ21069	A_23_P417363	298801	-1.712	0.00853
HSMPP8	A_24_P287403	75339	-1.71347	0.00097
RP11-367J7.1	A_23_P103803	115352	-1.7147	0.00052
MAP4K4	A_23_P102192	26921	-1.71578	0.00047
GPX4	A_23_P28075	29328	-1.71604	0.0002
INSR	A_32_P27041		-1.71636	1.12E-10
pps22-1 protein	A_23_P383698	641298	-1.71659	0.00048
THC1808978	A_24_P914095		-1.7169	0.00019
arachidonate 5	A_24_P347378	241	-1.718	0.00001
TIC	A_23_P68121	311785	-1.71817	0.00932
DKFZP727C091	A_32_P95541		-1.71899	0
PAG	A_23_P347070	55824	-1.71978	0.00013
KAB	A_23_P23151	545389	-1.7198	0.00255
UNQ6228	A_24_P935682	100131541	-1.72066	0.00436
C6orf80	A_23_P31085	25901	-1.72071	3.07E-14
AKAP1	A_32_P132438	114124	-1.72094	3.29E-11
A_24_P745960	A_24_P745960		-1.72138	4.52E-06
FAT2	A_23_P81507	245827	-1.72381	5.14E-07
OTTHUMP00000016909	A_32_P224566	380669	-1.7243	0.00143
STX16	A_24_P36457	362283	-1.72441	5.53E-07
MAWBP	A_23_P149998	68371	-1.72722	0.00396
PUS1	A_23_P60753		-1.72769	0.00013
TBC1D4	A_23_P88095	210789	-1.72771	1.02E-06
LOC339047	A_32_P215170	100133970	-1.72824	1.05E-08
LOC128102	A_24_P350397		-1.72839	0.00295
MUC3	A_24_P630109	100133790	-1.72887	0.00007
IMP-2	A_32_P170206		-1.73081	0.00988

PFN2	A_23_P253301	18645	-1.73213	2.61E-09
MSRA	A_23_P61426	110265	-1.73271	0.00736
SPRR1A	A_23_P348208	6698	-1.73546	6.19E-06
NR0B1	A_23_P73632	11614	-1.73548	0.00714
A_24_P853410	A_24_P853410		-1.73553	0.00037
DKFZp434K1210	A_23_P146077	55893	-1.73569	1.19E-14
THC1827152	A_24_P795662		-1.73587	0.00199
SLC2A11	A_23_P404565	66035	-1.73602	0.00858
TIAM2	A_24_P303454	24001	-1.73618	0.00063
VMLS30621	A_32_P167577		-1.73657	0.00028
UGT2B28	A_24_P180243	54490	-1.73663	0.00053
CD104030	A_32_P115749		-1.73666	1.08E-10
MYH3	A_23_P26865	24583	-1.73762	0.00015
chromosome 10 open reading frame 125	A_23_P97952	69064	-1.73769	0.001
CR1L	A_23_P63547	1379	-1.73772	0.007
TLR1	A_32_P4934		-1.73796	0.00086
Nup43	A_23_P31055	348995	-1.73868	0.00002
SNRK	A_24_P102151		-1.73899	8.50E-09
MAGEA4	A_24_P185945		-1.7398	1.86E-06
A_32_P23517	A_32_P23517		-1.74067	0.00538
LOC148203	A_32_P81806		-1.74071	0.00721
PTCH	A_24_P106910	19206	-1.74081	6.89E-08
FLJ21159	A_23_P92370	310544	-1.74105	0.00128
LOC92017	A_32_P233834		-1.74125	0.00051
LOC115294	A_32_P63858		-1.74181	0.0006
GPSM3	A_24_P144465	106512	-1.74288	0.00109
FLJ13710	A_23_P148249	207596	-1.74394	1.90E-10
LOC388716	A_32_P191696		-1.74555	0.00494
ZNF439	A_23_P434430	90594	-1.74814	6.62E-11
IFI16	A_23_P160025	3428	-1.74886	2.91E-07
DKFZp547P183	A_24_P721699		-1.74933	0.00063
A_32_P8971	A_32_P8971		-1.74943	1.06E-13
MTERF	A_32_P232704		-1.75147	1.10E-07
CYCS	A_24_P29665	54205	-1.75209	0.00132
FLJ32130	A_24_P944063	146540	-1.75243	0.00125
UNQ306	A_23_P206501	353287	-1.75487	0.00019
MAT2A	A_32_P221337		-1.7555	9.22E-14
GDPD1	A_24_P918891		-1.76092	0.00367
SNX12	A_32_P140228		-1.76175	8.26E-08
APOM	A_24_P89426	55939	-1.76199	0.00192
RPS19	A_24_P65597		-1.76202	0.00481
LOXL1	A_23_P124084	4016	-1.76299	0.00003
NR1H4	A_23_P25396	60351	-1.76547	0.00002
SLC3A1	A_24_P217234	29484	-1.76571	1.00E-10
ZDHHC21	A_23_P302125	298184	-1.76661	1.59E-23
LOC222171	A_23_P431346	78004	-1.76675	0.00228
KIAA1327	A_24_P264928	665775	-1.76678	0.00017
RC1	A_24_P924185		-1.76682	0.00011
pps22-1 protein	A_24_P358084	729978	-1.76723	0.00004
ZNF559	A_24_P284584	84527	-1.76754	7.72E-10
CYP3A4	A_24_P389251	266682	-1.77066	0.00031
LOC93082	A_23_P328740	93082	-1.77116	0.0004

FXR2	A_23_P4007	23879	-1.77323	0.00003
transmembrane protease, serine 9	A_23_P209176	360200	-1.77399	0.00052
NGEF	A_23_P102364	246217	-1.77538	9.59E-07
AJ001827	A_32_P179572		-1.77564	0.00901
SMURF2	A_23_P100754	66313	-1.77574	0.00059
MTATP8	A_23_P337726		-1.77747	0.00006
THC1933786	A_32_P142334		-1.77928	7.73E-07
FNDC1	A_23_P407840	308099	-1.78035	5.45E-06
HIVEP3	A_32_P59302	313557	-1.7814	0.00237
NIN	A_23_P54147	18080	-1.78289	0.00025
SPIC	A_32_P148275	121599	-1.78812	0.00149
DKFZp686F01145	A_32_P101313		-1.78896	0.00002
LOC388221	A_24_P693321		-1.78949	1.55E-12
BX103476	A_32_P185766		-1.79075	8.10E-12
SAST	A_23_P101480	56527	-1.79113	1.30E-10
7A5	A_32_P144599	238455	-1.79186	2.41E-06
A_32_P235293	A_32_P235293		-1.7925	4.25E-10
ROPN1	A_32_P184464	76378	-1.79438	0.00989
CD84	A_32_P58215		-1.7957	0.00023
TRIM6	A_24_P381199	117854	-1.79705	0.00227
ZNF530	A_24_P697345		-1.79745	0.00082
NKX2-8	A_24_P253293	26257	-1.79747	0.0007
GOLGA6	A_32_P103669		-1.79994	6.90E-07
F10	A_23_P205177	29243	-1.80055	6.99E-10
VHL	A_23_P132611	7428	-1.80206	3.23E-06
LOC388221	A_32_P168853		-1.80233	2.06E-18
ANKRD3	A_24_P125871	72388	-1.80377	3.02E-17
PBX4	A_23_P90419	80714	-1.80486	0.00118
EPHB4	A_23_P168443	13846	-1.80691	0.00207
mucin 3A, intestinal	A_23_P349147	100131514	-1.80967	0.00059
DD5	A_24_P450172		-1.80999	0.00005
IL11RA	A_23_P83277	245983	-1.81047	7.68E-42
THC1839040	A_32_P139634		-1.81052	4.56E-06
RTN4	A_23_P56933	57142	-1.811	0.00172
CHES1	A_23_P140405	1112	-1.81184	1.56E-11
LOC441242	A_32_P185701		-1.81185	9.70E-10
ATPase, Class V, type 10A	A_24_P215765	11982	-1.81299	3.11E-07
EBI2	A_23_P25566	1880	-1.814	8.25E-06
polyhomeotic-like 1	A_23_P204246	1911	-1.81411	0.00368
TRERF1	A_24_P217904	55809	-1.81598	0.00329
A_32_P44073	A_32_P44073		-1.81625	0.00089
FLJ11535	A_23_P67569	314614	-1.8168	3.47E-06
THC1891841	A_32_P66843	100170765	-1.81703	0.00069
LOC442578	A_32_P45894	442578	-1.81749	1.27E-14
FLJ10178	A_23_P96369	102871	-1.81792	0.00008
LOC283663	A_32_P8813	283663	-1.81906	0.00002
SIAT1	A_24_P397043	20440	-1.81916	2.19E-07
TBCD	A_24_P169258	108903	-1.81972	0.00005
A_32_P49116	A_32_P49116		-1.82	2.87E-07
LOC51270	A_23_P10518	51270	-1.82027	0.00141
RANBP9	A_24_P226355	56705	-1.82069	0.00169
FLJ22341	A_23_P329870	79651	-1.82114	0.00006

FLJ46385	A_24_P804267		-1.82162	8.50E-25
LOC284422	A_23_P397120	72273	-1.82457	0.00011
UNC13A	A_23_P365494	64829	-1.82544	0.00001
MYO1A	A_23_P162288	4640	-1.82544	0.00309
origin recognition complex, subunit 6 homolog-like (yeast)	A_23_P100341	56452	-1.82658	7.46E-18
CYBRD1	A_24_P345451	73649	-1.82703	0.00278
DHRS6	A_23_P92490	69772	-1.82708	0.00004
FLJ00312	A_23_P115902		-1.82763	2.16E-08
FLJ20668	A_23_P7262	55016	-1.82779	0.00269
FLJ10671	A_24_P115287		-1.82976	1.66E-07
VAMP1	A_23_P105545	6843	-1.83148	4.00E-06
SIGLEC10	A_23_P208182	292844	-1.83148	4.67E-06
PI-3-kinase-related kinase	A_32_P142881	233789	-1.8326	2.12E-10
RPS26	A_32_P90987		-1.83328	5.64E-18
PIP5K2A	A_24_P673786	5305	-1.83452	0.00007
LOC340344	A_32_P47027		-1.83466	1.69E-07
CD3G	A_23_P98410	300678	-1.83571	0.00821
C10orf121	A_32_P104334		-1.83606	9.40E-09
LOC145741	A_32_P509169	691703	-1.83635	4.79E-07
LOC388760	A_23_P158997		-1.83862	0.00124
SLITRK5	A_32_P180111		-1.83966	0.00706
TRIM	A_23_P212568	77647	-1.84135	3.41E-09
GLI	A_23_P105251	2735	-1.84145	0.00819
VIT	A_23_P56578	313831	-1.84234	5.09E-12
PTPN7	A_23_P201778	5778	-1.84256	0.00866
MBD2	A_32_P107777		-1.84494	0.00523
A_24_P926484	A_24_P926484		-1.84555	1.01E-08
COCH	A_24_P184803	1690	-1.84646	1.05E-17
GLS	A_23_P39766	2744	-1.85144	0.00042
SCARF2	A_24_P108738	224024	-1.85258	2.16E-06
A_24_P462330	A_24_P462330		-1.85512	5.62E-13
similar to hypothetical protein LOC231503	A_23_P110412	360916	-1.85513	0.00409
LOC388335	A_23_P4069	388335	-1.85551	0.00167
RBMX	A_32_P56392		-1.85741	0.00957
NALP8	A_23_P351866	126205	-1.85805	0.00034
LOC283537	A_23_P105856	283537	-1.85816	0.00032
NR3C1	A_24_P787914		-1.85851	1.27E-17
RAFTLIN	A_23_P315571	76438	-1.85884	0.00091
SOX3	A_24_P113725	6658	-1.85894	0.00201
FLJ13621	A_24_P140481	305288	-1.86072	0.00067
KIAA0542	A_23_P80278	305467	-1.86117	1.12E-11
AQP3	A_23_P112481	65133	-1.86179	0.00006
CAM-KIIN	A_23_P18406	73047	-1.86262	5.28E-26
AL080082	A_32_P93045		-1.86363	0.00265
C20orf9	A_23_P165962	245866	-1.86419	0.00162
MYL6	A_32_P3600		-1.86568	4.71E-10
GLCCI1	A_23_P336198	500026	-1.86742	0.0001
THC1942218	A_32_P51524		-1.86804	3.39E-14
KPRT30847	A_32_P195788		-1.87052	0.00027
HOXA7	A_23_P70968	15404	-1.87279	0.00004

TXNRD1	A_32_P149416		-1.87456	0.00004
PHKA1	A_23_P258531	18679	-1.87538	0.00785
LOC92270	A_24_P807031	92270	-1.87575	3.88E-12
mannosidase, alpha,	A_23_P157943	499751	-1.87618	5.90E-06
TTRAP	A_23_P8311	51567	-1.87753	0.00022
KIAA1789	A_23_P125748	84460	-1.87967	0.0088
GPR18	A_23_P14165	110168	-1.88051	0.00074
THC1891432	A_32_P9931		-1.88121	0.00002
VKRH31259	A_32_P30831	729029	-1.88185	0.00256
similar to phosphatidylinositol	A_32_P507710	100131322	-1.8852	0.00118
CL683	A_23_P73972	298376	-1.88603	0.00039
CACNA1D	A_24_P880000		-1.88749	8.10E-11
LOC374405	A_32_P69333		-1.88865	0.00209
C14orf4	A_32_P466514	238330	-1.88944	4.74E-10
FLJ38359	A_24_P11737	100132017	-1.88948	1.32E-08
A_23_P130187	A_23_P130187		-1.89094	0.00002
KIAA0103	A_32_P115277		-1.89283	0.0036
FNBP1	A_24_P485105		-1.89569	0.00003
AQP1	A_23_P372834	25240	-1.89621	3.00E-09
CHDH	A_32_P73507		-1.89675	7.07E-07
FLJ20519	A_24_P234116	54964	-1.89728	0.00027
EIF4EBP2	A_23_P115922	361845	-1.89962	0.00092
PITPNC1	A_32_P3342		-1.89977	0.00006
PLA2G4C	A_23_P50508	8605	-1.90154	7.43E-12
VAV3	A_23_P201551	295378	-1.9022	3.61E-12
unknown	A_24_P586264		-1.90262	0.00001
KIAA1975	A_32_P34138	643161	-1.90296	0.00046
BC042469	A_32_P77102	100128420	-1.9049	1.93E-09
TRAF1	A_24_P89891	22029	-1.9066	0.00002
LOC441748	A_24_P350708		-1.90685	0.00048
SLC17A8	A_24_P124647	266767	-1.90821	0.00057
KHK	A_23_P5845	25659	-1.90942	0.00361
PCAF	A_23_P41128	8850	-1.90975	0.00333
ZHX2	A_32_P91328		-1.91031	0.00728
GLRX	A_23_P69908	2745	-1.91065	0.00002
FLJ39873	A_23_P80528	363784	-1.91257	0.0008
RBPSUH	A_32_P101002		-1.91261	5.26E-07
hIAN6	A_24_P132383	243374	-1.91323	0.00169
ZNF198	A_23_P105815		-1.9149	0.00679
ASAHL	A_24_P354488	67111	-1.91494	0.00035
RAPGEF6	A_24_P923934		-1.91576	4.68E-12
FLJ10613	A_23_P22499	237107	-1.9159	0.00013
KST1	A_23_P37914	252854	-1.91915	0.0013
FLJ35961	A_23_P51213	242702	-1.92099	0.00045
A_32_P161327	A_32_P161327		-1.92194	0.0073
CYP4F2	A_24_P168494	4051	-1.92366	0.00001
EVER2	A_23_P152992		-1.92422	4.72E-17
FUT6	A_23_P252664		-1.92528	6.80E-06
ASPA	A_24_P373475	443	-1.92648	0.00025
ITPR1	A_23_P92042	3708	-1.92709	0.00004
FLJ39647	A_23_P335388	284099	-1.92744	6.37E-07
BLNK	A_24_P565390		-1.92752	5.78E-08

