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- (54) **Title:** METHODS, SYSTEMS, AND KITS FOR TREATING INFLAMMATORY DISEASE TARGETING SKAP2

FIG. 1

PHENOTYPE	dbSNP	p_value	A1	n_miss	OR_Z_B	base_ pair_CH 7	snp_ location	cis_ eGENE	eqtl_beta	eqtl_p	priority	MAF
CD vs. Ctrl	rs73069541	5.75E-14	G	94095	0.089594991	26904928	intronic	HIBADH, HOXA11-AS	- 0.1186890 17417339, 0.0941114 404455934	0.04652407 2405745, 0.04990810 58041685	0, 0	0.244
CD vs. Ctrl	rs10486483	8.54E-14	A	89783	0.088948057	26892440	intronic	NA	NA	NA	NA	0.2596
CD vs. Ctrl	rs3801810	9.76E-14	A	86890	0.090776716	26892531	intronic	NA	NA	NA	NA	0.2576
CD vs. Ctrl	rs73069540	1.31E-13	A	94100	0.088305501	26904770	intronic	HIBADH, HOXA11-AS	- 0.1186890 17417339, 0.0941114 404455934	0.04652407 2405745, 0.04990810 58041685	0, 0	0.2438
CD vs. Ctrl	rs3801844	1.37E-13	G	94067	0.086962835	26829759	intronic	NA	NA	NA	NA	0.2502
CD vs. Ctrl	rs17323934	1.51E-13	G	94084	0.088080968	26904330	UTR5	HIBADH, HOXA11-AS	- 0.1186890 17417339, 0.0941114 404455934	0.04652407 2405745, 0.04990810 58041685	0, 0	0.2438
CD vs. Ctrl	rs10276471	1.51E-13	G	94076	0.086758459	26837940	intronic	NA	NA	NA	NA	0.2501
CD vs. Ctrl	rs3801820	1.70E-13	G	94094	0.086579542	26861353	intronic	NA	NA	NA	NA	0.2528
CD vs. Ctrl	rs10272303	1.72E-13	G	94080	0.086616253	26827815	intronic	NA	NA	NA	NA	0.2502
CD vs. Ctrl	rs3801842	1.79E-13	A	94021	0.086550335	26830263	intronic	NA	NA	NA	NA	0.2502
CD vs. Ctrl	rs3801831	1.85E-13	G	94081	0.086412272	26853470	intronic	NA	NA	NA	NA	0.2529
CD vs. Ctrl	rs73065517	1.91E-13	G	94090	0.086421813	26830555	intronic	NA	NA	NA	NA	0.2501

- (57) **Abstract:** Described herein are methods, systems, compositions, and kits useful for the diagnosis and/or treatment of a disease or condition in a subject. The present disclosure relates to methods and systems for identifying and stratifying patients suitable for treatment with a SKAP2 modulator, as described herein.

Declarations under Rule 4.17:

- *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*
- *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))*

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- *with international search report (Art. 21(3))*
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- *with sequence listing part of description (Rule 5.2(a))*

METHODS, SYSTEMS, AND KITS FOR TREATING INFLAMMATORY DISEASE TARGETING SKAP2

CROSS-REFERENCE

[001] This application claims the benefit of U.S. Provisional Application No. 62/803,290, filed February 8, 2019, which is herein incorporated by reference in its entirety.

SEQUENCE LISTING

[002] The instant application contains a Sequence Listing which has been submitted electronically in ASCII format and is hereby incorporated by reference in its entirety. Said ASCII copy, created on January 28, 2020, is named 56884-757_601_SL.txt and is 15,348 bytes in size.

SUMMARY

[003] Inflammatory bowel diseases (IBD) is a heterogeneous group of chronic, relapsing inflammatory disorders of the gastrointestinal (GI) tract affecting more than 3 million adults in the United States, according to the most recent Centers for Disease and Prevention (CDC) survey. The two most common manifestations of IBD are Crohn's disease (CD) and ulcerative colitis (UC). Each of these forms of IBD has various subclinical phenotypes that manifest in certain IBD patients. For example, the chronic inflammation of the GI tract caused by CD and UC leads to the formation of scar tissue (fibrosis) and stenosis (fibrostenosis) in the intestinal wall in some IBD patients, that is largely unresponsive to current therapeutic interventions. For these patients endoscopic or surgical treatment is often the only treatment available.

[004] IBD, including CD and UC, is characterized by an uncontrolled activity of the immune response within the intestinal mucosal, which depends on genetic susceptibility to developing the IBD, subclinical phenotypes of IBD, as well as to various stimuli related to IBD pathogenesis (*e.g.*, intestinal microbiome). Genome Wide Association Studies (GWAS) have enabled scientists to identify genetic variants in certain IBD susceptibility gene loci useful for the selection of IBD patients for treatment with targeted therapeutic strategies and identifying drugable targets in the development of novel therapies.

[005] Few treatment options are available to patients that suffer from IBD. Current therapeutic regimens include one or more of anti-inflammatory medication (*e.g.*, corticosteroids) and immunomodulatory therapy (*e.g.*, anti-TNF therapy). However, nearly half of all patients treated with an anti-TNF therapy do not respond to the induction of the therapy or experience a loss of response to the treatment after a period, during which, disease severity has progressed significantly. Therefore, there remains a significant need for targeted and effective treatment options that respond to the underlying immunopathogenesis of IBD.

[006] Aspects disclosed herein provide methods of treating a subject in need thereof with a modulator of Src Kinase Associated Phosphoprotein 2 (SKAP2) activity or expression, wherein the subject has

moderate to severe Crohn's disease (CD), and wherein the subject has a genotype characterized by the presence of one or more SNPs. In some embodiments, the methods further comprise determining the genotype of the subject. In some embodiments, the genotype of the subject comprises determining the presence or absence of the one or more SNPs provided in FIG. 1. In some embodiments, the genotype is detected with an assay comprising polymerase chain reaction (PCR), quantitative reverse-transcription PCR (qPCR), automated sequencing, genotype array, or a combination thereof. In some embodiments, the subject does not comprise the minor allele shown in FIG. 1. In some embodiments, the SNP is associated with at least one of stricturing and penetrating. In some embodiments, the at least one of stricturing and penetrating is isolated to at least one of a colon, an ileum, and an ileocolonic region of an intestine. In some embodiments, the SNP is associated with one or more serological markers. In some embodiments, the SNP is associated with one or more subclinical phenotypes.

[007] Aspects disclosed herein provide methods of reducing activity or expression of Src Kinase Associated Phosphoprotein 2 (SKAP2) in a subject having a genotype characterized by the presence of one or more SNPs provided in FIG. 1, the method comprising administering to the subject a modulator of SKAP2. In some embodiments, the methods further comprise determining the genotype of the subject. In some embodiments, the genotype of the subject comprises determining the presence or absence of the one or more SNPs provided in FIG. 1. In some embodiments, the genotype is detected with an assay comprising polymerase chain reaction (PCR), quantitative reverse-transcription PCR (qPCR), automated sequencing, genotype array, or a combination thereof. In some embodiments, the subject does not comprise the minor allele shown in FIG. 1. In some embodiments, the SNP is associated with at least one of stricturing and penetrating. In some embodiments, the at least one of stricturing and penetrating is isolated to at least one of a colon, an ileum, and an ileocolonic region of an intestine. In some embodiments, the SNP is associated with one or more serological markers. In some embodiments, the SNP is associated with one or more subclinical phenotypes.

[008] Aspects disclosed herein provide methods of treating a subject in need thereof with a modulator of Src Kinase Associated Phosphoprotein 2 (SKAP2) activity or expression, wherein the subject has moderate to severe inflammatory bowel disease (IBD), and wherein the subject has a genotype characterized by the presence of one or more SNPs. In some embodiments, methods further comprise determining the genotype of the subject. In some embodiments, the genotype of the subject comprises determining the presence or absence of the one or more SNPs provided in FIG. 1. In some embodiments, the genotype is detected with an assay comprising polymerase chain reaction (PCR), quantitative reverse-transcription PCR (qPCR), automated sequencing, genotype array, or a combination thereof. In some embodiments, the subject does not comprise the minor allele shown in FIG. 1. In some embodiments, the SNP is associated with at least one of stricturing and penetrating. In some embodiments, the at least one of stricturing and penetrating is isolated to at least one of a colon, an ileum, and an ileocolonic region of an intestine. In some embodiments, the SNP is associated with

one or more serological markers. In some embodiments, the SNP is associated with one or more subclinical phenotypes.

[009] Aspects disclosed herein provide methods of treating a subject in need thereof with a modulator of Src Kinase Associated Phosphoprotein 2 (SKAP2) activity or expression, wherein the subject has moderate to severe ulcerative colitis, and wherein the subject has a genotype characterized by the presence of one or more SNPs. In some embodiments, methods further comprise determining the genotype of the subject. In some embodiments, the genotype of the subject comprises determining the presence or absence of the one or more SNPs provided in FIG. 1. In some embodiments, the genotype is detected with an assay comprising polymerase chain reaction (PCR), quantitative reverse-transcription PCR (qPCR), automated sequencing, genotype array, or a combination thereof. In some embodiments, the subject does not comprise the minor allele shown in FIG. 1. In some embodiments, the SNP is associated with at least one of stricturing and penetrating. In some embodiments, the at least one of stricturing and penetrating is isolated to at least one of a colon, an ileum, and an ileocolonic region of an intestine. In some embodiments, the SNP is associated with one or more serological markers. In some embodiments, the SNP is associated with one or more subclinical phenotypes.

BRIEF DESCRIPTION OF THE DRAWINGS

[0010] Fig. 1 illustrates meta-analysis of SKAP2 single nucleotide polymorphism in association with Crohn's disease (CD), inflammatory bowel disease (IBD), or ulcerative colitis (UC), and various subclinical phenotypes of CD, IBD, and UC.

DETAILED DESCRIPTION OF THE DISCLOSURE

[0011] While preferred embodiments of the present disclosure have been shown and described herein, it will be obvious to those skilled in the art that such embodiments are provided by way of example only. Numerous variations, changes, and substitutions will now occur to those skilled in the art without departing from the disclosure. It should be understood that various alternatives to the embodiments of the disclosure described herein may be employed in practicing the disclosure. It is intended that the following claims define the scope of the disclosure and that methods and structures within the scope of these claims and their equivalents be covered thereby.

Certain Terminologies

[0012] The terminology used herein is for the purpose of describing particular cases only and is not intended to be limiting. As used herein, the singular forms "a", "an" and "the" are intended to include the plural forms as well, unless the context clearly indicates otherwise. Furthermore, to the extent that the terms "including", "includes", "having", "has", "with", or variants thereof are used in either the detailed description and/or the claims, such terms are intended to be inclusive in a manner similar to the term "comprising."

[0013] The term “about” or “approximately” means within an acceptable error range for the particular value as determined by one of ordinary skill in the art, which will depend in part on how the value is measured or determined, e.g., the limitations of the measurement system. For example, “about” can mean within 1 or more than 1 standard deviation, per the practice in the given value. Where particular values are described in the application and claims, unless otherwise stated the term “about” should be assumed to mean an acceptable error range for the particular value.

[0014] As used herein “consisting essentially of” when used to define compositions and methods, shall mean excluding other elements of any essential significance to the combination for the stated purpose. Thus, a composition consisting essentially of the elements as defined herein would not exclude other materials or steps that do not materially affect the basic and novel characteristic(s) of the claimed disclosure, such as compositions for treating skin disorders like acne, eczema, psoriasis, and rosacea.

[0015] The terms "homologous," "homology," or "percent homology" are used herein to generally mean an amino acid sequence or a nucleic acid sequence having the same, or similar sequence to a reference sequence. Percent homology of sequences can be determined using the most recent version of BLAST, as of the filing date of this application.

[0016] The terms “increased,” or “increase” are used herein to generally mean an increase by a statically significant amount. In some embodiments, the terms “increased,” or “increase,” mean an increase of at least 10% as compared to a reference level, for example an increase of at least about 10%, at least about 20%, or at least about 30%, or at least about 40%, or at least about 50%, or at least about 60%, or at least about 70%, or at least about 80%, or at least about 90% or up to and including a 100% increase or any increase between 10-100% as compared to a reference level, standard, or control. Other examples of “increase” include an increase of at least 2-fold, at least 5-fold, at least 10-fold, at least 20-fold, at least 50-fold, at least 100-fold, at least 1000-fold or more as compared to a reference level.

[0017] The terms “decreased” or “decrease” are used herein generally to mean a decrease by a statistically significant amount. In some embodiments, “decreased” or “decrease” means a reduction by at least 10% as compared to a reference level, for example a decrease by at least about 20%, or at least about 30%, or at least about 40%, or at least about 50%, or at least about 60%, or at least about 70%, or at least about 80%, or at least about 90% or up to and including a 100% decrease (e.g., absent level or non-detectable level as compared to a reference level), or any decrease between 10-100% as compared to a reference level. In the context of a marker or symptom, by these terms is meant a statistically significant decrease in such level. The decrease can be, for example, at least 10%, at least 20%, at least 30%, at least 40% or more, and is preferably down to a level accepted as within the range of normal for an individual without a given disease.

[0018] The terms “patient” or “subject” are used interchangeably herein and encompass mammals. Non-limiting examples of mammal include, any member of the mammalian class: humans, non-

human primates such as chimpanzees, and other apes and monkey species; farm animals such as cattle, horses, sheep, goats, swine; domestic animals such as rabbits, dogs, and cats; laboratory animals including rodents, such as rats, mice and guinea pigs, and the like. In one aspect, the mammal is a human. The term “animal” as used herein comprises human beings and non-human animals. In one embodiment, a “non-human animal” is a mammal, for example a rodent such as rat or a mouse.

[0019] The term “gene,” as used herein, refers to a segment of nucleic acid that encodes an individual protein or RNA (also referred to as a “coding sequence” or “coding region”), optionally together with associated regulatory region such as promoter, operator, terminator and the like, which may be located upstream or downstream of the coding sequence.

[0020] The term “genetic variant” as used herein refers to an aberration in (e.g., a mutation), or of (e.g., copy number variation), a nucleic acid sequence, as compared to the nucleic acid sequence in a reference population. In some embodiments, the genetic variant is common in the reference population. In some embodiments, the genetic variant is rare in the reference population.

[0021] The term, “genotype” as disclosed herein, refers to the chemical composition of polynucleotide sequences within the genome of an individual. In some embodiments, the genotype comprises single nucleotide variant (SNV), a single nucleotide polymorphism (SNP), or and indel (insertion or deletion, of a nucleobase within a polynucleotide sequence). In some embodiments, a genotype for a particular SNV, SNP, or indel is heterozygous. In some embodiments, a genotype for a particular SNV, SNP, or indel is homozygous.

[0022] The term, “single nucleotide polymorphism” or “SNP”, as disclosed herein, refers to a variation in a single nucleotide within a polynucleotide sequence. The variation of an SNP may have multiple different forms. A single form of an SNP is referred to as an “allele.” An SNP can be mono-, bi-, tri, or tetra-allelic. An SNV may include a “risk allele,” a “protective allele,” or neither. By way of example, a reference polynucleotide sequence reading 5’ to 3’ is TTACG. A SNP at allele position 3 (of 5’-TTACG-3’) comprise a substitution of the reference allele, “A” to a non-reference allele, “C.” If the “C” allele of the SNV is associated with an increased probability of developing a phenotypic trait, the allele is considered a “risk” allele. However, the same SNP may also comprise a substitution of the “A” allele to a “T” allele at position 3. If the T allele of the SNP is associated with a decreased probability of developing a phenotypic trait, the allele is considered a “protective” allele. The term “SNP,” should not be interpreting as placing a restriction on the observance rate in a given population. In some embodiments, the SNP is represented by an “rs” number, which refers to the accession of reference cluster of one more submitted SNPs in the dbSNP bioinformatics database as of the filing date of this patent application, and which is included within a sequence that comprises the total number of nucleobases from 5’ to 3’. In some embodiments, a SNP may be further defined by the position of the SNP (nucleobase) within the dbSNP sequence, the position of which is always with reference to 5’ length of the sequence plus 1. In some embodiments, a SNP is defined as the genomic position in a reference genome and the allele change (e.g. chromosome 7 at position 234,123,567

from G allele to A allele in the reference human genome build 37). In some embodiments, the SNV is defined as the genomic position identified with a non-nucleotide code (e.g., IPUAC) or [brackets] in a sequence disclosed herein.

[0023] The term, “indel,” as disclosed herein, refers to an insertion, or a deletion, of a nucleobase within a polynucleotide sequence. An indel can be mono-, bi-, tri-, or tetra-allelic. An indel may be “risk,” a “protective,” or neither, for a phenotypic trait. In some embodiments, the indel is represented by an “rs” number, which refers to the accession of reference cluster of one more submitted indels in the dbSNP bioinformatics database as of the filing date of this patent application, and which is included in a sequence that comprises the total number of nucleobases from 5’ to 3’. In some embodiments, an indel may be further defined by the position of the insertion/deletion within the dbSNP sequence, the position of which is always with reference to the 5’ length of the sequence plus 1. In some embodiments, an indel is defined as the genomic position in a reference genome and the allele change. In some embodiments, the indel is defined as the genomic position identified with [brackets] in a sequence disclosed herein.

[0024] “Haplotype” as used herein, encompasses a group of one or more genotypes, SNVs, SNPs, or indels, which tend to be inherited together in a reference population. In some embodiments, a haplotype comprises particular SNVs, SNPs, or indels, and any SNV, SNP, or indel in linkage disequilibrium therewith.

[0025] “Linkage disequilibrium,” or “LD,” as used herein refers to the non-random association of alleles or indels in different gene loci in a given population. LD may be defined by a D' value corresponding to the difference between an observed and expected allele or indel frequencies in the population ($D = P_{AB} - P_A P_B$), which is scaled by the theoretical maximum value of D . LD may be defined by an r^2 value corresponding to the difference between an observed and expected unit of risk frequencies in the population ($D = P_{AB} - P_A P_B$), which is scaled by the individual frequencies of the different loci. In some embodiments, D' comprises at least 0.20. In some embodiments, r^2 comprises at least 0.70.

[0026] The terms “treat,” “treating,” and “treatment” as used herein refers to alleviating or abrogating a disorder, disease, or condition; or one or more of the symptoms associated with the disorder, disease, or condition; or alleviating or eradicating a cause of the disorder, disease, or condition itself. Desirable effects of treatment can include, but are not limited to, preventing occurrence or recurrence of disease, alleviation of symptoms, diminishing any direct or indirect pathological consequences of the disease, preventing metastasis, decreasing the rate of disease progression, amelioration or palliation of the disease state and remission or improved prognosis.

[0027] The term “therapeutically effective amount” refers to the amount of a compound or therapy that, when administered, is sufficient to prevent development of, or alleviate to some extent, one or more of the symptoms of a disorder, disease, or condition of the disease; or the amount of a

compound that is sufficient to elicit biological or medical response of a cell, tissue, system, animal, or human that is being sought by a researcher, veterinarian, medical doctor, or clinician.

[0028] The term “pharmaceutically acceptable carrier,” “pharmaceutically acceptable excipient,” “physiologically acceptable carrier,” or “physiologically acceptable excipient” refers to a pharmaceutically-acceptable material, composition, or vehicle, such as a liquid or solid filler, diluent, excipient, solvent, or encapsulating material. A component can be “pharmaceutically acceptable” in the sense of being compatible with the other ingredients of a pharmaceutical formulation. It can also be suitable for use in contact with the tissue or organ of humans and animals without excessive toxicity, irritation, allergic response, immunogenicity, or other problems or complications, commensurate with a reasonable benefit/risk ratio. See, Remington: The Science and Practice of Pharmacy, 21st Edition; Lippincott Williams & Wilkins: Philadelphia, PA, 2005; Handbook of Pharmaceutical Excipients, 5th Edition; Rowe et al., Eds., The Pharmaceutical Press and the American Pharmaceutical Association: 2005; and Handbook of Pharmaceutical Additives, 3rd Edition; Ash and Ash Eds., Gower Publishing Company: 2007; Pharmaceutical Preformulation and Formulation, Gibson Ed., CRC Press LLC: Boca Raton, FL, 2004).

[0029] The term “pharmaceutical composition” refers to a mixture of a compound disclosed herein with other chemical components, such as diluents or carriers. The pharmaceutical composition can facilitate administration of the compound to an organism. Multiple techniques of administering a compound exist in the art including, but not limited to, oral, injection, aerosol, parenteral, and topical administration.

[0030] The term “inflammatory bowel disease” or “IBD” as used herein refers to gastrointestinal disorders of the gastrointestinal tract. Non-limiting examples of IBD include, Crohn's disease (CD), ulcerative colitis (UC), indeterminate colitis (IC), microscopic colitis, diversion colitis, Bechet's disease, and other inconclusive forms of IBD. In some instances, IBD comprises fibrosis, fibrostenosis, stricturing and/or penetrating disease, obstructive disease, or a disease that is refractory (e.g., mrUC, refractory CD), perianal CD, or other complicated forms of IBD.

[0031] Non-limiting examples of “sample” include any material from which nucleic acids and/or proteins can be obtained. As non-limiting examples, this includes whole blood, peripheral blood, plasma, serum, saliva, mucus, urine, semen, lymph, fecal extract, cheek swab, cells or other bodily fluid or tissue, including but not limited to tissue obtained through surgical biopsy or surgical resection. In various embodiments, the sample comprises tissue from the large and/or small intestine. In various embodiments, the large intestine sample comprises the cecum, colon (the ascending colon, the transverse colon, the descending colon, and the sigmoid colon), rectum and/or the anal canal. In some embodiments, the small intestine sample comprises the duodenum, jejunum, and/or the ileum. Alternatively, a sample can be obtained through primary patient derived cell lines or archived patient samples in the form of preserved samples, or fresh frozen samples.

[0032] The term “biomarker” comprises a measurable substance in a subject whose presence, level, or activity, is indicative of a phenomenon (e.g., phenotypic expression or activity; disease, condition, subclinical phenotype of a disease or condition, infection; or environmental stimuli). In some embodiments, a biomarker comprises a gene, or gene expression product. In some embodiments, a biomarker comprises a cytokine (e.g., IL-1 α , IL-1 β , IL-2, IL-3, IL-4, IL-5, IL-6, IL-8, IL-9, IL-10, IL-13, IL-17, IL-17F, IL-22, TNF- α , TNF- β , IFN- α 1/- α 2, IFN- β , IFN- γ , TNFSF superfamily: TNF, TL1A, FasL, LIGHT, TRAIL, and TWEAK). In some embodiments, a biomarker comprises a cell type (e.g., Natural Killer (NK) cells, T cells, Effector T cells (Teff), Regulatory T cells (Treg) B cells, T helper (Th) cells, cluster of differentiation (CD) cells, innate lymphoid cells (ILC), antigen-presenting cells (APC), monocytes Paneth cells, granulocytes, dendritic cells, and macrophages).

[0033] The term “serological marker,” as used herein refers to a type of biomarker representing an antigenic response in a subject that may be detected in the serum of the subject. In some embodiments, a serological marker comprises an antibody against various fungal antigens. Non-limiting examples of a serological marker comprise anti-Saccharomyces cerevisiae antibody (ASCA), an anti-neutrophil cytoplasmic antibody (ANCA), E.coli outer membrane porin protein C (OmpC), anti-Malassezia restricta antibody, anti-Malassezia pachydermatis antibody, anti-Malassezia furfur antibody, anti-Malassezia globosa antibody, anti-Cladosporium albicans antibody, anti-laminaribiose antibody (ALCA), anti-chitobioside antibody (ACCA), anti-laminarin antibody, anti-chitin antibody, pANCA antibody, anti-I2 antibody, and anti-Cbir1 flagellin antibody.

[0034] The term “microbiome” and its variation used herein describe the populations and interactions of the bacteria, fungi, protists, and virus that align the gastrointestinal tract of a subject. A subject afflicted with IBD may possess presence, absence, excess, diminished, or a combination thereof of a microbiome as compared to a healthy subject. Non-limiting examples of bacteria associated with IBD includes strains, sub-strains, and enterotypes of enterobacteriaceae, pasteuraceae, fusobacteriaceae, neisseriaceae, veillonellaceae, gemellaceae, bacteroidales, clostridiales, erysipelotrichaceae, bifidobacteriaceae bacteroides, faecalibacterium, roseburia, blautia, ruminococcus, coprococcus, streptococcus, dorea, blautia, ruminococcus, lactobacillus, enterococcus, streptococcus, escherichia coli, fusobacterium nucleatum, haemophilus parainfluenzae (pasteurellaceae), veillonella parvula, eikenella corrodens (neisseriaceae), and gemella moribundum, bacteroides vulgatus, bacteroides caccae, bifidobacterium bifidum, bifidobacterium longum, bifidobacterium adolescentis, bifidobacterium dentum, blautia hansenii, ruminococcus gnavus, clostridium nexile, faecalibacterium prausnitzii, ruminococcus torques, clostridium bolteae, eubacterium rectale, roseburia intestinalis, coprococcus comes, actinomyces, lactococcus, roseburia, streptococcus, blautia, dialister, desulfovibrio, escherichia, lactobacillus, coprococcus, clostridium, bifidobacterium, klebsiella, granulatella, eubacterium, anaerostipes, parabacteroides, coprobacillus, gordonibacter, collinsella, bacteroides, faecalibacterium, anaerotruncus, alistipes, haemophilus, anaerococcus, veillonella, arevotella, akkermansia, bilophila, sutterella, eggerthella, holdemania, gemella,

peptoniphilus, rothia, enterococcus, pediococcus, citrobacter, odoribacter, enterobacteria, fusobacterium, and proteus. Non-limiting examples of viruses associated with IBD include picovirinae, lactococcus phage, cellulophaga phage, bacteroides phage, C2 like virus, enterococcus phage, caudivirales, cellulophaga phage, phiCD119 like virus, croceibacter phage, clostridium phage, spounavirinae, riemerella phage, lambda like virus, bacillus phage, terenvirinae, lactobacillus phage, enterobacteria phage, thermoanaerobacterium phage, streptococcus phage, and pseudomonas phage. Non-limiting examples of fungi genera associated with IBD includes Malassezia, Cladosporium, Aureobasidium, Fusarium, Candida, Pichia, Saccharomyces, and Escherichia.

[0035] The term “medically refractory,” or “refractory,” as used herein, refers to the failure of a standard treatment to induce remission of a disease. In some embodiments, the disease comprises an inflammatory disease disclosed herein. A non-limiting example of refractory inflammatory disease includes refractory Crohn’s disease, and refractory ulcerative colitis (*e.g.*, mrUC). Non-limiting examples of standard treatment include glucocorticosteroids, anti-TNF therapy, anti-a4-b7 therapy (vedolizumab), anti-IL12p40 therapy (ustekinumab), Thalidomide, and Cytosin.

[0036] The term “anti-tumor necrosis factor (TNF) non-response,” or “anti-TNF non-response,” as used herein, refers to a subject not responding to the induction of an anti-TNF therapy (primary non-response), or loss of response during maintenance after a successful induction of the anti-TNF therapy (secondary loss of response). In some embodiments, the induction of the anti-TNF therapy comprises 1, 2, 3, 4, or 5, doses of the therapy. In some embodiments, loss of response is characterized by a reappearance of symptoms consistent with a flare after an initial response to the anti-TNF therapy.

METHODS

[0037] Disease or Condition

[0038] Aspects disclosed herein provide methods of treating, diagnosing, prognosing, or monitoring, a disease or condition. In some cases, the disease or condition comprises an inflammatory disease, fibrostenotic disease, and/or fibrotic disease. Non-limiting examples of inflammatory diseases include diseases of the gastrointestinal (GI) tract, liver, gallbladder, and joints. In some cases, the inflammatory disease inflammatory bowel disease (IBD), Crohn’s disease (CD), or ulcerative colitis, systemic lupus erythematosus (SLE), or rheumatoid arthritis. A subject may suffer from fibrosis, fibrostenosis, or a fibrotic disease, either isolated or in combination with an inflammatory disease. An exemplary fibrotic disease is primary sclerosing cholangitis (PSC).

[0039] In some instances, the disease or condition is refractory, which refers a quality of the disease or condition such that there is an observed failure of a standard treatment to induce remission of a disease or condition. Non-limiting examples of refractory inflammatory disease include refractory Crohn’s disease, and medically refractory ulcerative colitis (*e.g.*, mrUC). Non-limiting examples of standard treatment include glucocorticosteroids, anti-TNF therapy, anti-a4-b7 therapy (vedolizumab), anti-IL12p40 therapy (ustekinumab), Thalidomide, and Cytosin. In some instances, the refractory

disease or condition is characterized by an increase in colitis, inflammation, fibrosis, fibrostenosis, stricturing, penetrating, obstructive, or otherwise complicated, disease of the GI tract.

[0040] Subject

[0041] Disclosed herein, in some embodiments, are methods of treating, diagnosing, prognosing, or monitoring, a disease or condition in a subject. In some instances, the subject is a mammal. In some embodiments, the subject comprises a mouse, rat, guinea pig, rabbit, chimpanzee, or farm animal. In some instances, the subject is human. In some instances, the subject is diagnosed with the disease or condition disclosed herein. Non-limiting methods for diagnosis using existing indices and scoring systems include Crohn's Disease Activity Index (CDAI), Ulcerative Colitis Disease Activity Index (UCDAI), guidelines from American College of Gastroenterology (ACG) and European Crohn's and Colitis Organization (ECCO), patient-reported outcomes (PRO-2), Harvey-Bradshaw Index, Van Hess Index, Perianal Disease Activity Index (PDAI), Rachmilewitz score, Mayo score, Powell-Tuck index, Patient Simple Clinical Colitis Activity Index (P-SCCAI), Lichtiger index, Seo index, Inflammatory Bowel Disease Questionnaire (IBDQ), Manitoba IBD Index, Crohn's Disease Endoscopic Index of Severity (CDEIS), Simple Endoscopic Score for Crohn Disease (SES-CD), Lewis score (capsule endoscopy), Rutgeert's Score, and the Montreal Classification, and IBD questionnaire. In some instances, the subject is not diagnosed with the disease or condition. In some instances, the subject is suffering from a symptom related to a disease or condition disclosed herein (e.g., abdominal pain, cramping, diarrhea, rectal bleeding, fever, weight loss, fatigue, loss of appetite, dehydration, and malnutrition, anemia, or ulcers).