STK17B	A_24_P636882		-1.9295	2.12E-07
NDRG1	A_24_P655888		-1.92965	4.05E-13
DOCK11	A_23_P148584	139818	-1.93203	6.19E-08
LOC440133	A_32_P151747		-1.93416	0.0007
FLJ14399	A_23_P203115	689172	-1.93489	0.00015
SSR1	A_32_P226073		-1.93671	5.09E-07
LIN7A	A_24_P867201		-1.9374	0.00002
TEGT	A_24_P355876	7009	-1.93751	0.00002
LOC123688	A_24_P602507	300723	-1.93962	0.00206
SLC1A2	A_23_P162068	20511	-1.94048	0.00066
AATK	A_23_P10559	690853	-1.9409	0.00032
EBF	A_32_P197561	13591	-1.94343	0.0002
LOC388221	A_24_P926025		-1.94481	0.00009
GP1BA	A_23_P152926		-1.94758	0.0042
FLJ10094	A_23_P128574	306038	-1.94949	0.00007
ENST00000315091	A_32_P2148		-1.95155	0.00844
SOAT2	A_23_P25475	223920	-1.9561	0.0026
KIAA0922	A_23_P257250	229473	-1.9575	1.20E-08
PCK1	A_23_P408249	362282	-1.95855	0.00553
ABCG5	A_23_P119763	64240	-1.9592	0.0016
LOC388077	A_24_P177844		-1.96183	0.0005
TLX2	A_24_P328446	3196	-1.96393	0.00001
PHTF2	A_24_P323944	57157	-1.96415	0.0086
FGB	A_24_P550411		-1.96669	1.62E-09
PTGDR	A_23_P3083	498475	-1.9673	0.00094
LOC388221	A_32_P89087		-1.96742	0.0011
APBB1IP	A_23_P12549	307171	-1.9688	0.00914
NBEA	A_23_P65278	26960	-1.96884	3.89E-06
CD48	A_32_P175934	962	-1.96952	0.00224
NIN	A_23_P396353	18080	-1.97359	4.16E-07
DGAT1	A_23_P112162	84497	-1.97442	0.00031
C10orf81	A_24_P286951	499377	-1.97479	5.57E-08
GPR64	A_23_P253692	266735	-1.97541	0.00641
MGAT3	A_24_P245838	17309	-1.97653	0.00009
THC1946056	A_32_P128603		-1.97898	0.00074
GPNMB	A_23_P134426	10457	-1.97902	0.0004
MALT1	A_32_P76576		-1.97986	0.00016
C21orf93	A_24_P100190	246704	-1.98065	4.35E-16
FLJ32028	A_23_P361584	320782	-1.98088	0.00404
FZD7	A_23_P209449	8324	-1.98129	5.15E-18
JARID2	A_24_P914102		-1.98675	1.83E-19
PLEKHA2	A_32_P35603		-1.98861	0.00317
ARPC2	A_32_P465526		-1.98895	4.22E-08
LAPTM5	A_23_P86283	89783	-1.99013	0.00047
A_32_P192853	A_32_P192853		-1.99117	0.00682
CUBN	A_23_P127027	8029	-1.99685	1.34E-06
TM4SF1	A_32_P25419		-1.99709	0.00175
zinc finger protein 292	A_24_P937119	30046	-2.00223	7.68E-09
ND4	A_23_P360209		-2.00321	0.00001
APOA4	A_23_P87036	337	-2.00414	0.00019
SFMBT2	A_32_P84714		-2.00428	3.72E-06
BM689022	A_24_P670342		-2.0069	0.00008

GGA2	A_32_P42149		-2.00913	0.00007
FLJ22570	A_32_P121085	306760	-2.00985	0.0027
BTG1	A_23_P87560	12226	-2.01014	1.15E-34
MSN	A_23_P73589		-2.01234	1.60E-06
ZNF264	A_24_P176805	9422	-2.01307	0.0004
CYBRD1	A_23_P209564	73649	-2.01499	0.00057
SLC19A3	A_23_P39871	316559	-2.01551	0.00002
ADCY7	A_24_P416177	84420	-2.01607	2.66E-06
RPS20	A_32_P171790		-2.01852	5.87E-06
GNB5	A_23_P205778	10681	-2.01919	0.00071
RPEL1	A_32_P52018	221692	-2.02207	0.00053
CYB5	A_23_P101208	1528	-2.02338	0.00018
SLC5A1	A_23_P17826	6523	-2.02365	0.00569
BG213769	A_32_P20040		-2.02456	0.00276
GLIPR1	A_24_P390096	299783	-2.02604	0.00008
FOXP1	A_32_P146844		-2.0263	1.97E-06
GDA	A_24_P393571	83585	-2.02805	0.00035
FLJ21195	A_24_P40626	64388	-2.02917	0.00009
C9orf71	A_24_P725998		-2.0294	0.00009
DKFZp434C0328	A_23_P253012	360717	-2.02977	0.00002
LUM	A_23_P99063	81682	-2.03242	1.27E-07
AGT	A_23_P115261	183	-2.03393	0.00003
DSCR8	A_23_P6252	84677	-2.03437	0.0006
TCF4	A_24_P931428	84382	-2.03754	0.00032
XPNPEP2	A_23_P83659	7512	-2.04041	0.00077
SLC23A2	A_23_P21990	50621	-2.04475	0.00038
RSAFD1	A_24_P883109		-2.04611	3.30E-07
RetSDR2	A_23_P21644	114664	-2.04701	9.28E-10
FLJ22814	A_24_P254106		-2.05244	0.00007
KIAA1582	A_24_P857624		-2.05519	0.00002
MGC9515	A_32_P187715		-2.05623	0.00017
RP11-57K17.2	A_24_P865	387119	-2.05672	0.00006
CLU	A_32_P113322		-2.05735	0.00077
CD1E	A_23_P201160	913	-2.05961	1.16E-07
CYP2J2	A_23_P103486	13110	-2.06413	0.00003
LOC91526	A_23_P209347	91526	-2.06755	0.00183
SPAP1	A_23_P160751	79368	-2.06853	0.0085
MMP12	A_23_P150316	17381	-2.07026	4.20E-08
RUFY1	A_32_P159787		-2.07368	1.06E-08
CST	A_23_P120863	9514	-2.07371	0.00001
SMPDL3A	A_23_P72117	10924	-2.07415	5.28E-08
LOC344760	A_24_P739355		-2.0777	5.04E-06
P2RX5	A_23_P433785	94045	-2.08372	0.00018
A_32_P57013	A_32_P57013		-2.08862	4.73E-07
MTBP	A_23_P357794	27085	-2.08968	0.00196
LOC400509	A_32_P47200		-2.09039	5.91E-06
EVER1	A_24_P152743		-2.09088	0.0006
CD44	A_23_P24870	960	-2.09493	6.51E-09
GSTA2	A_24_P300394	2939	-2.09978	0.00004
RBP5	A_24_P386746	83758	-2.10312	0.00006
taxilin	A_23_P51361	109658	-2.10346	0.00003
MAF	A_23_P397376	4094	-2.10523	0.0001

ITIH5	A_32_P44878		-2.10598	0.00067
PRO1073	A_24_P935147	238055	-2.1079	0.00098
THC1818940	A_32_P212108		-2.11332	3.96E-08
ZHX2	A_32_P227657		-2.11829	0.00653
KIAA1586	A_24_P101047	57691	-2.1229	0.00981
kinesin family member 14	A_23_P149668	360849	-2.1245	0.00073
LOC152573	A_23_P41476	330096	-2.12589	5.03E-07
retSDR4	A_23_P117506	299135	-2.12602	2.03E-08
zinc finger protein,	A_23_P124934		-2.12774	0.00214
PLXNC1	A_24_P196351		-2.13272	5.64E-06
RQNF14971	A_24_P548415		-2.13633	0.00399
MAML2	A_32_P61708		-2.13707	4.78E-07
CD3D	A_23_P138985	12500	-2.14422	0.00002
LOC197322	A_24_P239309		-2.14992	0.00007
PLA2G12B	A_24_P700562		-2.15026	2.34E-09
KCNH6	A_23_P390984		-2.15059	0.00017
FOXO1A	A_24_P930391		-2.15359	0.00879
FOXP4	A_24_P371892	363185	-2.15498	0.00919
LOC91614	A_23_P385126	91614	-2.15686	0.00007
PC-LKC	A_23_P133338	54825	-2.15835	0.00005
C20orf39	A_23_P251043	79953	-2.1608	0.00057
G6PC	A_23_P207371	25634	-2.16365	4.68E-10
ASPA	A_23_P164436	443	-2.16962	6.36E-10
CA503163	A_32_P15756		-2.17545	3.89E-13
KIAA0470	A_23_P348857	645455	-2.17876	0.008
ZNF434	A_32_P330691		-2.17934	0.00002
SLC7A7	A_23_P99642	9056	-2.18101	0.00015
FKSG28	A_24_P192727	293997	-2.19054	8.21E-09
FBP1	A_23_P257111	24362	-2.19146	0.00392
FLJ32191	A_23_P380951	499120	-2.19615	0.00343
ABHD6	A_23_P211850	57406	-2.19635	4.52E-13
STAU2	A_24_P374634	27067	-2.19796	0.00002
FKBP6	A_32_P132883		-2.19819	0.00071
CCRK	A_23_P20752	105278	-2.19844	2.48E-07
A_32_P89277	A_32_P89277		-2.19853	0.00005
LOC54103	A_23_P416894	212167	-2.20308	1.28E-07
COCH	A_24_P184799	1690	-2.20426	0.00004
ARHGAP15	A_23_P255166	295635	-2.20847	0.00088
TAF1	A_23_P11237	6872	-2.21044	9.21E-07
NAP1L1	A_23_P53646	89825	-2.21316	9.79E-16
A_32_P213103	A_32_P213103		-2.21523	0.00084
BCCIP	A_24_P1255	66165	-2.21578	0.00146
A_32_P57213	A_32_P57213		-2.21606	0.00877
PEPD	A_23_P83436	18624	-2.21784	0.00071
HIC	A_23_P327022	16543	-2.21799	4.56E-09
FLI1	A_24_P355649	2313	-2.21826	3.91E-10
IRF5	A_23_P500271	27056	-2.2197	2.82E-11
PIK3CG	A_24_P637651		-2.22388	3.74E-06
similar to Ab2-183	A_32_P101352	158830	-2.22788	0.00059
MAF	A_24_P256219	4094	-2.22841	0.00069
AVP	A_23_P109133	24221	-2.22937	0.00006
FYN	A_32_P184039		-2.23759	0.00003

CREB-H	A_23_P108082	208677	-2.23826	2.29E-06
CPO_2	A_23_P102172	130749	-2.23982	0.00002
ADAM28	A_23_P10356	10863	-2.24042	0.00455
SWAP70	A_24_P359165		-2.24316	1.20E-08
C7orf23	A_32_P37584		-2.24558	1.58E-06
SORL1	A_23_P87049	6653	-2.2467	2.34E-09
BLK	A_23_P31725	640	-2.24703	0.00114
BCNP1	A_24_P940348	199786	-2.24824	0.00361
CYP2C9	A_23_P12767	29277	-2.25883	2.96E-06
BPNT1	A_24_P122636	10380	-2.26006	1.69E-08
PCOLCE2	A_23_P57709	26577	-2.26206	0.00836
MGC52019	A_23_P12928	159963	-2.26641	0.00004
THC1835187	A_24_P494658		-2.26693	5.15E-08
SLC17A8	A_23_P159076	266767	-2.27021	0.00017
CD69	A_23_P87879	12515	-2.27109	0.00353
GPR65	A_23_P14564	299242	-2.27119	1.03E-06
HPS3	A_32_P109078		-2.27153	8.42E-08
SLC26A1	A_24_P37665	64076	-2.27214	1.42E-12
CD96	A_23_P44155	84544	-2.28697	8.32E-09
CYP3A7	A_23_P358917	13113	-2.28845	3.59E-12
MSI2	A_32_P86264		-2.29397	0.00072
TRPM6	A_23_P216712	140803	-2.2953	1.57E-09
DKFZP586A0522	A_24_P941773	25840	-2.29749	0.0022
OSCAR	A_23_P50368	232790	-2.29973	0.00004
PRG1	A_23_P86653	19073	-2.30853	1.48E-08
PLEKHG1	A_32_P137819		-2.31139	0.00049
ALPP	A_23_P79587	367308	-2.31653	0.00004
C4ST3	A_23_P80473	166012	-2.3269	1.04E-09
DNASE1	A_23_P66311	13419	-2.32766	0.00192
ALDH1A3	A_23_P205959	56847	-2.33337	0.00795
SLC9A9	A_32_P46214	331004	-2.33359	0.00047
KIAA0053	A_23_P142974	500246	-2.33426	0.00013
DATF1	A_32_P19917		-2.33648	9.65E-18
REG1A	A_23_P90743	19692	-2.34031	2.55E-06
KCNK7	A_23_P86874	16530	-2.34108	1.34E-11
BCL2	A_23_P352266	12043	-2.34109	3.33E-12
GPR78	A_23_P69652	27201	-2.34684	1.31E-10
RAN	A_32_P125233		-2.35288	0.00291
BX115350	A_32_P228886		-2.35717	7.62E-10
PLA2G7	A_23_P145096	27226	-2.36266	0.00012
BG182941	A_24_P920135		-2.36521	1.14E-13
SLC7A9	A_23_P142250	11136	-2.3664	2.14E-06
TFEC	A_32_P184394	26296	-2.36922	0.00058
LOC201175	A_23_P401626	70559	-2.37547	0.00005
PDE7A	A_23_P123478	81744	-2.37783	5.39E-08
MME	A_24_P260101	17380	-2.38279	0.00157
SLC6A5	A_23_P116624	104245	-2.38498	1.51E-06
PCK2	A_23_P140207	361042	-2.38513	0.00051
CD48	A_23_P74145	962	-2.38619	0.00505
LOC388235	A_32_P62106		-2.38845	7.11E-17
OLFM1	A_24_P406601	10439	-2.38984	0.00036
UNQ1971	A_23_P76136		-2.39543	0.00016

LOC439949	A_32_P232559	439949	-2.39705	6.49E-42
IRTA2	A_23_P201211	83416	-2.40494	0.00798
GNGT1	A_32_P108938		-2.4053	2.00E-06
FLJ00267	A_23_P35045	226652	-2.40625	0.00937
CBR1	A_23_P29046	873	-2.40654	0.00036
GUCA2B	A_23_P63032	14916	-2.41266	0.00027
FCHSD2	A_32_P138409		-2.415	0.00015
GNG4	A_23_P335329	2786	-2.41732	9.77E-09
ITGAL	A_23_P206806	308995	-2.41815	0.00002
MMP12	A_23_P340698	17381	-2.41873	3.44E-08
LIN7A	A_23_P99253	108030	-2.42177	0.00001
LOC388235	A_32_P48198	400509	-2.43346	0.00013
CYP2B6	A_24_P339514	1556	-2.43913	5.48E-07
BLR1	A_24_P252945	12145	-2.4435	0.00039
SNRPN	A_23_P335143		-2.44555	0.00398
KIAA1789	A_24_P11100	84460	-2.44946	0.00011
SLC39A4	A_23_P20502	300051	-2.4519	1.75E-10
FLJ34870 protein	A_24_P298224	363974	-2.46258	7.01E-12
UGT2B7	A_23_P136671	286989	-2.46691	2.57E-16
FOXD1	A_32_P34920	2297	-2.46954	1.16E-18
AX775927	A_32_P148627		-2.47047	1.11E-06
LOC340152	A_24_P187826		-2.4717	2.41E-08
THC1902708	A_32_P879150		-2.48042	0.00057
DKFZp761P0423	A_23_P250212	244418	-2.49024	8.75E-35
ATM	A_23_P35916	651610	-2.49607	5.44E-08
TNNC2	A_23_P131825	7125	-2.49715	0.00061
RGS13	A_23_P500093	246709	-2.49872	0.00039
NOD3	A_23_P340019		-2.5056	0.00005
LAMA1	A_32_P313405	16772	-2.50721	3.71E-09
GZMK	A_23_P156218	3003	-2.50735	4.61E-07
ABCG2	A_23_P18713	312382	-2.51192	0.0001
DTX4	A_24_P153568	17476	-2.51343	6.20E-06
GSTA1	A_23_P135417	2938	-2.51963	0.00006
AK129584	A_32_P93328	100131931	-2.52192	7.77E-12
G6PC	A_23_P385017	25634	-2.52387	3.44E-11
PDZK1	A_23_P52121	5174	-2.54091	0.00017
SLIC1	A_24_P364825		-2.54345	9.03E-08
apolipoprotein A-IV	A_24_P252934	337	-2.54814	1.12E-06
A_32_P138666	A_32_P138666		-2.5484	0.00004
LOC440666	A_32_P34365		-2.56933	1.12E-24
GSTA5	A_23_P93141	14858	-2.58283	0.00015
MS4A6A	A_23_P203376	64231	-2.60145	0.00041
GUCA2A	A_23_P11968	25656	-2.61323	0.00034
SLC10A2	A_23_P140009	6555	-2.62446	0.00017
CES2	A_24_P13790	436059	-2.63753	1.11E-07
RASSF2	A_23_P166087	215653	-2.642	2.13E-06
TNFSF11	A_23_P99386	21943	-2.65562	7.09E-06
THC1814602	A_32_P162862		-2.65678	0.00367
AA151106	A_32_P209778		-2.66032	0.00098
DPEP1	A_23_P152262	1800	-2.67446	1.20E-06
HAK	A_23_P15876	498875	-2.68556	0.00029
ACTG2	A_23_P39955	72	-2.69074	3.68E-13

OTTHUMP00000019572	A_24_P346859	69069	-2.69326	4.03E-08
FLJ00026	A_32_P181077	81704	-2.70285	0.00001
SIAT8A	A_23_P354705	20449	-2.7087	0.00235
ND4	A_23_P360213		-2.70947	1.48E-06
A_23_P21882	A_23_P21882		-2.72151	8.79E-09
P2RY8	A_24_P340128	286530	-2.73216	1.55E-06
PNLIPRP2	A_23_P24083	117554	-2.74255	0.00065
C8FW	A_32_P38821		-2.74842	0.00084
UPA	A_23_P202275	60574	-2.75694	4.56E-09
IL16	A_24_P73599	16170	-2.75792	0.00849
ZDHHC11	A_24_P153456	79844	-2.76328	0.00001
similar to MGC9515 protein	A_32_P215143		-2.77556	0.00577
COL25A1	A_32_P115087		-2.79406	0.00017
HLA-DOB	A_32_P193194		-2.80245	0.00044
ZDHHC11	A_23_P256008	79844	-2.80372	0.00002
GBA3	A_23_P18672	289687	-2.8088	6.43E-06
TMC7	A_32_P8351		-2.83038	8.81E-20
THC1873675	A_32_P17343		-2.83605	6.33E-07
SEPP1	A_23_P121926	29360	-2.83947	7.40E-06
CCR6	A_24_P234921	75296	-2.84182	1.43E-14
UST	A_32_P62371		-2.85739	0.00025
similar to FLJ43276 protein	A_24_P555170		-2.88872	0.00192
KIF1C	A_23_P107369	16562	-2.90963	9.22E-09
A_24_P110601	A_24_P110601		-2.91932	6.87E-11
ACE2	A_23_P252981	302668	-2.93761	5.94E-10
LEAP-2	A_24_P268993	497901	-2.93858	1.21E-09
ITGA4	A_24_P915464		-2.95079	0.00002
SULT2A1	A_24_P224684	20859	-2.95333	0.00003
CML2	A_24_P308506	51471	-2.99026	2.36E-14
ANKRD17	A_24_P220771	289521	-3.00861	0.00839
GSTA1	A_23_P214300	2939	-3.01367	0.00007
DJ434O14.3	A_23_P323761	360900	-3.01729	0.00025
PMP22	A_23_P100711	5376	-3.03801	0.00003
IL27RA	A_24_P348326	9466	-3.0412	5.56E-07
SSAT2	A_23_P15402	360547	-3.04695	8.67E-06
TM4SF5	A_23_P27107	75604	-3.07196	5.21E-08
LIPA	A_23_P97860	25055	-3.07513	0.00019
ECT2	A_24_P366033	1894	-3.08247	0.00009
CD1C	A_23_P51767	911	-3.09825	1.26E-08
ARHGAP15	A_23_P84154	295635	-3.10217	2.68E-10
MEF2B	A_24_P282013	100133072	-3.13545	4.31E-11
APOM	A_23_P42265	55939	-3.1532	2.63E-09
PDE7A	A_24_P360529	81744	-3.16143	6.45E-13
THC1906402	A_32_P105694		-3.1615	3.58E-06
CARD11	A_24_P945262		-3.16488	3.10E-06
CXCL13	A_23_P121695	55985	-3.18101	2.06E-06
LTF	A_23_P166848	4057	-3.18891	0.0005
LIMD1	A_23_P434965	8994	-3.19562	0.00043
FLVCR	A_32_P201958		-3.19978	6.06E-16
CRIP2	A_23_P44674	1396	-3.23307	8.33E-13
FYB	A_24_P393740	499537	-3.30763	7.94E-10
LOC283892	A_32_P64016		-3.32168	0.00294

MGAM	A_23_P42897	8972	-3.36198	1.92E-06
SLC6A4	A_23_P152995	6532	-3.37499	0.00043
LGALS2	A_23_P120902	171134	-3.37686	3.28E-10
LOC51152	A_24_P214184	51152	-3.40822	0.00081
NAT8	A_23_P154379	68396	-3.43094	2.71E-16
LOC440345	A_32_P11359		-3.48394	2.55E-17
TEP1	A_24_P201973	7011	-3.52629	0.00001
FCHSD2	A_32_P163594		-3.55842	6.82E-08
PLB1	A_23_P56356	665270	-3.56248	1.84E-06
AIM2	A_32_P44394	383619	-3.61905	5.49E-10
NELL2	A_23_P10025	81734	-3.62091	9.93E-17
LOC91526	A_24_P128713	91526	-3.64893	0.00035
LEF1	A_24_P20630	16842	-3.65274	0
P2RY10	A_23_P217187		-3.72966	0.00048
TARSH	A_23_P218858	25890	-3.73628	0.00216
GSTA3	A_23_P253495	14859	-3.73688	1.76E-06
CD28	A_23_P91095	940	-3.76214	1.77E-17
ENST00000333536	A_32_P64461	100129513	-3.76941	5.53E-07
MGC32805	A_32_P888644		-3.86994	0.00176
PDE7A	A_32_P137382		-3.91006	0.00002
OAT	A_23_P98092	64313	-4.03563	1.20E-07
AGXT2	A_23_P156076	83784	-4.07194	7.83E-17
PRODH2	A_32_P13555	4868	-4.12052	0.00361
C4orf7	A_23_P362694	260436	-4.22845	0.00903
APOB	A_23_P79591	238055	-4.24795	0.0001
TNFRSF13C	A_24_P621701		-4.32485	6.71E-06
HEBP1	A_23_P117082	15199	-4.43185	3.24E-09
ARHGAP24	A_32_P72067		-4.48983	7.05E-10
LOC375180	A_32_P49764		-4.52586	3.49E-12
SUSD2	A_23_P314101	294335	-4.683	6.76E-06
AGXT2	A_24_P63468	83784	-4.84685	0.00011
CYFIP2	A_24_P465879		-4.89606	0.0001
FNBP1	A_24_P899020		-4.92271	7.33E-19
SLC28A2	A_23_P48816	60423	-5.02797	1.05E-15
OTTHUMP00000011522	A_23_P45821	338094	-5.03803	2.68E-08
PAX8	A_23_P324916	18510	-5.80485	0.00263
CXCR4	A_23_P102000	12767	-6.01856	8.18E-18
CGGA17790	A_32_P203728		-6.46865	0.00016
APOA1	A_23_P203191	11806	-6.8623	0.00305
C6orf32	A_24_P941359	306934	-7.02034	1.09E-13
NPPC	A_24_P174353		-7.14015	0.00395
CCL23	A_24_P133905	6368	-7.14857	1.62E-10
APOC3	A_23_P203183	345	-8.17858	7.02E-08
IRTA1	A_23_P115200	83417	-9.62094	6.82E-06
MGC27169	A_23_P407695	338094	-9.89477	4.82E-08
IRTA1	A_23_P115201	83417	-11.4284	4.72E-12

Figure 26

Sequence Name(s)	Sequence Code	Entrez Gene	Fold Change	P-value
SAA1	A_24_P335092	6288	6.33671	5.34E-08
PRO1073	A_24_P829261		3.52163	4.74E-22
IGSF6	A_23_P106629	10261	3.20438	4.44E-07
GPNMB	A_23_P134426	10457	3.06185	7.08E-14
hypothetical protein FLJ34236	A_24_P172600	283373	2.86324	5.80E-06
cig5	A_24_P316965	91543	2.81735	1.58E-07
UNG2	A_23_P92860	499528	2.60157	1.21E-10
SECTM1	A_24_P48204	6398	2.55036	0.00003
chromosome 10 open reading frame 81	A_23_P23980	499377	2.51416	0.00031
AF267875	A_24_P179107		2.45637	0.00001
FLJ31842	A_32_P19539		2.45126	1.06E-07
immunoglobulin kappa constant	A_24_P263786	651751	2.37967	0.00078
MS4A4A	A_23_P75769	361734	2.37141	7.41E-11
immunoglobulin lambda constant 1 (Mcg marker)	A_23_P72252	28793	2.33179	2.02E-08
APP	A_24_P314159	351	2.29136	2.69E-08
FLJ00310	A_32_P109604		2.27024	2.30E-11
TRIM31	A_23_P122493	294208	2.26583	9.38E-10
NEK3	A_24_P921966		2.25049	0.00373
AQP8	A_23_P26522	343	2.24191	2.51E-07
SLC26A2	A_23_P250951	13521	2.20102	9.54E-14
MGC27165	A_24_P100684	28396	2.19846	4.36E-06
hypothetical protein FLJ22671	A_23_P60990	71874	2.1952	0.0003
hypothetical protein MGC27165	A_24_P590547		2.19192	6.57E-11
LOC402619	A_24_P548795		2.17797	0.00035
OTTHUMP00000064579	A_32_P4792		2.14534	0.0005
SEPP1	A_23_P121926	29360	2.11948	3.39E-06
LOC204777	A_24_P204374		2.06686	9.62E-07
THC1975338	A_24_P681218		2.04814	1.24E-11
IgH	A_24_P15388		2.04428	6.87E-07
hypothetical protein FLJ14966	A_23_P2041	84953	2.03083	2.69E-07
IGLC2	A_24_P465799		2.02945	1.49E-06
IGHG1	A_24_P604784		2.02842	0.00035
CLDN8	A_23_P427014	54420	2.01686	3.96E-10
HLA-C	A_23_P70539	3107	2.01468	3.77E-18
MGC27165	A_24_P488083	28396	2.01433	6.73E-06
CNGA1	A_24_P256722	1259	2.01334	0.0001
LOC129026	A_23_P435390		1.99807	0.00017
C6orf123	A_23_P70813	1001330 56	1.99653	4.17E-07
P5-1	A_32_P220770		1.99121	2.58E-06
Sprn	A_24_P930415	503542	1.98392	0.00928
LIMK1	A_23_P215461	65172	1.98193	3.59E-09
immunoglobulin lambda constant 1 (Mcg marker)	A_24_P605563	28815	1.96567	0.00005
IGLL1	A_24_P83102	3543	1.95395	0.00003
AB063751	A_23_P21249		1.94372	1.03E-07
TEX11	A_23_P96501	56159	1.94274	0.00005
DKFZp761N1114	A_24_P51115	213006	1.93269	4.92E-06

ATP8A1	A_23_P30075	11980	1.92913	0.00322
LOC153328	A_23_P424051	328258	1.92026	0.00003
C14orf81	A_24_P323298		1.91886	0.00002
FLJ31952	A_23_P332413	146857	1.91634	0.00214
PLCB4	A_23_P28898	25031	1.91617	3.81E-18
FRMD3	A_23_P135132	298141	1.91455	0.0073
ADAMTSL3	A_23_P43940	269959	1.90545	0.00682
DKFZp686N02209	A_23_P124632	3493	1.90251	0.00003
IFIT2	A_24_P304071	15958	1.90225	0.00101
LOC285189	A_32_P197825	100134363	1.89372	0.00416
PRV1	A_23_P259868	499099	1.8812	2.19E-07
FBXO13	A_32_P137632	64839	1.8649	4.27E-15
OTTHUMP00000028776	A_24_P239076	91353	1.86172	0.00016
SST	A_23_P252817	6750	1.86114	0.00366
LOC441430	A_24_P851132		1.85431	2.81E-06
SEMA6A	A_24_P857669		1.84652	2.38E-22
HLA-G	A_24_P263767	649853	1.84117	6.54E-10
TPM1	A_24_P179244		1.839	0.00246
LAX	A_24_P370952	54900	1.83893	0.0056
CTSZ	A_23_P40240	1522	1.83791	0.00683
TSSL31215	A_32_P189781	645687	1.82521	2.41E-09
MLSTD1	A_24_P341646		1.82118	0.0017
similar to Ankyrin repeat domain protein 18A	A_24_P84220	645626	1.81876	1.99E-06
IGHM	A_24_P813550		1.80962	0.00093
EFNA1	A_23_P254512	13636	1.80887	8.36E-07
CaMKIINalpha	A_23_P11800	287005	1.80787	2.01E-19
MGC27165	A_24_P702749	28396	1.8064	0.00067
similar to polycythemia rubra vera 1; cell surface receptor	A_32_P157213		1.80108	5.54E-07
ITGB6	A_23_P154217	311061	1.79716	0.0042
MUC20	A_23_P92222	200958	1.79458	7.40E-13
HCG3 gene	A_32_P2362	414061	1.7847	0.00001
FN1	A_24_P119745	14268	1.77961	0.00432
FLJ45422	A_24_P110012		1.77204	2.12E-16
NMA	A_23_P52207	68010	1.77147	0.00005
TTTY1	A_24_P323131	50858	1.76728	0.00889
UGT2B11	A_23_P212968	24862	1.76701	0.00071
MGC14407	A_24_P300610		1.76631	0.001
BTNL8	A_24_P851254		1.76165	0.00014
SGK2	A_23_P131801	171497	1.76012	5.01E-08
EEF1A1	A_32_P44316		1.75257	1.35E-09
A_23_P96191	A_23_P96191		1.74999	4.81E-08
LOC388820	A_32_P49516		1.74914	0.00006
MGC27165	A_23_P259763		1.749	0.00242
immunoglobulin lambda constant 1 (Mcg marker)	A_24_P318990		1.7479	2.42E-07
UNQ2492	A_23_P44335	72090	1.74658	0.00002
GSCL	A_23_P109382	2928	1.73427	0.0041
CDON	A_23_P98335	50938	1.7277	0.00138
ZNF483	A_24_P198044	158399	1.72746	0.00127
CREB-H	A_23_P108082	208677	1.7262	0.00295
NMNAT3	A_23_P69089		1.72612	0.00856
major histocompatibility complex, class I, B	A_24_P101771	3107	1.7257	4.46E-06