[0042] In some embodiments, the subject is susceptible to, or is inflicted with, thiopurine toxicity, or a disease caused by thiopurine toxicity (such as pancreatitis or leukopenia). In further embodiments provided, the subject is, or is suspected of being, non-responsive to a standard treatment (e.g., anti-TNF alpha therapy, anti-a4-b7 therapy (vedolizumab), anti-IL12p40 therapy (ustekinumab), Thalidomide, or Cytosin). In some cases, the subject is not responsive to the induction of said therapy. In some cases, the subject loses response to said standard treatment after a period of time during treatment.

[0043] Src Kinase Associated Phosphoprotein 2 (SKAP2)

[0044] Src Kinase Associated Phosphoprotein 2 SKAP2) (UniProtKB: O75563) is encoded by the gene *SKAP2* (Entrez Gene: 8935), which shares homology with Src kinase-associated phosphoprotein 1, and is a substrate of Src family kinases. SKAP2 is an adaptor protein that is thought to play an essential role in the Src signaling pathway, and in regulating proper activation of the immune system. *SKAP2* is located on chromosome 7.

[0045] Method of Detection

[0046] Disclosed herein, in some embodiments, are methods of detecting a presence, absence, or level, of a genotype or biomarker in a sample obtained from a subject. In some instances, the methods

of detection disclosed herein are useful for the diagnosis, prognosis, monitoring of disease progression, selection for treatment, monitoring of treatment, and/or treatment of inflammatory bowel disease (e.g., Crohn's disease, ulcerative colitis, and the like) disclosed herein.

[0047] In some embodiments, methods of detecting a presence, absence, or level of a genotype or biomarker in the sample obtained from the subject involve detecting a nucleic acid sequence. In some cases, the nucleic acid sequence comprises deoxyribonucleic acid (DNA). In some instances, the nucleic acid sequence comprises a denatured DNA molecule or fragment thereof. In some instances, the nucleic acid sequence comprises DNA selected from: genomic DNA, viral DNA, mitochondrial DNA, plasmid DNA, amplified DNA, circular DNA, circulating DNA, cell-free DNA, or exosomal DNA. In some instances, the DNA is single-stranded DNA (ssDNA), double-stranded DNA, denaturing double-stranded DNA, synthetic DNA, and combinations thereof. The circular DNA may be cleaved or fragmented. In some instances, the nucleic acid sequence comprises ribonucleic acid (RNA). In some instances, the nucleic acid sequence comprises fragmented RNA. In some instances, the nucleic acid sequence comprises partially degraded RNA. In some instances, the nucleic acid sequence comprises a microRNA or portion thereof. In some instances, the nucleic acid sequence comprises an RNA molecule or a fragmented RNA molecule (RNA fragments) selected from: a microRNA (miRNA), a pre-miRNA, a pri-miRNA, a mRNA, a pre-mRNA, a viral RNA, a viroid RNA, a virusoid RNA, circular RNA (circRNA), a ribosomal RNA (rRNA), a transfer RNA (tRNA), a pre-tRNA, a long non-coding RNA (lncRNA), a small nuclear RNA (snRNA), a circulating RNA, a cell-free RNA, an exosomal RNA, a vector-expressed RNA, an RNA transcript, a synthetic RNA, and combinations thereof.

[0048] Disclosed herein, in some embodiments, the genotype or biomarker is detected by subjecting a sample obtained from the subject to a nucleic acid-based detection assay. In some instances, the nucleic acid-based detection assay comprises quantitative polymerase chain reaction (qPCR), gel electrophoresis (including for e.g., Northern or Southern blot), immunochemistry, *in situ* hybridization such as fluorescent *in situ* hybridization (FISH), cytochemistry, or sequencing. In some embodiments, the sequencing technique comprises next generation sequencing. In some embodiments, the methods involve a hybridization assay such as fluorogenic qPCR (e.g., TaqMan™, SYBR green, SYBR green I, SYBR green II, SYBR gold, ethidium bromide, methylene blue, Pyronin Y, DAPI, acridine orange, Blue View or phycoerythrin), which involves a nucleic acid amplification reaction with a specific primer pair, and hybridization of the amplified nucleic acid probes comprising a detectable moiety or molecule that is specific to a target nucleic acid sequence. In some instances, a number of amplification cycles for detecting a target nucleic acid in a qPCR assay is about 5 to about 30 cycles. In some instances, the number of amplification cycles for detecting a target nucleic acid is at least about 5 cycles. In some instances, the number of amplification cycles for detecting a target nucleic acid is at most about 30 cycles. In some instances, the number of amplification cycles for detecting a target nucleic acid is about 5 to about 10, about 5 to about 15, about 5 to about 20, about 5

to about 25, about 5 to about 30, about 10 to about 15, about 10 to about 20, about 10 to about 25, about 10 to about 30, about 15 to about 20, about 15 to about 25, about 15 to about 30, about 20 to about 25, about 20 to about 30, or about 25 to about 30 cycles. For TaqMan™ methods, the probe may be a hydrolysable probe comprising a fluorophore and quencher that is hydrolyzed by DNA polymerase when hybridized to a target nucleic acid. In some cases, the presence of a target nucleic acid is determined when the number of amplification cycles to reach a threshold value is less than 30, 29, 28, 27, 26, 25, 24, 23, 22, 21, or 20 cycles. In some instances, hybridization may occur at standard hybridization temperatures, e.g., between about 35 °C and about 65 °C in a standard PCR buffer.

[0049] An additional exemplary nucleic acid-based detection assay comprises the use of nucleic acid probes conjugated or otherwise immobilized on a bead, multi-well plate, or other substrate, wherein the nucleic acid probes are configured to hybridize with a target nucleic acid sequence. In some instances, the nucleic acid probe is specific to one or more genetic variants disclosed herein is used. In some instances, the nucleic acid probe specific to a SNP or SNV comprises a nucleic acid probe sequence sufficiently complementary to a risk or protective allele of interest, such that hybridization is specific to the risk or protective allele. In some instances, the nucleic acid probe specific to an indel comprises a nucleic acid probe sequence sufficiently complementary to an insertion of a nucleobase within a polynucleotide sequence flanking the insertion, such that hybridization is specific to the indel. In some instances, the nucleic acid probe specific to an indel comprises a probe sequence sufficiently complementary to a polynucleotide sequence flanking a deletion of a nucleobase within the polynucleotide sequence, such that hybridization is specific to the indel. In some instances, the nucleic acid probe specific to a biomarker comprises a nucleic acid probe sequence sufficiently complementary to the polynucleotide sequence of the biomarker. In some instances, the biomarker comprises a transcribed polynucleotide sequence (e.g., RNA, cDNA). In some embodiments, the nucleic acid probe can be, for example, a full-length cDNA, or a portion thereof, such as an oligonucleotide of at least about 7, 8, 9, 10, 11, 12, 13, 14, 15, 20, 25, 30, 35, 40, 45, or 50 nucleotides in length and sufficient to specifically hybridize under standard hybridization conditions to the target nucleic acid sequence. In some embodiments, the target nucleic acid sequence is immobilized on a solid surface and contacted with a probe, for example by running the isolated target nucleic acid sequence on an agarose gel and transferring the target nucleic acid sequence from the gel to a membrane, such as nitrocellulose. In some embodiments, the probe(s) are immobilized on a solid surface, for example, in an Affymetrix gene chip array, and the probe(s) are contacted with the target nucleic acid sequence.

[0050] In some embodiments, the term “probe” with regards to nucleic acids, refers to any nucleic acid molecule that is capable of selectively binding to a specifically intended target nucleic acid sequence. In some instances, probes are specifically designed to be labeled, for example, with a radioactive label, a fluorescent label, an enzyme, a chemiluminescent tag, a colorimetric tag, or other labels or tags that are known in the art. In some instances, the fluorescent label comprises a

fluorophore. In some instances, the fluorophore is an aromatic or heteroaromatic compound. In some instances, the fluorophore is a pyrene, anthracene, naphthalene, acridine, stilbene, benzoxazole, indole, benzindole, oxazole, thiazole, benzothiazole, canine, carbocyanine, salicylate, anthranilate, xanthenes dye, coumarin. Exemplary xanthene dyes include, e.g., fluorescein and rhodamine dyes. Fluorescein and rhodamine dyes include, but are not limited to 6-carboxyfluorescein (FAM), 2',7'-dimethoxy-4',5'-dichloro-6-carboxyfluorescein (JOE), tetrachlorofluorescein (TET), 6-carboxyrhodamine (R6G), N,N,N', N'-tetramethyl-6-carboxyrhodamine (TAMRA), 6-carboxy-X-rhodamine (ROX). Suitable fluorescent probes also include the naphthylamine dyes that have an amino group in the alpha or beta position. For example, naphthylamino compounds include 1-dimethylaminonaphthyl-5-sulfonate, 1-anilino-8-naphthalene sulfonate and 2-p-toluidinyl-6-naphthalene sulfonate, 5-(2'-aminoethyl)aminonaphthalene-1-sulfonic acid (EDANS). Exemplary coumarins include, e.g., 3-phenyl-7-isocyanatocoumarin; acridines, such as 9-isothiocyanatoacridine and acridine orange; N-(p-(2-benzoxazolyl)phenyl) maleimide; cyanines, such as, e.g., indodicarbocyanine 3 (Cy3), indodicarbocyanine 5 (Cy5), indodicarbocyanine 5.5 (Cy5.5), 3-(-carboxy-pentyl)-3'-ethyl-5,5'-dimethyloxacarboxyanine (CyA); 1H, 5H, 11H, 15H-Xantheno[2,3, 4-ij:5,6, 7-i'j']diquinolizin-18-ium, 9-[2 (or 4)-[[[6-[2,5-dioxo-1-pyrrolidinyl]oxy]-6-oxohexyl]amino]sulfonyl]-4 (or 2)-sulfophenyl]-2,3, 6,7, 12,13, 16,17-octahydro-inner salt (TR or Texas Red); or BODIPY™ dyes. In some cases, the probe comprises FAM as the dye label.

[0051] Disclosed herein, in some embodiments, a genotype or biomarker is detected by subjecting a sample obtained from the subject to a nucleic acid amplification assay. In some instances, the amplification assay comprises polymerase chain reaction (PCR), qPCR, self-sustained sequence replication, transcriptional amplification system, Q-Beta Replicase, rolling circle replication, or any suitable other nucleic acid amplification technique. A suitable nucleic acid amplification technique is configured to amplify a region of a nucleic acid sequence comprising one or more genetic risk variants disclosed herein. In some instances, the amplification assays requires primers. The nucleic acid sequence for the genetic risk variants and/or genes known or provided herein is sufficient to enable one of skill in the art to select primers to amplify any portion of the gene or genetic variants. A DNA sample suitable as a primer may be obtained, e.g., by polymerase chain reaction (PCR) amplification of genomic DNA, fragments of genomic DNA, fragments of genomic DNA ligated to adaptor sequences or cloned sequences. A person of skill in the art would utilize computer programs to design of primers with the desired specificity and optimal amplification properties, such as Oligo version 7.0 (National Biosciences). Controlled robotic systems are useful for isolating and amplifying nucleic acids and can be used.

[0052] In some embodiments, detecting the biomarker or genotype of the subject comprises sequencing genetic material obtained from a biological sample from the subject. Sequencing can be performed with any appropriate sequencing technology, including but not limited to single-molecule real-time (SMRT) sequencing, Polony sequencing, sequencing by ligation, reversible terminator

sequencing, proton detection sequencing, ion semiconductor sequencing, nanopore sequencing, electronic sequencing, pyrosequencing, Maxam-Gilbert sequencing, chain termination (*e.g.*, Sanger) sequencing, +S sequencing, or sequencing by synthesis. Sequencing methods also include next-generation sequencing, *e.g.*, modern sequencing technologies such as Illumina sequencing (*e.g.*, Solexa), Roche 454 sequencing, Ion torrent sequencing, and SOLiD sequencing. In some cases, next-generation sequencing involves high-throughput sequencing methods. Additional sequencing methods available to one of skill in the art may also be employed.

[0053] In some instances, a number of nucleotides that are sequenced are at least 5, 10, 15, 20, 25, 30, 35, 40, 45, 50, 100, 150, 200, 300, 400, 500, 2000, 4000, 6000, 8000, 10000, 20000, 50000, 100000, or more than 100000 nucleotides. In some instances, the number of nucleotides sequenced is in a range of about 1 to about 100000 nucleotides, about 1 to about 10000 nucleotides, about 1 to about 1000 nucleotides, about 1 to about 500 nucleotides, about 1 to about 300 nucleotides, about 1 to about 200 nucleotides, about 1 to about 100 nucleotides, about 5 to about 100000 nucleotides, about 5 to about 10000 nucleotides, about 5 to about 1000 nucleotides, about 5 to about 500 nucleotides, about 5 to about 300 nucleotides, about 5 to about 200 nucleotides, about 5 to about 100 nucleotides, about 10 to about 100000 nucleotides, about 10 to about 10000 nucleotides, about 10 to about 1000 nucleotides, about 10 to about 500 nucleotides, about 10 to about 300 nucleotides, about 10 to about 200 nucleotides, about 10 to about 100 nucleotides, about 20 to about 100000 nucleotides, about 20 to about 10000 nucleotides, about 20 to about 1000 nucleotides, about 20 to about 500 nucleotides, about 20 to about 300 nucleotides, about 20 to about 200 nucleotides, about 20 to about 100 nucleotides, about 30 to about 100000 nucleotides, about 30 to about 10000 nucleotides, about 30 to about 1000 nucleotides, about 30 to about 500 nucleotides, about 30 to about 300 nucleotides, about 30 to about 200 nucleotides, about 30 to about 100 nucleotides, about 50 to about 100000 nucleotides, about 50 to about 10000 nucleotides, about 50 to about 1000 nucleotides, about 50 to about 500 nucleotides, about 50 to about 300 nucleotides, about 50 to about 200 nucleotides, or about 50 to about 100 nucleotides.

[0054] Disclosed herein, in some embodiments, are methods for detecting a transcriptomic risk signature or transcriptomic risk profile in a sample obtained from the subject. In some embodiments, the presence, level, or activity of two or more biomarkers in a sample is determined by detecting a transcribed or reverse transcribed polynucleotide, or portion thereof (*e.g.*, mRNA, or cDNA), of a target gene making up the transcriptomic risk signature or transcriptomic risk profile. Any suitable method of detecting a biomarker, such as those disclosed herein, may be utilized to detect a transcriptomic risk signature or transcriptomic risk profile, such as those disclosed herein. A transcriptomic risk signature or transcriptomic risk profile can also be detected at the protein level, using a detection reagent that detects the protein product encoded by the mRNA of the biomarker, directly or indirectly, such the detection reagents disclosed herein.

[0055] Disclosed herein, in some embodiments, genetic material is extracted from a sample obtained from a subject, e.g., a sample of blood or serum. In certain embodiments where nucleic acids are extracted, the nucleic acids are extracted using any technique that does not interfere with subsequent analysis. In certain embodiments, this technique uses alcohol precipitation using ethanol, methanol or isopropyl alcohol. In certain embodiments, this technique uses phenol, chloroform, or any combination thereof. In certain embodiments, this technique uses cesium chloride. In certain embodiments, this technique uses sodium, potassium or ammonium acetate or any other salt commonly used to precipitate DNA. In certain embodiments, this technique utilizes a column or resin based nucleic acid purification scheme such as those commonly sold commercially, one non-limiting example would be the GenElute Bacterial Genomic DNA Kit available from Sigma Aldrich. In certain embodiments, after extraction the nucleic acid is stored in water, Tris buffer, or Tris-EDTA buffer before subsequent analysis. In an exemplary embodiment, the nucleic acid material is extracted in water. In some cases, extraction does not comprise nucleic acid purification. In certain embodiments, RNA may be extracted from cells using RNA extraction techniques including, for example, using acid phenol/guanidine isothiocyanate extraction (RNAzol B; Biogenesis), RNeasy RNA preparation kits (Qiagen) or PAXgene (PreAnalytix, Switzerland).

[0056] In some embodiments, methods of detecting a presence, absence, or level of a target protein (e.g., biomarker) in the sample obtained from the subject involve detecting protein activity or expression. A target protein may be detected by use of an antibody-based assay, where an antibody specific to the target protein is utilized. In some embodiments, antibody-based detection methods utilize an antibody that binds to any region of target protein. An exemplary method of analysis comprises performing an enzyme-linked immunosorbent assay (ELISA). The ELISA assay may be a sandwich ELISA or a direct ELISA. Another exemplary method of analysis comprises a single molecule array, e.g., Simoa. Other exemplary methods of detection include immunohistochemistry and lateral flow assay. Additional exemplary methods for detecting target protein include, but are not limited to, gel electrophoresis, capillary electrophoresis, high performance liquid chromatography (HPLC), thin layer chromatography (TLC), hyperdiffusion chromatography, and the like, or various immunological methods such as fluid or gel precipitation reactions, immunodiffusion (single or double), immunoelectrophoresis, radioimmunoassay (RIA), immunofluorescent assays, and Western blotting. In some embodiments, antibodies, or antibody fragments, are used in methods such as Western blots or immunofluorescence techniques to detect the expressed proteins. The antibody or protein can be immobilized on a solid support for Western blots and immunofluorescence techniques. Suitable solid phase supports or carriers include any support capable of binding an antigen or an antibody. Exemplary supports or carriers include glass, polystyrene, polypropylene, polyethylene, dextran, nylon, amylases, natural and modified celluloses, polyacrylamides, gabbros, and magnetite.

[0057] In some cases, a target protein may be detected by detecting binding between the target protein and a binding partner of the target protein. In some cases, the target protein comprises SKAP2. In

some instances, the binding partner of SKAP2 is a Src kinase. Exemplary methods of analysis of protein-protein binding comprise performing an assay *in vivo* or *in vitro*, or *ex vivo*. In some instances, the method of analysis comprises an assay such as a co-immunoprecipitation (co-IP), pull-down, crosslinking protein interaction analysis, labeled transfer protein interaction analysis, or Far-western blot analysis, FRET based assay, including, for example FRET-FLIM, a yeast two-hybrid assay, BiFC, or split luciferase assay.

[0058] Disclosed herein, in some embodiments, are methods of detecting a presence or a level of one or more serological markers in a sample obtained from a subject. In some embodiments, the one or more serological markers comprises anti-Saccharomyces cerevisiae antibody (ASCA), an anti-neutrophil cytoplasmic antibody (ANCA), E.coli outer membrane porin protein C (OmpC), anti-Malassezia restricta antibody, anti-Malassezia pachydermatis antibody, anti-Malassezia furfur antibody, anti-Malassezia globosa antibody, anti-Cladosporium albicans antibody, anti-laminaribiose antibody (ALCA), anti-chitobioside antibody (ACCA), anti-laminarin antibody, anti-chitin antibody, pANCA antibody, anti-I2 antibody, and anti-Cbir1 flagellin antibody. In some embodiments, the antibodies comprises immunoglobulin A (IgA), immunoglobulin G (IgG), immunoglobulin E (IgE), or immunoglobulin M (IgM), immunoglobulin D (IgD), or a combination thereof. Any suitable method for detecting a target protein or biomarker disclosed herein may be used to detect a presence, absence, or level of a serological marker. In some embodiments, the presence or the level of the one or more serological markers is detected using an enzyme-linked immunosorbent assay (ELISA), a single molecule array (Simoa), immunohistochemistry, internal transcribed spacer (ITS) sequencing, or any combination thereof. In some embodiments, the ELISA is a fixed leukocyte ELISA. In some embodiments, the ELISA is a fixed neutrophil ELISA. A fixed leukocyte or neutrophil ELISA may be useful for the detection of certain serological markers, such as those described in Saxon *et al.*, A distinct subset of antineutrophil cytoplasmic antibodies is associated with inflammatory bowel disease, *J. Allergy Clin. Immuno.* 86:2; 202-210 (August 1990). In some embodiments, ELISA units (EU) are used to measure positivity of a presence or level of a serological marker (e.g., seropositivity), which reflects a percentage of a standard or reference value. In some embodiments, the standard comprises pooled sera obtained from well-characterized patient population (e.g., diagnosed with the same disease or condition the subject has, or is suspected of having) reported as being seropositive for the serological marker of interest. In some embodiments, the control or reference value comprises 10, 20, 30, 40, 50, 60, 70, 80, 90, or 100 EU. In some instances, a quartile sum scores are calculated using, for example, the methods reported in Landers C J, Cohavy O, Misra R. *et al.*, Selected loss of tolerance evidenced by Crohn's disease-associated immune responses to auto- and microbial antigens. *Gastroenterology* (2002)123:689–699.

[0059] Methods of Diagnosis and Prognosis

[0060] Disclosed herein, in some embodiments, are methods of diagnosing a disease or condition in a subject. In some cases, the disease or condition comprises an inflammatory disease, fibrostenotic

disease, and/or fibrotic disease. Non-limiting examples of inflammatory diseases include diseases of the GI tract, liver, gallbladder, and joints. In some cases, the inflammatory disease IBD, CD, UC, systemic lupus erythematosus (SLE), or rheumatoid arthritis. In some embodiments, the disease or condition comprises fibrosis, fibrostenosis, or a fibrotic disease, either isolated or in combination with an inflammatory disease. An exemplary fibrotic disease is PSC. In some embodiments, a subtype of the disease or condition is diagnosed in the subject. Non-limiting examples of subtypes of IBD include, stricturing disease, penetrating disease, stricturing and penetrating disease, obstructive disease, refractory disease, or another complicated form of IBD. In some instances, the subject is diagnosed with, or predicted to develop, one disease or condition, two disease or conditions, three disease or conditions, or more.

[0061] Disclosed herein, in some embodiments, are methods of diagnosing a disease or condition in a subject comprising: (a) obtaining a sample from a subject; (b) subjecting the sample to an assay configured to detect a presence, absence, or level, of one or more SNPs of SKAP2; (c) diagnosing the subject with the disease or condition, provided the presence, absence, or level of one or more SNPs of SKAP2 is detected in the sample obtained from the subject. In some embodiments, the one or more SNPs of SKAP2 is detected using one or more methods of detection, kits and/or compositions disclosed herein. In some embodiments, the subject is treated by administering a therapeutically effective amount of a therapeutic agent and/or additional agent disclosed herein to the subject, provided the subject is diagnosed with the disease or condition. In some embodiments, the therapeutic agent comprises an antagonist of SKAP2. In some embodiments, the one or more SNPs of SKAP2 is associated with Crohn's disease. In some embodiments, the one or more SNPs of SKAP2 is associated with inflammatory bowel disease. In some embodiments, the one or more SNPs of SKAP2 is associated with ulcerative colitis.

[0062] Disclosed herein, in some embodiments, are methods of predicting whether a subject will develop a disease a disease or condition, the method comprising: (a) obtaining a sample from a subject; (b) subjecting the sample to an assay configured to detect a presence, absence, or level, of one or more SNPs of SKAP2; (c) predicting that the subject will develop the disease or condition, provided the presence, absence, or level of the one or more SNPs of SKAP2 is detected in the sample obtained from the subject. In some embodiments, the one or more SNPs of SKAP2 is detected using one or more methods of detection, kits and/or compositions disclosed herein. In some embodiments, the subject is treated by administering a therapeutically effective amount of a therapeutic agent and/or additional agent disclosed herein to the subject, provided the subject is predicted to develop the disease or condition. In some embodiments, the therapeutic agent comprises an antagonist of SKAP2. In some embodiments, the one or more SNPs of SKAP2 is associated with Crohn's disease. In some embodiments, the one or more SNPs of SKAP2 is associated with inflammatory bowel disease. In some embodiments, the one or more SNPs of SKAP2 is associated with ulcerative colitis. In some embodiments, the one or more SNPs of SKAP2 comprises a SNP provided in Figure 1.

[0063] Methods of Characterizing a Subtype of a Disease or Condition

[0064] Disclosed herein, in some embodiments, are methods of characterizing a disease or condition, or a subtype of a disease or condition. In some cases, the disease or condition comprises an inflammatory disease, fibrostenotic disease, and/or fibrotic disease. Non-limiting examples of inflammatory diseases include diseases of the GI tract, liver, gallbladder, and joints. In some cases, the inflammatory disease IBD, CD, UC, systemic lupus erythematosus (SLE), or rheumatoid arthritis. In some embodiments, the disease or condition comprises fibrosis, fibrostenosis, or a fibrotic disease, either isolated or in combination with an inflammatory disease. An exemplary fibrotic disease is PSC. Non-limiting examples of subtypes of IBD include, stricturing disease, penetrating disease, stricturing and penetrating disease, obstructive disease, refractory disease, or another complicated form of IBD.

[0065] Disclosed herein, in some embodiments, are methods of characterizing a disease a disease or condition, or a subtype of a disease or condition comprising: (a) obtaining a sample from a subject; (b) subjecting the sample to an assay configured to detect a presence, absence, or level, of one or more SNPs of SKAP2; (c) characterizing the disease or condition as being associated with at least one of non-stricturing and non-penetrating, stricturing, and penetrating, provided the presence, absence, or level of one or more SNPs of SKAP2 is detected in the sample obtained from the subject. In some embodiments, the one or more SNPs of SKAP2 is detected using one or more methods of detection, kits and/or compositions disclosed herein. In some embodiments, the subject is treated by administering a therapeutically effective amount of a therapeutic agent and/or additional agent disclosed herein to the subject, provided the subject is disease or condition is characterized as being associated with at least one of non-stricturing and non-penetrating, stricturing, and penetrating. In some embodiments, the therapeutic agent comprises an antagonist of SKAP2.

[0066] Disclosed herein, in some embodiments, are methods of characterizing a disease a disease or condition, or a subtype of a disease or condition comprising: (a) obtaining a sample from a subject; (b) subjecting the sample to an assay configured to detect a presence, absence, or level, of one or more SNPs of SKAP2; (c) characterizing the disease or condition as being associated with at least one of non-stricturing and non-penetrating, stricturing, and penetrating that is isolated to an ileum, ileocolonic region of an intestine, or colon, provided the presence, absence, or level of one or more SNPs of SKAP2 is detected in the sample obtained from the subject. In some embodiments, the one or more SNPs of SKAP2 is detected using one or more methods of detection, kits and/or compositions disclosed herein. In some embodiments, the subject is treated by administering a therapeutically effective amount of a therapeutic agent and/or additional agent disclosed herein to the subject, provided the subject is disease or condition is characterized as being associated with the at least one of non-stricturing and non-penetrating, stricturing, and penetrating is isolated to an ileum, ileocolonic region of an intestine, or colon. In some embodiments, the therapeutic agent comprises an antagonist of SKAP2.

[0067] Disclosed herein, in some embodiments, are methods of characterizing a disease a disease or condition, or a subtype of a disease or condition comprising: (a) obtaining a sample from a subject; (b) subjecting the sample to an assay configured to detect a presence, absence, or level, of one or more SNPs of SKAP2; (c) characterizing the disease or condition as being associated with morphological defects in ileal Paneth cells, provided the presence, absence, or level of one or more SNPs of SKAP2 is detected in the sample obtained from the subject. In some embodiments, the one or more SNPs of SKAP2 is detected using one or more methods of detection, kits and/or compositions disclosed herein. In some embodiments, the subject is treated by administering a therapeutically effective amount of a therapeutic agent and/or additional agent disclosed herein to the subject, provided the subject is disease or condition is characterized as being associated with morphological defects in ileal Paneth cells. In some embodiments, the therapeutic agent comprises an antagonist of SKAP2.

[0068] In some embodiments, the one or more SNPs of SKAP2 comprises a SNP provided in Figure 1.

[0069] **Methods of Treatment**

[0070] Disclosed herein, in some embodiments, are methods of treating a disease or condition, or a symptom of the disease or condition, in a subject, comprising administering of therapeutic effective amount of one or more therapeutic agents to the subject. In some embodiments, the one or more therapeutic agents is administered to the subject alone (e.g., standalone therapy). In some embodiments, the one or more therapeutic agents is administered in combination with an additional agent. In some embodiments, the therapeutic agent is a first-line therapy for the disease or condition. In some embodiments, the therapeutic agent is a second-line, third-line, or fourth-line therapy, for the disease or condition.

[0071] **Therapeutic Agent**

[0072] Disclosed herein, in some embodiments, are therapeutic agents useful for the treatment of a disease or condition, or symptom of the disease or condition, disclosed herein. In some embodiments, the therapeutic agent comprises a modulator, agonist, and/or antagonist of Src Kinase Associated Phosphoprotein 2 (SKAP2). Methods disclosed herein may comprise and/or utilize a therapeutic agent or use thereof, wherein the therapeutic agent is effective to modify expression and/or activity of SKAP2 (e.g., modulator of SKAP2). Therapeutic agents that modify expression and/or activity of SKAP2 may also be referred to herein as SKAP2-targeting agents. Alternatively, or additionally, compositions, kits and methods disclosed herein may comprise and/or utilize a therapeutic agent or use thereof, wherein the therapeutic agent modifies expression and/or activity of a protein that functions upstream or downstream of a pathway that involves SKAP2. In some embodiments, the modulator of SKAP2 is effective to increase or activate the activity or expression of SKAP2 in the subject (e.g., agonist or partial agonist). In some embodiments, the modulator of SKAP2 is effective to decrease or reduce the activity or expression of SKAP2 (e.g., antagonist or partial antagonist).