IGHM	A_24_P417352	100133862	1.72159	4.27E-12
HOXA5	A_23_P93772	3202	1.71886	1.98E-10
LOC134147	A_23_P144668	134147	1.71504	5.95E-15
MT1G	A_23_P206707	4495	1.71293	3.96E-07
12MelaCE5B3CD	A_24_P920573		1.71245	0.00186
FLRT1	A_23_P47168	23769	1.70994	0.00007
MGC27165	A_32_P51988		1.70979	0.00003
SLC4A4	A_23_P22205	54403	1.70293	1.72E-11
HHLA2	A_23_P368805	11148	1.70126	5.13E-07
AQP12	A_23_P142856	367316	1.69963	0.00012
LOC285016	A_24_P561341	285016	1.69889	0.00036
UBR1	A_24_P102203	22222	1.69754	0.00009
COLM	A_24_P698125		1.68876	0.0019
similar to ankyrin repeat domain 20A	A_32_P66222	391269	1.68828	2.21E-08
RASSF6	A_23_P302404	73246	1.6861	8.24E-06
AK092468	A_32_P46404		1.68346	1.57E-07
ENST00000327386	A_24_P247117		1.68205	0.00221
SECTM1	A_23_P207905	6398	1.68168	4.97E-13
IGLJ3	A_24_P519504		1.68032	0.00103
BF675806	A_32_P702236		1.67896	0.00788
LUM	A_23_P99063	81682	1.67784	0.00014
MUCDHL	A_24_P352388	53841	1.67637	0.0064
HIST1H1C	A_23_P122443	3006	1.67564	4.06E-12
01-Sep	A_24_P393353	300944	1.67422	0.0025
IGLJ3	A_24_P510357		1.67166	7.59E-08
LU	A_23_P55716	57278	1.6693	0.00001
BC020923	A_23_P311895	94272	1.66904	2.24E-11
RIPK3	A_23_P14559	11035	1.66866	0.00002
11-Sep	A_24_P934008		1.66865	0.0087
LOC283970	A_24_P870101		1.66683	7.55E-06
similar to Ankyrin repeat domain protein 18A	A_32_P150086		1.66499	4.84E-08
FLJ22944	A_24_P38722	365476	1.66424	0.00979
DKFZp667J0810	A_24_P538459		1.66378	0.00002
LOC93082	A_23_P328740	93082	1.66324	7.52E-07
MAWBP	A_23_P149998	68371	1.66211	7.05E-09
P2RY1	A_24_P225845		1.66208	7.54E-07
KIAA1109	A_24_P937135	229227	1.66199	0.00821
WCV29794	A_32_P152586		1.65913	0.00222
PRV1	A_32_P143589	499099	1.6587	0.00004
EMP1	A_23_P76488	13730	1.65693	8.10E-07
ENST00000333419	A_24_P229447		1.65591	7.85E-08
tumor differentially expressed 2-like	A_24_P145629	313057	1.65518	2.53E-10
AK127222	A_24_P848126		1.64842	0.00307
ECGP	A_23_P27822	292810	1.64532	4.23E-07
CA3	A_23_P20316	54232	1.64471	0.00743
A_23_P84791	A_23_P84791		1.64169	2.24E-06
FLJ10824	A_23_P311847	253725	1.63841	2.41E-31
hypothetical LOC401131	A_32_P79190		1.638	1.96E-07
MAML3	A_32_P132936		1.63572	0.00078
CRG-L2	A_24_P49199	342035	1.63544	0.0046
MYLIP	A_23_P31041	218203	1.63505	2.52E-12
GPR105	A_24_P165864	9934	1.63416	0.00465

IGLV8S1	A_23_P159435		1.63407	0.00012
C1QB	A_23_P137366	29687	1.6297	0.00053
TCF7L2	A_23_P149798	79938	1.62951	8.69E-18
FMO5	A_24_P71341	14263	1.62495	5.25E-13
LOC440361	A_24_P144346	100132941	1.6238	0.0003
similar to immunoglobulin heavy chain VH3	A_24_P384119		1.62256	9.83E-06
cig5	A_24_P28722	65190	1.62145	0.00271
ZDHHC11	A_24_P153456	79844	1.62131	0.00196
IGJ	A_23_P167168	360922	1.62119	0.00782
FLJ14146	A_23_P160433	79762	1.61885	0.00145
HLA-E	A_23_P30848	3133	1.61731	2.79E-09
KIAA1239	A_23_P396934		1.61588	0.00001
CNK2	A_23_P428887	302703	1.61545	1.30E-10
EFNA5	A_32_P11673		1.61511	0.00644
CDC2L2	A_24_P355772	315362	1.61487	3.73E-07
SCNN1G	A_23_P206626	20278	1.61468	0.00717
Ig V<kappa}	A_23_P361654		1.61362	0.00555
FLJ31614	A_32_P231568	242505	1.60467	0.00007
DAO	A_23_P139635	114027	1.60376	0.00016
ABHD2	A_24_P924920		1.60278	0.00558
RPIB9	A_23_P111724	154661	1.60122	1.88E-08
PLEKHB2	A_24_P20200	226971	1.59845	5.83E-08
A_32_P42137	A_32_P42137		1.59628	0.0035
MLLT4	A_23_P344694		1.59556	0.00075
C21orf81	A_23_P392529	114035	1.5949	5.66E-09
A_23_P158699	A_23_P158699		1.59318	0.00165
C10orf74	A_23_P75033	28193	1.59174	3.08E-16
MYO7B	A_23_P209799	4648	1.58912	0.00019
BU729325	A_24_P816073		1.58891	7.36E-07
selenium binding protein 1	A_23_P74619	8991	1.58853	8.11E-07
UNQ338	A_23_P94434	646962	1.58846	0.00666
LOC124199	A_24_P714620		1.58832	0.00002
OTTHUMP00000031241	A_23_P28797		1.58775	3.76E-16
DIP13B	A_23_P105747	362860	1.58705	0.00002
major histocompatibility complex, class I, B	A_23_P125107	3106	1.58684	4.68E-10
SATB2	A_24_P928408		1.58626	8.94E-07
F2RL1	A_23_P58835	14063	1.58337	2.12E-07
similar to tripartite motif-containing 43	A_23_P12972	642446	1.58268	0.00008
FLJ25224	A_24_P59430	78252	1.58258	0.00003
CDC14B	A_24_P69525	8555	1.58227	0.00231
NRAP	A_23_P402765	18175	1.58209	0.00001
PDCD6IP	A_32_P22338	10015	1.58088	3.44E-08
LOC388503	A_32_P14582	388503	1.58065	0.00807
IgH	A_24_P24053		1.57785	0.00284
ZFP67	A_24_P19884	51043	1.57751	3.07E-08
LOC346113	A_24_P58647		1.57599	9.07E-17
VPS13A	A_23_P9472	271564	1.57561	6.54E-10
unknown	A_24_P51316		1.57212	0.00412
similar to ankyrin repeat domain 20A	A_32_P168326		1.56933	4.85E-09
A_24_P773958	A_24_P773958		1.56925	5.70E-15
FLJ21687	A_23_P84941	54634	1.56889	5.34E-06
TRIM15	A_23_P214554	89870	1.56777	0.00003

UGT1A10	A_23_P158330	54576	1.56753	2.47E-07
BCL2L14	A_23_P128050	500348	1.56747	8.48E-13
UGT2B10	A_23_P7342	305264	1.56698	0.00029
CST3	A_24_P216294	25307	1.5652	2.10E-12
NOS2A	A_23_P502464	18126	1.56417	4.66E-10
HIST1H1E	A_23_P170713		1.56293	3.24E-10
APOC1	A_24_P109214	11812	1.56219	0.00718
FLJ10787	A_23_P41470	234311	1.56197	3.99E-08
eukaryotic translation initiation factor 4E	A_32_P176066	13684	1.56188	0.00207
ACMSD	A_23_P376727	171385	1.5617	0.00094
COLEC12	A_23_P27306	361289	1.56116	0.00515
IKIP	A_23_P53467	121457	1.55822	9.10E-12
CB136271	A_32_P127009		1.55694	0.00046
HLA-A	A_32_P234459	3136	1.55595	5.62E-06
SLIT1	A_24_P910566	20562	1.55451	0.00147
LOC340012	A_24_P895836		1.55262	1.01E-09
ANKRD20A	A_24_P868583	441430	1.55205	2.30E-06
CGN	A_24_P45728	70737	1.54934	0.00001
SAT	A_23_P378722	302642	1.54547	8.82E-11
FLJ22622	A_23_P391198	75767	1.54431	7.56E-09
FLJ21308	A_23_P121898	294762	1.54386	0.00024
SLC3A1	A_24_P217234	29484	1.54212	0.00026
FGFR2	A_24_P206624	14183	1.54175	0.00018
PTK6	A_23_P56978	366275	1.54097	1.88E-12
SLC4A4	A_32_P349145	54403	1.54045	0.00006
APOB	A_23_P79591	238055	1.53988	0.0002
ZNF217	A_23_P210608	7764	1.53932	6.05E-11
FLJ20035	A_24_P334361	234311	1.53898	0.00009
AL109696	A_24_P810476	18213	1.53879	0.00533
RIOK3	A_23_P55584	66878	1.53873	5.43E-06
ZBP1	A_23_P259141	81030	1.53835	9.19E-07
ACSL6	A_24_P941526	23305	1.5376	0.00245
SEC6L1	A_24_P316046		1.53701	0.00015
LCN2	A_23_P169437	16819	1.53661	0.0065
A_24_P255303	A_24_P255303		1.53631	1.22E-17
ABCB1	A_23_P82523	170913	1.53545	0.0001
ERP70	A_32_P192804		1.53529	0.00369
CaMKIINalpha	A_24_P117620	287005	1.53521	1.98E-13
KIAA1775	A_23_P149946	93662	1.53445	7.57E-07
insulin-like growth factor 2 receptor	A_23_P156953	16004	1.53435	4.64E-28
immunoglobulin kappa constant	A_23_P61068		1.53431	0.00124
SGK2	A_24_P151356	171497	1.53084	0.00003
LRP4	A_24_P403561	228357	1.53066	2.04E-09
TRPM6	A_23_P216712	140803	1.53055	0.00129
ZNF17	A_32_P401723		1.52931	0.00776
A_24_P631625	A_24_P631625		1.52915	5.70E-06
LOC90271	A_32_P199998		1.52897	1.68E-06
KIAA0573	A_32_P62508		1.52883	0.00005
CKB	A_23_P25674	1152	1.52784	0.00004
KIAA1671	A_24_P678743	85379	1.52626	1.96E-06
IGKV	A_24_P484904		1.52486	0.00026
C6orf85	A_32_P226941		1.52436	0.00002

CDC14A	A_23_P405110	229776	1.52432	0.00921
PRKG1	A_32_P137149		1.5231	0.00478
cytochrome P450, family 2, subfamily A, polypeptide 7 pseudogene 1	A_24_P203696	1548	1.5224	0.00612
COLM	A_32_P46456		1.52033	7.88E-14
similar to ankyrin repeat domain 20A	A_32_P68942	440482	1.52024	9.10E-13
MCOLN2	A_23_P23639	68279	1.51967	0.00133
HSD3B1	A_24_P925818		1.51962	0.00567
KIAA1311	A_24_P927222	225432	1.51588	9.35E-13
HLA-A	A_24_P376483	3105	1.51567	0.00001
RAB8A	A_23_P164752	17274	1.51564	0.00011
PPARGC1B	A_32_P31832		1.51376	8.22E-11
CEACAM7	A_24_P228302	1087	1.51325	0.00037
EFHD2	A_24_P251053	298609	1.51137	4.07E-14
NDP52	A_24_P322191	10241	1.51075	1.61E-17
HBG2	A_23_P53137	502359	1.5103	0.00003
HIST1H1D	A_24_P260639	14957	1.51013	3.36E-11
A_24_P894345	A_24_P894345		1.50995	0.00275
myosin regulatory light chain interacting protein	A_24_P917123	218203	1.509	5.87E-08
PDE4D	A_32_P18034		1.50687	0.0005
interleukin 1 receptor, type II	A_24_P63019	7850	1.50646	0.00184
HLA-B57	A_23_P95917	3107	1.50629	1.90E-06
RASD1	A_24_P348006	64455	1.50513	0.00191
ENMV29985	A_32_P216369	100134159	1.50481	1.02E-07
C21orf23	A_32_P157516		1.50267	0.00029
MGC27165	A_23_P136026	3493	1.5019	0.00023
MGC27165	A_24_P860662		1.50184	0.00513
S100A5	A_23_P115467	295211	1.50105	0.00012
FKSG14	A_23_P155989	60411	-1.5005	2.41E-12
RRM1	A_23_P87351	365320	-1.50121	2.20E-19
DJ667H12.2	A_23_P318904	56256	-1.50197	0.00016
DSCA17079	A_32_P840463		-1.50404	3.08E-08
ART3	A_23_P80918	305235	-1.50443	0.00351
SUMF1	A_24_P612890		-1.50554	9.58E-06
STX16	A_24_P36457	362283	-1.50609	0.00252
ZNF337	A_24_P318939	26152	-1.50657	2.26E-06
UBD	A_23_P81898	54393	-1.50674	0.00097
myelin transcription factor 1	A_24_P164815	311726	-1.50684	0.0011
similar to Tetratricopeptide repeat protein 4 (My044 protein)	A_24_P92411		-1.50685	0.00226
TA-LRRP	A_24_P345131	433926	-1.50857	6.63E-14
MGC5528	A_23_P252740	72107	-1.50866	5.58E-21
LOC133374	A_24_P811954		-1.50874	0.00181
KIAA1804	A_24_P130952	84451	-1.50906	0.00698
MYO5A	A_24_P255218	25017	-1.51088	0.00025
EVER2	A_23_P346093	217356	-1.51108	1.15E-06
CARP	A_23_P161218	27063	-1.5111	0.00231
LMNB2	A_23_P67725	84823	-1.51143	2.56E-11
SNRPE	A_23_P126291	20643	-1.51211	8.76E-16
BIRC5	A_23_P118815	332	-1.51226	0.00002
SSR1	A_32_P226073		-1.51288	0.00002
EFHC2	A_24_P221285		-1.51357	1.43E-08

RAB39B	A_24_P408603	67790	-1.51399	0.00788
MGC2714	A_23_P127533	76863	-1.51501	1.53E-16
CHES1	A_32_P192745		-1.51602	0.00502
ANP32B	A_32_P114146		-1.51642	1.46E-07
BRIP1	A_23_P15844	360588	-1.51655	0.00154
KSP37	A_23_P41528	83888	-1.51733	0.00425
PAICS	A_24_P200427	67054	-1.51859	8.07E-16
LOC284454	A_24_P734060		-1.51901	1.16E-08
LOC286434	A_24_P538495		-1.52029	0.00624
AP1S2	A_24_P190804	8905	-1.52037	0.0002
A_32_P195461	A_32_P195461		-1.52083	0.00019
FLJ00412	A_23_P79069	314596	-1.5211	4.01E-06
FLJ32745	A_32_P234391		-1.52195	0.00418
ESAM	A_24_P13190		-1.52301	0.0001
LOC51079	A_32_P207243		-1.52524	0.00003
PPIL1	A_23_P133995	68816	-1.52695	3.72E-18
NOXA1	A_23_P256973		-1.5276	0.00044
LST-3	A_24_P713267		-1.52803	0.00316
A_24_P84268	A_24_P84268		-1.52854	4.50E-08
PLAB	A_23_P16523	29455	-1.52893	8.19E-06
DATF1	A_32_P19917		-1.52923	3.62E-08
FLJ20105	A_23_P96325	236930	-1.53065	3.38E-06
solute carrier family 25 (mitochondrial carrier; phosphate carrier), member 25	A_23_P9435	227731	-1.5312	0.00198
P2RX5	A_23_P433785	94045	-1.5315	3.92E-06
NOD3	A_23_P340019		-1.53251	0.00068
KLHL5	A_24_P17710	51088	-1.53302	0.00584
LOC440345	A_32_P11359		-1.53305	0.00037
FLJ21120	A_23_P112016	10395	-1.53423	0.0064
RASGRP2	A_23_P64058	10235	-1.53431	8.46E-09
FLJ10520	A_24_P287826	361409	-1.53483	9.96E-07
polyhomeotic-like 1 (Drosophila)	A_23_P204246	1911	-1.53487	0.00294
EME1	A_23_P368225	287634	-1.5356	1.43E-11
PRDM15	A_32_P145989	114604	-1.53745	0.00003
ZNF516	A_24_P910325	291406	-1.53767	7.27E-07
MALT1	A_32_P76576		-1.53835	1.98E-06
AA151106	A_32_P209778		-1.53874	0.0015
CD96	A_23_P44155	84544	-1.53887	0.0081
DDHD1	A_23_P205623	80821	-1.53889	0.00438
DKFZp451M2119	A_24_P400172	285023	-1.53917	0.0005
PIGR	A_24_P844984	25046	-1.53963	6.79E-06
NR4A3	A_23_P398566	18124	-1.54167	6.39E-07
THC1891432	A_32_P9931		-1.54183	2.36E-06
TPPS32037	A_32_P11181		-1.54214	3.10E-17
RPS26	A_32_P90987		-1.54231	3.35E-35
ODC1	A_23_P165840	24609	-1.54578	1.84E-16
NOLC1	A_23_P202143	70769	-1.54597	4.32E-13
TIMELESS	A_23_P53276	83508	-1.54664	4.08E-19
MCM4	A_23_P370989	17217	-1.54674	1.81E-19
NAP1L1	A_24_P304458		-1.5493	0.00717
LOC440362	A_32_P139738	440362	-1.55044	0.00027
RAD18	A_23_P121222	58186	-1.55161	4.72E-06
FLJ12604	A_23_P380208	72789	-1.55233	0.00806

HNRPR	A_24_P724984		-1.55301	0.00006
A_32_P57013	A_32_P57013		-1.55397	2.03E-08
KIAA1287	A_23_P420269	360589	-1.55432	1.13E-07
A_32_P8971	A_32_P8971		-1.55464	4.43E-18
POLR2D	A_32_P219753	5433	-1.55488	1.63E-09
NBEA	A_23_P65278	26960	-1.55501	0.0015
AKAP13	A_24_P7642	642956	-1.5553	2.22E-07
PDE4DIP	A_32_P110550		-1.55563	0.00628
ZNF6	A_23_P340149	245595	-1.55653	0.00003
H63 breast cancer expressed gene	A_23_P140469	113201	-1.55668	0.00625
MALT1	A_24_P116909	240354	-1.55821	0.00499
DUSP1	A_23_P110712	19252	-1.55895	0.00021
A_32_P327750	A_32_P327750		-1.56008	0.00112
PRKAA2	A_23_P52109	78975	-1.5602	0.00435
RAB6IP1	A_23_P321201	308942	-1.56095	1.30E-10
GARNL1	A_24_P922969	253959	-1.56184	0.00524
TIMM10	A_32_P115162		-1.56287	0.00064
A_24_P636179	A_24_P636179		-1.56323	0.0015
C6orf173	A_32_P143245	689399	-1.56345	1.96E-11
CHEK1	A_23_P116123	1111	-1.5635	1.49E-15
PTGIS	A_24_P48723	25527	-1.56406	0.00253
WDR4	A_23_P211302	10785	-1.56591	1.87E-18
LOC344760	A_24_P739355		-1.56659	1.32E-13
MTBP	A_23_P357794	27085	-1.5672	0.00001
CENPA	A_24_P413884	12615	-1.56789	4.09E-07
OLFM1	A_24_P406601	10439	-1.56825	2.05E-07
HCAP-G	A_32_P169679		-1.56826	0.00026
AK093202	A_24_P256404		-1.56885	0.00228
AK001796	A_24_P825942		-1.56992	0.00187
SQLE	A_23_P146284	6713	-1.57075	0.00049
WASF3	A_24_P176079	245880	-1.57119	5.08E-06
THOC1	A_23_P78372	9984	-1.57136	0.00045
CDCA2	A_23_P385861	108912	-1.57404	1.90E-12
KLF15	A_24_P20327	28999	-1.57457	0.00071
stress-associated endoplasmic reticulum protein 1	A_24_P579862	100129720	-1.57616	0.00499
SLC30A6	A_24_P342807	298786	-1.5767	5.28E-07
LOC440823	A_24_P595223		-1.57787	2.52E-07
BCL2A1	A_23_P152002	12044	-1.57903	0.0007
ST7	A_24_P141019	7982	-1.5808	0.0016
OATA12672	A_32_P49211		-1.58185	0.00631
CAV1	A_32_P56489		-1.58208	0.00062
KHGF15301	A_24_P854896		-1.58435	0.00469
PTGDS2	A_23_P21907	54486	-1.58438	0.00344
RABEP1	A_24_P399174	54189	-1.58528	0.00001
UNQ1971	A_23_P76136		-1.58557	0.00084
A_24_P349648	A_24_P349648		-1.58715	0.00424
C18orf1	A_32_P31206		-1.58733	0.0003
KIAA0470	A_23_P348857	645455	-1.59013	0.00243
PAICS	A_23_P41280	67054	-1.5905	2.68E-22
KCNJ1	A_23_P501781	56379	-1.59383	0.00001
ZWINT	A_23_P63789	11130	-1.59391	1.01E-24
KIAA0562	A_23_P200047	230967	-1.59458	0.0006

FLJ21069	A_23_P417363	298801	-1.59475	0.0039
MELK	A_23_P94422	362510	-1.59477	4.29E-22
MCM6	A_23_P90612	4175	-1.59888	8.48E-19
BC011998	A_32_P42104		-1.59906	2.09E-13
ENO1	A_32_P229365		-1.59942	0.00037
MGC39571	A_23_P423462	221241	-1.6009	0.00533
HNRPD	A_24_P123245	79256	-1.60123	4.90E-09
LOC146909	A_24_P680947	70218	-1.60224	7.17E-11
C10orf3	A_23_P115872	55165	-1.60237	1.58E-07
C6orf192	A_24_P85418		-1.60449	0.00036
A_32_P201976	A_32_P201976		-1.60605	0.00003
D15Wsu75e	A_23_P68966	315160	-1.60644	0.0058
ZNF594	A_23_P321160	84622	-1.60699	0.00025
A_32_P17439	A_32_P17439		-1.60874	0.00041
AKT1	A_23_P2960	24185	-1.60889	8.71E-06
RPL23	A_24_P205242		-1.61006	0.00004
DDEF1	A_23_P71526	50807	-1.61029	0.00624
LPL	A_23_P146233	24539	-1.61102	9.09E-06
FLJ23311 protein	A_23_P35871	108961	-1.61161	5.55E-10
APG-1	A_23_P363936	18415	-1.61185	0.00018
COL4A3	A_23_P170679	12828	-1.61193	0.00466
THC1808895	A_32_P202082		-1.61328	0.00765
LRLE1	A_32_P846696		-1.61526	0.00827
A_32_P138666	A_32_P138666		-1.61738	0.00145
ZNF559	A_24_P284584	84527	-1.61912	0.00082
ZDHHC22	A_32_P75243		-1.61953	0.00736
ZNF25	A_23_P381577	219749	-1.62122	0.00087
HEC	A_23_P50108	67052	-1.6216	7.06E-16
FLJ20641	A_23_P87773	55010	-1.62183	0.0008
AF15Q14	A_24_P940678	311327	-1.62437	0.00099
CYR61	A_24_P370946	16007	-1.62574	0.00257
C3	A_23_P101407	12266	-1.62846	8.90E-07
STYX	A_24_P910262	56291	-1.62914	1.52E-07
KIAA0101	A_23_P117852	300795	-1.63426	6.46E-16
ATOH1	A_23_P332246	474	-1.6348	0.00001
WWOX	A_24_P929558		-1.63515	0.00013
TYMS	A_23_P50096	22171	-1.6358	6.33E-11
CD2	A_23_P161076	497761	-1.63594	1.61E-06
NCR1	A_23_P108042	17086	-1.6371	0.00482
MASP1	A_23_P212263	5648	-1.6381	0.0017
LOC93081	A_23_P362046	75623	-1.63988	2.27E-15
similar to Zinc-alpha-2-glycoprotein precursor (Zn-alpha-2-glycoprotein) (Zn-alpha-2-GP)	A_24_P49267		-1.64128	0.00166
KIAA1430	A_32_P30153	306469	-1.64152	0.00062
CD3Z	A_23_P34676	12503	-1.64208	0.00012
C14orf118	A_24_P927311		-1.64208	0.00793
DKFZp779P0659	A_24_P937306		-1.64323	0.00224
GTP binding protein 6 (putative)	A_24_P358381	8225	-1.64641	0.00077
PTPN11	A_23_P105436		-1.64871	0.00003
RRS1	A_23_P146187	59014	-1.64937	7.68E-13
FXR1	A_24_P345781		-1.64962	0.00081
WDR32	A_32_P133005	79269	-1.65022	0.00214
NEIL3	A_23_P155711	290729	-1.65133	1.39E-08

A_24_P944275	A_24_P944275		-1.65138	0.00105
CENPF	A_24_P96780	257649	-1.6521	0.00007
UNQ496	A_24_P311577	70681	-1.65245	6.12E-08
INPP5E	A_23_P94875	64436	-1.65353	0.00994
PPP1R12A	A_23_P204564	17931	-1.65486	0.00148
LOC151648	A_24_P923984		-1.65498	0.0001
DNA2L	A_24_P366107	309762	-1.65833	1.74E-06
CDC2	A_23_P138507	983	-1.65866	6.14E-15
LOC400509	A_32_P78809		-1.66164	0.00002
LOC441124	A_32_P234294		-1.66177	0.00428
STAC	A_24_P234415	363152	-1.66221	0.0001
FYB	A_24_P393740	499537	-1.66252	3.25E-06
UHRF1	A_23_P208880		-1.66424	2.39E-10
SNX27	A_32_P31300		-1.6657	1.31E-06
A_32_P119154	A_32_P119154		-1.66687	1.00E-08
RBBP4	A_24_P912095	5928	-1.67234	9.22E-06
THC1933749	A_24_P833191		-1.67257	0.0002
MGC32020	A_23_P338505	502320	-1.67589	0.00888
AD024	A_23_P51085	66442	-1.67801	2.14E-14
CLTB	A_23_P252671	74325	-1.68216	0.00053
FABP5	A_23_P59877	728641	-1.68366	7.90E-12
CCR6	A_24_P234921	75296	-1.68375	0.00186
CCR7	A_23_P343398	12775	-1.68663	0.00006
EFHA2	A_32_P202502	364601	-1.6885	5.89E-08
CDCA5	A_23_P104651	67849	-1.69129	1.07E-11
LOC116068	A_24_P15658		-1.69999	0.00149
MBD2	A_32_P107777		-1.70036	4.27E-09
MGC4308	A_23_P132874	66497	-1.70138	4.14E-18
TA-KRP	A_23_P431252	243574	-1.70547	7.69E-06
RPS3	A_24_P218765		-1.71179	1.30E-07
EVA1	A_24_P278552	300679	-1.71391	0.00189
ANGPT2	A_24_P932435	11601	-1.71451	0.00914
ZNF251	A_23_P418204	90987	-1.71518	0.00177
TACR1	A_23_P95125	6869	-1.71685	0.00915
DKFZp313L052	A_32_P489920		-1.72121	0.00195
FBXO36	A_23_P422981	130888	-1.72291	0.00203
LSAMP	A_24_P794631		-1.72707	2.37E-06
LOC51270	A_23_P10518	51270	-1.72817	0.00995
TTID	A_23_P110764	9499	-1.72846	0.00756
RPS6KB2	A_24_P392201	108995	-1.73119	4.69E-09
MONDOA	A_24_P415618	208104	-1.73215	2.19E-15
CTCFL	A_23_P40225	664799	-1.73245	4.73E-06
FLJ23047	A_24_P920355	304007	-1.73432	0.00486
ARHGEF10	A_23_P356216		-1.73527	0.00159
KITLG	A_24_P929231		-1.73793	0.00017
TIMP3	A_23_P211468		-1.73836	0.00003
ZNF509	A_24_P154573	75079	-1.73888	0.00001
NPTX1	A_23_P124905	266777	-1.73914	0.00004
SNF1LK	A_23_P132115	150094	-1.74113	0.00004
C1orf24	A_23_P217832	63913	-1.74294	0.00059
LOC338819	A_24_P255845		-1.74794	9.94E-08
KIAA1524	A_24_P351466	360711	-1.75465	0.00301

A_32_P192853	A_32_P192853		-1.75509	0.00007
BCCIP	A_24_P1255	66165	-1.75653	0.00061
SYNCRIP	A_24_P940599		-1.75804	0.00064
WDHD1	A_32_P148602		-1.76104	0.00017
B3GALT4	A_24_P845082		-1.7633	4.85E-10
C8FW	A_23_P123503	78969	-1.76337	0.00281
ZAP70	A_23_P39682	301348	-1.7702	1.05E-21
DKFZP564G092	A_24_P936041		-1.77094	0.00085
FLJ43663	A_24_P522976		-1.77203	0.00843
LOC441220	A_24_P925635		-1.77231	0.00001
K-ALPHA-1	A_32_P119998		-1.77489	3.03E-09
PRO2964	A_23_P430156	55415	-1.77918	0.00036
AATK	A_23_P10559	690853	-1.79189	0.00019
COL8A1	A_24_P139152		-1.79505	1.46E-08
LOC401588	A_32_P66570		-1.79573	0.00011
LOC339903	A_23_P80551	26172	-1.79603	0.00001
EIF3S5	A_24_P940944	66085	-1.80204	0.00139
ARTS-1	A_24_P63537	80897	-1.80209	0.00271
TWSG1	A_24_P211064	65960	-1.80266	0.00023
VMP1	A_32_P9753		-1.80956	7.49E-14
HCAP-G	A_23_P155815	64151	-1.81083	5.84E-15
HSPH1	A_23_P88119	10808	-1.81233	1.29E-18
C8FW	A_32_P38821		-1.81799	0.00003
RAB3IP	A_24_P93624	216363	-1.82817	0.00002
LRP8	A_23_P200222	7804	-1.82902	5.15E-15
SHOX	A_23_P22761	6473	-1.8329	0.00002
CXCR4	A_23_P102000	12767	-1.83681	1.38E-08
BC043195	A_32_P94160	78975	-1.83731	0.00095
CNP	A_23_P10798	25275	-1.83824	0.00165
NYD-SP16	A_23_P7744	294594	-1.84121	0.00088
CLIC6	A_23_P385067	209195	-1.8417	1.53E-07
JAK3	A_24_P59667	25326	-1.84278	5.98E-09
EEF1A1P2	A_24_P603453		-1.85096	0.00036
NDE1	A_24_P210675	83836	-1.8521	0.0015
PAX8	A_23_P324916	18510	-1.85478	0.00027
FERD3L	A_23_P422849	114712	-1.86086	1.48E-09
ZNF367	A_32_P183218	238673	-1.86233	1.48E-11
PHKA1	A_23_P258531	18679	-1.86618	0.00006
ADAMTS1	A_23_P342275	11504	-1.86963	1.21E-07
MYL6	A_32_P3600		-1.87229	2.94E-14
LOC339967	A_24_P109101	339967	-1.87695	0.00661
chromosome 8 open reading frame 4	A_23_P253350	56892	-1.88932	0.00001
UBQLN1	A_24_P338121	29979	-1.89073	0.00595
ZFP30	A_23_P119735	22693	-1.89182	0.00088
CHD2	A_24_P85317	244059	-1.89208	0.00076
HSPC154	A_24_P74088	307210	-1.91901	1.12E-08
ARPP-21	A_23_P315602	10777	-1.9239	0.00113
CANP	A_24_P332314	374393	-1.92867	2.06E-06
KIAA0620	A_23_P80752	23129	-1.93192	0.00052
CYFIP2	A_24_P465879		-1.93263	0.00027
C6orf198	A_23_P434398	167838	-1.94145	0.00145
C10orf82	A_23_P314876	67507	-1.94368	0.00045