[0073] In some embodiments, the SKAP2 modulator is an antibody, an antigen binding fragment, an RNA interfering agent (RNAi), a small interfering RNA (siRNA), a short hairpin RNA (shRNA), a microRNA (miRNA), an antisense oligonucleotide, a peptide, a peptidomimetic, a small molecule, or an aptamer.

[0074]] In some instances, the therapeutic agent is an antagonist of SKAP2. In some instances, the antagonist acts as an inverse agonist. In some instances, the therapeutic agent is an allosteric modulator of SKAP2. Methods disclosed herein may comprise administering SKAP2-targeting agents alone. In other instances, methods disclosed herein may comprise administering SKAP2-targeting agents along with another therapeutic agent disclosed herein, a nutritional-based therapy, a nature-based therapy, a diet-based therapy, or a combination thereof.

[0075] In some instances, the subject has a SNP that is associated with, or causes, an increased expression of SKAP2. In some instances, the subject has a SNP that is associated with, or causes increased activity of SKAP2. In some instances, the SNP is associated with, or causes and increase expression of SKAP2. In some instances, the SNP is associated with, or causes an increase activity of SKAP2. In these instances, it may be suitable to use an SKAP2 antagonist to bring SKAP2 activity back to a normal level, e.g., that of a person without the IBD of the subject.

[0076] In some instances, the subject has a SNP that is associated with, or causes decreased expression of SKAP2. In some instances, the subject has a SNP is associated with, or causes, decreased activity of SKAP2. In some instances, the SNP is associated with, or causes, a decrease in expression of SKAP2. In some instances, the SNP is associated with, or causes, decreased activity of SKAP2. In these instances, it may be suitable to use an SKAP2 agonist to bring SKAP2 activity back to a normal level, e.g., that of a person without the IBD of the subject.

[0077] In some instances, the therapeutic agent is a small molecule drug. By way of non-limiting example, a small molecule drug may be a chemical compound. In some instances, the therapeutic agent is a large molecule drug. Large molecule drugs generally comprise a peptide or nucleic acid. By way of non-limiting example, the large molecule drug may comprise an antibody or antigen binding antibody fragment. In some instances, the therapeutic agent comprises a small molecule and a large molecule. By way of non-limiting example, the therapeutic agent may comprise an antibody-drug conjugate.

[0078] In some instances, the therapeutic agent is a small molecule that binds SKAP2. In some instances, the small molecule that binds SKAP2 is an SKAP2 agonist. In some instances, the small molecule that binds SKAP2 is an SKAP2 partial agonist. In some instances, the small molecule that binds SKAP2 is an SKAP2 antagonist. In some instances, the small molecule that binds SKAP2 is an SKAP2 partial agonist.

[0079] In some embodiments, the agonist of SKAP2 comprises an SKAP2 polypeptide. In some embodiments, the SKAP2 polypeptide comprises a human SKAP2 protein (huSKAP2), or a homolog thereof. In some instances the polypeptide is an antagonist, agonist or modulator (e.g., allosteric

modulator, orthosteric modulator) of SKAP2. In some embodiments, the SKAP2 polypeptide comprises a recombinant SKAP2 polypeptide. In some embodiments, the recombinant huSKAP2 precursor protein comprises SEQ ID NO: 1)(

MPNPSSTSSPYPLPEEIRNLLADVETVADILKGENLSKKAKEKRESLIKKIKDVKSIYLQEFQD
KGDAEDGEEYDDPFAGPPDTISLASERYDKDDEAPSDGAQFPPIAAQDLPFVLKAGYLEKRR
KDHSFLGFQWQKRWALSKTVFYYYGSDKDKQKGEFAIDGYSVRMNTLRKDGKKDCCF
EISAPDKRIYQFTAASPKDAEEWVQQLKFVLQDMESDIIPEDYDERGELYDDVDHPLPISNPLT
SSQPIDDEIYEELPEEEEDSAPVKVEEQRKMSQDSVHHTSGDKSTDYANFYQGLWDCTGAFS
DELSFKRGDVIYILSKEYNRYGWWVGEMKGAIGLVPKAYIMEMYDI), which is the amino acid
sequence of human SKAP2 protein (NCBI Reference Sequence No. NP_003921.2). In some
embodiments, the SKAP2 polypeptide comprises a recombinant SKAP2 polypeptide. In some
embodiments, the huSKAP2 comprises an amino acid sequence about 99%, 98%, 97%, 96%, 95%,
94%, 93%, 92%, 91%, or 90% homologous to SEQ ID NO: 1. In some embodiments, the
recombinant huSKAP2 precursor protein comprises SEQ ID NO: 2

(MNNTLRKDGKKDCCFEISAPDKRIYQFTAASPKDAEEWVQQLKFVLQDMESDIIPEDYDER
GELYDDVDHPLPISNPLTSSQPIDDEIYEELPEEEEDSAPVKVEEQRKMSQDSVHHTSGDKSTD
YANFYQGLWDCTGAFSDELSFKRGDVIYILSKEYNRYGWWVGEMKGAIGLVPKAYIMEMY
DI), which is the amino acid sequence of human SKAP2 (NCBI Reference Sequence No.
NP_001290397.1). In some embodiments, the huSKAP2 comprises an amino acid sequence about
99%, 98%, 97%, 96%, 95%, 94%, 93%, 92%, 91%, or 90% homologous to SEQ ID NO: 2.

[0080] In some instances, the SKAP2 polypeptide is truncated. In some instances, the truncation is an N-terminal deletion. In other instances, the truncation is a C-terminal deletion. In additional instances, the truncation comprises both N-terminal and C-terminal deletions. For example, the truncation can be a deletion of at least or about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 20, or more residues from either the N-terminus or the C-terminus, or both termini. In some cases, the SKAP2 polypeptide comprises an N-terminal deletion of at least or about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 20, or more residues. In some cases, the SKAP2 polypeptide comprises an N-terminal deletion of at least or about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 residues. In some cases, the SKAP2 polypeptide comprises an N-terminal deletion of at least or about 2 residues. In some cases, the SKAP2 polypeptide comprises an N-terminal deletion of at least or about 3 residues. In some cases, the SKAP2 polypeptide comprises an N-terminal deletion of at least or about 4 residues. In some cases, the SKAP2 polypeptide comprises an N-terminal deletion of at least or about 5 residues. In some cases, the SKAP2 polypeptide comprises an N-terminal deletion of at least or about 6 residues. In some cases, the SKAP2 polypeptide comprises an N-terminal deletion of at least or about 7 residues. In some cases, the SKAP2 polypeptide comprises an N-terminal deletion of at least or about 8 residues. In some cases, the SKAP2 polypeptide comprises an N-terminal deletion of at least or about 9 residues. In some cases, the SKAP2 polypeptide comprises an N-terminal deletion of at least or about 10 residues.

[0081] In some embodiments, the SKAP2 polypeptide has an enhanced plasma half-life. In some instances, the plasma half-life comprises at least 30 minutes, 45 minutes, 60 minutes, 75 minutes, or 90 minutes, 2 hours, 3 hours, 4 hours, 5 hours, 6 hours, 7 hours, 8 hours, 9 hours, 10 hours, 11 hours, 12 hours, 18 hours, 24 hours, 36 hours, 48 hours, 3 days, 4 days, 5 days, 6 days, 7 days, 10 days, 12 days, 14 days, 21 days, 28 days, 30 days, or longer than the plasma half-life of the wild-type SKAP2 protein.

[0082] In some embodiments, the SKAP2 polypeptide is a conjugate. In some embodiments, the SKAP2 conjugate comprises an SKAP2 polypeptide comprising at least one amino acid and a conjugating moiety bound to the at least one amino acid. In some embodiments, the at least one amino acid is located proximal to the N-terminus (e.g., proximal to the N-terminal residue). For example, the at least one amino acid is located optionally within the first 10, 20, 30, 40, or 50 residues from the N-terminus. In some cases, the at least one amino acid is located at the N-terminus (i.e., the at least one amino acid is the N-terminal residue of the SKAP2 polypeptide). In other embodiments, the at least one amino acid is located proximal to the C-terminus (e.g., proximal to the C-terminal residue). For example, the at least one amino acid is located optionally within the first 10, 20, 30, 40, or 50 residues from the C-terminus. In some cases, the at least one amino acid is located at the C-terminus (i.e., the at least one amino acid is the C-terminal residue of the SKAP2 polypeptide). In some instances, the SKAP2 conjugate has an enhanced plasma half-life, such as the half-lives described herein. In some embodiments, the SKAP2 conjugate is functionally active (e.g., retains activity). In some embodiments, the SKAP2 conjugate is not functionally active (e.g., devoid of activity). In some embodiments, the conjugating moiety comprises a polymer comprising Polyethylene glycol (PEG).

[0083] In some embodiments, the SKAP2 polypeptide is fused with a second polypeptide. In some embodiments, the second polypeptide comprises a polypeptide with a long plasma half-life relative to the plasma half-life of the SKAP2 polypeptide. In some embodiments, the second polypeptide comprises an antibody or antibody fragment. In some embodiments, the antibody or antibody fragment comprises an IgG1, IgG2, IgG4, IgG3, or IgE. In some embodiments, the IgG is an Fc. In some embodiments, the IgG Fc is human. In some instances, the long plasma half-life polypeptide comprises HSA, transferrin, IgA monomer, Retinol-binding protein, Factor H, Factor XIII, C-reactive protein, Factor IX, Fibrinogen, IFN-alpha, Pentameric IgM, IL-2, or Thyroglobulin.

[0084] Dosages and Routes of Administration

[0085] In general, methods disclosed herein comprise administering a therapeutic agent by oral administration. However, in some instances, methods comprise administering a therapeutic agent by intraperitoneal injection. In some instances, methods comprise administering a therapeutic agent in the form of an anal suppository. In some instances, methods comprise administering a therapeutic agent by intravenous ("i.v.") administration. It is conceivable that one may also administer therapeutic agents disclosed herein by other routes, such as subcutaneous injection, intramuscular injection,

intradermal injection, transdermal injection percutaneous administration, intranasal administration, intralymphatic injection, rectal administration intragastric administration, or any other suitable parenteral administration. In some embodiments, routes for local delivery closer to site of injury or inflammation are preferred over systemic routes. Routes, dosage, time points, and duration of administering therapeutics may be adjusted. . In some embodiments, administration of therapeutics is prior to, or after, onset of either, or both, acute and chronic symptoms of the disease or condition.

[0086] An effective dose and dosage of therapeutics to prevent or treat the disease or condition disclosed herein is defined by an observed beneficial response related to the disease or condition, or symptom of the disease or condition. Beneficial response comprises preventing, alleviating, arresting, or curing the disease or condition, or symptom of the disease or condition (e.g., reduced instances of diarrhea, rectal bleeding, weight loss, and size or number of intestinal lesions or strictures, reduced fibrosis or fibrogenesis, reduced fibrostenosis, reduced inflammation). In some embodiments, the beneficial response may be measured by detecting a measurable improvement in the presence, level, or activity, of biomarkers, transcriptomic risk profile, or intestinal microbiome in the subject. An “improvement,” as used herein refers to shift in the presence, level, or activity towards a presence, level, or activity, observed in normal individuals (e.g. individuals who do not suffer from the disease or condition). In instances wherein the therapeutic agent is not therapeutically effective or is not providing a sufficient alleviation of the disease or condition, or symptom of the disease or condition, then the dosage amount and/or route of administration may be changed, or an additional agent may be administered to the subject, along with the therapeutic agent. In some embodiments, as a patient is started on a regimen of a therapeutic agent, the patient is also weaned off (e.g., step-wise decrease in dose) a second treatment regimen.

[0087] Suitable dose and dosage administered to a subject is determined by factors including, but not limited to, the particular therapeutic agent, disease condition and its severity, the identity (e.g., weight, sex, age) of the subject in need of treatment, and can be determined according to the particular circumstances surrounding the case, including, e.g., the specific agent being administered, the route of administration, the condition being treated, and the subject or host being treated. In general, however, doses employed for adult human treatment are typically in the range of 0.01 mg-5000 mg per day. In one aspect, doses employed for adult human treatment are from about 1 mg to about 1000 mg per day. In one embodiment, the desired dose is conveniently presented in a single dose or in divided doses administered simultaneously (or over a short period of time) or at appropriate intervals, for example as two, three, four or more sub-doses per day. Non-limiting examples of effective dosages of for oral delivery of a therapeutic agent include between about 0.1 mg/kg and about 100 mg/kg of body weight per day, and preferably between about 0.5 mg/kg and about 50 mg/kg of body weight per day. In other instances, the oral delivery dosage of effective amount is about 1 mg/kg and about 10 mg/kg of body weight per day of active material. Non-limiting examples of effective dosages for intravenous administration of the therapeutic agent include at a rate between about 0.01 to 100 pmol/kg body

weight/min. In some embodiments, the daily dosage or the amount of active in the dosage form are lower or higher than the ranges indicated herein, based on a number of variables in regard to an individual treatment regime. In various embodiments, the daily and unit dosages are altered depending on a number of variables including, but not limited to, the activity of the therapeutic agent used, the disease or condition to be treated, the mode of administration, the requirements of the individual subject, the severity of the disease or condition being treated, and the judgment of the practitioner.

[0088] In some embodiments, the administration of the therapeutic agent is hourly, once every 2 hours, 3 hours, 4 hours, 5 hours, 6 hours, 7 hours, 8 hours, 9 hours, 10 hours, 11 hours, 12 hours, 13 hours, 14 hours, 15 hours, 16 hours, 17 hours, 18 hours, 19 hours, 20 hours, 21 hours, 22 hours, 23 hours, 1 day, 2 days, 3 days, 4 days, 5 days, 6 days, 7 days, 8 days, 9 days, 10 days, 11 days, 12 days, 13 days, 14 days, 15 days, 1 month, 2 months, 3 months, 4 months, 5 months, 6 months, 7 months, 8 months, 9 months, 10 months, 11 months, 1 year, 2 years, 3 years, 4 years, or 5 years, or 10 years. The effective dosage ranges may be adjusted based on subject's response to the treatment. Some routes of administration will require higher concentrations of effective amount of therapeutics than other routes.

[0089] In certain embodiments wherein the patient's condition does not improve, upon the doctor's discretion the administration of therapeutic agent is administered chronically, that is, for an extended period of time, including throughout the duration of the patient's life in order to ameliorate or otherwise control or limit the symptoms of the patient's disease or condition. In certain embodiments wherein a patient's status does improve, the dose of therapeutic agent being administered may be temporarily reduced or temporarily suspended for a certain length of time (i.e., a "drug holiday"). In specific embodiments, the length of the drug holiday is between 2 days and 1 year, including by way of example only, 2 days, 3 days, 4 days, 5 days, 6 days, 7 days, 10 days, 12 days, 15 days, 20 days, 28 days, or more than 28 days. The dose reduction during a drug holiday is, by way of example only, by 10%-100%, including by way of example only 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, and 100%. In certain embodiments, the dose of drug being administered may be temporarily reduced or temporarily suspended for a certain length of time (i.e., a "drug diversion"). In specific embodiments, the length of the drug diversion is between 2 days and 1 year, including by way of example only, 2 days, 3 days, 4 days, 5 days, 6 days, 7 days, 10 days, 12 days, 15 days, 20 days, 28 days, or more than 28 days. The dose reduction during a drug diversion is, by way of example only, by 10%-100%, including by way of example only 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, and 100%. After a suitable length of time, the normal dosing schedule is optionally reinstated.

[0090] In some embodiments, once improvement of the patient's conditions has occurred, a maintenance dose is administered if necessary. Subsequently, in specific embodiments, the dosage or the frequency of administration, or both, is reduced, as a function of the symptoms, to a level at which

the improved disease, disorder or condition is retained. In certain embodiments, however, the patient requires intermittent treatment on a long-term basis upon any recurrence of symptoms.

[0091] Toxicity and therapeutic efficacy of such therapeutic regimens are determined by standard pharmaceutical procedures in cell cultures or experimental animals, including, but not limited to, the determination of the LD50 and the ED50. The dose ratio between the toxic and therapeutic effects is the therapeutic index and it is expressed as the ratio between LD50 and ED50. In certain embodiments, the data obtained from cell culture assays and animal studies are used in formulating the therapeutically effective daily dosage range and/or the therapeutically effective unit dosage amount for use in mammals, including humans. In some embodiments, the daily dosage amount of the therapeutic agent described herein lies within a range of circulating concentrations that include the ED50 with minimal toxicity. In certain embodiments, the daily dosage range and/or the unit dosage amount varies within this range depending upon the dosage form employed and the route of administration utilized.

[0092] *Additional Therapeutic*

[0093] A therapeutic agent may be used alone or in combination with an additional therapeutic agent. In some cases, an “additional therapeutic agent” as used herein is administered alone. The therapeutic agents may be administered together or sequentially. The combination therapies may be administered within the same day, or may be administered one or more days, weeks, months, or years apart. In some cases, a therapeutic agent provided herein is administered if the subject is determined to be non-responsive to a first line of therapy, e.g., such as TNF inhibitor. Such determination may be made by treatment with the first line therapy and monitoring of disease state and/or diagnostic determination that the subject would be non-responsive to the first line therapy.

[0094] In some embodiments, the additional therapeutic agent comprises an anti-TNF therapy, e.g., an anti-TNF α therapy. In some embodiments, the additional therapeutic agent comprises a second-line treatment to an anti-TNF therapy. In some embodiments, the additional therapeutic agent comprises an immunosuppressant, or a class of drugs that suppress, or reduce, the strength of the immune system. In some embodiments, the immunosuppressant is an antibody. Non-limiting examples of immunosuppressant therapeutic agents include STELARA® (ustekinumab) azathioprine (AZA), 6-mercaptopurine (6-MP), methotrexate, cyclosporin A. (CsA).

[0095] In some embodiments, the additional therapeutic agent comprises a selective anti-inflammatory drug, or a class of drugs that specifically target pro-inflammatory molecules in the body. In some embodiments, the anti-inflammatory drug comprises an antibody. In some embodiments, the anti-inflammatory drug comprises a small molecule. Non-limiting examples of anti-inflammatory drugs include ENTYVIO (vedolizumab), corticosteroids, aminosalicylates, mesalamine, balsalazide (Colazal) and olsalazine (Dipentum).

[0096] In some embodiments, the additional therapeutic agent comprises a stem cell therapy. The stem cell therapy may be embryonic or somatic stem cells. The stem cells may be isolated from a

donor (allogeneic) or isolated from the subject (autologous). The stem cells may be expanded adipose-derived stem cells (eASCs), hematopoietic stem cells (HSCs), mesenchymal stem (stromal) cells (MSCs), or induced pluripotent stem cells (iPSCs) derived from the cells of the subject. In some embodiments, the therapeutic agent comprises Cx601 / Alofisel® (darvadstrocel).

[0097] In some embodiments, the additional therapeutic agent comprises a small molecule. The small molecule may be used to treat inflammatory diseases or conditions, or fibrostenotic or fibrotic disease. Non-limiting examples of small molecules include Otezla® (apremilast), alicaforsen, or ozanimod (RPC-1063).

[0098] In some embodiments, the additional therapeutic agent comprises an agonist of TL1A, JAK1, GPR35, ADCY7, IFNG, TNFSF8, PFKFB3, SKAP2 GPR65, SPRED2, IL18RAP, GSDMB, and gene expression products from genes implicated in the pathogenesis of inflammatory, fibrotic, or fibrostenotic disease. The therapeutic agent may be an allosteric modulator of TL1A, JAK1, GPR35, ADCY7, IFNG, TNFSF8, PFKFB3, SKAP2 GPR65, SPRED2, IL18RAP, GSDMB, and gene expression products from genes implicated in the pathogenesis of inflammatory, fibrotic, or fibrostenotic disease.

[0099] In some embodiments, the additional therapeutic agent comprises an antagonist. The antagonist may comprise an inhibitor of the activity or expression of TL1A, JAK1, GPR35, ADCY7, IFNG, TNFSF8, PFKFB3, SKAP2 GPR65, SPRED2, IL18R1, GSDMB, and gene expression products from genes implicated in the pathogenesis of inflammatory, fibrotic, or fibrostenotic disease. Non-limiting examples of JAK1 inhibitors include Ruxolitinib (INCB018424), S-Ruxolitinib (INCB018424), Baricitinib (LY3009104, INCB028050), Filgotinib (GLPG0634), Momelotinib (CYT387), Cerdulatinib (PRT062070, PRT2070), LY2784544, NVP-BSK805, 2HCl, Tofacitinib (CP-690550, Tasocitinib), XL019, Pacritinib (SB1518), or ZM 39923 HCl.

[00100] In some embodiments the additional therapeutic agent comprises an inhibitor of TL1A expression or activity. In some cases, the inhibitor of TL1A expression or activity is effective to inhibit TL1A-DR3 binding. In some embodiments, the inhibitor of TL1A expression or activity comprises an allosteric modulator of TL1A. An allosteric modulator of TL1A may indirectly influence the effects TL1A on DR3, or TR6/DcR3 on TL1A or DR3. The inhibitor of TL1A expression or activity may be a direct inhibitor or indirect inhibitor. Non-limiting examples of an inhibitor of TL1A expression include RNA to protein TL1A translation inhibitors, antisense oligonucleotides targeting the TNFSF15 mRNA (such as miRNAs, or siRNA), epigenetic editing (such as targeting the DNA-binding domain of TNFSF15, or post-translational modifications of histone tails and/or DNA molecules). Non-limiting examples of an inhibitor of TL1A activity include antagonists to the TL1A receptors, (DR3 and TR6/DcR3), antagonists to TL1A antigen, and antagonists to gene expression products involved in TL1A mediated disease. Antagonists as disclosed herein, may include, but are not limited to, an anti-TL1A antibody, an anti-TL1A-binding antibody fragment, or a small molecule. The small molecule may be a small molecule that binds to TL1A or

DR3. The anti-TL1A antibody may be monoclonal or polyclonal. The anti-TL1A antibody may be humanized or chimeric. The anti-TL1A antibody may be a fusion protein. The anti-TL1A antibody may be a blocking anti-TL1A antibody. A blocking antibody blocks binding between two proteins, e.g., a ligand and its receptor. Therefore, a TL1A blocking antibody includes an antibody that prevents binding of TL1A to DR3 or TR6/DcR3 receptors. In a non-limiting example, the TL1A blocking antibody binds to DR3. In another example, the TL1A blocking antibody binds to DcR3. In some cases, the TL1A antibody is an anti-TL1A antibody that specifically binds to TL1A.

[00101] In some embodiments the additional therapeutic agent comprises an inhibitor of CD30L expression or activity. The inhibitor of CD30L expression or activity may be a direct inhibitor or indirect inhibitor. Non-limiting examples of an inhibitor of CD30L expression include RNA to protein TL1A translation inhibitors, antisense oligonucleotides targeting the mRNA (such as miRNAs, or siRNA), epigenetic editing (such as targeting the DNA-binding domain of CD30L, or post-translational modifications of histone tails and/or DNA molecules). In some embodiments, the CD30L inhibitor is an anti-CD30L antibody. The anti-CD30L antibody may be monoclonal or polyclonal. The anti-CD30L antibody may be humanized or chimeric.

[00102] In some instances, the additional therapeutic agent comprises administering to the subject an active agent that modulates CARD9 activity or expression. In various embodiments, the inhibitor of CARD9 activity or expression comprises a CARD9 antibody, a small molecule, a direct inhibitor of CARD9, an indirect inhibitor of CARD9, an allosteric modulator of CARD9, an anti-CARD9 antibody or antibody fragment, antibody or antibody fragment that specifically binds to Rubicon, an anti-tripartite Motif Containing 62 (TRIM62) antibody or antibody fragment, an antibody or antibody fragment that specifically binds to B Cell CLL/Lymphoma 10 (BCL10), an inhibitor of CARD9-Rubicon interaction, an inhibitor of CARD9-Tripertite Motif Containing 62 (TRIM62) interaction, an inhibitor of CARD9-B Cell CLL/Lymphoma 10 (BCL10) interaction, a small molecule that specifically binds CARD9 a small molecule that specifically binds to Rubicon, a small molecule that specifically binds to Tripertite Motif Containing 62 (TRIM62), a small molecule that specifically binds to B Cell CLL/Lymphoma 10 (BCL10), an inhibitor of CARD9-Rubicon interaction, an inhibitor of CARD9-Tripertite Motif Containing 62 (TRIM62) interaction, an inhibitor of B Cell CLL/Lymphoma 10 (BCL10)-CARD9 interaction, or a combination thereof. In some other embodiments, the inhibitor of CARD9 activity or expression comprises the small molecule inhibitor BRD5529, BRD4203, BRD8991, BRD4098 or a combination thereof. In some embodiments, the CARD9 antibody recognizes the total CARD9 protein. In other embodiments, the CARD9 antibody recognizes 90%, 80%, 70%, 60%, 50%, 40%, 30%, 20%, or 10% of the total CARD9 protein. In some embodiments, the modulator of CARD9 comprises a stem cell therapy. The stem cell therapy may be embryonic or somatic stem cells. The stem cells may be isolated from a donor (allogeneic) or isolated from the subject (autologous). The stem cells may be expanded adipose-derived stem cells (eASCs),

hematopoietic stem cells (HSCs), mesenchymal stem (stromal) cells (MSCs), or induced pluripotent stem cells (iPSCs) derived from the cells of the subject.

[00103] In some embodiments, the additional therapeutic agent comprises administering to the subject an antibody or antibody fragment, a small molecule, an allosteric modulator, an agonist, an antagonist, a direct modulator of Dectin-1A, an indirect modulator of Dectin-1A, or a combination thereof. In other embodiments, the treatment is an inhibitor of C-type lectin-like receptors. In various embodiments, the agonist is soluble β -glucan antagonist laminarin. In various other embodiments, the antagonist is soluble β -glucan antagonist laminarin. In some embodiments, the antibody binds to the C-type lectin-like receptors. In some embodiments, the Dectin-1 antibody recognizes the total Dectin-1 protein. In other embodiments, the Dectin-1 antibody recognizes 90%, 80%, 70%, 60%, 50%, 40%, 30%, 20%, or 10% of the total Dectine-1A protein. In some embodiments, the modulator of Dectin-1A comprises a stem cell therapy. The stem cell therapy may be embryonic or somatic stem cells. The stem cells may be isolated from a donor (allogeneic) or isolated from the subject (autologous). The stem cells may be expanded adipose-derived stem cells (eASCs), hematopoietic stem cells (HSCs), mesenchymal stem (stromal) cells (MSCs), or induced pluripotent stem cells (iPSCs) derived from the cells of the subject.

[00104] In some instances, the additional therapeutic agent comprises administering to the subject an antimycotic agent. In some instances, the antimycotic agent comprises an active agent that inhibits growth of a fungus. In some instances, the antimycotic agent comprises an active agent that kills a fungus. In some embodiments, the antimycotic agent comprises polyene, an azole, an echinocandin, an flucytosine, an allylamine, a tolnaftate, or griseofulvin, or a combination thereof. In other embodiments, the azole comprises triazole, imidazole, clotrimazole, ketoconazole, itraconazole, terconazole, oxiconazole, miconazole, econazole, tioconazole, voriconazole, fluconazole, isavuconazole, itraconazole, pramiconazole, ravuconazole, or posaconazole. In some other embodiments, the polyene comprises amphotericin B, nystatin, or natamycin. In yet other embodiments, the echinocandin comprises caspofungin, anidulafungin, or micafungin. In various other embodiments, the allylamine comprises naftifine or terbinafine.

[00105] Pharmaceutical Composition

[00106] A pharmaceutical composition, as used herein, refers to a mixture of a therapeutic agent, with other chemical components (i.e. pharmaceutically acceptable inactive ingredients), such as carriers, excipients, binders, filling agents, suspending agents, flavoring agents, sweetening agents, disintegrating agents, dispersing agents, surfactants, lubricants, colorants, diluents, solubilizers, moistening agents, plasticizers, stabilizers, penetration enhancers, wetting agents, anti-foaming agents, antioxidants, preservatives, or one or more combination thereof. Optionally, the compositions include two or more therapeutic agent (e.g., one or more therapeutic agents and one or more additional agents) as discussed herein. In practicing the methods of treatment or use provided herein, therapeutically effective amounts of therapeutic agents described herein are administered in a

pharmaceutical composition to a mammal having a disease, disorder, or condition to be treated, e.g., an inflammatory disease, fibrostenotic disease, and/or fibrotic disease. In some embodiments, the mammal is a human. A therapeutically effective amount can vary widely depending on the severity of the disease, the age and relative health of the subject, the potency of the therapeutic agent used and other factors. The therapeutic agents can be used singly or in combination with one or more therapeutic agents as components of mixtures.

[00107] The pharmaceutical formulations described herein are administered to a subject by appropriate administration routes, including but not limited to, intravenous, intraarterial, oral, parenteral, buccal, topical, transdermal, rectal, intramuscular, subcutaneous, intraosseous, transmucosal, inhalation, or intraperitoneal administration routes. The pharmaceutical formulations described herein include, but are not limited to, aqueous liquid dispersions, self-emulsifying dispersions, solid solutions, liposomal dispersions, aerosols, solid dosage forms, powders, immediate release formulations, controlled release formulations, fast melt formulations, tablets, capsules, pills, delayed release formulations, extended release formulations, pulsatile release formulations, multiparticulate formulations, and mixed immediate and controlled release formulations.

[00108] Pharmaceutical compositions including a therapeutic agent are manufactured in a conventional manner, such as, by way of example only, by means of conventional mixing, dissolving, granulating, dragee-making, levigating, emulsifying, encapsulating, entrapping or compression processes.