A_32_P164477	A_32_P164477		-1.94672	0.00026
DLX2	A_24_P45980	1746	-1.95106	0.00359
LOC285331	A_23_P396981	320234	-1.95707	0.00399
EPHB4	A_23_P168443	13846	-1.95748	0.00001
ADAMTS1	A_23_P211039	9510	-1.96396	0.00003
DSVL30277	A_24_P822931		-1.97534	0.00084
DMRT2	A_32_P213459	226049	-1.97754	0.00032
MGC33653	A_23_P350591	139105	-1.98786	0.00117
RC1	A_24_P924185		-1.98854	2.84E-14
ULBP3	A_24_P672143		-1.99705	0.00025
FLJ10808	A_32_P158053		-2.00704	0.00022
C22orf1	A_24_P325025		-2.01135	0.00162
BC031872	A_24_P25498		-2.01586	0.0001
NR4A1	A_23_P128230	15370	-2.02029	1.42E-06
CD69	A_23_P87879	12515	-2.02309	9.15E-11
FYGN18466	A_24_P101200		-2.02704	0.00039
COLEC11	A_24_P388322	71693	-2.02755	8.03E-14
BC030635	A_24_P145216		-2.02884	0.00019
MGC5347	A_24_P922252		-2.03053	0.00126
NLN	A_32_P891680		-2.03671	2.12E-07
DKFZp686O04253	A_24_P913819	242594	-2.03737	0.00059
TRAPPC6B	A_24_P942132	78232	-2.03761	0.00116
CP110 protein	A_23_P26501	9738	-2.03825	0.00472
SE20-4	A_23_P170608	52808	-2.04322	0.00584
PDE7A	A_32_P137382		-2.04507	3.47E-07
LOC339881	A_24_P846810		-2.05671	0.0006
RBMX	A_32_P56392		-2.05918	0.00397
A_24_P745635	A_24_P745635		-2.05939	0.00173
MAX	A_24_P932488		-2.05956	0.00295
KIAA1432	A_24_P306136	226089	-2.06054	0.00008
A_32_P191066	A_32_P191066		-2.06831	0.00681
EGR3	A_23_P216225	13655	-2.07232	0.00276
NHLRC2	A_23_P35376		-2.10235	0.00849
LOC441207	A_24_P911310		-2.11782	0.00003
C4orf7	A_23_P362694	260436	-2.12262	8.17E-11
KIAA0103	A_32_P115277		-2.12557	1.12E-07
HIST1H1B	A_23_P250385	3009	-2.13668	1.93E-07
A_24_P693768	A_24_P693768		-2.14378	1.25E-08
C12orf2	A_23_P116712	312846	-2.15256	3.50E-06
MGC10814	A_23_P79032		-2.15611	2.07E-11
FLJ90396	A_24_P382401	163049	-2.18019	0.00043
C6orf155	A_23_P156408	79940	-2.198	2.85E-06
OTTHUMP00000016909	A_24_P769529	380669	-2.2099	0.00025
A_24_P238386	A_24_P238386		-2.21197	4.86E-08
SESTD1	A_23_P367610	295678	-2.21611	0.00036
SLC22A18	A_32_P174121		-2.27022	0.00125
RAN	A_32_P125233		-2.29257	0.00018
C20orf160	A_23_P91414	140706	-2.32223	2.27E-06
AF035297	A_24_P737492		-2.32936	0.00636
FOS	A_23_P106194	2353	-2.33116	4.44E-07
TSLP	A_23_P121987	85480	-2.3473	2.72E-06
POLK	A_24_P919863		-2.36932	0.00252

LOC51152	A_24_P214184	51152	-2.3724	0.00917
NKD1	A_24_P304881		-2.37731	0.00054
REST	A_24_P942579	5978	-2.41803	0.00032
CCL19	A_23_P123853	6363	-2.47667	2.81E-08
SNIP1	A_23_P23175	313588	-2.53055	0.00016
FLJ11342	A_24_P268662	303953	-2.53093	0.00165
KIAA1586	A_24_P101047	57691	-2.57808	0.00002
GTPBP2	A_24_P77826		-2.64576	1.27E-08
C6orf32	A_24_P941359	306934	-2.72357	5.37E-06
CXCL13	A_23_P121695	55985	-2.76064	0.00528
EGR1	A_23_P214080	24330	-2.77022	4.79E-06
LOC284058	A_32_P210106		-2.99167	0.00006
MMP1	A_23_P1691	4312	-3.27706	2.35E-15
LOC284058	A_24_P316381		-3.61807	0.00006

Figure 27

Sequence Name(s)	Sequence Code	Entrez Gene	Fold Change	P-value
OLFM4	A_24_P181254	290409	6.19335	2.92E-14
ribosomal protein S4	A_23_P324384	690845	3.92713	0.00841
FLJ25393	A_24_P305993	315438	3.82528	0.00211
FLJ21162	A_23_P386478	79931	3.63174	2.30E-10
TTTY15	A_24_P348861	100133422	3.61598	3.07E-09
EIF1AY	A_24_P237511	317163	3.61305	0.00032
DBY	A_23_P217797	8653	3.5582	7.53E-17
CYorf15A	A_23_P364792	246126	3.54097	0.00055
GW112	A_23_P2789	290409	3.37203	3.95E-10
CLECSF9	A_24_P78531	56619	3.33298	0.00135
S100A9	A_23_P23048	94195	3.26362	0.00009
regenerating islet-derived 3 gamma	A_32_P65628	24618	3.20387	0.00004
ART3	A_23_P80918	305235	3.14924	0.00007
CXCL3	A_24_P183150	20310	3.02695	6.16E-08
KIAA1404 protein	A_23_P68462	98999	2.96907	4.13E-06
CXCL11	A_23_P125278	56066	2.87122	0.00007
DEFA6	A_24_P363711	1671	2.63504	0.00358
TFEC	A_32_P184394	26296	2.63059	0.00028
BCL2A1	A_23_P152002	12044	2.63023	5.42E-08
C6orf32	A_23_P358394	306934	2.58744	0.00255
CHRDL2	A_23_P13548	69121	2.5535	0.00013
SAA1	A_24_P335092	6288	2.51707	0.00881
ECT2	A_24_P366033	1894	2.49818	0.00193
UTY	A_23_P329835	7404	2.46771	0.00003
CYorf15B	A_23_P96658	84663	2.46762	1.97E-06
FLJ10884	A_23_P137484	685355	2.42911	1.94E-07
SELL	A_23_P103522	20343	2.41679	0.00589
AIM2	A_32_P44394	383619	2.41618	0.00045
MGC10814	A_23_P79032		2.36847	3.15E-13
IL2RA	A_23_P127288	25704	2.31902	1.37E-07
LCN2	A_23_P169437	16819	2.31046	2.47E-06
MMP3	A_23_P161698	171045	2.30314	0.00286
TPO	A_24_P257224	7173	2.2722	4.21E-07
A_24_P238386	A_24_P238386		2.27147	3.40E-13
CXCR6	A_23_P109913	80901	2.26698	1.37E-06
TRIM22	A_23_P203498	10346	2.22541	2.09E-08
VSNL1	A_23_P209978	26950	2.2098	0.00013
RBMX	A_32_P56392		2.19717	0.00118
KCNJ10	A_24_P387875	16513	2.18892	7.56E-06
A_32_P327750	A_32_P327750		2.18518	2.83E-08
REG4	A_24_P58673	445583	2.16598	0.00005
FLJ30469	A_24_P323148	502308	2.15915	0.00257
TDO2	A_23_P80974	56720	2.14203	0.00322
AKAP12	A_23_P111311	83425	2.14102	0.0065
BRDG1	A_23_P7185	56792	2.13689	0.00055
SYCP2	A_24_P333644	320558	2.1332	0.00625
K5B	A_23_P331098	332131	2.1108	0.00511
KCND3	A_32_P140268	56543	2.09083	0.00859

HLA-DQB2	A_23_P136683		2.0842	6.00E-10
CYP2U1	A_24_P913156		2.0744	0.00473
DIAPH2	A_23_P254212	29935	2.07003	2.91E-06
similar to RIKEN cDNA A630077B13 gene; RIKEN cDNA 2810048G17	A_23_P7827	215900	2.05787	0.00011
LRRC2	A_23_P155463	74249	2.05097	0.00014
GBP1	A_23_P62890	304266	2.04986	0.00008
ARFD1	A_23_P167384	373	2.03847	0.00011
LRP8	A_23_P200222	7804	2.03014	2.67E-09
CYFIP2	A_24_P465879		2.03006	0.00085
FLJ90396	A_24_P382401	163049	2.02063	0.00456
HLA-DMB	A_24_P481844		2.01735	5.74E-06
SOCS3	A_23_P207058	9021	2.01071	3.43E-07
OAS2	A_24_P343929	363938	2.00087	0.0007
IFNG	A_23_P151294	3458	2.0007	0.00801
PCSK9	A_32_P142440	298296	1.97869	2.22E-16
VH4	A_23_P158817	3492	1.97817	2.74E-06
EPHB4	A_23_P168443	13846	1.95229	9.90E-06
FLJ21616	A_24_P932736	79618	1.94832	0.00022
KIAA1115	A_23_P119448	361502	1.94246	0.00067
ADPRTP1	A_24_P726495		1.94022	0.0038
SLC6A14	A_24_P365721	298340	1.93357	0.00001
HLA-DRB5	A_23_P45099	731247	1.93256	0.00003
BQ013066	A_32_P107994		1.9311	0.00079
MMP1	A_23_P1691	4312	1.926	0.0056
CMIP	A_23_P377935		1.92496	0.00855
CD86	A_24_P131589	56822	1.92217	0.00092
IRTA2	A_23_P201211	83416	1.9198	3.22E-09
CCR6	A_24_P234921	75296	1.91903	0.00176
RP11-53I24.2	A_24_P366644		1.91469	8.09E-06
BF	A_23_P156687	294257	1.90484	7.92E-07
HLA-DRB3	A_24_P845223		1.8941	8.80E-06
PSMB9	A_23_P111000	16912	1.88857	7.31E-10
CXCL10	A_24_P303091	3627	1.8841	0.00124
ASPN	A_23_P216429	306805	1.88323	0.00334
FOS	A_23_P106194	2353	1.87816	0.00012
COVA1	A_24_P391468	209224	1.87411	0.00053
IRX5	A_23_P9779	54352	1.87305	0.00055
C20orf174	A_32_P206479	128611	1.86005	0.00844
SESTD1	A_23_P367610	295678	1.85227	0.00364
CEACAM6	A_23_P218442	4680	1.8458	0.00048
DKFZp451J1719	A_24_P32790	55432	1.84546	0.00114
EGR3	A_23_P216225	13655	1.8454	0.00919
PRKY	A_24_P186030	5616	1.84191	2.06E-06
GPCR	A_23_P214267	301266	1.84079	0.00032
CHD2	A_24_P85317	244059	1.83918	0.00819
A_24_P925966	A_24_P925966		1.8387	0.00213
FLJ12443	A_24_P406006	361467	1.8355	0.00039
A_32_P188127	A_32_P188127		1.82847	0.0004
ankyrin repeat and IBR domain containing 1	A_23_P93912	368062	1.82718	0.00134
VMP1	A_32_P9753		1.82449	1.47E-19

UBQLN1	A_24_P338121	29979	1.82449	0.00315
FLJ32191	A_23_P380951	499120	1.82069	0.00113
LOC133374	A_24_P811954		1.81944	0.00003
H6PD	A_24_P626850	9563	1.81915	0.00347
LOC339903	A_23_P80551	26172	1.81873	0.0002
ATF3	A_23_P34915	11910	1.81707	4.97E-09
C14orf79	A_23_P376870	122616	1.81595	0.00157
APG-1	A_23_P363936	18415	1.81584	0.00001
SSH2	A_32_P142943		1.81541	0.00048
ME1	A_23_P8196	17436	1.81454	1.18E-07
APOL1	A_23_P17837	8542	1.81406	0.00831
MGC19764	A_32_P67223		1.81254	0.00171
IFI44	A_23_P23074	310969	1.80962	9.01E-07
C3	A_23_P101407	12266	1.80857	0.00036
LOC285331	A_23_P396981	320234	1.80814	0.00644
FLJ21069	A_23_P417363	298801	1.80622	0.00006
G1P2	A_23_P819	9636	1.80311	2.88E-13
ADRBK2	A_23_P251686	320129	1.79001	0.00002
DMBT1	A_23_P86599	170568	1.78828	0.00002
TORC3	A_32_P80016		1.78443	0.00225
LAX	A_23_P438	54900	1.78089	5.34E-06
CNP	A_23_P10798	25275	1.77792	0.0017
PIM3	A_23_P61398	223775	1.7758	3.03E-09
CRSP6	A_24_P941459		1.77493	0.00002
ARHGEF10	A_23_P356216		1.76766	0.00151
KAL1	A_23_P429950	3730	1.76533	0.00378
similar to Nuclear protein SkiP (Ski-interacting protein) (SNW1 protein) (Nuclear receptor coactivator NCoA-62)	A_32_P82119		1.76409	0.00006
C18orf1	A_32_P31206		1.75717	1.05E-06
FLJ13612	A_32_P187126		1.75618	0.00046
UNC5CL	A_23_P428298	301225	1.7518	0.00393
CCL20	A_23_P17065	29538	1.74566	0.00003
CLDN1	A_23_P57784	9076	1.74398	0.00002
INPP5E	A_23_P94875	64436	1.74296	0.00522
DDX3X	A_23_P317657	13205	1.74055	9.17E-14
TRIM5	A_23_P356526	667823	1.73687	4.98E-07
YES1	A_23_P164507	7525	1.73461	0.00133
ropporin 1-like	A_32_P335921	685646	1.73143	0.00837
IF	A_23_P7212	79126	1.72986	0.00027
PIK3R3	A_23_P22970	8503	1.72671	0.00071
TAGAP	A_24_P354724	308097	1.72647	0.00214
GALNAC4S-6ST	A_32_P94176		1.72585	2.19E-06
LOC93349	A_23_P337753	93349	1.7238	0.00001
KLHL3	A_23_P133543	26249	1.71317	4.28E-09
BMP7	A_24_P91566	12162	1.71263	0.00084
FLJ38984	A_23_P321377	127703	1.7113	0.00284
oxoglutarate (alpha-ketoglutarate) receptor 1	A_24_P39195	27199	1.71	0.00663
TOM1L2	A_23_P152570		1.70704	0.0022
LOC51270	A_23_P10518	51270	1.70618	0.00885
KIAA1026	A_24_P246573	23254	1.70417	3.58E-06

AK124173	A_32_P235358		1.70142	0.00012
BLZF1	A_24_P119259	8548	1.69859	0.00042
SOX14	A_32_P183652		1.69716	0.00516
BATF	A_23_P128974	10538	1.69514	0.00405
ST3GAL2	A_32_P184746		1.69452	0.00003
FLJ27099	A_32_P200144		1.69278	0.00066
HLA-DRB3	A_23_P145336	731247	1.69205	0.00005
HGEL18516	A_24_P42373		1.68606	0.00644
HLA-DQB2	A_23_P19510	3120	1.68354	3.23E-07
protein phosphatase 1F (PP2C domain containing)	A_24_P125894	9647	1.68302	0.00099
HLA-DQB1	A_32_P191417		1.6825	0.0097
TK2	A_24_P219324	7084	1.68054	0.003
LOC440823	A_24_P595223		1.67752	0.0012
PLEK	A_23_P209678	5341	1.67491	0.00723
BTN3A3	A_24_P311917	10384	1.67471	0.00008
RBMS3	A_32_P139551		1.66868	0.00236
BLP1	A_23_P10927	83877	1.66713	0.00602
NNMT	A_23_P127584	4837	1.66355	0.0001
SLCO4A1	A_23_P5903		1.66268	6.17E-12
C14orf161	A_23_P77043	79820	1.66202	0.001
TRB@	A_23_P352861	28619	1.65978	0.00171
PLAC8	A_24_P183128	360914	1.65785	0.00037
SP5	A_32_P183718	296510	1.65609	0.00003
TCEA1P	A_24_P712193		1.65525	0.00361
LOC343981	A_24_P212997		1.65216	2.99E-10
MSCP	A_23_P216004		1.65064	7.32E-06
FUT1	A_23_P107963	81919	1.64961	0.00989
LOC374392	A_24_P229426	643637	1.64822	0.00122
NUCB2	A_24_P595460		1.64807	0.00136
SNX16	A_23_P258891	64089	1.64683	0.00017
LSAMP	A_24_P794631		1.64574	0.00007
RBL1	A_24_P276102	19650	1.64502	0.00021
ASSP6	A_24_P900555		1.64419	0.00242
KIAA0103	A_32_P115277		1.64383	0.00739
HLA-DRA	A_32_P115555		1.64327	8.87E-07
BCR	A_24_P127235		1.64115	0.00565
GGA1	A_24_P926400	26088	1.64017	0.00012
NLF2	A_24_P788878	75697	1.63861	5.98E-06
VNN1	A_23_P255345	29142	1.63853	0.00067
PLAC8	A_23_P81219	360914	1.63356	2.07E-06
KIAA0844	A_23_P86610	216049	1.6332	0.00312
SPINK1	A_23_P214079	20730	1.63281	5.51E-08
UNQ6077	A_24_P323421	338366	1.63258	0.00693
CABP7	A_24_P177236	360970	1.63235	0.00431
MAP3K8	A_23_P23947	116596	1.63198	0.00004
STX16	A_24_P36457	362283	1.62911	0.00064
FLJ45832	A_32_P29408	100130623	1.62716	0.00124
RNF34	A_24_P278839	80196	1.61904	0.003
EPSTI1	A_23_P105794	108670	1.61885	0.00243
G0S2	A_23_P74609	50486	1.61632	0.00484
BIRC5	A_23_P118815	332	1.61483	0.00001
CARD11	A_24_P945262		1.61479	0.0015

ACE2	A_23_P252981	302668	1.61464	5.76E-06
MMP7	A_23_P52761	25335	1.61421	0.00924
HSXIAPAF1	A_24_P557479	54739	1.61262	8.59E-07
IER3	A_23_P42257	8870	1.61182	2.04E-12
FLJ34790	A_23_P362191	284029	1.60783	0.0071
THC1849214	A_32_P144390		1.60691	2.32E-06
TCF7L1	A_23_P142872	21415	1.60225	0.00135
FCHSD2	A_32_P163594		1.6014	0.00009
LDLR	A_23_P208595	300438	1.60015	0.0003
HLA-A	A_23_P408353	3105	1.59971	3.73E-06
AFP	A_23_P58205	11576	1.59945	0.00818
PI3	A_23_P210465	5266	1.59758	1.93E-09
TACC3	A_23_P212844	21335	1.58777	0.00032
A_32_P68443	A_32_P68443		1.58752	0.00056
CDH6	A_32_P134764		1.58374	0.00776
NCF4	A_23_P109508	4689	1.58295	0.00563
TPM4	A_23_P141974		1.58102	4.70E-11
CHI3L1	A_23_P137665	89824	1.57649	0.00769
C11orf23	A_24_P261488	52036	1.57505	0.00535
THC1873675	A_32_P17343		1.57445	0.00258
BCCIP	A_24_P1255	66165	1.5742	0.00579
ATCV32560	A_23_P373126		1.57002	0.00003
MIA	A_23_P4714	81510	1.56961	1.65E-06
FLJ20542	A_24_P328231	54973	1.56726	0.00621
DKFZP564I0422	A_24_P350437	66816	1.56699	0.00749
MGC19764	A_24_P707530		1.56514	0.00004
COL4A3	A_23_P170679	12828	1.56484	0.00422
NR4A1	A_23_P128230	15370	1.56452	0.00051
ID1	A_23_P252306	15901	1.56401	4.82E-08
KIAA1554	A_23_P95172	57674	1.56155	0.00116
C7orf6	A_23_P145874	500015	1.55915	0.00005
TCF19	A_24_P349965	6941	1.55884	0.00167
PCSK1	A_23_P213508	18548	1.5586	0.00007
HLA-G histocompatibility antigen, class I, G	A_23_P370707	3136	1.55802	0.00001
AK023647	A_24_P889070		1.55795	0.00122
PHKA1	A_23_P258531	18679	1.55779	0.00656
ITGAX	A_23_P312132	16411	1.55689	7.71E-06
LOC284134	A_32_P44349		1.55552	0.00651
NCF1	A_23_P42746	654817	1.55286	0.00001
TRIAD3	A_23_P42724	304294	1.55284	0.00003
IGHM	A_24_P367432	100133862	1.54923	0.00502
C14orf81	A_24_P323298		1.54859	0.00287
DIAPH3	A_23_P419254	290396	1.54629	0.00027
UNQ5783	A_24_P272451		1.54528	0.00397
PHIP	A_24_P931503		1.54054	0.00617
mannosidase, alpha, class 1A, member 2	A_24_P213548	10905	1.539	0.00005
ZNF25	A_23_P381577	219749	1.53774	0.0047
PRG4	A_23_P160286	289104	1.53724	0.00446
PPP1R12A	A_23_P204564	17931	1.5372	0.00349
GLRX	A_23_P69908	2745	1.53578	1.04E-06
APOL4	A_23_P380857	80832	1.53567	6.24E-06

DAPP1	A_23_P255444	27071	1.53424	4.85E-06
A_24_P7570	A_24_P7570		1.5333	0.00012
STAT3	A_24_P116805	25125	1.53309	0.00447
AREG	A_23_P259071	374	1.53302	0.0008
GIMAP2	A_23_P368681	26157	1.53185	0.00024
hypothetical protein FLJ33318	A_23_P38388	544806	1.53141	5.49E-06
ZNF251	A_23_P418204	90987	1.53059	0.00459
MNDA	A_23_P137935	4332	1.52916	0.00028
ASSP8	A_24_P367100		1.52861	0.00862
DPLK24430	A_23_P338113		1.52855	0.00081
LOC124976	A_24_P8371	124976	1.52827	3.43E-07
ZFY	A_24_P942743	7544	1.52821	0.00021
NOD3	A_23_P340019		1.5279	0.0003
KIAA0802	A_23_P360605	68617	1.52525	0.00586
HLA-G histocompatibility antigen, class I, G	A_23_P350295	3136	1.52434	6.27E-09
FLJ22761	A_23_P202427	216019	1.52412	0.00025
TGM2	A_32_P86763	21817	1.52407	0.00714
BC064349	A_32_P2807		1.52363	0.00036
RGC32	A_24_P10137	28984	1.5233	0.00016
KIAA1033	A_23_P394545	23325	1.52284	0.00903
USP18	A_32_P132206	11274	1.52206	3.55E-08
THC1805416	A_24_P561165		1.52116	0.0003
PCM1	A_24_P932661		1.5202	0.00189
FYB	A_24_P393740	499537	1.51965	0.00583
DNAJC5	A_24_P934565		1.51957	4.74E-06
LARP	A_24_P7211	23367	1.51849	2.01E-06
ARL7	A_23_P317620	10123	1.51691	0.00002
CASP10	A_23_P209408	843	1.51625	3.44E-07
BC042469	A_32_P77102	100128420	1.51575	0.00042
KHGF15301	A_24_P854896		1.51519	0.00574
IFIT2	A_23_P24004		1.51367	2.54E-07
DGKB	A_23_P61919	1607	1.51364	0.00367
LOC440441	A_24_P221327		1.51318	2.34E-07
Sej	A_24_P942969	14344	1.51121	0.00043
PLA2G2A	A_23_P321949	29692	1.51033	0.00051
GGIT32015	A_32_P175098		1.51027	1.26E-07
ZNF543	A_24_P913119		1.51013	0.00304
ARHT1	A_24_P59765	55288	1.50965	0.00037
RAD54B	A_23_P94141	100128414	1.50947	0.00021
LOC64744	A_24_P225325	298500	1.50709	0.00651
MTRR	A_23_P252211	210009	1.50628	6.45E-09
PTPN7	A_23_P201778	5778	1.5045	0.00021
LOC389667	A_32_P21993		1.50413	1.85E-11
FADS1	A_23_P203419	76267	1.50362	5.78E-07
ENST00000327829	A_24_P212949		1.50325	0.00136
SLC8A1	A_32_P110372	6546	1.50223	0.00517
MGC7036	A_23_P76109	288652	1.50179	0.00002
similar to KIAA0592 protein	A_24_P677639		1.50075	0.00011
ETFDH	A_32_P120484		-1.5009	0.00069
PHYH	A_23_P115919	114209	-1.50211	4.48E-08
AMACR	A_24_P106297	25284	-1.50313	0.00002
SLC30A1	A_24_P937095		-1.50325	1.12E-10

EIF4EBP2	A_24_P115621		-1.50331	9.00E-09
DXS1283E	A_23_P159797	363471	-1.50431	5.89E-09
ANK3	A_23_P301530		-1.50448	0.0002
FLJ12768	A_23_P143935	239827	-1.50781	0.00106
ARRDC4	A_23_P339818	91947	-1.51024	1.35E-06
KLF5	A_23_P53891	688	-1.5107	9.54E-06
ENPP1	A_32_P192376	85496	-1.51337	0.00002
DKK3	A_24_P261417	27122	-1.51705	0.00049
PPARGC1A	A_23_P18447	83516	-1.51945	3.54E-08
SLC4A4	A_32_P358887	54403	-1.52087	0.00005
C1orf179	A_23_P407695	338094	-1.52695	0.00006
THC1903690	A_32_P14222		-1.52916	0.00771
APOBEC3D	A_23_P369966	140564	-1.52956	3.84E-06
CD164	A_23_P254756	8763	-1.53008	2.66E-08
THC1913569	A_32_P117322		-1.53229	2.66E-07
GGTLA4	A_23_P57199	92086	-1.53905	8.44E-06
DKFZP586A0522	A_23_P415021	25840	-1.53927	1.48E-06
DAO	A_23_P139635	114027	-1.54044	0.00128
RetSDR2	A_23_P21644	114664	-1.54116	0.00009
LOC440498	A_32_P46981		-1.54197	0.00002
MSTP9	A_23_P340376		-1.54252	0.00309
SORL1	A_23_P87049	6653	-1.54449	4.28E-08
GLI3	A_23_P111531	2737	-1.54534	0.0002
VIL1	A_23_P16866	22349	-1.54559	8.04E-12
immunoglobulin lambda constant 1 (Mcg marker)	A_23_P72252	28793	-1.54631	0.00718
RUNX3	A_24_P918561		-1.54647	0.00508
MT1J	A_24_P74828	4498	-1.54658	0.00044
CKMT2	A_23_P144778	1160	-1.54671	0.00219
KIAA0931	A_23_P418234	23035	-1.54747	0.00013
similar to polycythemia rubra vera 1; cell surface receptor	A_32_P157213		-1.54749	0.00018
NMA	A_23_P52207	68010	-1.5491	0.00623
RVAG28856	A_32_P115717		-1.55264	1.12E-06
TXNIP	A_23_P97700	10628	-1.55326	7.04E-09
caveolin 1, caveolae protein, 22kDa	A_24_P12626	12389	-1.55674	0.00171
NRAP	A_23_P402765	18175	-1.56079	0.00018
GPC6	A_32_P97169		-1.56119	0.00239
LAMA4	A_23_P133656	16775	-1.56571	0.00002
C2orf10	A_32_P316136	91752	-1.56799	0.00669
PZP	A_23_P139682	5858	-1.57171	8.17E-06
KUB3	A_23_P53363	299828	-1.57333	1.14E-09
sphingomyelin phosphodiesterase, acid-like 3A	A_32_P223859	10924	-1.57444	6.41E-06
ANK3	A_23_P202269	361833	-1.57458	3.82E-08
MT1X	A_23_P303242	4501	-1.57664	0.0008
FLJ25224	A_24_P59430	78252	-1.587	3.83E-06
MT1B	A_23_P37983	4490	-1.58821	0.00075
MBD3L2	A_23_P378450	729458	-1.59367	0.00671
CNGA1	A_23_P92536	1259	-1.59729	0.00213
FLJ32954	A_23_P102160	151393	-1.59768	2.13E-09
PMP22	A_23_P100711	5376	-1.5998	0.00056
MCP-3	A_23_P78037	6354	-1.60253	0.00465

MT1H	A_23_P163782	4496	-1.60456	0.00015
ANPEP	A_23_P88626	81641	-1.60494	0.0026
MGC4248	A_23_P63660	361118	-1.60854	8.91E-10
MT2A	A_24_P361896	4502	-1.60931	0.00091
COMMD1	A_24_P879933		-1.61095	0.00952
similar to RIKEN cDNA 4921536K21	A_32_P227930		-1.61764	0.00547
UGT1A10	A_24_P222872	113992	-1.62073	0.0001
TRPM6	A_23_P216712	140803	-1.62478	0.00063
UGT1A4	A_23_P60599	113992	-1.62629	1.07E-06
RPIB9	A_23_P111724	154661	-1.62768	0.00003
ADH1A	A_24_P291658	124	-1.63033	2.63E-11
MAWBP	A_23_P149998	68371	-1.63181	0.00012
DKFZP566K1924	A_23_P329353	364208	-1.63261	0.00006
LOC134147	A_23_P144668	134147	-1.63648	1.46E-09
ANTXR1	A_24_P131522	69538	-1.63856	0.00022
PDZK1	A_23_P52121	5174	-1.64096	0.00002
RNF157	A_32_P57810	114804	-1.64884	1.09E-06
UGT1A10	A_23_P158330	54576	-1.65404	6.84E-06
MGAT2	A_24_P278603		-1.65425	4.39E-08
CTRB1	A_23_P431139	1504	-1.66037	0.00107
EMP1	A_23_P76488	13730	-1.66215	0.00016
ANGPTL1	A_23_P126706	679942	-1.66349	0.00406
GPNMB	A_23_P134426	10457	-1.67603	0.00226
PXMP2	A_23_P124122	29533	-1.68646	1.29E-10
CASPR4	A_23_P355405	85445	-1.69279	0.0032
FLJ20674	A_23_P72059	54621	-1.69574	2.50E-12
hypothetical protein FLJ22671	A_23_P60990	71874	-1.70185	0.00506
ENST00000334429	A_32_P122373		-1.70414	0.00036
GSTA1	A_23_P135417	2938	-1.71632	0.00086
COLEC12	A_23_P27306	361289	-1.71665	0.00036
Unknown	A_24_P51316		-1.72075	0.00544
BTNL8	A_24_P851254		-1.73357	0.00033
KIAA0828	A_24_P72518	312192	-1.73894	0.00001
TAS2R38	A_23_P359746	387513	-1.74156	0.00846
CLDN8	A_23_P427014	54420	-1.74343	0.00021
PAX6	A_32_P306001		-1.75584	0.00084
PNLIPRP2	A_23_P24083	117554	-1.77278	0.00207
TTTY1	A_24_P323131	50858	-1.77666	0.00115
COL6A2	A_23_P211233	361821	-1.77759	0.00004
SCN9A	A_24_P792124	78956	-1.77947	0.00086
PDLIM2	A_23_P20285	290354	-1.78682	8.84E-10
TM4SF2	A_23_P114185	7102	-1.7931	4.25E-12
HMGCS2	A_23_P103588	15360	-1.80628	7.36E-07
LOC285016	A_24_P561341	285016	-1.80711	0.00003
ZDHHC11	A_23_P256008	79844	-1.80969	0.00016
MT1I	A_23_P60933	4495	-1.81166	0.00008
MT1H	A_23_P414343	4498	-1.81952	0.00005
UGT2B10	A_23_P7342	305264	-1.82402	8.23E-06
LOC440572	A_24_P854586		-1.83156	0.00812
THC1969420	A_32_P3322		-1.84451	0.00447
ITGAD	A_24_P366652	381924	-1.8461	0.00715
C14orf31	A_24_P330303	319710	-1.85383	0.00006