[00109] The pharmaceutical compositions may include at least a therapeutic agent as an active ingredient in free-acid or free-base form, or in a pharmaceutically acceptable salt form. In addition, the methods and pharmaceutical compositions described herein include the use of *N*-oxides (if appropriate), crystalline forms, amorphous phases, as well as active metabolites of these compounds having the same type of activity. In some embodiments, therapeutic agents exist in unsolvated form or in solvated forms with pharmaceutically acceptable solvents such as water, ethanol, and the like. The solvated forms of the therapeutic agents are also considered to be disclosed herein.

[00110] In some embodiments, a therapeutic agent exists as a tautomer. All tautomers are included within the scope of the agents presented herein. As such, it is to be understood that a therapeutic agent or a salt thereof may exhibit the phenomenon of tautomerism whereby two chemical compounds that are capable of facile interconversion by exchanging a hydrogen atom between two atoms, to either of which it forms a covalent bond. Since the tautomeric compounds exist in mobile equilibrium with each other they may be regarded as different isomeric forms of the same compound.

[00111] In some embodiments, a therapeutic agent exists as an enantiomer, diastereomer, or other stereoisomeric form. The agents disclosed herein include all enantiomeric, diastereomeric, and epimeric forms as well as mixtures thereof.

[00112] In some embodiments, therapeutic agents described herein may be prepared as prodrugs. A "prodrug" refers to an agent that is converted into the parent drug *in vivo*. Prodrugs are often useful

because, in some situations, they may be easier to administer than the parent drug. They may, for instance, be bioavailable by oral administration whereas the parent is not. The prodrug may also have improved solubility in pharmaceutical compositions over the parent drug. An example, without limitation, of a prodrug would be a therapeutic agent described herein, which is administered as an ester (the "prodrug") to facilitate transmittal across a cell membrane where water solubility is detrimental to mobility but which then is metabolically hydrolyzed to the carboxylic acid, the active entity, once inside the cell where water-solubility is beneficial. A further example of a prodrug might be a short peptide (polyaminoacid) bonded to an acid group where the peptide is metabolized to reveal the active moiety. In certain embodiments, upon in vivo administration, a prodrug is chemically converted to the biologically, pharmaceutically or therapeutically active form of the therapeutic agent. In certain embodiments, a prodrug is enzymatically metabolized by one or more steps or processes to the biologically, pharmaceutically or therapeutically active form of the therapeutic agent.

[00113] Prodrug forms of the therapeutic agents, wherein the prodrug is metabolized in vivo to produce an agent as set forth herein are included within the scope of the claims. Prodrug forms of the herein described therapeutic agents, wherein the prodrug is metabolized in vivo to produce an agent as set forth herein are included within the scope of the claims. In some cases, some of the therapeutic agents described herein may be a prodrug for another derivative or active compound. In some embodiments described herein, hydrazones are metabolized in vivo to produce a therapeutic agent.

[00114] In certain embodiments, compositions provided herein include one or more preservatives to inhibit microbial activity. Suitable preservatives include mercury-containing substances such as merfen and thiomersal; stabilized chlorine dioxide; and quaternary ammonium compounds such as benzalkonium chloride, cetyltrimethylammonium bromide and cetylpyridinium chloride.

[00115] In some embodiments, formulations described herein benefit from antioxidants, metal chelating agents, thiol containing compounds and other general stabilizing agents. Examples of such stabilizing agents, include, but are not limited to: (a) about 0.5% to about 2% w/v glycerol, (b) about 0.1% to about 1% w/v methionine, (c) about 0.1% to about 2% w/v monothioglycerol, (d) about 1 mM to about 10 mM EDTA, (e) about 0.01% to about 2% w/v ascorbic acid, (f) 0.003% to about 0.02% w/v polysorbate 80, (g) 0.001% to about 0.05% w/v. polysorbate 20, (h) arginine, (i) heparin, (j) dextran sulfate, (k) cyclodextrins, (l) pentosan polysulfate and other heparinoids, (m) divalent cations such as magnesium and zinc; or (n) combinations thereof.

[00116] The pharmaceutical compositions described herein are formulated into any suitable dosage form, including but not limited to, aqueous oral dispersions, liquids, gels, syrups, elixirs, slurries, suspensions, solid oral dosage forms, aerosols, controlled release formulations, fast melt formulations, effervescent formulations, lyophilized formulations, tablets, powders, pills, dragees, capsules, delayed release formulations, extended release formulations, pulsatile release formulations, multiparticulate formulations, and mixed immediate release and controlled release formulations. In one aspect, a therapeutic agent as discussed herein, e.g., therapeutic agent is formulated into a pharmaceutical

composition suitable for intramuscular, subcutaneous, or intravenous injection. In one aspect, formulations suitable for intramuscular, subcutaneous, or intravenous injection include physiologically acceptable sterile aqueous or non-aqueous solutions, dispersions, suspensions or emulsions, and sterile powders for reconstitution into sterile injectable solutions or dispersions. Examples of suitable aqueous and non-aqueous carriers, diluents, solvents, or vehicles include water, ethanol, polyols (propyleneglycol, polyethylene-glycol, glycerol, cremophor and the like), suitable mixtures thereof, vegetable oils (such as olive oil) and injectable organic esters such as ethyl oleate. Proper fluidity can be maintained, for example, by the use of a coating such as lecithin, by the maintenance of the required particle size in the case of dispersions, and by the use of surfactants. In some embodiments, formulations suitable for subcutaneous injection also contain additives such as preserving, wetting, emulsifying, and dispensing agents. Prevention of the growth of microorganisms can be ensured by various antibacterial and antifungal agents, such as parabens, chlorobutanol, phenol, sorbic acid, and the like. In some cases it is desirable to include isotonic agents, such as sugars, sodium chloride, and the like. Prolonged absorption of the injectable pharmaceutical form can be brought about by the use of agents delaying absorption, such as aluminum monostearate and gelatin.

[00117] For intravenous injections or drips or infusions, a therapeutic agent described herein is formulated in aqueous solutions, preferably in physiologically compatible buffers such as Hank's solution, Ringer's solution, or physiological saline buffer. For transmucosal administration, penetrants appropriate to the barrier to be permeated are used in the formulation. Such penetrants are generally known in the art. For other parenteral injections, appropriate formulations include aqueous or nonaqueous solutions, preferably with physiologically compatible buffers or excipients. Such excipients are known.

[00118] Parenteral injections may involve bolus injection or continuous infusion. Formulations for injection may be presented in unit dosage form, e.g., in ampoules or in multi-dose containers, with an added preservative. The pharmaceutical composition described herein may be in a form suitable for parenteral injection as a sterile suspensions, solutions or emulsions in oily or aqueous vehicles, and may contain formulatory agents such as suspending, stabilizing and/or dispersing agents. In one aspect, the active ingredient is in powder form for constitution with a suitable vehicle, e.g., sterile pyrogen-free water, before use.

[00119] For administration by inhalation, a therapeutic agent is formulated for use as an aerosol, a mist or a powder. Pharmaceutical compositions described herein are conveniently delivered in the form of an aerosol spray presentation from pressurized packs or a nebuliser, with the use of a suitable propellant, e.g., dichlorodifluoromethane, trichlorofluoromethane, dichlorotetrafluoroethane, carbon dioxide or other suitable gas. In the case of a pressurized aerosol, the dosage unit may be determined by providing a valve to deliver a metered amount. Capsules and cartridges of, such as, by way of

example only, gelatin for use in an inhaler or insufflator may be formulated containing a powder mix of the therapeutic agent described herein and a suitable powder base such as lactose or starch.

[00120] Representative intranasal formulations are described in, for example, U.S. Pat. Nos. 4,476,116, 5,116,817 and 6,391,452. Formulations that include a therapeutic agent are prepared as solutions in saline, employing benzyl alcohol or other suitable preservatives, fluorocarbons, and/or other solubilizing or dispersing agents known in the art. See, for example, Ansel, H. C. *et al.*, *Pharmaceutical Dosage Forms and Drug Delivery Systems*, Sixth Ed. (1995). Preferably these compositions and formulations are prepared with suitable nontoxic pharmaceutically acceptable ingredients. These ingredients are known to those skilled in the preparation of nasal dosage forms and some of these can be found in REMINGTON: THE SCIENCE AND PRACTICE OF PHARMACY, 21st edition, 2005. The choice of suitable carriers is dependent upon the exact nature of the nasal dosage form desired, e.g., solutions, suspensions, ointments, or gels. Nasal dosage forms generally contain large amounts of water in addition to the active ingredient. Minor amounts of other ingredients such as pH adjusters, emulsifiers or dispersing agents, preservatives, surfactants, gelling agents, or buffering and other stabilizing and solubilizing agents are optionally present. Preferably, the nasal dosage form should be isotonic with nasal secretions.

[00121] Pharmaceutical preparations for oral use are obtained by mixing one or more solid excipient with one or more of the therapeutic agents described herein, optionally grinding the resulting mixture, and processing the mixture of granules, after adding suitable auxiliaries, if desired, to obtain tablets or dragee cores. Suitable excipients include, for example, fillers such as sugars, including lactose, sucrose, mannitol, or sorbitol; cellulose preparations such as, for example, maize starch, wheat starch, rice starch, potato starch, gelatin, gum tragacanth, methylcellulose, microcrystalline cellulose, hydroxypropylmethylcellulose, sodium carboxymethylcellulose; or others such as: polyvinylpyrrolidone (PVP or povidone) or calcium phosphate. If desired, disintegrating agents are added, such as the cross-linked croscarmellose sodium, polyvinylpyrrolidone, agar, or alginic acid or a salt thereof such as sodium alginate. In some embodiments, dyestuffs or pigments are added to the tablets or dragee coatings for identification or to characterize different combinations of active therapeutic agent doses.

[00122] In some embodiments, pharmaceutical formulations of a therapeutic agent are in the form of capsules, including push-fit capsules made of gelatin, as well as soft, sealed capsules made of gelatin and a plasticizer, such as glycerol or sorbitol. The push-fit capsules contain the active ingredients in admixture with filler such as lactose, binders such as starches, and/or lubricants such as talc or magnesium stearate and, optionally, stabilizers. In soft capsules, the active therapeutic agent is dissolved or suspended in suitable liquids, such as fatty oils, liquid paraffin, or liquid polyethylene glycols. In some embodiments, stabilizers are added. A capsule may be prepared, for example, by placing the bulk blend of the formulation of the therapeutic agent inside of a capsule. In some embodiments, the formulations (non-aqueous suspensions and solutions) are placed in a soft gelatin

capsule. In other embodiments, the formulations are placed in standard gelatin capsules or non-gelatin capsules such as capsules comprising HPMC. In other embodiments, the formulation is placed in a sprinkle capsule, wherein the capsule is swallowed whole or the capsule is opened and the contents sprinkled on food prior to eating.

[00123] All formulations for oral administration are in dosages suitable for such administration. In one aspect, solid oral dosage forms are prepared by mixing a therapeutic agent with one or more of the following: antioxidants, flavoring agents, and carrier materials such as binders, suspending agents, disintegration agents, filling agents, surfactants, solubilizers, stabilizers, lubricants, wetting agents, and diluents. In some embodiments, the solid dosage forms disclosed herein are in the form of a tablet, (including a suspension tablet, a fast-melt tablet, a bite-disintegration tablet, a rapid-disintegration tablet, an effervescent tablet, or a caplet), a pill, a powder, a capsule, solid dispersion, solid solution, bioerodible dosage form, controlled release formulations, pulsatile release dosage forms, multiparticulate dosage forms, beads, pellets, granules. In other embodiments, the pharmaceutical formulation is in the form of a powder. Compressed tablets are solid dosage forms prepared by compacting the bulk blend of the formulations described above. In various embodiments, tablets will include one or more flavoring agents. In other embodiments, the tablets will include a film surrounding the final compressed tablet. In some embodiments, the film coating can provide a delayed release of a therapeutic agent from the formulation. In other embodiments, the film coating aids in patient compliance (e.g., Opadry® coatings or sugar coating). Film coatings including Opadry® typically range from about 1% to about 3% of the tablet weight. In some embodiments, solid dosage forms, e.g., tablets, effervescent tablets, and capsules, are prepared by mixing particles of a therapeutic agent with one or more pharmaceutical excipients to form a bulk blend composition. The bulk blend is readily subdivided into equally effective unit dosage forms, such as tablets, pills, and capsules. In some embodiments, the individual unit dosages include film coatings. These formulations are manufactured by conventional formulation techniques.

[00124] In another aspect, dosage forms include microencapsulated formulations. In some embodiments, one or more other compatible materials are present in the microencapsulation material. Exemplary materials include, but are not limited to, pH modifiers, erosion facilitators, anti-foaming agents, antioxidants, flavoring agents, and carrier materials such as binders, suspending agents, disintegration agents, filling agents, surfactants, solubilizers, stabilizers, lubricants, wetting agents, and diluents. Exemplary useful microencapsulation materials include, but are not limited to, hydroxypropyl cellulose ethers (HPC) such as Klucel® or Nisso HPC, low-substituted hydroxypropyl cellulose ethers (L-HPC), hydroxypropyl methyl cellulose ethers (HPMC) such as Seppifilm-LC, Pharmacoat®, Metolose SR, Methocel®-E, Opadry YS, PrimaFlo, Benecel MP824, and Benecel MP843, methylcellulose polymers such as Methocel®-A, hydroxypropylmethylcellulose acetate stearate Aqoat (HF-LS, HF-LG, HF-MS) and Metolose®, Ethylcelluloses (EC) and mixtures thereof such as E461, Ethocel®, Aqualon®-EC, Surelease®, Polyvinyl alcohol (PVA) such as Opadry AMB,

hydroxyethylcelluloses such as Natrosol®, carboxymethylcelluloses and salts of carboxymethylcelluloses (CMC) such as Aqualon®-CMC, polyvinyl alcohol and polyethylene glycol co-polymers such as Kollicoat IR®, monoglycerides (Myverol), triglycerides (KLX), polyethylene glycols, modified food starch, acrylic polymers and mixtures of acrylic polymers with cellulose ethers such as Eudragit® EPO, Eudragit® L30D-55, Eudragit® FS 30D Eudragit® L100-55, Eudragit® L100, Eudragit® S100, Eudragit® RD100, Eudragit® E100, Eudragit® L12.5, Eudragit® S12.5, Eudragit® NE30D, and Eudragit® NE 40D, cellulose acetate phthalate, sepiifilms such as mixtures of HPMC and stearic acid, cyclodextrins, and mixtures of these materials.

[00125] Liquid formulation dosage forms for oral administration are optionally aqueous suspensions selected from the group including, but not limited to, pharmaceutically acceptable aqueous oral dispersions, emulsions, solutions, elixirs, gels, and syrups. See, e.g., Singh et al., Encyclopedia of Pharmaceutical Technology, 2nd Ed., pp. 754-757 (2002). In addition to therapeutic agent the liquid dosage forms optionally include additives, such as: (a) disintegrating agents; (b) dispersing agents; (c) wetting agents; (d) at least one preservative, (e) viscosity enhancing agents, (f) at least one sweetening agent, and (g) at least one flavoring agent. In some embodiments, the aqueous dispersions further includes a crystal-forming inhibitor.

[00126] In some embodiments, the pharmaceutical formulations described herein are self-emulsifying drug delivery systems (SEDDS). Emulsions are dispersions of one immiscible phase in another, usually in the form of droplets. Generally, emulsions are created by vigorous mechanical dispersion. SEDDS, as opposed to emulsions or microemulsions, spontaneously form emulsions when added to an excess of water without any external mechanical dispersion or agitation. An advantage of SEDDS is that only gentle mixing is required to distribute the droplets throughout the solution. Additionally, water or the aqueous phase is optionally added just prior to administration, which ensures stability of an unstable or hydrophobic active ingredient. Thus, the SEDDS provides an effective delivery system for oral and parenteral delivery of hydrophobic active ingredients. In some embodiments, SEDDS provides improvements in the bioavailability of hydrophobic active ingredients. Methods of producing self-emulsifying dosage forms include, but are not limited to, for example, U.S. Pat. Nos. 5,858,401, 6,667,048, and 6,960,563.

[00127] Buccal formulations that include a therapeutic agent are administered using a variety of formulations known in the art. For example, such formulations include, but are not limited to, U.S. Pat. Nos. 4,229,447, 4,596,795, 4,755,386, and 5,739,136. In addition, the buccal dosage forms described herein can further include a bioerodible (hydrolysable) polymeric carrier that also serves to adhere the dosage form to the buccal mucosa. For buccal or sublingual administration, the compositions may take the form of tablets, lozenges, or gels formulated in a conventional manner.

[00128] For intravenous injections, a therapeutic agent is optionally formulated in aqueous solutions, preferably in physiologically compatible buffers such as Hank's solution, Ringer's solution, or physiological saline buffer. For transmucosal administration, penetrants appropriate to the barrier to

be permeated are used in the formulation. For other parenteral injections, appropriate formulations include aqueous or nonaqueous solutions, preferably with physiologically compatible buffers or excipients.

[00129] Parenteral injections optionally involve bolus injection or continuous infusion. Formulations for injection are optionally presented in unit dosage form, e.g., in ampoules or in multi dose containers, with an added preservative. In some embodiments, a pharmaceutical composition described herein is in a form suitable for parenteral injection as a sterile suspensions, solutions or emulsions in oily or aqueous vehicles, and contain formulatory agents such as suspending, stabilizing and/or dispersing agents. Pharmaceutical formulations for parenteral administration include aqueous solutions of an agent that modulates the activity of a carotid body in water soluble form. Additionally, suspensions of an agent that modulates the activity of a carotid body are optionally prepared as appropriate, e.g., oily injection suspensions.

[00130] Conventional formulation techniques include, e.g., one or a combination of methods: (1) dry mixing, (2) direct compression, (3) milling, (4) dry or non-aqueous granulation, (5) wet granulation, or (6) fusion. Other methods include, e.g., spray drying, pan coating, melt granulation, granulation, fluidized bed spray drying or coating (e.g., wurster coating), tangential coating, top spraying, tableting, extruding and the like.

[00131] Suitable carriers for use in the solid dosage forms described herein include, but are not limited to, acacia, gelatin, colloidal silicon dioxide, calcium glycerophosphate, calcium lactate, maltodextrin, glycerine, magnesium silicate, sodium caseinate, soy lecithin, sodium chloride, tricalcium phosphate, dipotassium phosphate, sodium stearyl lactylate, carrageenan, monoglyceride, diglyceride, pregelatinized starch, hydroxypropylmethylcellulose, hydroxypropylmethylcellulose acetate stearate, sucrose, microcrystalline cellulose, lactose, mannitol and the like.

[00132] Suitable filling agents for use in the solid dosage forms described herein include, but are not limited to, lactose, calcium carbonate, calcium phosphate, dibasic calcium phosphate, calcium sulfate, microcrystalline cellulose, cellulose powder, dextrose, dextrans, dextran, starches, pregelatinized starch, hydroxypropylmethylcellulose (HPMC), hydroxypropylmethylcellulose phthalate, hydroxypropylmethylcellulose acetate stearate (HPMCAS), sucrose, xylitol, lactitol, mannitol, sorbitol, sodium chloride, polyethylene glycol, and the like.

[00133] Suitable disintegrants for use in the solid dosage forms described herein include, but are not limited to, natural starch such as corn starch or potato starch, a pregelatinized starch, or sodium starch glycolate, a cellulose such as methylcrystalline cellulose, methylcellulose, microcrystalline cellulose, croscarmellose, or a cross-linked cellulose, such as cross-linked sodium carboxymethylcellulose, cross-linked carboxymethylcellulose, or cross-linked croscarmellose, a cross-linked starch such as sodium starch glycolate, a cross-linked polymer such as crospovidone, a cross-linked polyvinylpyrrolidone, alginate such as alginic acid or a salt of alginic acid such as sodium alginate, a

gum such as agar, guar, locust bean, Karaya, pectin, or tragacanth, sodium starch glycolate, bentonite, sodium lauryl sulfate, sodium lauryl sulfate in combination starch, and the like.

[00134] Binders impart cohesiveness to solid oral dosage form formulations: for powder filled capsule formulation, they aid in plug formation that can be filled into soft or hard shell capsules and for tablet formulation, they ensure the tablet remaining intact after compression and help assure blend uniformity prior to a compression or fill step. Materials suitable for use as binders in the solid dosage forms described herein include, but are not limited to, carboxymethylcellulose, methylcellulose, hydroxypropylmethylcellulose, hydroxypropylmethylcellulose acetate stearate, hydroxyethylcellulose, hydroxypropylcellulose, ethylcellulose, and microcrystalline cellulose, microcrystalline dextrose, amylose, magnesium aluminum silicate, polysaccharide acids, bentonites, gelatin, polyvinylpyrrolidone/vinyl acetate copolymer, crospovidone, povidone, starch, pregelatinized starch, tragacanth, dextrin, a sugar, such as sucrose, glucose, dextrose, molasses, mannitol, sorbitol, xylitol, lactose, a natural or synthetic gum such as acacia, tragacanth, ghatti gum, mucilage of isapol husks, starch, polyvinylpyrrolidone, larch arabogalactan, polyethylene glycol, waxes, sodium alginate, and the like.

[00135] In general, binder levels of 20-70% are used in powder-filled gelatin capsule formulations. Binder usage level in tablet formulations varies whether direct compression, wet granulation, roller compaction, or usage of other excipients such as fillers which itself can act as moderate binder. Binder levels of up to 70% in tablet formulations is common.

[00136] Suitable lubricants or glidants for use in the solid dosage forms described herein include, but are not limited to, stearic acid, calcium hydroxide, talc, corn starch, sodium stearyl fumarate, alkali-metal and alkaline earth metal salts, such as aluminum, calcium, magnesium, zinc, stearic acid, sodium stearates, magnesium stearate, zinc stearate, waxes, Stearowet[®], boric acid, sodium benzoate, sodium acetate, sodium chloride, leucine, a polyethylene glycol or a methoxypolyethylene glycol such as Carbowax[™], PEG 4000, PEG 5000, PEG 6000, propylene glycol, sodium oleate, glyceryl behenate, glyceryl palmitostearate, glyceryl benzoate, magnesium or sodium lauryl sulfate, and the like.

[00137] Suitable diluents for use in the solid dosage forms described herein include, but are not limited to, sugars (including lactose, sucrose, and dextrose), polysaccharides (including dextrans and maltodextrin), polyols (including mannitol, xylitol, and sorbitol), cyclodextrins and the like.

[00138] Suitable wetting agents for use in the solid dosage forms described herein include, for example, oleic acid, glyceryl monostearate, sorbitan monooleate, sorbitan monolaurate, triethanolamine oleate, polyoxyethylene sorbitan monooleate, polyoxyethylene sorbitan monolaurate, quaternary ammonium compounds (e.g., Polyquat 10[®]), sodium oleate, sodium lauryl sulfate, magnesium stearate, sodium docusate, triacetin, vitamin E TPGS and the like.

[00139] Suitable surfactants for use in the solid dosage forms described herein include, for example, sodium lauryl sulfate, sorbitan monooleate, polyoxyethylene sorbitan monooleate, polysorbates,

polaxomers, bile salts, glyceryl monostearate, copolymers of ethylene oxide and propylene oxide, e.g., Pluronic® (BASF), and the like.

[00140] Suitable suspending agents for use in the solid dosage forms described here include, but are not limited to, polyvinylpyrrolidone, e.g., polyvinylpyrrolidone K12, polyvinylpyrrolidone K17, polyvinylpyrrolidone K25, or polyvinylpyrrolidone K30, polyethylene glycol, e.g., the polyethylene glycol can have a molecular weight of about 300 to about 6000, or about 3350 to about 4000, or about 7000 to about 5400, vinyl pyrrolidone/vinyl acetate copolymer (S630), sodium carboxymethylcellulose, methylcellulose, hydroxy-propylmethylcellulose, polysorbate-80, hydroxyethylcellulose, sodium alginate, gums, such as, e.g., gum tragacanth and gum acacia, guar gum, xanthans, including xanthan gum, sugars, cellulosics, such as, e.g., sodium carboxymethylcellulose, methylcellulose, sodium carboxymethylcellulose, hydroxypropylmethylcellulose, hydroxyethylcellulose, polysorbate-80, sodium alginate, polyethoxylated sorbitan monolaurate, polyethoxylated sorbitan monolaurate, povidone and the like.

[00141] Suitable antioxidants for use in the solid dosage forms described herein include, for example, e.g., butylated hydroxytoluene (BHT), sodium ascorbate, and tocopherol.

[00142] It should be appreciated that there is considerable overlap between additives used in the solid dosage forms described herein. Thus, the above-listed additives should be taken as merely exemplary, and not limiting, of the types of additives that can be included in solid dosage forms of the pharmaceutical compositions described herein. The amounts of such additives can be readily determined by one skilled in the art, according to the particular properties desired.

[00143] In various embodiments, the particles of a therapeutic agents and one or more excipients are dry blended and compressed into a mass, such as a tablet, having a hardness sufficient to provide a pharmaceutical composition that substantially disintegrates within less than about 30 minutes, less than about 35 minutes, less than about 40 minutes, less than about 45 minutes, less than about 50 minutes, less than about 55 minutes, or less than about 60 minutes, after oral administration, thereby releasing the formulation into the gastrointestinal fluid.

[00144] In other embodiments, a powder including a therapeutic agent is formulated to include one or more pharmaceutical excipients and flavors. Such a powder is prepared, for example, by mixing the therapeutic agent and optional pharmaceutical excipients to form a bulk blend composition. Additional embodiments also include a suspending agent and/or a wetting agent. This bulk blend is uniformly subdivided into unit dosage packaging or multi-dosage packaging units.

[00145] In still other embodiments, effervescent powders are also prepared. Effervescent salts have been used to disperse medicines in water for oral administration.

[00146] In some embodiments, the pharmaceutical dosage forms are formulated to provide a controlled release of a therapeutic agent. Controlled release refers to the release of the therapeutic agent from a dosage form in which it is incorporated according to a desired profile over an extended period of time. Controlled release profiles include, for example, sustained release, prolonged release,

pulsatile release, and delayed release profiles. In contrast to immediate release compositions, controlled release compositions allow delivery of an agent to a subject over an extended period of time according to a predetermined profile. Such release rates can provide therapeutically effective levels of agent for an extended period of time and thereby provide a longer period of pharmacologic response while minimizing side effects as compared to conventional rapid release dosage forms. Such longer periods of response provide for many inherent benefits that are not achieved with the corresponding short acting, immediate release preparations.

[00147] In some embodiments, the solid dosage forms described herein are formulated as enteric coated delayed release oral dosage forms, i.e., as an oral dosage form of a pharmaceutical composition as described herein which utilizes an enteric coating to affect release in the small intestine or large intestine. In one aspect, the enteric coated dosage form is a compressed or molded or extruded tablet/mold (coated or uncoated) containing granules, powder, pellets, beads or particles of the active ingredient and/or other composition components, which are themselves coated or uncoated. In one aspect, the enteric coated oral dosage form is in the form of a capsule containing pellets, beads or granules, which include a therapeutic agent that are coated or uncoated.

[00148] Any coatings should be applied to a sufficient thickness such that the entire coating does not dissolve in the gastrointestinal fluids at pH below about 5, but does dissolve at pH about 5 and above. Coatings are typically selected from any of the following: Shellac - this coating dissolves in media of pH >7; Acrylic polymers - examples of suitable acrylic polymers include methacrylic acid copolymers and ammonium methacrylate copolymers. The Eudragit series E, L, S, RL, RS and NE (Rohm Pharma) are available as solubilized in organic solvent, aqueous dispersion, or dry powders. The Eudragit series RL, NE, and RS are insoluble in the gastrointestinal tract but are permeable and are used primarily for colonic targeting. The Eudragit series E dissolve in the stomach. The Eudragit series L, L-30D and S are insoluble in stomach and dissolve in the intestine; Poly Vinyl Acetate Phthalate (PVAP) - PVAP dissolves in pH >5, and it is much less permeable to water vapor and gastric fluids. Conventional coating techniques such as spray or pan coating are employed to apply coatings. The coating thickness must be sufficient to ensure that the oral dosage form remains intact until the desired site of topical delivery in the intestinal tract is reached.

[00149] In other embodiments, the formulations described herein are delivered using a pulsatile dosage form. A pulsatile dosage form is capable of providing one or more immediate release pulses at predetermined time points after a controlled lag time or at specific sites. Exemplary pulsatile dosage forms and methods of their manufacture are disclosed in U.S. Pat. Nos. 5,011,692, 5,017,381, 5,229,135, 5,840,329 and 5,837,284. In one embodiment, the pulsatile dosage form includes at least two groups of particles, (i.e. multiparticulate) each containing the formulation described herein. The first group of particles provides a substantially immediate dose of a therapeutic agent upon ingestion by a mammal. The first group of particles can be either uncoated or include a coating and/or sealant. In one aspect, the second group of particles comprises coated particles. The coating on the second

group of particles provides a delay of from about 2 hours to about 7 hours following ingestion before release of the second dose. Suitable coatings for pharmaceutical compositions are described herein or known in the art.

[00150] In some embodiments, pharmaceutical formulations are provided that include particles of a therapeutic agent and at least one dispersing agent or suspending agent for oral administration to a subject. The formulations may be a powder and/or granules for suspension, and upon admixture with water, a substantially uniform suspension is obtained.

[00151] In some embodiments, particles formulated for controlled release are incorporated in a gel or a patch or a wound dressing.

[00152] In one aspect, liquid formulation dosage forms for oral administration and/or for topical administration as a wash are in the form of aqueous suspensions selected from the group including, but not limited to, pharmaceutically acceptable aqueous oral dispersions, emulsions, solutions, elixirs, gels, and syrups. See, e.g., Singh *et al.*, Encyclopedia of Pharmaceutical Technology, 2nd Ed., pp. 754-757 (2002). In addition to the particles of a therapeutic agent, the liquid dosage forms include additives, such as: (a) disintegrating agents; (b) dispersing agents; (c) wetting agents; (d) at least one preservative, (e) viscosity enhancing agents, (f) at least one sweetening agent, and (g) at least one flavoring agent. In some embodiments, the aqueous dispersions can further include a crystalline inhibitor.

[00153] In some embodiments, the liquid formulations also include inert diluents commonly used in the art, such as water or other solvents, solubilizing agents, and emulsifiers. Exemplary emulsifiers are ethyl alcohol, isopropyl alcohol, ethyl carbonate, ethyl acetate, benzyl alcohol, benzyl benzoate, propyleneglycol, 1,3-butyleneglycol, dimethylformamide, sodium lauryl sulfate, sodium docusate, cholesterol, cholesterol esters, taurocholic acid, phosphatidylcholine, oils, such as cottonseed oil, groundnut oil, corn germ oil, olive oil, castor oil, and sesame oil, glycerol, tetrahydrofurfuryl alcohol, polyethylene glycols, fatty acid esters of sorbitan, or mixtures of these substances, and the like.

[00154] Furthermore, pharmaceutical compositions optionally include one or more pH adjusting agents or buffering agents, including acids such as acetic, boric, citric, lactic, phosphoric and hydrochloric acids; bases such as sodium hydroxide, sodium phosphate, sodium borate, sodium citrate, sodium acetate, sodium lactate and tris-hydroxymethylaminomethane; and buffers such as citrate/dextrose, sodium bicarbonate and ammonium chloride. Such acids, bases and buffers are included in an amount required to maintain pH of the composition in an acceptable range.

[00155] Additionally, pharmaceutical compositions optionally include one or more salts in an amount required to bring osmolality of the composition into an acceptable range. Such salts include those having sodium, potassium or ammonium cations and chloride, citrate, ascorbate, borate, phosphate, bicarbonate, sulfate, thiosulfate or bisulfite anions; suitable salts include sodium chloride, potassium chloride, sodium thiosulfate, sodium bisulfite and ammonium sulfate.

[00156] Other pharmaceutical compositions optionally include one or more preservatives to inhibit microbial activity. Suitable preservatives include mercury-containing substances such as merfen and thiomersal; stabilized chlorine dioxide; and quaternary ammonium compounds such as benzalkonium chloride, cetyltrimethylammonium bromide and cetylpyridinium chloride.

[00157] In one embodiment, the aqueous suspensions and dispersions described herein remain in a homogenous state, as defined in The USP Pharmacists' Pharmacopeia (2005 edition, chapter 905), for at least 4 hours. In one embodiment, an aqueous suspension is re-suspended into a homogenous suspension by physical agitation lasting less than 1 minute. In still another embodiment, no agitation is necessary to maintain a homogeneous aqueous dispersion.

[00158] Examples of disintegrating agents for use in the aqueous suspensions and dispersions include, but are not limited to, a starch, e.g., a natural starch such as corn starch or potato starch, a pregelatinized starch, or sodium starch glycolate; a cellulose such as methylcrystalline cellulose, methylcellulose, croscarmellose, or a cross-linked cellulose, such as cross-linked sodium carboxymethylcellulose, cross-linked carboxymethylcellulose, or cross-linked croscarmellose; a cross-linked starch such as sodium starch glycolate; a cross-linked polymer such as crospovidone; a cross-linked polyvinylpyrrolidone; alginate such as alginic acid or a salt of alginic acid such as sodium alginate; a gum such as agar, guar, locust bean, Karaya, pectin, or tragacanth; sodium starch glycolate; bentonite; a natural sponge; a surfactant; a resin such as a cation-exchange resin; citrus pulp; sodium lauryl sulfate; sodium lauryl sulfate in combination starch; and the like.

[00159] In some embodiments, the dispersing agents suitable for the aqueous suspensions and dispersions described herein include, for example, hydrophilic polymers, electrolytes, Tween[®] 60 or 80, PEG, polyvinylpyrrolidone, and the carbohydrate-based dispersing agents such as, for example, hydroxypropylcellulose and hydroxypropyl cellulose ethers, hydroxypropyl methylcellulose and hydroxypropyl methylcellulose ethers, carboxymethylcellulose sodium, methylcellulose, hydroxyethylcellulose, hydroxypropylmethyl-cellulose phthalate, hydroxypropylmethyl-cellulose acetate stearate, noncrystalline cellulose, magnesium aluminum silicate, triethanolamine, polyvinyl alcohol (PVA), polyvinylpyrrolidone/vinyl acetate copolymer, 4-(1,1,3,3-tetramethylbutyl)-phenol polymer with ethylene oxide and formaldehyde (also known as tyloxapol), poloxamers; and poloxamines. In other embodiments, the dispersing agent is selected from a group not comprising one of the following agents: hydrophilic polymers; electrolytes; Tween[®] 60 or 80; PEG; polyvinylpyrrolidone (PVP); hydroxypropylcellulose and hydroxypropyl cellulose ethers; hydroxypropyl methylcellulose and hydroxypropyl methylcellulose ethers; carboxymethylcellulose sodium; methylcellulose; hydroxyethylcellulose; hydroxypropylmethyl-cellulose phthalate; hydroxypropylmethyl-cellulose acetate stearate; non-crystalline cellulose; magnesium aluminum silicate; triethanolamine; polyvinyl alcohol (PVA); 4-(1,1,3,3-tetramethylbutyl)-phenol polymer with ethylene oxide and formaldehyde; poloxamers; or poloxamines.

[00160] Wetting agents suitable for the aqueous suspensions and dispersions described herein include, but are not limited to, cetyl alcohol, glycerol monostearate, polyoxyethylene sorbitan fatty acid esters (e.g., the commercially available Tweens[®] such as e.g., Tween 20[®] and Tween 80[®], and polyethylene glycols, oleic acid, glyceryl monostearate, sorbitan monooleate, sorbitan monolaurate, triethanolamine oleate, polyoxyethylene sorbitan monooleate, polyoxyethylene sorbitan monolaurate, sodium oleate, sodium lauryl sulfate, sodium docusate, triacetin, vitamin E TPGS, sodium taurocholate, simethicone, phosphatidylcholine and the like.

[00161] Suitable preservatives for the aqueous suspensions or dispersions described herein include, for example, potassium sorbate, parabens (e.g., methylparaben and propylparaben), benzoic acid and its salts, other esters of parahydroxybenzoic acid such as butylparaben, alcohols such as ethyl alcohol or benzyl alcohol, phenolic compounds such as phenol, or quaternary compounds such as benzalkonium chloride. Preservatives, as used herein, are incorporated into the dosage form at a concentration sufficient to inhibit microbial growth.

[00162] Suitable viscosity enhancing agents for the aqueous suspensions or dispersions described herein include, but are not limited to, methyl cellulose, xanthan gum, carboxymethyl cellulose, hydroxypropyl cellulose, hydroxypropylmethyl cellulose, Plasdon[®] S-630, carbomer, polyvinyl alcohol, alginates, acacia, chitosans and combinations thereof. The concentration of the viscosity enhancing agent will depend upon the agent selected and the viscosity desired.

[00163] Examples of sweetening agents suitable for the aqueous suspensions or dispersions described herein include, for example, acacia syrup, acesulfame K, alitame, aspartame, chocolate, cinnamon, citrus, cocoa, cyclamate, dextrose, fructose, ginger, glycyrrhetinate, glycyrrhiza (licorice) syrup, monoammonium glycyrrhizinate (MagnaSweet[®]), malitol, mannitol, menthol, neohesperidine DC, neotame, Prosweet[®] Powder, saccharin, sorbitol, stevia, sucralose, sucrose, sodium saccharin, saccharin, aspartame, acesulfame potassium, mannitol, sucralose, tagatose, thaumatin, vanilla, xylitol, or any combination thereof.

[00164] In some embodiments, a therapeutic agent is prepared as transdermal dosage form. In some embodiments, the transdermal formulations described herein include at least three components: (1) a therapeutic agent; (2) a penetration enhancer; and (3) an optional aqueous adjuvant. In some embodiments the transdermal formulations include additional components such as, but not limited to, gelling agents, creams and ointment bases, and the like. In some embodiments, the transdermal formulation is presented as a patch or a wound dressing. In some embodiments, the transdermal formulation further include a woven or non-woven backing material to enhance absorption and prevent the removal of the transdermal formulation from the skin. In other embodiments, the transdermal formulations described herein can maintain a saturated or supersaturated state to promote diffusion into the skin.

[00165] In one aspect, formulations suitable for transdermal administration of a therapeutic agent described herein employ transdermal delivery devices and transdermal delivery patches and can be

lipophilic emulsions or buffered, aqueous solutions, dissolved and/or dispersed in a polymer or an adhesive. In one aspect, such patches are constructed for continuous, pulsatile, or on demand delivery of pharmaceutical agents. Still further, transdermal delivery of the therapeutic agents described herein can be accomplished by means of iontophoretic patches and the like. In one aspect, transdermal patches provide controlled delivery of a therapeutic agent. In one aspect, transdermal devices are in the form of a bandage comprising a backing member, a reservoir containing the therapeutic agent optionally with carriers, optionally a rate controlling barrier to deliver the therapeutic agent to the skin of the host at a controlled and predetermined rate over a prolonged period of time, and means to secure the device to the skin.

[00166] In further embodiments, topical formulations include gel formulations (e.g., gel patches which adhere to the skin). In some of such embodiments, a gel composition includes any polymer that forms a gel upon contact with the body (e.g., gel formulations comprising hyaluronic acid, pluronic polymers, poly(lactic-co-glycolic acid (PLGA)-based polymers or the like). In some forms of the compositions, the formulation comprises a low-melting wax such as, but not limited to, a mixture of fatty acid glycerides, optionally in combination with cocoa butter which is first melted. Optionally, the formulations further comprise a moisturizing agent.

[00167] In certain embodiments, delivery systems for pharmaceutical therapeutic agents may be employed, such as, for example, liposomes and emulsions. In certain embodiments, compositions provided herein can also include an mucoadhesive polymer, selected from among, for example, carboxymethylcellulose, carbomer (acrylic acid polymer), poly(methylmethacrylate), polyacrylamide, polycarboxiphil, acrylic acid/butyl acrylate copolymer, sodium alginate and dextran.

[00168] In some embodiments, a therapeutic agent described herein may be administered topically and can be formulated into a variety of topically administrable compositions, such as solutions, suspensions, lotions, gels, pastes, medicated sticks, balms, creams or ointments. Such pharmaceutical therapeutic agents can contain solubilizers, stabilizers, tonicity enhancing agents, buffers and preservatives.

KITS AND COMPOSITIONS

[00169] Compositions

[00170] Disclosed herein, in some embodiments, are compositions useful for the detection of a genotype or biomarker in a sample obtained from a subject according to the methods described herein. Aspects disclosed herein provide compositions comprising a polynucleotide sequence comprising at least 10 but less than 50 contiguous nucleotides encoding one or more SNPs of SKAP2, wherein the contiguous polynucleotide sequence comprises a detectable molecule. In various embodiments, the detectable molecule comprises a fluorophore. In other embodiments, the polynucleotide sequences further comprise a quencher.

[00171] Also disclosed herein are compositions comprising an antibody or antigen-binding fragment that specifically binds to SKAP2, wherein the antibody or antigen-binding fragment comprises a

detectable molecule. In various embodiments, the antibody comprises a monoclonal antibody, a chimeric antibody, a CDR-grafted antibody, a Fab, a Fab', a F(ab')₂, a Fv, a disulfide linked Fv, a scFv, a single domain antibody, a diabody, a multispecific antibody, a dual specific antibody, an anti-idiotypic antibody, or a bispecific antibody. In some embodiments, the antibody or antigen-binding fragment comprises an IgG antibody, an IgM antibody, and/or an IgE antibody. In some embodiments, the detectable molecule comprises a fluorophore. In some embodiments, the antibody or antigen-binding fragment is conjugated to a paramagnetic particle (e.g., bead).

[00172] Kits

[00173] Disclosed herein, in some embodiments, are kits useful for to detect the genotypes and/or biomarkers disclosed herein. In some embodiments, the kits disclosed herein may be used to diagnose and/or treat a disease or condition in a subject; or select a patient for treatment and/or monitor a treatment disclosed herein. In some embodiments, the kit comprises the compositions described herein, which can be used to perform the methods described herein. Kits comprise an assemblage of materials or components, including at least one of the compositions. Thus, in some embodiments the kit contains a composition including of the pharmaceutical composition, for the treatment of IBD. In other embodiments, the kits contains all of the components necessary and/or sufficient to perform an assay for detecting and measuring IBD markers, including all controls, directions for performing assays, and any necessary software for analysis and presentation of results.

[00174] In some instances, the kits described herein comprise components comprising the compositions described herein for detecting the presence, absence, and/or quantity of a target nucleic acid (e.g., SKAP2, SKAP2 SNPs) and/or protein (e.g., SKAP2) described herein. In some embodiments, the kit further comprises components for detecting the presence, absence, and/or quantity of a serological marker described herein. In some embodiments, the kit comprises the compositions (e.g., primers, probes, antibodies) described herein. The disclosure provides kits suitable for assays such as enzyme-linked immunosorbent assay (ELISA), single-molecular array (Simoa), PCR, and qPCR. The exact nature of the components configured in the kit depends on its intended purpose. For example, some embodiments are configured for the purpose of treating a disease or condition disclosed herein (e.g., IBD, CD, UC) in a subject. In some embodiments, the kit is configured particularly for the purpose of treating mammalian subjects. In some embodiments, the kit is configured particularly for the purpose of treating human subjects. In further embodiments, the kit is configured for veterinary applications, treating subjects such as, but not limited to, farm animals, domestic animals, and laboratory animals. In some embodiments, the kit is configured to select a subject for a therapeutic agent, such as those disclosed herein. In some embodiments, the kit is configured to select a subject for treatment with Crohn's disease, inflammatory bowel disease, or ulcerative colitis.

[00175] Instructions for use may be included in the kit. Optionally, the kit also contains other useful components, such as, diluents, buffers, pharmaceutically acceptable carriers, syringes, catheters,

applicators, pipetting or measuring tools, bandaging materials or other useful paraphernalia. The materials or components assembled in the kit can be provided to the practitioner stored in any convenient and suitable ways that preserve their operability and utility. For example the components can be in dissolved, dehydrated, or lyophilized form; they can be provided at room, refrigerated or frozen temperatures. The components are typically contained in suitable packaging material(s). As employed herein, the phrase “packaging material” refers to one or more physical structures used to house the contents of the kit, such as compositions and the like. The packaging material is constructed by well-known methods, preferably to provide a sterile, contaminant-free environment. The packaging materials employed in the kit are those customarily utilized in gene expression assays and in the administration of treatments. As used herein, the term “package” refers to a suitable solid matrix or material such as glass, plastic, paper, foil, and the like, capable of holding the individual kit components. Thus, for example, a package can be a glass vial or prefilled syringes used to contain suitable quantities of the pharmaceutical composition. The packaging material has an external label which indicates the contents and/or purpose of the kit and its components.

SYSTEMS

[00176] Disclosed herein, in some embodiments, is a system for detecting a particular SNP in SKAP2 in a subject. The system is configured to implement the methods described in this disclosure, including, but not limited to, detecting the presence of a particular CD subtype to determine whether the subject is suitable for treatment with a particular therapy.

[00177] In some embodiments, disclosed herein is a system for detecting one or more SNPs in SKAP2 in a subject, comprising: (a) a computer processing device, optionally connected to a computer network; and (b) a software module executed by the computer processing device to analyze a target nucleic acid sequence of one or more SNPS in SKAP2 in a sample from a subject. In some instances, the system comprises a central processing unit (CPU), memory (e.g., random access memory, flash memory), electronic storage unit, computer program, communication interface to communicate with one or more other systems, and any combination thereof. In some instances, the system is coupled to a computer network, for example, the Internet, intranet, and/or extranet that is in communication with the Internet, a telecommunication, or data network. In some embodiments, the system comprises a storage unit to store data and information regarding any aspect of the methods described in this disclosure. Various aspects of the system are a product or article or manufacture.

[00178] One feature of a computer program includes a sequence of instructions, executable in the digital processing device's CPU, written to perform a specified task. In some embodiments, computer readable instructions are implemented as program modules, such as functions, features, Application Programming Interfaces (APIs), data structures, and the like, that perform particular tasks or implement particular abstract data types. In light of the disclosure provided herein, those of skill in

the art will recognize that a computer program may be written in various versions of various languages.

[00179] The functionality of the computer readable instructions are combined or distributed as desired in various environments. In some instances, a computer program comprises one sequence of instructions or a plurality of sequences of instructions. A computer program may be provided from one location. A computer program may be provided from a plurality of locations. In some embodiment, a computer program includes one or more software modules. In some embodiments, a computer program includes, in part or in whole, one or more web applications, one or more mobile applications, one or more standalone applications, one or more web browser plug-ins, extensions, add-ins, or add-ons, or combinations thereof.

[00180] **Web application**

[00181] In some embodiments, a computer program includes a web application. In light of the disclosure provided herein, those of skill in the art will recognize that a web application may utilize one or more software frameworks and one or more database systems. A web application, for example, is created upon a software framework such as Microsoft® .NET or Ruby on Rails (RoR). A web application, in some instances, utilizes one or more database systems including, by way of non-limiting examples, relational, non-relational, feature oriented, associative, and XML database systems. Suitable relational database systems include, by way of non-limiting examples, Microsoft® SQL Server, MySQL™, and Oracle®. Those of skill in the art will also recognize that a web application may be written in one or more versions of one or more languages. In some embodiments, a web application is written in one or more markup languages, presentation definition languages, client-side scripting languages, server-side coding languages, database query languages, or combinations thereof. In some embodiments, a web application is written to some extent in a markup language such as Hypertext Markup Language (HTML), Extensible Hypertext Markup Language (XHTML), or eXtensible Markup Language (XML). In some embodiments, a web application is written to some extent in a presentation definition language such as Cascading Style Sheets (CSS). In some embodiments, a web application is written to some extent in a client-side scripting language such as Asynchronous Javascript and XML (AJAX), Flash® Actionscript, Javascript, or Silverlight®. In some embodiments, a web application is written to some extent in a server-side coding language such as Active Server Pages (ASP), ColdFusion®, Perl, Java™, JavaServer Pages (JSP), Hypertext Preprocessor (PHP), Python™, Ruby, Tcl, Smalltalk, WebDNA®, or Groovy. In some embodiments, a web application is written to some extent in a database query language such as Structured Query Language (SQL). A web application may integrate enterprise server products such as IBM® Lotus Domino®. A web application may include a media player element. A media player element may utilize one or more of many suitable multimedia technologies including, by way of non-limiting examples, Adobe® Flash®, HTML 5, Apple® QuickTime®, Microsoft® Silverlight®, Java™, and Unity®.

[00182] Mobile application

[00183] In some instances, a computer program includes a mobile application provided to a mobile digital processing device. The mobile application may be provided to a mobile digital processing device at the time it is manufactured. The mobile application may be provided to a mobile digital processing device via the computer network described herein.

[00184] A mobile application is created by techniques known to those of skill in the art using hardware, languages, and development environments known to the art. Those of skill in the art will recognize that mobile applications may be written in several languages. Suitable programming languages include, by way of non-limiting examples, C, C++, C#, Featureive-C, Java™, Javascript, Pascal, Feature Pascal, Python™, Ruby, VB.NET, WML, and XHTML/HTML with or without CSS, or combinations thereof.

[00185] Suitable mobile application development environments are available from several sources. Commercially available development environments include, by way of non-limiting examples, AirplaySDK, alcheMo, Appcelerator®, Celsius, Bedrock, Flash Lite, .NET Compact Framework, Rhomobile, and WorkLight Mobile Platform. Other development environments may be available without cost including, by way of non-limiting examples, Lazarus, MobiFlex, MoSync, and Phonegap. Also, mobile device manufacturers distribute software developer kits including, by way of non-limiting examples, iPhone and iPad (iOS) SDK, Android™ SDK, BlackBerry® SDK, BREW SDK, Palm® OS SDK, Symbian SDK, webOS SDK, and Windows® Mobile SDK.

[00186] Those of skill in the art will recognize that several commercial forums are available for distribution of mobile applications including, by way of non-limiting examples, Apple® App Store, Android™ Market, BlackBerry® App World, App Store for Palm devices, App Catalog for webOS, Windows® Marketplace for Mobile, Ovi Store for Nokia® devices, Samsung® Apps, and Nintendo® DSi Shop.

[00187] Standalone application

[00188] In some embodiments, a computer program includes a standalone application, which is a program that may be run as an independent computer process, not an add-on to an existing process, e.g., not a plug-in. Those of skill in the art will recognize that standalone applications are sometimes compiled. In some instances, a compiler is a computer program(s) that transforms source code written in a programming language into binary feature code such as assembly language or machine code. Suitable compiled programming languages include, by way of non-limiting examples, C, C++, Featureive-C, COBOL, Delphi, Eiffel, Java™, Lisp, Python™, Visual Basic, and VB .NET, or combinations thereof. Compilation may be often performed, at least in part, to create an executable program. In some instances, a computer program includes one or more executable compiled applications.

[00189] Web browser plug-in

[00190] A computer program, in some aspects, includes a web browser plug-in. In computing, a plug-in, in some instances, is one or more software components that add specific functionality to a larger software application. Makers of software applications may support plug-ins to enable third-party developers to create abilities which extend an application, to support easily adding new features, and to reduce the size of an application. When supported, plug-ins enable customizing the functionality of a software application. For example, plug-ins are commonly used in web browsers to play video, generate interactivity, scan for viruses, and display particular file types. Those of skill in the art will be familiar with several web browser plug-ins including, Adobe® Flash® Player, Microsoft® Silverlight®, and Apple® QuickTime®. The toolbar may comprise one or more web browser extensions, add-ins, or add-ons. The toolbar may comprise one or more explorer bars, tool bands, or desk bands.

[00191] In view of the disclosure provided herein, those of skill in the art will recognize that several plug-in frameworks are available that enable development of plug-ins in various programming languages, including, by way of non-limiting examples, C++, Delphi, Java™, PHP, Python™, and VB .NET, or combinations thereof.

[00192] In some embodiments, Web browsers (also called Internet browsers) are software applications, designed for use with network-connected digital processing devices, for retrieving, presenting, and traversing information resources on the World Wide Web. Suitable web browsers include, by way of non-limiting examples, Microsoft® Internet Explorer®, Mozilla® Firefox®, Google® Chrome, Apple® Safari®, Opera Software® Opera®, and KDE Konqueror. The web browser, in some instances, is a mobile web browser. Mobile web browsers (also called microbrowsers, mini-browsers, and wireless browsers) may be designed for use on mobile digital processing devices including, by way of non-limiting examples, handheld computers, tablet computers, netbook computers, subnotebook computers, smartphones, music players, personal digital assistants (PDAs), and handheld video game systems. Suitable mobile web browsers include, by way of non-limiting examples, Google® Android® browser, RIM BlackBerry® Browser, Apple® Safari®, Palm® Blazer, Palm® WebOS® Browser, Mozilla® Firefox® for mobile, Microsoft® Internet Explorer® Mobile, Amazon® Kindle® Basic Web, Nokia® Browser, Opera Software® Opera® Mobile, and Sony® PSP™ browser.

[00193] Software modules

[00194] The medium, method, and system disclosed herein comprise one or more softwares, servers, and database modules, or use of the same. In view of the disclosure provided herein, software modules may be created by techniques known to those of skill in the art using machines, software, and languages known to the art. The software modules disclosed herein may be implemented in a multitude of ways. In some embodiments, a software module comprises a file, a section of code, a programming feature, a programming structure, or combinations thereof. A software module may

comprise a plurality of files, a plurality of sections of code, a plurality of programming features, a plurality of programming structures, or combinations thereof. By way of non-limiting examples, the one or more software modules comprise a web application, a mobile application, and/or a standalone application. Software modules may be in one computer program or application. Software modules may be in more than one computer program or application. Software modules may be hosted on one machine. Software modules may be hosted on more than one machine. Software modules may be hosted on cloud computing platforms. Software modules may be hosted on one or more machines in one location. Software modules may be hosted on one or more machines in more than one location.

[00195] Databases

[00196] The medium, method, and system disclosed herein comprise one or more databases, or use of the same. In view of the disclosure provided herein, those of skill in the art will recognize that many databases are suitable for storage and retrieval of geologic profile, operator activities, division of interest, and/or contact information of royalty owners. Suitable databases include, by way of non-limiting examples, relational databases, non-relational databases, feature oriented databases, feature databases, entity-relationship model databases, associative databases, and XML databases. In some embodiments, a database is internet-based. In some embodiments, a database is web-based. In some embodiments, a database is cloud computing-based. A database may be based on one or more local computer storage devices.

[00197] Data transmission

[00198] The subject matter described herein, including methods for detecting a particular CD subtype, are configured to be performed in one or more facilities at one or more locations. Facility locations are not limited by country and include any country or territory. In some instances, one or more steps are performed in a different country than another step of the method. In some instances, one or more steps for obtaining a sample are performed in a different country than one or more steps for detecting the presence or absence of a particular CD subtype from a sample. In some embodiments, one or more method steps involving a computer system are performed in a different country than another step of the methods provided herein. In some embodiments, data processing and analyses are performed in a different country or location than one or more steps of the methods described herein. In some embodiments, one or more articles, products, or data are transferred from one or more of the facilities to one or more different facilities for analysis or further analysis. An article includes, but is not limited to, one or more components obtained from a subject, e.g., processed cellular material. Processed cellular material includes, but is not limited to, cDNA reverse transcribed from RNA, amplified RNA, amplified cDNA, sequenced DNA, isolated and/or purified RNA, isolated and/or purified DNA, and isolated and/or purified polypeptide. Data includes, but is not limited to, information regarding the stratification of a subject, and any data produced by the methods disclosed herein. In some embodiments of the methods and systems described herein, the analysis is performed and a subsequent data transmission step will convey or transmit the results of the analysis.

[00199] In some embodiments, any step of any method described herein is performed by a software program or module on a computer. In additional or further embodiments, data from any step of any method described herein is transferred to and from facilities located within the same or different countries, including analysis performed in one facility in a particular location and the data shipped to another location or directly to an individual in the same or a different country. In additional or further embodiments, data from any step of any method described herein is transferred to and/or received from a facility located within the same or different countries, including analysis of a data input, such as genetic or processed cellular material, performed in one facility in a particular location and corresponding data transmitted to another location, or directly to an individual, such as data related to the diagnosis, prognosis, responsiveness to therapy, or the like, in the same or different location or country.

[00200] **Business Methods Utilizing a Computer**

[00201] The methods described herein may utilize one or more computers. The computer may be used for managing customer and sample information such as sample or customer tracking, database management, analyzing molecular profiling data, analyzing cytological data, storing data, billing, marketing, reporting results, storing results, or a combination thereof. The computer may include a monitor or other graphical interface for displaying data, results, billing information, marketing information (e.g. demographics), customer information, or sample information. The computer may also include means for data or information input. The computer may include a processing unit and fixed or removable media or a combination thereof. The computer may be accessed by a user in physical proximity to the computer, for example via a keyboard and/or mouse, or by a user that does not necessarily have access to the physical computer through a communication medium such as a modem, an internet connection, a telephone connection, or a wired or wireless communication signal carrier wave. In some cases, the computer may be connected to a server or other communication device for relaying information from a user to the computer or from the computer to a user. In some cases, the user may store data or information obtained from the computer through a communication medium on media, such as removable media. It is envisioned that data relating to the methods can be transmitted over such networks or connections for reception and/or review by a party. The receiving party can be but is not limited to an individual, a health care provider or a health care manager. In one embodiment, a computer-readable medium includes a medium suitable for transmission of a result of an analysis of a biological sample, such as exosome bio-signatures. The medium can include a result regarding an exosome bio-signature of a subject, wherein such a result is derived using the methods described herein.

[00202] The entity obtaining a diagnosis, prognosis, or selecting a patient for a treatment with an antagonist of SKAP2 may enter sample information into a database for the purpose of one or more of the following: inventory tracking, assay result tracking, order tracking, customer management, customer service, billing, and sales. Sample information may include, but is not limited to: customer

name, unique customer identification, customer associated medical professional, indicated assay or assays, assay results, adequacy status, indicated adequacy tests, medical history of the individual, preliminary diagnosis, suspected diagnosis, sample history, insurance provider, medical provider, third party testing center or any information suitable for storage in a database. Sample history may include but is not limited to: age of the sample, type of sample, method of acquisition, method of storage, or method of transport.

[00203] The database may be accessible by a customer, medical professional, insurance provider, or other third party. Database access may take the form of electronic communication such as a computer or telephone. The database may be accessed through an intermediary such as a customer service representative, business representative, consultant, independent testing center, or medical professional. The availability or degree of database access or sample information, such as assay results, may change upon payment of a fee for products and services rendered or to be rendered. The degree of database access or sample information may be restricted to comply with generally accepted or legal requirements for patient or customer confidentiality.

EMBODIMENTS

1. A method of treating or preventing a disease or condition in a subject, the method comprising administering a modulator of Src Kinase Associated Phosphoprotein 2 (SKAP2) activity or expression to the subject, provided the subject has a genotype characterized by the presence of one or more SNPs provided in FIG. 1.
2. A method of reducing activity or expression of Src Kinase Associated Phosphoprotein 2 (SKAP2) in a subject having a genotype characterized by the presence of one or more SNPs provided in FIG. 1, the method comprising administering to the subject a modulator of SKAP2.
3. The method of embodiment 1 or embodiment 2, further comprising determining the genotype of the subject.
4. The method of embodiment 3, provided that determining the genotype of the subject comprises determining the presence or absence of the one or more SNPs provided in FIG. 1.
5. The method of any previous embodiment, wherein the genotype is detected with an assay comprising polymerase chain reaction (PCR), quantitative reverse-transcription PCR (qPCR), automated sequencing, genotype array, or a combination thereof.
6. The method of any previous embodiment, provided that the subject does not comprise the minor allele shown in FIG. 1.
7. The method of any previous embodiment, provided that the disease or condition is inflammatory bowel disease (IBD).
8. The method of embodiment 7, provided that the IBD comprises Crohn's disease and/or ulcerative colitis.