ELA3B	A_23_P200579	298567	-1.85567	0.00009
MT1L	A_23_P427703	4500	-1.86516	9.57E-06
GDF10	A_24_P355464	79216	-1.86569	0.00607
CREB-H	A_23_P108082	208677	-1.86976	0.00133
CA2	A_23_P8913	54231	-1.88005	0.00419
MST1	A_24_P148796	24566	-1.8851	2.65E-07
AKAP1	A_32_P542060		-1.8906	0.00576
FN1	A_24_P119745	14268	-1.89844	0.00085
LOC343574	A_24_P915406		-1.90395	0.00499
NPY1R	A_23_P69699	4886	-1.90487	0.0009
Hr44 antigen	A_24_P585676	27251	-1.93542	0.00546
TNNC2	A_23_P131825	7125	-1.95787	0.00001
PDE6A	A_23_P81590	307401	-1.96299	0.00002
KCNS3	A_23_P120103	83588	-1.96912	4.27E-08
EDN1	A_23_P214821	13614	-1.97642	5.67E-09
LOC389023	A_32_P86578	389023	-1.97738	0.00033
TTPA	A_24_P252462	50500	-1.99139	0.00327
ZDHHC11	A_24_P153456	79844	-1.99975	0.00002
MT1G	A_23_P206707	4495	-2.01106	1.20E-08
GHR	A_24_P72064	25235	-2.03736	0.00002
UGT2B15	A_23_P58407	243085	-2.06266	0.00711
AQP8	A_23_P26522	343	-2.07242	0.00001
FLJ21934	A_24_P334378	79799	-2.07974	0.00005
MT2A	A_23_P206724	4493	-2.0907	0.00005
UNQ305	A_32_P118397	253012	-2.112	0.00007
A_24_P575267	A_24_P575267		-2.11439	0.00004
TEX11	A_23_P96501	56159	-2.11698	0.00008
PRO0245	A_23_P10564		-2.13693	0.00012
C6orf89	A_32_P129416		-2.20273	0.00498
MT1X	A_24_P125096	4501	-2.24743	4.28E-08
FRMD1	A_32_P174285		-2.28648	3.04E-08
MT1F	A_23_P15174		-2.45287	2.28E-07
OSTalpha	A_24_P385732	200931	-2.4793	0.00822
UGT2B11	A_23_P212968	24862	-2.48593	0.00096
SLC26A2	A_23_P250951	13521	-2.52501	0.00001
SLC38A4	A_24_P321581	55089	-2.67208	0.00507
UGT2B10	A_24_P521559		-2.71169	0.0002
SLC3A1	A_24_P217234	29484	-2.74488	0.00034
MT1K	A_23_P66241	4499	-2.83286	2.38E-10
ECHDC3	A_23_P127033	67856	-3.11593	7.59E-07
LOC63928	A_23_P349463	63928	-3.15354	5.46E-28

Figure 28

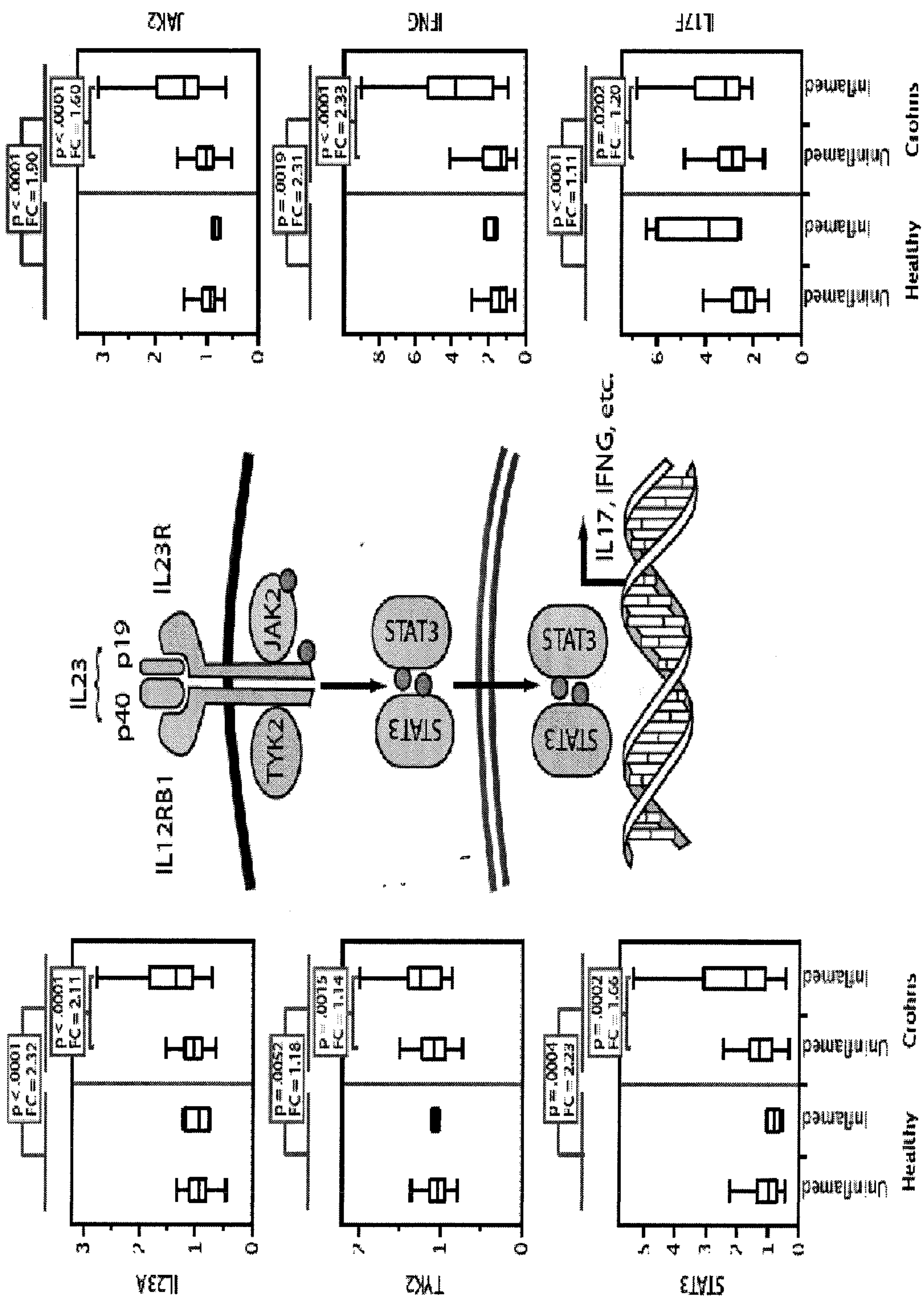

IL23A
TYK2
STAT3
JAK2
IFNG
IL17F
IL23
p40
p19
IL12RB1
IL23R
JAK2
TYK2
STAT3
IL17, IFNG, etc.
Healthy
Crohns
Uninflamed
Inflamed
p < .0001
FC = 2.32
p < .0001
FC = 2.11
p = .0052
FC = 1.18
p = .0015
FC = 1.14
p = .0004
FC = 2.23
p = .0002
FC = 1.66
p < .0001
FC = 1.90
p < .0001
FC = 1.60
p = .0019
FC = 2.31
p < .0001
FC = 2.33
p < .0001
FC = 1.11
p = .0202
FC = 1.20

Figure 29

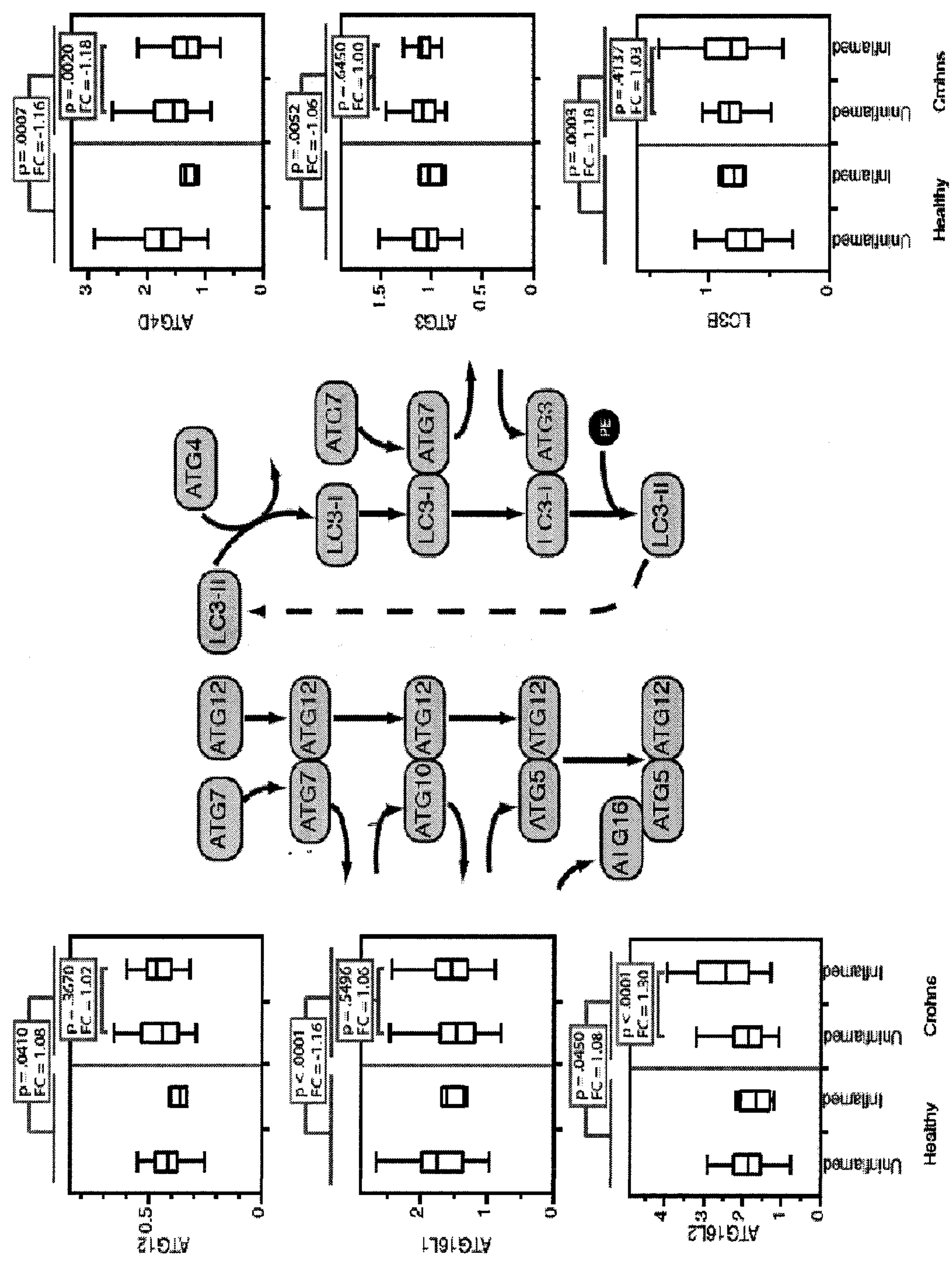
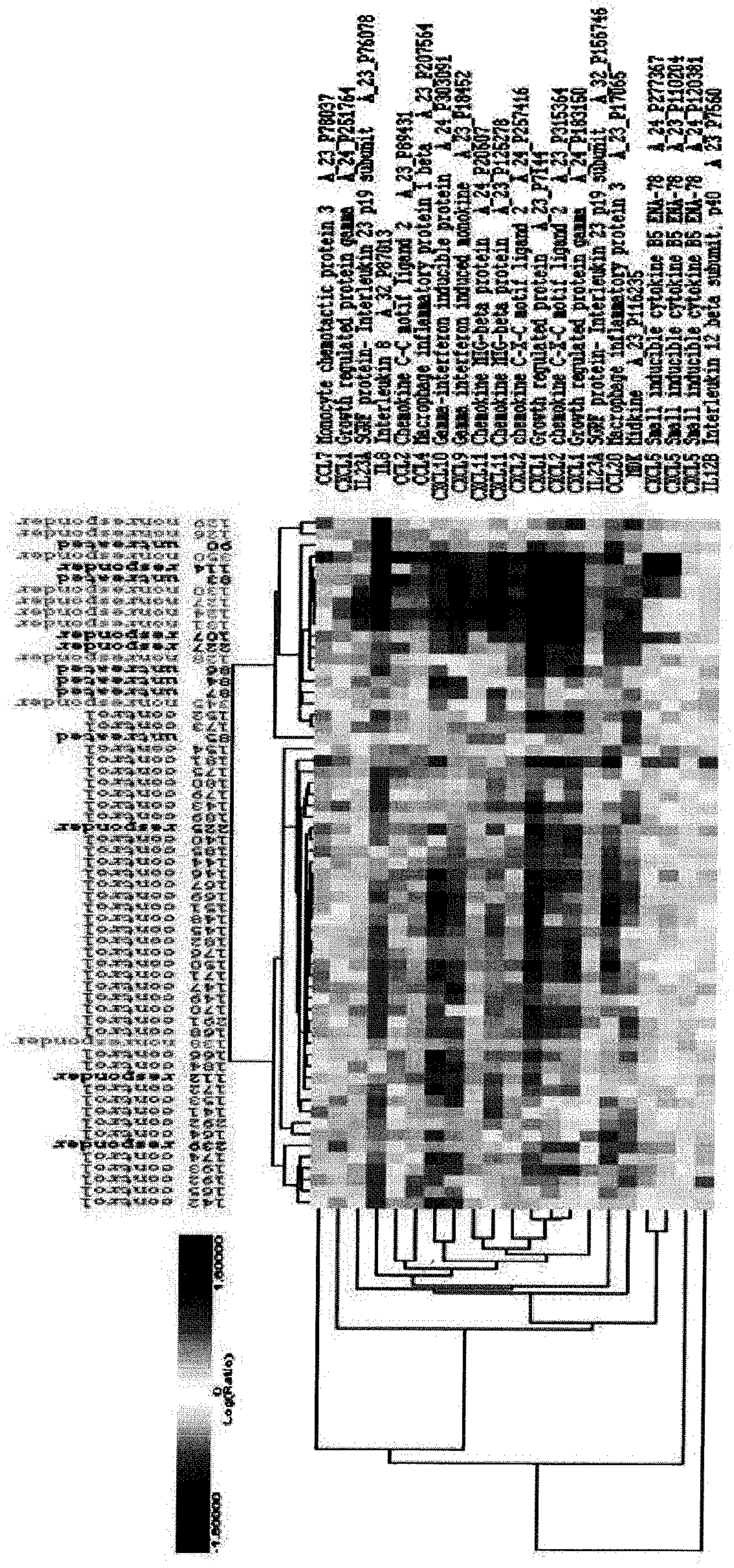

ATG4D
ATG3
LC3B
ATG12
ATG16L1
ATG16L2
ATG4
ATG7
ATG10
ATG5
ATG16
LC3-I
LC3-II
PE
Uninflamed
Inflamed
Healthy
Crohns

Figure 30


CCL7 Monocyte chemotactic protein 3 A_23_P78037
CXCL1 Growth regulated protein gamma A_24_P251764
IL23A SGRF protein- Interleukin 23 p19 subunit A_23_P76078
IL8 Interleukin 8 A_32_P87013
CCL2 Chemokine C-C motif ligand 2 A_23_P89431
CCL4 Macrophage inflammatory protein 1 beta A_23_P207564
CXCL10 Gamma-interferon inducible protein A_24_P303091
CXCL9 Gamma interferon induced monokine A_23_P18452
CXCL11 Chemokine HMG-beta protein A_24_P20607
CXCL11 Chemokine HMG-beta protein A_23_P125278
CXCL2 chemokine C-X-C motif ligand 2 A_24_P257416
CXCL1 Growth regulated protein A_23_P7144
CXCL2 chemokine C-X-C motif ligand 2 A_23_P315364
CXCL1 Growth regulated protein gamma A_24_P183150
IL23A SGRF protein- Interleukin 23 p19 subunit A_32_P156746
CCL20 Macrophage inflammatory protein 3 A_23_P17065
MDK Midkine A_23_P116235
CXCL5 Small inducible cytokine B5 ENA-78 A_24_P277367
CXCL5 Small inducible cytokine B5 ENA-78 A_23_P110204
CXCL5 Small inducible cytokine B5 ENA-78 A_24_P120381
IL12B Interleukin 12 beta subunit, p40 A_23_P7560
-1.50000
0
1.50000
Log(Ratio)