9. The method of any previous embodiment, provided that the subject has CD.
10. The method of embodiment 9, provided that the one or more SNPs comprises a SNP listed in FIG. 1.
11. The method of embodiment 9, wherein the single nucleotide polymorphism is associated with at least one of stricturing and penetrating.
12. The method of embodiment 11, wherein the at least one of structuring and penetrating is isolated to at least one of a colon, an ileum, and an ileocolonic region of an intestine.
13. The method of embodiment 11 or 12, provided that the one or more SNPs comprises a SNP listed in FIG. 1.
14. The method of embodiment 9, wherein the single nucleotide polymorphism is associated with a risk of a subject developing morphological defects in ileal Paneth cells.
15. The method of embodiment 14, provided that the one or more SNPs comprises a SNP listed in FIG. 1.
16. The method of any previous embodiment, provided that the subject has IBD.
17. The method of embodiment 16, provided that the one or more SNPs comprises a SNP listed in FIG. 1.
18. The method of any previous embodiment, provided that the subject has UC.
19. The method of embodiment 18, provided that the one or more SNPs comprises a SNP listed in FIG. 1.
20. The method of any previous embodiments, provided that the one or more SNPs comprises a SNP listed in FIG. 1.

EXAMPLES

[00204] Example 1. SKAP2 SNPs Associated with Crohn's Disease, Inflammatory Bowel Disease, and Ulcerative Colitis

[00205] Subjects were recruited and diagnosed as having or not having inflammatory bowel disease (IBD). Some IBD patients were further characterized as having Crohn's disease (CD) or ulcerative colitis (UC). Diagnosis was based on standard endoscopic, histologic, and/or radiographic features. Select subjects were further characterized based on genetic and/or phenotypic traits, as listed in FIG. 1.

[00206] Blood samples were collected from the subjects at the time of enrollment. Genotyping was performed on the samples using Illumina ImmunoChip (Illumina, San Diego, CA) per manufacturer's protocol. Markers were excluded from analysis based on: Hardy-Weinberg Equilibrium $p \leq 1.0E-5$; genotyping rate $< 95\%$; minor allele frequency $< 1\%$. Related individuals (P_i -hat scores > 0.25) were identified using identity-by-descent and excluded from analysis (PLINK). Admixture was used to generate ethnicity proportion estimations for all individuals. Only subjects identified by admixture as Caucasian (proportion < 0.75) were included in the analysis.

[00207] Multiple large-scale case-control association studies involving IBD, CD and UC in populations using gene-based single nucleotide polymorphism (SNP) markers were performed. The studies included subjects recruited at the Cedars-Sinai Inflammatory Bowel Disease Centers. The studies also included GWAS data derived from the International Inflammatory Bowel Diseases Genetic Consortium (IIBDGC) and cohorts from DeLange et al., “Genome-wide association study implicates immune activation of multiple integrin genes in inflammatory bowel disease,” *Nature Genetics*. Vol. 49, No. 2 (February 2017).

[00208] FIG. 1 provides meta-analysis of SNPs considered predictive of disease (IBD, CD, UC), phenotype, and/or suitability to treatment with a modulator of SKAP2.

[00209] Genotyping data was produced from small bowel tissue samples from patients diagnosed with IBD and healthy patients without IBD. eQTL mapping was performed on these samples. Transcriptomic data was generated on small bowel tissue. Briefly, uninflamed tissue from formalin-fixed paraffin-embedded (FFPE) small bowel resection margins of subjects requiring surgery at Cedars-Sinai Medical Center for Crohn’s disease was identified. Whole-thickness ileal tissue was scraped from the FFPE tissue sections followed by RNA extraction using the RNeasy FFPE kit (Qiagen) according to the manufacturer's instructions. The Transplex Whole Transcriptome Amplification kit (WTA2; Sigma) was used for cDNA synthesis and amplification. Subsequent purification of the cDNA product was performed with the PCR Purification kit (Qiagen). Sample quality was confirmed using the Agilent Bioanalyzer. For samples passing quality control, Cy5 labeling with the ULST Fluorescent Labeling kit (Kreatech) and hybridization (performed in duplicate for each sample) to Whole Human Genome 4x44k Microarrays (Agilent) was performed.

[00210] Single channel microarray expression data extracted using Agilent feature extraction software was received from Genome Technology Access Center at Washington University in St. Louis. Raw expression data available in technical duplicates was normalized using LIMMA package implemented in R version 3.2.2. The expression data preprocessing included background correction of the expression data, followed by log2-transformation and quantile-normalization. Unsupervised hierarchical clustering of expression data was used to remove outlier subjects. eQTL mapping was implemented in Matrix eQTL R package using the available expression and genotype data for independent Caucasian samples from patients undergoing surgery for small bowel disease and UC rectum tissues. Associations between genotype and probe expression level were performed using a linear regression model with additive genotype effects. All associations were adjusted for gender, age and population sub-structure using the first two principal components. Gene bounds were defined using a 1 Mb window around the transcription start position of given gene as obtained from UCSC Genome Browser. For cis-eQTL mapping, a 1Mb cis distance from gene bounds was used. Cis-eQTLs were defined as association signals from SNPs located within 1 Mb from each of the gene bounds. False discovery rates (FDR) were estimated to correct for multiple testing using Matrix eQTL according to the Benjamini and Hochberg method. Note that FDR calculation in matrix eQTL does

not take into account “linkage disequilibrium” between the SNPs and may be overly stringent. A negative beta value indicates a decrease in SKAP2 gene expression. A positive beta value indicates an increase in SKAP2 gene expression.

[00211] FIG. 1 provides meta-analysis of SNPs considered predictive of IBD, CD, UC, phenotype, and/or suitability to treatment with a modulator of SKAP2. These results show strong associations between the SNPs listed in the tables, and the associated diseases (IBD, CD, UC) and phenotypes (*see Figure 1*). The results also show that particular SNPs are associated with decreased or increased expression of various genes involved in the SKAP2 pathway, in patients diagnosed with IBD, CD, or UC having the provided phenotypes.

[00212] Example 2. SKAP2 Sequences

Table 1. SKAP2 Protein Sequences

SEQ ID NO.	NCBI Ref. No	Isoform	Sequence
1	NP_003921.2	1	MPNPSSTSSPYPLPEEIRNLLADVETFVADILKGENLSKKAKEKRE SLIKKIKDVKSIYLQEFQDKGDAEDGEEYDDPFAGPPDTISLASER YDKDDEAPSDGAQFPPIAAQDLFPVLKAGYLEKRRKDHSLGF WQKRWCALSKTVFYFYGGSDKDKQKGEFAIDGYSVRMNNTLR KDGKKDCCFEISAPDKRIYQFTAASPKDAEEWVQQLKFVLQDME SDIIPEDYDERGELYDDVDHPLPISNPLTSSQPIDDEIYEELPEEEED SAPVKVEEQRKMSQDSVHHTSGDKSTDYANFYQGLWDCTGAFS DELSFKRGDVIYILSKEYNRYGWWVGEMKGAIGLVPKAYIMEM YDI
2	NP_001290397.1	2	MNNTLRKDGKKDCCFEISAPDKRIYQFTAASPKDAEEWVQQLKF VLQDMESDIIPEDYDERGELYDDVDHPLPISNPLTSSQPIDDEIYEE LPEEEEDSAPVKVEEQRKMSQDSVHHTSGDKSTDYANFYQGLW DCTGAFSDELSFKRGDVIYILSKEYNRYGWWVGEMKGAIGLVPK AYIMEMYDI

Table 2. SKAP2 mRNA Sequences

SEQ ID NO.	NCBI Ref. No	Variant	Sequence
3	NM_003930.5	1	GACTTCCTTGTTGTGAGCCCCGGCCCGGCAGTGTCCCGACTCG TAGCCCCGCTGTTCTTAATCCGGGCGCTAGCCTGAGTCTAGG TCGCAGCCGCAGCCCCACCCCGTCGGTCACCTTTTCAGCGCAG GTCCTTTCCCCGCACGCCCTGCGCTCCCTAACATGCCCAACCC CAGCAGCACCTCCTCTCCCTACCCCTCCCTGAGGAAATTAGG AACCTGTTGGCAGATGTTGAAACATTTGTAGCAGATATACTGA AAGGAGAAAATTTATCCAAGAAAGCAAAGGAAAAAGAGAGAA TCCCTTATTAAGAAGATAAAAGATGTAAAGTCTATCTATCTTC AGGAATTTCAAGACAAAGGTGATGCAGAAGATGGGGAAGAA TATGATGACCCTTTTGCTGGGCCTCCAGACACTATTTTCATTAG CCTCAGAACGATATGATAAAGACGATGAAGCCCCCTCTGATG GAGCCCAGTTTCCTCCAATTGCAGCACAAGACCTTCCTTTTGT TCTAAAGGCTGGCTACCTTGAAAAACGCAGAAAAGATCACAG CTTTCTGGGATTTGAATGGCAGAAACGGTGGTGTGCTCTCAGT AAAACGGTATTCTATTATTATGGAAGTGATAAAGACAAACAA

		CAGAAAGGTGAATTTGCAATAGATGGCTACAGTGTGAGAATG AATAACACTCTAAGAAAGGATGGAAAGAAAGATTGCTGTTTT GAAATCTCTGCTCCTGATAAACGTATATATCAGTTTACAGCAG CTTCTCCCAAAGATGCTGAAGAATGGGTACAGCAGCTGAAAT TTGTATTGCAAGATATGGAATCTGATATTATTCTGAGGATTA TGATGAGAGAGGAGAATTATATGATGATGTTGATCATCCTCTA CCAATAAGCAATCCACTAACAAGCAGTCAACCAATAGATGAT GAAATTTATGAAGAACTTCCAGAAGAAGAAGAGGACAGTGCT CCAGTGAAAGTGGAAGAACAAAGGAAGATGAGTCAGGATAG TGTCCATCACACCTCAGGGGATAAGAGCACTGATTATGCTAAT TTTTACCAGGGATTGTGGGATTGTACTGGAGCTTTTTCTGATG AGTTGTCAATTAAGCGTGGTGATGTGATTTACATTCTTAGCAA GGAATACAATAGATATGGCTGGTGGGTAGGAGAAATGAAGGG AGCCATTGGCTTGGTGCCTAAAGCCTACATAATGGAGATGTAT GATATTTGAGAGTCCTGGAAAAGGAAAATTCTTCTGCTTGTCT GCAAATGCTTTGGATTAGAAAGCGTCATGAAAGCACGAGTGA CAGCTCCTAACCTCTCCTTGTATTTATTAAACATTACTTATCTTT GACTGTTATTTTATGCAGTCGCTCATTAATAATTTCTCTGATG TGAAATTAAATGAAGGATATTAATGTAAATTAGATGCAACCA GTTAAGTTATACCTGTTGCTATTTTGCAAAGAAATAATTATAG TTTTTATTTACCCATTTGATTTGTGTGAAGAATTCATCACTATT TTATACGTAACATATAGTCTACTATAGCATAGTATGCTACTAT TGCTACTTCTGGTGTGATTTGTAATGTTTCTTAATCATTGGACA TCAATTATTTTTAGAGAGTAATGTATAATTTCATAGCATTTTA AATTTAGTGTATCATGCGAGTTTTTTTTTGGTAGATGCTGAAGA ATGTGGTTGCTAAACAAAGAATGCTAAAGAATGTTCAAACCTTT ATAGATAACTTTATTGTTATTATTTATTTTCACACATTTAATTC CTATTAAGTACAGCCGCAAGAAAGAAAAAATGATGAAGTTGC AAATGGCAGTGTGCTGTCACTGCAACAGAAGTGCGTACCAG AAGTATGACTCATGCAAAGCATTTTACCGTACAAATATCCTGG TGCGATGATGGGCCTGGCAACATTTTCTACTGTACTTTTGTTTA AATTTAATGAAACAAAAAATTCCTAAGAAATACCACCTACC ACTAACAAAATGGTATAAAGAATCTCCCAGCCAGGCCAACAT GGTGAAACCCTGTCTCTACTAAAAATTAGCCAAGTGTGGTAAT GTTACCTGCAGTCCCAGCTACTTGGGAGGCCAAGGCACGAG AATTGCTTGAACAAGGTAGGCAGAGGTTGCAGTGAGCCAAGA TCGCGCCACTGCACTCCAGCCTGGGCGACAGAGTGAGACTCC ATCTCAGAAAAAAAAAAAAAAAAAAAAACAGAATCTCAGTGTAT TCTCAAAGTAAAAAGGCATAACCAAGCACTCTCTTATCTTGCC TTATTGCTATACTATTTACATCCCACTGCAGAACAGCAGATTT GAGGCTTTTCTATATACTTCTCAGAGCACTGAAAAGAAAGGA AGGGTTTGCAGAGGAGAGTGTAGAAATCCCAGTGGTAGCATG TACCAACAGGTGAGTAGAAAGGTAGTGTTAGCCTGACATTTG AGTTATACTCTGTGCTGCCTGAGCAAGATTTGTAGAATCATAT AATTACCTTTTCATGTATATTTGAAATCAGAGGTGTTTAAAT ACCTATGAGATACCAATGTAGCCTTAACATATGTCAAAATGCA TTGCTGGTTAGATAATTATTTGGACTACACATAAACTCCTAAT ATTGAATCATTACCTATCAGGTATTATCTTTATGGAACCTTTCA ATATCTTTGCTTTATAAAGATTCTAAACATGTATCTGAGCTGG TAATATTTTAAATCTCCATTATTTGTGTAAAACTGTTTATAAG CAGTGTTTGAGAGGGTCTGCTTTACCATTACCCCCTCAATATC ATGATCATCCAATCTCAAATGTGAAAAAAAAAAAAAGAAATTTG ATTTTAGGGATTGTGAGTAAACAAGTTTATATAGAGAGACATT GTGAAGTTAAAGTTTTTCAGAAGTTACATTTGTGCAGTTCCTTAC CTTTTCCTCATATAGTGCCATTGAAATAGACTGAAATTATCTT
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			GGCAAAAGTTAGACAACCAAAAGACGACTTTAGTGGACTGGTT TTCAAAACTTGAGCAGCTGAAAAGCAAAAGCCGTTGTTTCCC ATGACAATGTAGCCTTTGTGGATTTGGGTTTGTGCTTTGGGTT GAAAAGAAGTTTTTAGTCCTAGGCCAGTAGATGGCAGCAGCT TTTCATTGCAGACAAAACCTCTTGAAACCCTTCCCCCATGGCA CAAACCTCGCCCATGATGGAAAGCATCTAGATTTCTGCCTCCTT TTACAGTTAATCCAGGAGAGGGAGTCCTTTGCCAACTGATGAC CAACAGTTCCAAGCCAGATAGTCTCGTGAACAGTGACAATAC AGAAATAAGGTGTTATTTCTGTTTCAGATCTCCACCGGCCTTTG TTCTTTTAAAACTTGAATATAGGTGGGAGACATAAGAAAGGA AAGAAAAGACTTAAAACTGGAGTGACAGGACAAATAATCATT ACTTTCAATTCATGACTGCTTTATATTCAATTTGATGAAATCATT TGTATACAAACCAGGGAGAGTTTTCTTTACACCCTTGACAATA TATCACATACTCTTCAAGATCATAATAATATCATTAAATATAAA TTTAAACAACATGGCTTGTTAGAAAATATGCTAATTGCTATGG TCTCATTATGTTTGCTTAGCTTTTATTTGTTTTTCTGTGAACAG TTAGAGAGCTAATTTTTTTCAAAGGTGATTGTAAGTCATATTT TATATAGCATTTTGCTTGATTATTTGCTCTGTACTGAATTTGTA CTCTATTGCCATTAGATCTTACAATAATGTTCCACTCTGCAAA TTTTTAAGGTTCAAATAAAGTTTAATTGTTTGCAAA
4	NM_0 013034 68.1	2	ATTTGTCTAGTGAGGGCTCTGCCCCAGACCCGGCTCTCCATGC TCACTGCTCCGCTGAGAGGAACCCTGGGGTTTAACGCTGAA GTGCGTTTCTCAGAGGGCAGAGCTGGAGCATCTCGCAGCCCT ACAACCTTCTTGCGGCGCTTGGTCTGTCTTTGCGTTGCGAGAT CAGGATCGGTGTGTTGCTCAGACACCGGCCGAACGCCACCGG CACGTCTAGGAGTCTCCTGTGCCTGGAAGAGGCTGGTTTCATT CGATTCTAAAAGAAACGGATGTTGAAACATTTGTAGCAGATA TACTGAAAGGAGAAAATTTATCCAAGAAAGCAAAGGAAAAG AGAGAATCCCTTATTAAGAAGATAAAAAGATGTAAAGTCTATC TATCTTCAGGAATTTCAAGACAAAGGTGATGCAGAAGATGGG GAAGAATATGATGACCCTTTTGCTGGGCCTCCAGACACTATTT CATTAGCCTCAGAACGATATGATAAAGACGATGAAGCCCCCT CTGATGGAGCCCAGTTTCTCCAATTGCAGCACAAGACCTTCC TTTTGTTCTAAAGGCTGGCTACCTTGAAAAACGCAGAAAAGAT CACAGCTTTCTGGGATTTGAATGGCAGAAACGGTGGTGTGCTC TCAGTAAAACGGTATTCTATTATTATGGAAGTGATAAAGACA AACAACAGAAAGGTGAATTTGCAATAGATGGCTACAGTGTCA GAATGAATAACACTCTAAGAAAGGATGGAAAGAAAGATTGCT GTTTTGAAATCTCTGCTCCTGATAAACGTATATATCAGTTTAC AGCAGCTTCTCCCAAAGATGCTGAAGAATGGGTACAGCAGCT GAAATTTGTATTGCAAGATATGGAATCTGATATTATTCCTGAG GATTATGATGAGAGAGGAGAATTATATGATGATGTTGATCAT CCTCTACCAATAAGCAATCCACTAACAAGCAGTCAACCAATA GATGATGAAATTTATGAAGAACTTCCAGAAGAAGAAGAGGAC AGTGCTCCAGTGAAAGTGGAAGAACAAAGGAAGATGAGTCA GGATAGTGTCCATCACACCTCAGGGGATAAGAGCACTGATTA TGCTAATTTTACCAGGGATTGTGGGATTGTACTGGAGCTTTT TCTGATGAGTTGTCATTTAAGCGTGGTGTGATTACATTC TTAGCAAGGAATACAATAGATATGGCTGGTGGGTAGGAGAAA TGAAGGGAGCCATTGGCTTGGTGCCTAAAGCCTACATAATGG AGATGTATGATATTTGAGAGTCCTGGAAAAGGAAAATTCTTCT GCTTGTCTGCAATGCTTTGGATTTAGAAGCGTCATGAAAGCA CGAGTGACAGCTCCTAACCTCTCCTTGTTTTATTAAACATTACT TATCTTTGACTGTTATTTTATGCAGTCGCTCATTAATAATATTC TCTGATGTGAAATTAATGAAGGATATTAATGTAAATTAGATG

		CAACCAGTTAAGTTATACCTGTTGCTATTTTGCAAAGAAATAA TTATAGTTTTTATTTACCCATTTGATTTGTGTGAAGAATTCATC ACTATTTTATACGTAACATATAGTCTACTATAGCATAGTATGC TACTATTGCTACTTCTGGTGTGATTTGTAATGTTTCTTAATCAT TGGACATCAATTATTTTATAGAGAGTAATGTATAATTTTCATAGC ATTTTAAATTTAGTGTATCATGCGAGTTTTTTTTTGGTAGATGCT GAAGAATGTGGTTGCTAAACAAAGAATGCTAAAGAATGTTCA AACTTTATAGATAACTTTATTGTTATTATTTATTTTCACACATT TAATTCCTATTAAGTACAGCCGCAAGAAAGAAAAAATGATGA AGTTGCAAATGGCAGTGTGCTGTCACCTGCAACAGAAGTGCG TACCAGAAGTATGACTCATGCAAAGCATTTTACCGTACAAATA TCCTGGTGCGATGATGGGCCTGGCAACATTTTCTACTGTACTT TTGTTTAAATTTAATGAAACAAAAAATTCCTAAGAAATACCAC CCTACCACTAACAAAAATGGTATAAAGAATCTCCAGCCAGGC CAACATGGTGAAACCCTGTCTCTACTAAAAATTAGCCAAGTGT GGTAATGTTACCTGCAGTCCCAGCTACTTGGGAGGCCAAGG CACGAGAATTGCTTGAACAAGGTAGGCAGAGGTTGCAGTGAG CCAAGATCGCGCCACTGCACTCCAGCCTGGGCGACAGAGTGA GACTCCATCTCAGAAAAAAGGCAATAACCAAGCACTCTCTTAT GTGTATTCTCAAAGTAAAAAGGCATAACCAAGCACTCTCTTAT CTTGCCTTATTGCTATACTATTTACATCCCACTGCAGAACAGC AGATTTGAGGCTTTTCTATATACTTCTCAGAGCACTGAAAAGA AAGGAAGGGTTTGCAGAGGAGAGTGTAGAAATCCCAGTGGTA GCATGTACCAACAGGTGAGTAGAAAGGTAGTGTAGCCTGAC ATTTGAGTTATACTCTGTGCTGCCTGAGCAAGATTTGTAGAAT CATATAATTACCTTTTCATGTATATTTGAAATCAGAGGTGTTT AAAAATACCTATGAGATACCAATGTAGCCTTAACATATGTCAA AATGCATTGCTGGTTAGATAATTATTTGGACTACACATAAACT CCTAATATTGAATCATTACCTATCAGGTATTATCTTTATGGAA CTTTTCAATATCTTTGCTTTATAAAGATTCTAAACATGTATCTG AGCTGGTAATATTTTAAAATCTCCATTATTTGTGTAAAAGTGT TTATAAGCAGTGTGAGAGGGTCTGCTTTACCATTACCCCT CAATATCATGATCATCCAATCTCAAATGTGAAAAAAGAAAG AAATTTGATTTTAGGGATTGTGAGTAAACAAGTTTATATAGAG AGACATTGTGAAGTTAAAGTTTTTCAGAAGTTACATTTGTGCAG TTCTTACCTTTTCCTCATATAGTGCCATTGAAATAGACTGAAA TTATCTTGGCAAAAGTTAGACAACCAAAGACGACTTTAGTGG ACTGGTTTTCAAACTTGAGCAGCTGAAAAGCAAAAGCCGTT GTTTCCCATGACAATGTAGCCTTTGTGGATTGGGTTTGTGCTT TGGGTTGAAAAGAAGTTTTTAGTCCTAGGCCAGTAGATGGCA GCAGCTTTTCATTGCAGACAAAACCTCTTGAAACCCCTTCCCC ATGGCACAACTCGCCCATGATGGAAAGCATCTAGATTTCTGC CTCCTTTTACAGTTAATCCAGGAGAGGGAGTCCTTTGCCAACT GATGACCAACAGTTCCAAGCCAGATAGTCTCGTGAACAGTGA CAATACAGAAATAAGGTGTTATTTCTGTTTCAATCTCCACCGG CCTTTGTTCTTTTAAAACCTGAATATAGGTGGGAGACATAAGA AAGGAAAGAAAAGACTTAAAACCTGGAGTGACAGGACAAATA ATCATTACTTTCAATTCATGACTGCTTTATATTCATTTGATGAA ATCATTTGTATACAAACCAGGGAGAGTTTTCTTTACACCCTTG ACAATATATCATACTCTTCAAGATCATAATAATATCATTA TATAAATTTAAACAACATGGCTTGTTAGAAAAATATGCTAATTG CTATGGTCTCATTATGTTTGCTTAGCTTTTATTTGTTTTTCTGTG AACAGTTAGAGAGCTAATTTTTTTTCAAAGGTGATTGTAAGTCA TATTTTATATAGCATTTTGCTTGATTATTTGCTCTGTACTGAAT TTGTACTCTATTGCCATTAGATCTTACAATAATGTTCCACTCTG
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			CAAATTTTAAAGGTTCAAATAAAGTTTAATTGTTTGCAAACGTG TTAAAAAAAAAAAAAAAAAAAAA
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[00213] Example 3.

Table 3. Description of Abbreviations Used in Disclosed Tables

Term	Description
dbSNP	dbSNP 147 rsID for SNP associated with phenotype
A1	Minor allele for SNP
n_miss	Number of subjects in cohort
OR_Z_B	Odds ratio for logistic regression(OR) or Z (Hazard ratio for coxph regression) or Beta for linear regression or meta-analysis (B) If OR<1 ;(Z<1); (B <0) the minor allele correlates to a reduced risk of a patient exhibiting the listed phenotype If OR>1; (Z>1); (B >0), the minor allele correlates to an increased risk of a patient exhibiting the listed phenotype
p_value	Statistical significance of association between phenotype and SNP presence
base_pair	Base pair; Genomic location in hg19 coordinates
Chr	Chromosome
snp location	Location of SNP on gene
cis_eGene	Local gene on same chromosome as the SNP that is differentially regulated in patients having the related SNP
eql_beta	Negative value indicates decreased expression of cis gene in subjects having the related SNP; positive value indicates increased expression of cis gene in subjects having the related SNP
eql_p	Statistical significance of association between cisgene and SNP presence
priority	Defined as eQTL where the SNP is part of the cis-eGene that it regulates

Table 4. Description of phenotype abbreviations

Phenotype/Disease location	Description
L1	Disease location – ileal
L2	Disease location – colonic
L2_colonic	Disease location – colonic
L3	Disease location – ileocolonic
B1	Non-stricturing/non-penetrating
B2a	Stricturing
B2b	Stricturing and penetrating
B2a + B2b	
B3	Isolated internal penetrating
E_Nodosum	Erythema nodosum
Paneth-D0	% normal Paneth cells
Paneth-D1	% abnormal Paneth cells
Paneth-D1234	% abnormal Paneth cells
Paneth-D3	% abnormal Paneth cells
Paneth-D4	% abnormal Paneth cells
Paneth-D5	% abnormal Paneth cells

anti-TNF time to loss of response	Subjects non-responsive to anti-TNF in months. The loss of response was characterized by a reappearance of symptoms consistent with a flare after initial anti-TNF response, and the time from induction of therapy to loss of response was recorded (see attached reference).
ANCA	Antineutrophil cytoplasmic antibody
Arthralgias	Arthralgias
ASCA	<i>Saccharomyces cerevisiae</i> Antibodies
IGA ASCA	<i>Saccharomyces cerevisiae</i> Antibodies IGA
IGG ASCA	<i>Saccharomyces cerevisiae</i> Antibodies IGG
OMPC	Anti-outer-membrane porin C antibody
Cbir	Antibody against flagellin
i2	Antibody against <i>Pseudomonas fluorescens</i>
PDM	Perianal disease modifier
Oral ulcers	Oral ulcers
PSC	Primary sclerosing cholangitis
Psoriasis	Psoriasis

[00214] While preferred embodiments of the present examples have been shown and described herein, it will be obvious to those skilled in the art that such embodiments are provided by way of example only. Numerous variations, changes, and substitutions will now occur to those skilled in the art without departing from the disclosure. It should be understood that various alternatives to the embodiments of the disclosure described herein may be employed in practicing the disclosure. It is intended that the following claims define the scope of the disclosure and that methods and structures within the scope of these claims and their equivalents be covered thereby.

CLAIMS

What is claimed is

1. A method of treating inflammatory bowel disease (IBD) in a subject, the method comprising administering a modulator of Src Kinase Associated Phosphoprotein 2 (SKAP2) activity or expression to the subject, provided a genotype characterized by the presence of one or more SNPs provided in FIG. 1 is detected in the subject.
2. The method of claim 1, further comprising determining the genotype of the subject using an assay.
3. The method of claim 2, wherein the assay comprises quantitative reverse-transcription PCR (qPCR), automated sequencing, genotype array, or a combination thereof.
4. The method of claim 1, wherein the one or more SNPs provided in FIG. 1 is predictive of at least one of stricturing and penetrating disease.
5. The method of claim 4, wherein the at least one of stricturing and penetrating disease is isolated to at least one of a colon, an ileum, and an ileocolonic region of an intestine.
6. The method of claim 4, wherein the at least one of stricturing and penetrating disease is isolated to the ileocolonic region of the intestine.
7. A method of reducing activity or expression of Src Kinase Associated Phosphoprotein 2 (SKAP2) in a subject having a genotype characterized by the presence of one or more SNPs provided in FIG. 1, the method comprising administering to the subject a modulator of SKAP2.
8. The method of claim 7, further comprising determining the genotype of the subject using an assay.
9. The method of claim 8, wherein the assay comprises quantitative reverse-transcription PCR (qPCR), automated sequencing, genotype array, or a combination thereof.
10. The method of claim 7, wherein the one or more SNPs provided in FIG. 1 is predictive of at least one of stricturing and penetrating disease.
11. The method of claim 10, wherein the at least one of stricturing and penetrating disease is isolated to at least one of a colon, an ileum, and an ileocolonic region of an intestine.
12. The method of claim 11, wherein the at least one of stricturing and penetrating disease is isolated to the ileocolonic region of the intestine.
13. A method of predicting whether a subject will develop an inflammatory bowel disease, the method comprising:
 - a) obtaining a sample from a subject;
 - b) subjecting the sample to an assay configured to detect a presence, absence, or level, of one or more single nucleotide polymorphisms (SNPs) of Src Kinase Associated Phosphoprotein 2 (SKAP2) provided in FIG. 1;

- c) predicting that the subject will develop IBD, provided the presence, absence, or level of the one or more SNPs of SKAP2 is detected in the sample obtained from the subject.
- 14. The method of claim 13, provided that a presence of the one or more SNPs of SKAP2 is detected in the sample obtained from the subject.
- 15. The method of claim 13, further comprising administering a therapeutically effective amount of an antagonist of SKAP2 to the subject, provided the subject is predicted to develop the IBD.
- 16. The method of claim 13, wherein the IBD is Crohn's disease.
- 17. A method of characterizing an inflammatory bowel disease in a subject, the method comprising:
 - a) obtaining a sample from a subject;
 - b) subjecting the sample to an assay configured to detect a presence, absence, or level, of one or more SNPs of SKAP2 provided in FIG. 1;
 - c) characterizing the IBD as being associated with at least one of non-stricturing and non-penetrating, stricturing, and penetrating, provided the presence of the one or more SNPs of SKAP2 is detected in the sample obtained from the subject.
- 18. The method of claim 17, provided that a presence of the one or more SNPs of SKAP2 is detected in the sample obtained from the subject.
- 19. The method of claim 17, further comprising administering a therapeutically effective amount of an antagonist of SKAP2 to the subject.
- 20. The method of claim 17, wherein the IBD is Crohn's disease.

FIG. 1

PHENOTYPE	dbSNP	p_value	A1	n_miss	OR_Z_B	base_ pair_CH 7	snp_ location	cis_ eGENE	eqtl_beta	eqtl_p	priority	MAF
CD vs. Ctrl	rs73069541	5.75E-14	G	94095	0.089594991	26904928	intronic	HIBADH, HOXA11-AS	- 0.1186890 17417339, 0.04990810 0.0941114 404455934	0.04652407 2405745, 0.04990810 58041685	0, 0	0.244
CD vs. Ctrl	rs10486483	8.54E-14	A	89783	0.088948057	26892440	intronic	NA	NA	NA	NA	0.2596
CD vs. Ctrl	rs3801810	9.76E-14	A	86890	0.090776716	26892531	intronic	NA	NA	NA	NA	0.2576
CD vs. Ctrl	rs73069540	1.31E-13	A	94100	0.088305501	26904770	intronic	HIBADH, HOXA11-AS	- 0.1186890 17417339, 0.04990810 0.0941114 404455934	0.04652407 2405745, 0.04990810 58041685	0, 0	0.2438
CD vs. Ctrl	rs3801844	1.37E-13	G	94067	0.086962835	26829759	intronic	NA	NA	NA	NA	0.2502
CD vs. Ctrl	rs17323934	1.51E-13	G	94084	0.088080968	26904330	UTR5	HIBADH, HOXA11-AS	- 0.1186890 17417339, 0.04990810 0.0941114 404455934	0.04652407 2405745, 0.04990810 58041685	0, 0	0.2438
CD vs. Ctrl	rs10276471	1.51E-13	G	94076	0.086758459	26837940	intronic	NA	NA	NA	NA	0.2501
CD vs. Ctrl	rs3801820	1.70E-13	G	94094	0.086579542	26861353	intronic	NA	NA	NA	NA	0.2528
CD vs. Ctrl	rs10272303	1.72E-13	G	94080	0.086616253	26827815	intronic	NA	NA	NA	NA	0.2502
CD vs. Ctrl	rs3801842	1.79E-13	A	94021	0.086550335	26830263	intronic	NA	NA	NA	NA	0.2502
CD vs. Ctrl	rs3801831	1.85E-13	G	94081	0.086412272	26853470	intronic	NA	NA	NA	NA	0.2529
CD vs. Ctrl	rs73065517	1.91E-13	G	94090	0.086421813	26830555	intronic	NA	NA	NA	NA	0.2501

FIG. 1 (Continued)

PHENOTYPE	dbSNP	p_value	A1	n_miss	OR_Z_B	base_ pair_CH 7	snp_ location	cis_ eGENE	eqtl_beta	eqtl_p	priority	MAF
CD vs. Ctrl	rs12333525	1.97E-13	A	94075	0.08634067	26847762	intronic	NA	NA	NA	NA	0.2529
CD vs. Ctrl	rs3801850	1.99E-13	G	94041	0.086114535	26820577	intronic	NA	NA	NA	NA	0.2509
CD vs. Ctrl	rs17315775	2.06E-13	G	88845	0.088347322	26860134	intronic	NA	NA	NA	NA	0.254
CD vs. Ctrl	rs10486478	2.08E-13	A	94078	0.086853482	26819465	intronic	NA	NA	NA	NA	0.2502
CD vs. Ctrl	rs2106905	2.11E-13	A	94097	0.084919006	26766851	intronic	NA	NA	NA	NA	0.264
CD vs. Ctrl	rs10267950	2.16E-13	A	93830	0.086435139	26826757	intronic	NA	NA	NA	NA	0.2493
CD vs. Ctrl	rs3213853	2.31E-13	G	94060	0.086063688	26893524	intronic	NA	NA	NA	NA	0.2533
CD vs. Ctrl	rs4722644	2.34E-13	A	94099	0.086045184	26845386	intronic	NA	NA	NA	NA	0.2529
CD vs. Ctrl	rs73067443	2.34E-13	G	94099	0.086045184	26851074	intronic	NA	NA	NA	NA	0.2529
CD vs. Ctrl	rs17376018	2.34E-13	G	94081	0.086071094	26889862	intronic	NA	NA	NA	NA	0.2532
Paneth-D5 phenotype	rs188468488	2.35E-13	G	155	1.924	27109617	intergenic	NA	NA	NA	NA	0.01245
CD vs. Ctrl	rs3801840	2.49E-13	G	94093	0.085931715	26832986	intronic	NA	NA	NA	NA	0.2525
CD vs. Ctrl	rs212857	2.54E-13	C	91392	0.086620233	26730200	intronic	NA	NA	NA	NA	0.2619
CD vs. Ctrl	rs6951065	2.56E-13	G	94087	0.084618214	26756162	intronic	NPVF	0.1119454 61	0.00957578 4	0	0.2634
CD vs. Ctrl	rs1327989	2.61E-13	A	94091	0.085956678	26833563	intronic	NA	NA	NA	NA	0.2501
CD vs. Ctrl	rs73065504	2.61E-13	G	94090	0.086176992	26825984	intronic	NA	NA	NA	NA	0.2497
CD vs. Ctrl	rs3801807	2.62E-13	G	93984	0.086121671	26897439	intronic	NA	NA	NA	NA	0.2528
CD vs. Ctrl	rs12536145	2.62E-13	T	94051	0.086063235	26894860	intronic	NA	NA	NA	NA	0.253
CD vs. Ctrl	rs3801805	2.62E-13	G	94096	0.086031172	26897640	intronic	NA	NA	NA	NA	0.2535
CD vs. Ctrl	rs73067456	2.63E-13	A	94067	0.085887972	26852998	intronic	NA	NA	NA	NA	0.2528
CD vs. Ctrl	rs4722630	2.64E-13	C	94085	0.084565081	26773364	intronic	NA	NA	NA	NA	0.264
CD vs. Ctrl	rs10281261	2.64E-13	A	94088	0.084565081	26789472	intronic	NA	NA	NA	NA	0.2639
CD vs. Ctrl	rs3801812	2.70E-13	A	94068	0.085846772	26887615	intronic	NA	NA	NA	NA	0.2531
CD vs. Ctrl	rs3801826	2.71E-13	A	94072	0.085842784	26856720	intronic	NA	NA	NA	NA	0.2526

FIG. 1 (Continued)

PHENOTYPE	dbSNP	p_value	A1	n_miss	OR_Z_B	base_ pair_CH 7	snp_ location	cis_ eGENE	eqtl_beta	eqtl_p	priority	MAF
CD vs. Ctrl	rs73069533	2.93E-13	A	94075	0.085967694	26892325	intronic	NA	NA	NA	NA	0.2525
CD vs. Ctrl	rs2031811	3.08E-13	G	94026	0.08564077	26890672	intronic	NA	NA	NA	NA	0.2531
CD vs. Ctrl	rs73067475	3.17E-13	A	94094	0.085569905	26857120	intronic	NA	NA	NA	NA	0.2528
CD vs. Ctrl	rs3801843	3.21E-13	G	94069	0.08565601	26830201	intronic	NA	NA	NA	NA	0.2502
CD vs. Ctrl	rs4719877	3.36E-13	A	94098	0.084137091	26736220	intronic	NPVF	0.1119454 61	0.00957578 4	0	0.2643
CD vs. Ctrl	rs3801823	3.42E-13	G	94087	0.085475968	26861031	intronic	NA	NA	NA	NA	0.2528
CD vs. Ctrl	rs7804620	3.46E-13	C	94092	0.08583601	26891831	intronic	NA	NA	NA	NA	0.2531
CD vs. Ctrl	rs6972378	3.47E-13	G	94094	0.084146287	26753074	intronic	NPVF	0.1119454 61	0.00957578 4	0	0.2635
CD vs. Ctrl	rs7457076	3.48E-13	G	94079	0.084134174	26793215	intronic	NA	NA	NA	NA	0.2639
CD vs. Ctrl	rs6461963	3.48E-13	G	94084	0.084134375	26772491	intronic	NA	NA	NA	NA	0.2641
CD vs. Ctrl	rs212848	3.53E-13	C	94100	0.084246717	26722155	intronic	NPVF	0.1119454 61	0.00957578 4	0	0.2643
CD vs. Ctrl	rs3823930	3.54E-13	G	93963	0.085476455	26856525	intronic	NA	NA	NA	NA	0.2528
CD vs. Ctrl	rs212856	3.54E-13	A	94098	0.084054623	26729205	intronic	NPVF	0.1119454 61	0.00957578 4	0	0.2643
CD vs. Ctrl	rs13438513	3.60E-13	C	94090	0.085364036	26860633	intronic	NA	NA	NA	NA	0.2528
CD vs. Ctrl	rs17375272	3.78E-13	A	94078	0.085374722	26866497	intronic	NA	NA	NA	NA	0.2524
CD vs. Ctrl	rs2189017	3.86E-13	A	94090	0.083974868	26795073	intronic	NA	NA	NA	NA	0.2639
CD vs. Ctrl	rs10272603	3.94E-13	G	94092	0.085251324	26888277	intronic	NA	NA	NA	NA	0.2532
CD vs. Ctrl	rs3801837	3.96E-13	G	94055	0.08543286	26851361	intronic	NA	NA	NA	NA	0.2529
CD vs. Ctrl	rs73069510	4.05E-13	G	94096	0.085391444	26877567	intronic	NA	NA	NA	NA	0.2529
CD vs. Ctrl	rs10236221	4.53E-13	T	94086	0.085060532	26884671	intronic	NA	NA	NA	NA	0.2526
CD vs. Ctrl	rs58760954	4.66E-13	A	93093	0.085850096	26850776	intronic	NA	NA	NA	NA	0.2496
CD vs. Ctrl	rs73067476	4.72E-13	G	94020	0.084962818	26857240	intronic	NA	NA	NA	NA	0.2528
CD vs. Ctrl	rs7804356	4.90E-13	G	94045	0.085118871	26891665	intronic	NA	NA	NA	NA	0.2533

FIG. 1 (Continued)

PHENOTYPE	dbSNP	p_value	A1	n_miss	OR_Z_B	base_ pair_CH 7	snp_ location	cis_ eGENE	eqtl_beta	eqtl_p	priority	MAF
CD vs. Ctrl	rs3823936	4.93E-13	G	94098	0.08505475	26853830	intronic	NA	NA	NA	NA	0.2528
CD vs. Ctrl	rs10272190	5.05E-13	A	94021	0.084857987	26887942	intronic	NA	NA	NA	NA	0.2532
CD vs. Ctrl	rs12532796	5.26E-13	G	94066	0.085010952	26854828	intronic	NA	NA	NA	NA	0.2524
CD vs. Ctrl	rs3801846	5.28E-13	A	88673	0.086388572	26828653	intronic	NA	NA	NA	NA	0.2625
CD vs. Ctrl	rs3823929	5.49E-13	G	93984	0.084749382	26856600	intronic	NA	NA	NA	NA	0.253
CD vs. Ctrl	rs73061894	5.73E-13	G	94085	0.083547118	26802085	intronic	NA	NA	NA	NA	0.264
CD vs. Ctrl	rs3823934	5.95E-13	G	94073	0.08481407	26853934	intronic	NA	NA	NA	NA	0.2524
CD vs. Ctrl	rs3801833	6.00E-13	A	94025	0.084797168	26852212	intronic	NA	NA	NA	NA	0.2528
CD vs. Ctrl	rs6971397	6.06E-13	G	94064	0.083296318	26782564	intronic	NA	NA	NA	NA	0.2634
CD vs. Ctrl	rs7785711	7.02E-13	A	92933	0.085829668	26861640	intronic	NA	NA	NA	NA	0.2497
CD vs. Ctrl	rs3823931	7.04E-13	G	94081	0.084510652	26854026	intronic	NA	NA	NA	NA	0.2528
CD vs. Ctrl	rs12535784	7.37E-13	A	94009	0.084306989	26882067	intronic	NA	NA	NA	NA	0.2525
CD vs. Ctrl	rs73069507	7.39E-13	G	94098	0.084430835	26877536	intronic	NA	NA	NA	NA	0.2529
CD vs. Ctrl	rs3823938	7.50E-13	G	94044	0.084391867	26853741	intronic	NA	NA	NA	NA	0.2534
CD vs. Ctrl	rs3801815	7.78E-13	G	94097	0.084161266	26881292	intronic	NA	NA	NA	NA	0.253
CD vs. Ctrl	rs10262414	7.88E-13	A	94079	0.084329306	26854266	intronic	NA	NA	NA	NA	0.2528
CD vs. Ctrl	rs3801829	8.01E-13	C	94094	0.084274745	26854996	intronic	NA	NA	NA	NA	0.2529
CD vs. Ctrl	rs28404962	8.51E-13	G	94085	0.084178633	26860324	intronic	NA	NA	NA	NA	0.2529
CD vs. Ctrl	rs3801822	1.08E-12	G	89629	0.085288492	26861201	intronic	NA	NA	NA	NA	0.2586
CD vs. Ctrl	rs3801836	1.12E-12	A	85914	0.087223002	26851400	intronic	NA	NA	NA	NA	0.2589
CD vs. Ctrl	rs3801813	1.12E-12	G	94066	0.083629081	26887069	intronic	NA	NA	NA	NA	0.2527
CD vs. Ctrl	rs10242572	1.14E-12	G	94086	0.083917452	26895065	intronic	NA	NA	NA	NA	0.2531
CD vs. Ctrl	rs6948584	1.23E-12	A	94075	0.083610046	26855732	intronic	NA	NA	NA	NA	0.2528
CD vs. Ctrl	rs3801821	1.36E-12	A	94082	0.0834463	26861206	intronic	NA	NA	NA	NA	0.2528
CD vs. Ctrl	rs17315334	1.41E-12	A	90456	0.085373428	26852860	intronic	NA	NA	NA	NA	0.2529

FIG. 1 (Continued)

PHENOTYPE	dbSNP	p_value	A1	n_miss	OR_Z_B	base_ pair_CH 7	snp_ location	cis_ eGENE	eqtl_beta	eqtl_p	priority	MAF
CD vs. Ctrl	rs3801816	1.45E-12	A	90440	0.085348285	26881177	intronic	NA	NA	NA	NA	0.2529
CD vs. Ctrl	rs10266759	1.60E-12	A	94094	0.083362136	26855282	intronic	NA	NA	NA	NA	0.2527
CD vs. Ctrl	rs28550029	2.03E-12	A	90472	0.085486066	26872581	intronic	NA	NA	NA	NA	0.2504
CD vs. Ctrl	rs2189019	2.07E-12	G	93991	0.081631443	26798581	intronic	NA	NA	NA	NA	0.2635
CD vs. Ctrl	rs10225904	2.12E-12	A	94062	0.083799732	26869888	intronic	NA	NA	NA	NA	0.2524
CD vs. Ctrl	rs212850	2.31E-12	A	92730	0.082091154	26724279	intronic	NPVF	0.1119454 61	0.00957578 4	0	0.2642
CD vs. Ctrl	rs212838	2.56E-12	A	94094	0.081751658	26698194	intergenic	NPVF	0.1082079 45	0.01310842 7	0	0.2572
CD vs. Ctrl	rs10225700	2.57E-12	A	94095	0.082610591	26869880	intronic	NA	NA	NA	NA	0.2524
CD vs. Ctrl	rs7785689	2.78E-12	A	93794	0.082685473	26861609	intronic	NA	NA	NA	NA	0.2519
CD vs. Ctrl	rs3757654	2.94E-12	A	93989	0.081387354	26711104	intronic	NPVF	0.1095317 04	0.01169563 2	0	0.258
CD vs. Ctrl	rs73069539	3.14E-12	A	94071	0.083075484	26903661	intronic	HIBADH, HOXA11-AS	- 0.1186890 17417339, 0.0941114 404455934	0.04652407 2405745, 0.04990810 58041685	0, 0	0.2472
CD vs. Ctrl	rs10486485	3.30E-12	A	94062	0.082420325	26900356	intronic	HIBADH, HOXA11-AS	- 0.1186890 17417339, 0.0941114 404455934	0.04652407 2405745, 0.04990810 58041685	0, 0	0.2478
CD vs. Ctrl	rs10227529	4.01E-12	A	88112	0.084062798	26886309	intronic	NA	NA	NA	NA	0.2534

FIG. 1 (Continued)

PHENOTYPE	dbSNP	p_value	A1	n_miss	OR_Z_B	base_ pair_CH 7	snp_ location	cis_ eGENE	eqtl_beta	eqtl_p	priority	MAF
CD vs. Ctrl	rs3801803	4.42E-12	G	94054	0.081957967	26901740	intronic	HIBADH, HOXA11-AS	- 0.1186890 17417339, 0.04990810 0.0941114 404455934	0.04652407 2405745, 0.04990810 58041685	0, 0	0.2481
CD vs. Ctrl	rs7272450	4.52E-12	G	93980	0.08051108	26787642	intronic	NA	NA	NA	NA	0.2633
CD vs. Ctrl	rs73067472	7.07E-12	G	88101	0.082977414	26855959	intronic	NA	NA	NA	NA	0.2529
CD vs. Ctrl	rs7805778	7.11E-12	A	94093	0.080114293	26694926	intergenic	NPVF	0.1082079 45	0.01310842 7	0	0.2574
CD vs. Ctrl	rs6964094	1.08E-11	NA	NA	0.083238057	26834380	intronic	NA	NA	NA	NA	#N/A
CD vs. Ctrl	rs3801814	1.11E-11	C	92682	0.080806031	26881302	intronic	NA	NA	NA	NA	0.2524
CD vs. Ctrl	rs55739485	1.29E-11	G	92623	0.080784281	26860741	intronic	NA	NA	NA	NA	0.2528
CD vs. Ctrl	rs3801809	1.63E-11	A	90411	0.081596658	26895456	intronic	NA	NA	NA	NA	0.2529
CD vs. Ctrl	rs12532199	1.65E-11	G	94047	0.079627778	26854375	intronic	NA	NA	NA	NA	0.2527
CD vs. Ctrl	rs3801828	1.72E-11	A	88675	0.08095703	26855284	intronic	NA	NA	NA	NA	0.2635
CD vs. Ctrl	rs2299101	3.68E-11	A	92190	- 0.069258208	26747041	intronic	NA	NA	NA	NA	0.4928
CD vs. Ctrl	rs7795313	3.82E-11	C	94090	- 0.068053758	26775626	intronic	NA	NA	NA	NA	0.4893
CD vs. Ctrl	rs7810109	5.05E-11	G	94099	0.069479818	26776874	intronic	NA	NA	NA	NA	0.3819
CD vs. Ctrl	rs11764558	5.16E-11	A	93995	- 0.067425675	26778732	intronic	NA	NA	NA	NA	0.4929
CD vs. Ctrl	rs7810127	5.51E-11	G	94089	0.069341857	26776999	intronic	NA	NA	NA	NA	0.382
CD vs. Ctrl	rs10256561	5.79E-11	A	94075	0.069871056	26827627	intronic	NA	NA	NA	NA	0.3681
CD vs. Ctrl	rs12700757	6.07E-11	G	94075	- 0.067321851	26770394	intronic	NA	NA	NA	NA	0.4921
CD vs. Ctrl	rs13234336	6.18E-11	G	94094	0.069131638	26777849	intronic	NA	NA	NA	NA	0.3827
CD vs. Ctrl	rs73065521	6.26E-11	A	83552	0.081494151	26831409	intronic	NA	NA	NA	NA	0.2587

FIG. 1 (Continued)

PHENOTYPE	dbSNP	p_value	A1	n_miss	OR_Z_B	base_ pair_CH 7	snp_ location	cis_ eGENE	eqtl_beta	eqtl_p	priority	MAF
CD vs. Ctrl	rs12700754	6.58E-11	G	94090	- 0.067218519	26754389	intronic	NA	NA	NA	NA	0.4937
CD vs. Ctrl	rs1982995	6.64E-11	C	87241	0.079543113	26884135	intronic	NA	NA	NA	NA	0.2633
CD vs. Ctrl	rs13229947	6.90E-11	A	94092	0.070534202	26767430	intronic	NA	NA	NA	NA	0.3419
CD vs. Ctrl	rs12700762	7.27E-11	A	94093	- 0.066876152	26793597	intronic	NA	NA	NA	NA	0.4932
CD vs. Ctrl	rs11772673	7.65E-11	A	94094	0.068825543	26774969	intronic	NA	NA	NA	NA	0.3819
CD vs. Ctrl	rs3801872	8.14E-11	C	94096	- 0.066867689	26744599	intronic	NA	NA	NA	NA	0.493
CD vs. Ctrl	rs3823939	8.19E-11	G	94099	0.069293546	26820850	intronic	NA	NA	NA	NA	0.368
CD vs. Ctrl	rs687254	9.48E-11	A	94093	0.066784927	26819774	intronic	NA	NA	NA	NA	0.4863
CD vs. Ctrl	rs12700756	1.09E-10	A	94096	- 0.066213374	26768482	intronic	NA	NA	NA	NA	0.4949
CD vs. Ctrl	rs212851	1.43E-10	A	94095	- 0.065986168	26725389	intronic	NA	NA	NA	NA	0.4928
CD vs. Ctrl	rs73061889	1.44E-10	C	92095	0.069898262	26799874	intronic	NA	NA	NA	NA	0.3512
CD vs. Ctrl	rs13234201	1.49E-10	G	94079	0.067721017	26777723	intronic	NA	NA	NA	NA	0.3829
CD vs. Ctrl	rs10227898	1.52E-10	G	94082	0.068594198	26764618	intronic	JAZF1	- 0.0216838 55	0.02995406 6	0	0.3525
CD vs. Ctrl	rs4722628	1.52E-10	C	94080	- 0.065919856	26735911	intronic	NA	NA	NA	NA	0.4922
CD vs. Ctrl	rs3801847	2.10E-10	G	93030	0.068483092	26821129	intronic	NA	NA	NA	NA	0.3615
CD vs. Ctrl	rs1548480	2.12E-10	A	94076	- 0.065375281	26787343	intronic	NA	NA	NA	NA	0.4936
CD vs. Ctrl	rs10250223	2.70E-10	A	93100	0.068066517	26821320	intronic	NA	NA	NA	NA	0.3615
CD vs. Ctrl	rs7802771	2.96E-10	A	94053	-0.06486436	26734838	intronic	NA	NA	NA	NA	0.4931
CD vs. Ctrl	rs56374720	2.96E-10	A	94093	0.067514411	26815776	intronic	JAZF1	- 0.0216838 55	0.02995406 6	0	0.352

FIG. 1 (Continued)

PHENOTYPE	dbSNP	p_value	A1	n_miss	OR_Z_B	base_ pair_CH 7	snp_ location	cis_ eGENE	eqtl_beta	eqtl_p	priority	MAF
CD vs. Ctrl	rs7795074	3.09E-10	A	94092	0.067391068	26742154	intronic	JAZF1	- 0.0216838 55	0.02995406 6	0	0.3527
CD vs. Ctrl	rs7782621	3.38E-10	G	94054	0.067293713	26790937	intronic	JAZF1	- 0.0216838 55	0.02995406 6	0	0.3518
CD vs. Ctrl	rs11980739	3.46E-10	G	94091	0.067253623	26818164	intronic	JAZF1	- 0.0216838 55	0.02995406 6	0	0.3521
CD vs. Ctrl	rs212837	3.53E-10	A	91720	0.067614078	26695215	intergenic	NPVF	0.0821950 54	0.03146251	0	0.3868
CD vs. Ctrl	rs7803699	3.94E-10	G	94100	0.067061779	26814173	intronic	JAZF1	- 0.0216838 55	0.02995406 6	0	0.3513
CD vs. Ctrl	rs763616	4.10E-10	T	94071	0.066946558	26784600	intronic	JAZF1	- 0.0216838 55	0.02995406 6	0	0.3521
CD vs. Ctrl	rs1468203	4.27E-10	C	94091	0.066904821	26791287	intronic	JAZF1	- 0.0216838 55	0.02995406 6	0	0.3518
CD vs. Ctrl	rs7802688	4.38E-10	A	94092	0.066885845	26785832	intronic	JAZF1	- 0.0216838 55	0.02995406 6	0	0.3514
CD vs. Ctrl	rs3801857	4.38E-10	A	94072	0.066883435	26811484	intronic	JAZF1	- 0.0216838 55	0.02995406 6	0	0.3519
CD vs. Ctrl	rs4719879	4.45E-10	A	94053	0.064224032	26780199	intronic	NA	NA	NA	NA	0.4709
CD vs. Ctrl	rs1023712	4.51E-10	C	94088	0.06681159	26803163	intronic	JAZF1	- 0.0216838 55	0.02995406 6	0	0.3521
CD vs. Ctrl	rs727449	5.74E-10	G	88231	0.068053917	26787577	intronic	NA	NA	NA	NA	0.3633
CD vs. Ctrl	rs1123158	8.09E-10	G	92199	0.064424384	26816648	intronic	NA	NA	NA	NA	0.47

FIG. 1 (Continued)

PHENOTYPE	dbSNP	p_value	A1	n_miss	OR_Z_B	base_ pair_CH 7	snp_ location	cis_ eGENE	eqtl_beta	eqtl_p	priority	MAF
CD vs. Ctrl	rs17372780	1.17E-09	C	94055	0.065320686	26804018	intronic	JAZF1	- 0.0216838 55	0.02995406 6	0	0.3518
CD vs. Ctrl	rs11773029	1.19E-09	G	94082	0.062733013	26793064	intronic	NA	NA	NA	NA	0.47
CD vs. Ctrl	rs11773050	1.24E-09	G	94067	0.062684822	26793094	intronic	NA	NA	NA	NA	0.47
CD vs. Ctrl	rs12700760	1.30E-09	T	94067	0.062568034	26793448	intronic	NA	NA	NA	NA	0.4703
CD vs. Ctrl	rs4345466	1.35E-09	G	94093	0.062525122	26815636	intronic	NA	NA	NA	NA	0.4699
CD vs. Ctrl	rs3801854	1.49E-09	G	94080	0.062364899	26812754	intronic	NA	NA	NA	NA	0.4692
CD vs. Ctrl	rs12700761	1.50E-09	G	94090	0.062372588	26793515	intronic	NA	NA	NA	NA	0.4706
CD vs. Ctrl	rs58988613	1.54E-09	A	94084	0.06230092	26769702	intronic	NA	NA	NA	NA	0.4706
CD vs. Ctrl	rs12700758	1.56E-09	G	94066	0.062281446	26790969	intronic	NA	NA	NA	NA	0.47
CD vs. Ctrl	rs10951149	1.86E-09	G	94100	0.061994086	26815857	intronic	NA	NA	NA	NA	0.4699
CD vs. Ctrl	rs1548478	1.90E-09	C	94076	0.061799502	26788153	intronic	NA	NA	NA	NA	0.4702
CD vs. Ctrl	rs1123156	1.90E-09	A	90387	0.06641208	26817044	intronic	JAZF1	- 0.0216838 55	0.02995406 6	0	0.352
CD vs. Ctrl	rs2023821	1.90E-09	G	84509	- 0.065201964	26700475	intergenic	NA	NA	NA	NA	0.4938
CD vs. Ctrl	rs4722631	1.96E-09	G	88551	0.063211891	26774325	intronic	NA	NA	NA	NA	0.4817
CD vs. Ctrl	rs3801853	2.04E-09	G	94087	0.061858159	26813025	intronic	NA	NA	NA	NA	0.4692
CD vs. Ctrl	rs989250	2.12E-09	G	91133	0.063456344	26803955	intronic	NA	NA	NA	NA	0.4642
CD vs. Ctrl	rs6461964	2.21E-09	A	94083	0.061688315	26775702	intronic	NA	NA	NA	NA	0.4754
CD vs. Ctrl	rs744611	2.26E-09	G	94082	0.061665673	26811840	intronic	NA	NA	NA	NA	0.4698
CD vs. Ctrl	rs891875	2.32E-09	G	94088	0.061624622	26811306	intronic	NA	NA	NA	NA	0.4699
CD vs. Ctrl	rs6973237	2.40E-09	C	94101	0.061566255	26800646	intronic	NA	NA	NA	NA	0.47
CD vs. Ctrl	rs3801855	2.46E-09	G	94096	0.061525203	26812669	intronic	NA	NA	NA	NA	0.47
CD vs. Ctrl	rs2391360	2.53E-09	G	94081	0.061477267	26816201	intronic	NA	NA	NA	NA	0.4699
CD vs. Ctrl	rs7811764	2.60E-09	A	94089	0.061403756	26742148	intronic	NA	NA	NA	NA	0.4701

FIG. 1 (Continued)

PHENOTYPE	dbSNP	p_value	A1	n_miss	OR_Z_B	base_ pair_CH 7	snp_ location	cis_ eGENE	eqtl_beta	eqtl_p	priority	MAF
CD vs. Ctrl	rs6461965	2.61E-09	C	93071	0.06204291	26794980	intronic	NA	NA	NA	NA	0.4644
CD vs. Ctrl	rs891874	2.69E-09	G	93997	0.061373088	26811191	intronic	NA	NA	NA	NA	0.4702
CD vs. Ctrl	rs2299102	3.03E-09	G	94081	0.061169551	26747064	intronic	NA	NA	NA	NA	0.4708
CD vs. Ctrl	rs3801866	3.18E-09	A	94084	0.061090952	26792512	intronic	NA	NA	NA	NA	0.4699
CD vs. Ctrl	rs2023819	3.40E-09	A	94074	0.060996948	26798067	intronic	NA	NA	NA	NA	0.4701
CD vs. Ctrl	rs12700755	3.51E-09	A	94050	0.060902812	26762452	intronic	NA	NA	NA	NA	0.4711
CD vs. Ctrl	rs12700759	3.70E-09	A	94097	0.060680823	26793350	intronic	NA	NA	NA	NA	0.4723
CD vs. Ctrl	rs212853	3.75E-09	A	94100	0.060806434	26726320	intronic	NA	NA	NA	NA	0.4703
CD vs. Ctrl	rs212858	3.76E-09	T	94071	0.060781382	26730869	intronic	NA	NA	NA	NA	0.4701
CD vs. Ctrl	rs3801864	3.85E-09	A	94094	0.060765514	26794831	intronic	NA	NA	NA	NA	0.4694
CD vs. Ctrl	rs3801835	3.89E-09	A	84484	0.066473709	26852053	intronic	NA	NA	NA	NA	0.3797
CD vs. Ctrl	rs212847	3.98E-09	G	94035	0.060726588	26722010	intronic	NA	NA	NA	NA	0.472
CD vs. Ctrl	rs7807640	3.99E-09	G	94094	0.06072697	26814394	intronic	NA	NA	NA	NA	0.4699
CD vs. Ctrl	rs212849	3.99E-09	A	94059	0.060700463	26722643	intronic	NA	NA	NA	NA	0.4712
CD vs. Ctrl	rs6461971	4.41E-09	G	94081	0.060534496	26814023	intronic	NA	NA	NA	NA	0.4714
CD vs. Ctrl	rs3801860	4.47E-09	A	94094	0.06051048	26800710	intronic	NA	NA	NA	NA	0.4705
CD vs. Ctrl	rs12668948	4.59E-09	G	94091	0.060463879	26744101	intronic	NA	NA	NA	NA	0.4708
CD vs. Ctrl	rs7802852	4.61E-09	G	92091	0.061487121	26787836	intronic	NA	NA	NA	NA	0.4701
CD vs. Ctrl	rs3801839	4.65E-09	A	93968	-	26833021	intronic	NA	NA	NA	NA	0.4622
					0.060630566							
CD vs. Ctrl	rs11770043	5.20E-09	G	94081	0.060100708	26789814	intronic	NA	NA	NA	NA	0.4723
CD vs. Ctrl	rs2282906	6.15E-09	A	94059	0.059963297	26747964	intronic	NA	NA	NA	NA	0.4725
CD vs. Ctrl	rs5012512	6.17E-09	C	94080	0.059959688	26812428	intronic	NA	NA	NA	NA	0.4714
CD vs. Ctrl	rs212842	6.23E-09	A	94089	0.059939646	26711817	intronic	NA	NA	NA	NA	0.4644
CD vs. Ctrl	rs212846	8.96E-09	G	94082	0.059286541	26721613	intronic	NA	NA	NA	NA	0.473
CD vs. Ctrl	rs10256799	9.15E-09	G	89689	0.060068153	26818890	intronic	NA	NA	NA	NA	0.4881

FIG. 1 (Continued)

PHENOTYPE	dbSNP	p_value	A1	n_miss	OR_Z_B	base_ pair_CH 7	snp_ location	cis_ eGENE	eqtl_beta	eqtl_p	priority	MAF
CD vs. Ctrl	rs2112852	1.01E-08	G	94056	0.059098982	26725984	intronic	NA	NA	NA	NA	0.4723
CD vs. Ctrl	rs10261915	1.21E-08	G	92662	0.05951317	26814630	intronic	NA	NA	NA	NA	0.4696
CD vs. Ctrl	rs2112840	1.64E-08	A	88435	0.059953097	26701002	intergenic	NA	NA	NA	NA	0.4807
CD vs. Ctrl	rs484426	1.76E-08	G	93071	- 0.058520162	26853846	intronic	NA	NA	NA	NA	0.4703
IBD vs. Ctrl	rs11764558	1.86E-08	A	128299	- 0.046993141	26778732	intronic	NA	NA	NA	NA	0.4929
CD vs. Ctrl	rs13186	1.97E-08	C	94068	0.057925289	26707657	UTR3	NFE2L3	0.0977858 55	0.03897937 3	0	0.4688
IBD vs. Ctrl	rs12700754	2.14E-08	G	128431	- 0.046766298	26754389	intronic	NA	NA	NA	NA	0.4937
CD vs. Ctrl	rs1548479	2.28E-08	G	85498	0.060282634	26787664	intronic	NA	NA	NA	NA	0.4907
IBD vs. Ctrl	rs2299101	2.44E-08	A	126223	- 0.047065323	26747041	intronic	NA	NA	NA	NA	0.4928
IBD vs. Ctrl	rs7795313	2.46E-08	C	128431	- 0.046582932	26775626	intronic	NA	NA	NA	NA	0.4893
IBD vs. Ctrl	rs12700756	2.58E-08	A	128438	- 0.046477257	26768482	intronic	NA	NA	NA	NA	0.4949
IBD vs. Ctrl	rs3801872	2.78E-08	C	128437	- 0.046385094	26744599	intronic	NA	NA	NA	NA	0.493
IBD vs. Ctrl	rs12700762	2.90E-08	A	128430	- 0.046327837	26793597	intronic	NA	NA	NA	NA	0.4932
CD vs. Ctrl	rs601106	3.04E-08	A	94082	- 0.056990259	26867957	intronic	NA	NA	NA	NA	0.4618
IBD vs. Ctrl	rs12700757	3.49E-08	G	128408	- 0.046051515	26770394	intronic	NA	NA	NA	NA	0.4921
IBD vs. Ctrl	rs2112851	3.93E-08	A	128436	-0.04588022	26725389	intronic	NA	NA	NA	NA	0.4928
IBD vs. Ctrl	rs687254	5.19E-08	A	128433	0.045787046	26819774	intronic	NA	NA	NA	NA	0.4863
IBD vs. Ctrl	rs1548480	6.49E-08	A	128407	- 0.045135465	26787343	intronic	NA	NA	NA	NA	0.4936

FIG. 1 (Continued)

PHENOTYPE	dbSNP	p_value	A1	n_miss	OR_Z_B	base_ pair_CH 7	snp_ location	cis_ eGENE	eqtl_beta	eqtl_p	priority	MAF
CD vs. Ctrl	rs78028110	6.73E-08	A	94088	0.10696121	26784056	intronic	EVX1, KIAA0087	0.3013987 74811087, 0.0311722 0.02933705 066916883	0.02256077 80515621, 0.02933705 87330475	0, 0	0.07211
IBD vs. Ctrl	rs4722628	6.83E-08	C	128419	-0.04505656	26735911	intronic	NA	NA	NA	NA	0.4922
IBD vs. Ctrl	rs7802771	6.96E-08	A	128373	- 0.045048493	26734838	intronic	NA	NA	NA	NA	0.4931
IBD vs. Ctrl	rs212857	9.86E-08	C	125149	0.051457222	26730200	intronic	NA	NA	NA	NA	0.2619
IBD vs. Ctrl	rs7810109	1.06E-07	G	128440	0.04589587	26776874	intronic	NA	NA	NA	NA	0.3819
IBD vs. Ctrl	rs7810127	1.07E-07	G	128428	0.045888156	26776999	intronic	NA	NA	NA	NA	0.382
IBD vs. Ctrl	rs10256561	1.12E-07	A	128408	0.046313033	26827627	intronic	NA	NA	NA	NA	0.3681
IBD vs. Ctrl	rs73069541	1.15E-07	G	128435	0.051896906	26904928	intronic	HIBADH, HOXA11-AS	- 0.1186890 17417339, 0.04990810 0.0941114 404455934	0.04652407 2405745, 0.04990810 58041685	0, 0	0.244
IBD vs. Ctrl	rs3823939	1.48E-07	G	128439	0.045853991	26820850	intronic	NA	NA	NA	NA	0.368
IBD vs. Ctrl	rs13234336	1.48E-07	G	128436	0.045357912	26777849	intronic	NA	NA	NA	NA	0.3827
IBD vs. Ctrl	rs73069540	1.57E-07	A	128439	0.051334188	26904770	intronic	HIBADH, HOXA11-AS	- 0.1186890 17417339, 0.04990810 0.0941114 404455934	0.04652407 2405745, 0.04990810 58041685	0, 0	0.2438
CD vs. Ctrl	rs6970591	1.78E-07	G	88339	0.056079813	26795244	intronic	NA	NA	NA	NA	0.4708
IBD vs. Ctrl	rs11772673	1.85E-07	A	128434	0.045023275	26774969	intronic	NA	NA	NA	NA	0.3819
CD vs. Ctrl	rs475238	1.91E-07	G	94076	- 0.053423527	26848278	intronic	NA	NA	NA	NA	0.4999

FIG. 1 (Continued)

PHENOTYPE	dbSNP	p_value	A1	n_miss	OR_Z_B	base_ pair_CH 7	snp_ location	cis_ eGENE	eqtl_beta	eqtl_p	priority	MAF
IBD vs. Ctrl	rs3801831	2.00E-07	G	128418	0.050125142	26853470	intrinsic	NA	NA	NA	NA	0.2529
IBD vs. Ctrl	rs17323934	2.01E-07	G	128424	0.050892073	26904330	UTR5	HIBADH, HOXA11-AS	- 0.1186890 17417339, 0.04990810 0.0941114 404455934	0.04652407 2405745, 0.04990810 58041685	0, 0	0.2438
IBD vs. Ctrl	rs13234201	2.03E-07	G	128413	0.044853307	26777723	intrinsic	NA	NA	NA	NA	0.3829
IBD vs. Ctrl	rs73069533	2.13E-07	A	128408	0.050033472	26892325	intrinsic	NA	NA	NA	NA	0.2525
IBD vs. Ctrl	rs4722644	2.24E-07	A	128441	0.049903593	26845386	intrinsic	NA	NA	NA	NA	0.2529
IBD vs. Ctrl	rs73067443	2.24E-07	G	128441	0.049903593	26851074	intrinsic	NA	NA	NA	NA	0.2529
IBD vs. Ctrl	rs3801844	2.35E-07	G	128402	0.049871431	26829759	intrinsic	NA	NA	NA	NA	0.2502
IBD vs. Ctrl	rs58760954	2.45E-07	A	127342	0.050173326	26850776	intrinsic	NA	NA	NA	NA	0.2496
IBD vs. Ctrl	rs73067456	2.51E-07	A	128400	0.049716092	26852998	intrinsic	NA	NA	NA	NA	0.2528
IBD vs. Ctrl	rs10281261	2.53E-07	A	128418	0.048833622	26789472	intrinsic	NA	NA	NA	NA	0.2639
IBD vs. Ctrl	rs7804620	2.61E-07	C	128432	0.049781994	26891831	intrinsic	NA	NA	NA	NA	0.2531
IBD vs. Ctrl	rs10250223	2.63E-07	A	127349	0.045313015	26821320	intrinsic	NA	NA	NA	NA	0.3615
IBD vs. Ctrl	rs17376018	2.67E-07	G	128414	0.04943155	26889862	intrinsic	NA	NA	NA	NA	0.2532
IBD vs. Ctrl	rs3801847	2.70E-07	G	127272	0.04526718	26821129	intrinsic	NA	NA	NA	NA	0.3615
IBD vs. Ctrl	rs12333525	2.72E-07	A	128411	0.049570962	26847762	intrinsic	NA	NA	NA	NA	0.2529
IBD vs. Ctrl	rs2031811	2.73E-07	G	128341	0.04940813	26890672	intrinsic	NA	NA	NA	NA	0.2531
IBD vs. Ctrl	rs3801810	2.74E-07	A	120492	0.051192864	26892531	intrinsic	NA	NA	NA	NA	0.2576
IBD vs. Ctrl	rs7457076	2.75E-07	G	128415	0.048688101	26793215	intrinsic	NA	NA	NA	NA	0.2639
IBD vs. Ctrl	rs2106905	2.75E-07	A	128437	0.04868701	26766851	intrinsic	NA	NA	NA	NA	0.264
IBD vs. Ctrl	rs73065517	2.76E-07	G	128423	0.049562005	26830555	intrinsic	NA	NA	NA	NA	0.2501
IBD vs. Ctrl	rs3801823	2.80E-07	G	128427	0.049503615	26861031	intrinsic	NA	NA	NA	NA	0.2528

FIG. 1 (Continued)

PHENOTYPE	dbSNP	p_value	A1	n_miss	OR_Z_B	base_ pair_CH 7	snp_ location	cis_ eGENE	eqtl_beta	eqtl_p	priority	MAF
IBD vs. Ctrl	rs6972378	2.80E-07	G	128435	0.048637279	26753074	intronic	NPVF	0.1119454 61	0.00957578 4	0	0.2635
IBD vs. Ctrl	rs6951065	2.84E-07	G	128426	0.048630341	26756162	intronic	NPVF	0.1119454 61	0.00957578 4	0	0.2634
IBD vs. Ctrl	rs3801812	2.88E-07	A	128401	0.049447994	26887615	intronic	NA	NA	NA	NA	0.2531
IBD vs. Ctrl	rs12536145	2.89E-07	T	128377	0.049447679	26894860	intronic	NA	NA	NA	NA	0.253
IBD vs. Ctrl	rs3801842	2.89E-07	A	128322	0.049498121	26830263	intronic	NA	NA	NA	NA	0.2502
IBD vs. Ctrl	rs73065504	2.89E-07	G	128431	0.049497391	26825984	intronic	NA	NA	NA	NA	0.2497
IBD vs. Ctrl	rs3213853	2.90E-07	G	128387	0.049439173	26893524	intronic	NA	NA	NA	NA	0.2533
IBD vs. Ctrl	rs10276471	2.95E-07	G	128409	0.049444226	26837940	intronic	NA	NA	NA	NA	0.2501
IBD vs. Ctrl	rs10272603	2.95E-07	G	128433	0.049248485	26888277	intronic	NA	NA	NA	NA	0.2532
IBD vs. Ctrl	rs10236221	2.98E-07	T	128426	0.049405183	26884671	intronic	NA	NA	NA	NA	0.2526
IBD vs. Ctrl	rs212848	3.00E-07	C	128442	0.04846241	26722155	intronic	NPVF	0.1119454 61	0.00957578 4	0	0.2643
CD vs. Ctrl	rs2769365	3.03E-07	C	82472	- 0.056076611	26844616	intronic	NA	NA	NA	NA	0.4996
IBD vs. Ctrl	rs3801820	3.13E-07	G	128431	0.049315027	26861353	intronic	NA	NA	NA	NA	0.2528
IBD vs. Ctrl	rs10486483	3.14E-07	A	124098	0.049989284	26892440	intronic	NA	NA	NA	NA	0.2596
IBD vs. Ctrl	rs17375272	3.24E-07	A	128416	0.049273522	26866497	intronic	NA	NA	NA	NA	0.2524
IBD vs. Ctrl	rs73067475	3.26E-07	A	128434	0.049067619	26857120	intronic	NA	NA	NA	NA	0.2528
IBD vs. Ctrl	rs3801840	3.29E-07	G	128434	0.04919969	26832986	intronic	NA	NA	NA	NA	0.2525
IBD vs. Ctrl	rs10272303	3.53E-07	G	128415	0.04911631	26827815	intronic	NA	NA	NA	NA	0.2502
IBD vs. Ctrl	rs3801826	3.57E-07	A	128404	0.049079245	26856720	intronic	NA	NA	NA	NA	0.2526
IBD vs. Ctrl	rs10267950	3.58E-07	A	128001	0.049200475	26826757	intronic	NA	NA	NA	NA	0.2493
IBD vs. Ctrl	rs3801805	3.61E-07	G	128437	0.049018974	26897640	intronic	NA	NA	NA	NA	0.2535
IBD vs. Ctrl	rs3823930	3.62E-07	G	128265	0.049066174	26856525	intronic	NA	NA	NA	NA	0.2528
CD vs. Ctrl	rs567124	3.64E-07	A	89824	-0.05283054	26845145	intronic	NA	NA	NA	NA	0.4873

FIG. 1 (Continued)

PHENOTYPE	dbSNP	p_value	A1	n_miss	OR_Z_B	base_ pair_CH 7	snp_ location	cis_ eGENE	eqtl_beta	eqtl_p	priority	MAF
IBD vs. Ctrl	rs6461963	3.66E-07	G	128423	0.048160813	26772491	intrinsic	NA	NA	NA	NA	0.2641
IBD vs. Ctrl	rs1327989	3.66E-07	A	128430	0.049066264	26833563	intrinsic	NA	NA	NA	NA	0.2501
IBD vs. Ctrl	rs4719877	3.74E-07	A	128439	0.048085	26736220	intrinsic	NPVF	0.1119454 61	0.00957578 4	0	0.2643
IBD vs. Ctrl	rs13438513	3.87E-07	C	128431	0.048913181	26860633	intrinsic	NA	NA	NA	NA	0.2528
IBD vs. Ctrl	rs4722630	3.94E-07	C	128417	0.048044767	26773364	intrinsic	NA	NA	NA	NA	0.264
IBD vs. Ctrl	rs3801850	3.95E-07	G	128371	0.048792156	26820577	intrinsic	NA	NA	NA	NA	0.2509
IBD vs. Ctrl	rs12532796	3.96E-07	G	128396	0.048907602	26854828	intrinsic	NA	NA	NA	NA	0.2524
IBD vs. Ctrl	rs10272190	3.97E-07	A	128344	0.048866908	26887942	intrinsic	NA	NA	NA	NA	0.2532
IBD vs. Ctrl	rs212856	4.03E-07	A	128439	0.047947963	26729205	intrinsic	NPVF	0.1119454 61	0.00957578 4	0	0.2643
IBD vs. Ctrl	rs28550029	4.24E-07	A	123240	0.049882214	26872581	intrinsic	NA	NA	NA	NA	0.2504
IBD vs. Ctrl	rs2189017	4.28E-07	A	128427	0.047877377	26795073	intrinsic	NA	NA	NA	NA	0.2639
CD vs. Ctrl	rs6461961	4.38E-07	G	88103	0.053493122	26738984	intrinsic	NA	NA	NA	NA	0.4792
IBD vs. Ctrl	rs7804356	4.39E-07	G	128383	0.048712141	26891665	intrinsic	NA	NA	NA	NA	0.2533
IBD vs. Ctrl	rs17315775	4.40E-07	G	123087	0.049829441	26860134	intrinsic	NA	NA	NA	NA	0.254
CD vs. Ctrl	rs471536	4.56E-07	A	84572	- 0.054881492	26848685	intrinsic	NA	NA	NA	NA	0.4945
IBD vs. Ctrl	rs3801837	4.70E-07	G	128369	0.048571867	26851361	intrinsic	NA	NA	NA	NA	0.2529
IBD vs. Ctrl	rs4719879	4.71E-07	A	128377	0.04237527	26780199	intrinsic	NA	NA	NA	NA	0.4709
IBD vs. Ctrl	rs3801807	4.85E-07	G	128291	0.048515425	26897439	intrinsic	NA	NA	NA	NA	0.2528
IBD vs. Ctrl	rs6971397	4.89E-07	G	128400	0.047654747	26782564	intrinsic	NA	NA	NA	NA	0.2634
IBD vs. Ctrl	rs73061894	4.93E-07	G	128424	0.047622357	26802085	intrinsic	NA	NA	NA	NA	0.264
IBD vs. Ctrl	rs3801813	5.03E-07	G	128400	0.048307834	26887069	intrinsic	NA	NA	NA	NA	0.2527
IBD vs. Ctrl	rs10486478	5.17E-07	A	128410	0.048690481	26819465	intrinsic	NA	NA	NA	NA	0.2502
IBD vs. Ctrl	rs3801833	5.17E-07	A	128341	0.048411854	26852212	intrinsic	NA	NA	NA	NA	0.2528

FIG. 1 (Continued)

PHENOTYPE	dbSNP	p_value	A1	n_miss	OR_Z_B	base_ pair_CH 7	snp_ location	cis_ eGENE	eqtl_beta	eqtl_p	priority	MAF
IBD vs. Ctrl	rs10486485	5.24E-07	A	128390	0.048646128	26900356	intronic	HIBADH, HOXA11-AS	- 0.1186890 17417339, 0.04990810 0.0941114 404455934	0.04652407 2405745, 0.04990810 58041685	0, 0	0.2478
IBD vs. Ctrl	rs6948584	5.69E-07	A	128410	0.048216242	26855732	intronic	NA	NA	NA	NA	0.2528
IBD vs. Ctrl	rs3823929	5.71E-07	G	128282	0.048228005	26856600	intronic	NA	NA	NA	NA	0.253
CD vs. Ctrl	rs503110	5.79E-07	T	94094	- 0.051218547	26857016	intronic	NA	NA	NA	NA	0.4998
IBD vs. Ctrl	rs3823936	6.02E-07	G	128439	0.048095657	26853830	intronic	NA	NA	NA	NA	0.2528
IBD vs. Ctrl	rs73067476	6.15E-07	G	128344	0.04807162	26857240	intronic	NA	NA	NA	NA	0.2528
IBD vs. Ctrl	rs3823934	6.32E-07	G	128406	0.048039872	26853934	intronic	NA	NA	NA	NA	0.2524
IBD vs. Ctrl	rs12535784	6.40E-07	A	128313	0.048033243	26882067	intronic	NA	NA	NA	NA	0.2525
IBD vs. Ctrl	rs3801829	6.50E-07	C	128430	0.047950796	26854996	intronic	NA	NA	NA	NA	0.2529
IBD vs. Ctrl	rs73069510	6.77E-07	G	128438	0.047891829	26877567	intronic	NA	NA	NA	NA	0.2529
IBD vs. Ctrl	rs73069539	6.78E-07	A	128405	0.048482812	26903661	intronic	HIBADH, HOXA11-AS	- 0.1186890 17417339, 0.04990810 0.0941114 404455934	0.04652407 2405745, 0.04990810 58041685	0, 0	0.2472
IBD vs. Ctrl	rs10262414	6.92E-07	A	128412	0.047852642	26854266	intronic	NA	NA	NA	NA	0.2528
IBD vs. Ctrl	rs73069507	7.10E-07	G	128439	0.047800937	26877536	intronic	NA	NA	NA	NA	0.2529
IBD vs. Ctrl	rs3801815	7.50E-07	G	128438	0.047699865	26881292	intronic	NA	NA	NA	NA	0.253
CD vs. Ctrl	rs622011	7.53E-07	G	93992	- 0.050753173	26855739	intronic	NA	NA	NA	NA	0.4996
IBD vs. Ctrl	rs12700758	8.06E-07	G	128405	0.041331761	26790969	intronic	NA	NA	NA	NA	0.47
IBD vs. Ctrl	rs11773050	8.06E-07	G	128402	0.041331761	26793094	intronic	NA	NA	NA	NA	0.47

FIG. 1 (Continued)

PHENOTYPE	dbSNP	p_value	A1	n_miss	OR_Z_B	base_ pair_CH 7	snp_ location	cis_ eGENE	eqtl_beta	eqtl_p	priority	MAF
IBD vs. Ctrl	rs3801843	8.55E-07	G	128399	0.047506072	26830201	intronic	NA	NA	NA	NA	0.2502
IBD vs. Ctrl	rs10242572	8.63E-07	G	128423	0.047568779	26895065	intronic	NA	NA	NA	NA	0.2531
IBD vs. Ctrl	rs3823931	8.81E-07	G	128416	0.047398917	26854026	intronic	NA	NA	NA	NA	0.2528
IBD vs. Ctrl	rs12700760	9.67E-07	T	128403	0.041165341	26793448	intronic	NA	NA	NA	NA	0.4703
IBD vs. Ctrl	rs10225904	9.75E-07	A	128392	0.047937578	26869888	intronic	NA	NA	NA	NA	0.2524
IBD vs. Ctrl	rs4345466	9.85E-07	G	128435	0.041152029	26815636	intronic	NA	NA	NA	NA	0.4699
IBD vs. Ctrl	rs10951149	1.04E-06	G	128442	0.041061548	26815857	intronic	NA	NA	NA	NA	0.4699
IBD vs. Ctrl	rs212850	1.07E-06	A	126723	0.046523978	26724279	intronic	NPVF	0.1119454 61	0.00957578 4	0	0.2642
IBD vs. Ctrl	rs10225700	1.08E-06	A	128432	0.04718043	26869880	intronic	NA	NA	NA	NA	0.2524
IBD vs. Ctrl	rs3801803	1.09E-06	G	128372	0.047282675	26901740	intronic	HIBADH, HOXA11-AS	- 0.1186890 17417339, 0.04990810 0.0941114 404455934	0.04652407 2405745, 0.04990810 58041685	0, 0	0.2481
IBD vs. Ctrl	rs3823938	1.09E-06	G	128367	0.046988635	26853741	intronic	NA	NA	NA	NA	0.2534
IBD vs. Ctrl	rs3801816	1.10E-06	A	123126	0.048036393	26881177	intronic	NA	NA	NA	NA	0.2529
IBD vs. Ctrl	rs28404962	1.10E-06	G	128424	0.046960391	26860324	intronic	NA	NA	NA	NA	0.2529
IBD vs. Ctrl	rs4722631	1.11E-06	G	122697	0.041751367	26774325	intronic	NA	NA	NA	NA	0.4817
IBD vs. Ctrl	rs11773029	1.13E-06	G	128421	0.040777008	26793064	intronic	NA	NA	NA	NA	0.47
IBD vs. Ctrl	rs58988613	1.14E-06	A	128422	0.040911382	26769702	intronic	NA	NA	NA	NA	0.4706
IBD vs. Ctrl	rs3801821	1.15E-06	A	128420	0.047032859	26861206	intronic	NA	NA	NA	NA	0.2528
IBD vs. Ctrl	rs2391360	1.21E-06	G	128416	0.040805481	26816201	intronic	NA	NA	NA	NA	0.4699
IBD vs. Ctrl	rs2189019	1.26E-06	G	128297	0.045961196	26798581	intronic	NA	NA	NA	NA	0.2635
IBD vs. Ctrl	rs12700755	1.26E-06	A	128376	0.0407347	26762452	intronic	NA	NA	NA	NA	0.4711
IBD vs. Ctrl	rs7785711	1.27E-06	A	127139	0.047441865	26861640	intronic	NA	NA	NA	NA	0.2497

FIG. 1 (Continued)

PHENOTYPE	dbSNP	p_value	A1	n_miss	OR_Z_B	base_ pair_CH 7	snp_ location	cis_ eGENE	eqtl_beta	eqtl_p	priority	MAF
IBD vs. Ctrl	rs3801853	1.29E-06	G	128423	0.040701268	26813025	intronic	NA	NA	NA	NA	0.4692
IBD vs. Ctrl	rs6461965	1.30E-06	C	127299	0.040878353	26794980	intronic	NA	NA	NA	NA	0.4644
IBD vs. Ctrl	rs17315334	1.31E-06	A	123151	0.047854498	26852860	intronic	NA	NA	NA	NA	0.2529
IBD vs. Ctrl	rs6973237	1.33E-06	C	128443	0.040502926	26800646	intronic	NA	NA	NA	NA	0.47
IBD vs. Ctrl	rs12700761	1.33E-06	G	128429	0.040502509	26793515	intronic	NA	NA	NA	NA	0.4706
IBD vs. Ctrl	rs3801855	1.34E-06	G	128438	0.040638089	26812669	intronic	NA	NA	NA	NA	0.47
IBD vs. Ctrl	rs1123158	1.36E-06	G	126237	0.041046282	26816648	intronic	NA	NA	NA	NA	0.47
IBD vs. Ctrl	rs6461964	1.38E-06	A	128420	0.040575906	26775702	intronic	NA	NA	NA	NA	0.4754
IBD vs. Ctrl	rs744611	1.40E-06	G	128416	0.040413202	26811840	intronic	NA	NA	NA	NA	0.4698
IBD vs. Ctrl	rs7811764	1.45E-06	A	128430	0.040345257	26742148	intronic	NA	NA	NA	NA	0.4701
IBD vs. Ctrl	rs891875	1.49E-06	G	128426	0.04031393	26811306	intronic	NA	NA	NA	NA	0.4699
IBD vs. Ctrl	rs212858	1.51E-06	T	128399	0.040427336	26730869	intronic	NA	NA	NA	NA	0.4701
IBD vs. Ctrl	rs891874	1.52E-06	G	128293	0.04028291	26811191	intronic	NA	NA	NA	NA	0.4702
IBD vs. Ctrl	rs2023821	1.52E-06	G	116666	-	26700475	intergenic	NA	NA	NA	NA	0.4938
IBD vs. Ctrl	rs212838	1.57E-06	A	128431	0.045868642	26698194	intergenic	NPVF	0.1082079 45	0.01310842 7	0	0.2572
IBD vs. Ctrl	rs12700759	1.58E-06	A	128438	0.040203724	26793350	intronic	NA	NA	NA	NA	0.4723
IBD vs. Ctrl	rs2299102	1.60E-06	G	128416	0.040198544	26747064	intronic	NA	NA	NA	NA	0.4708
IBD vs. Ctrl	rs3801846	1.61E-06	A	122399	0.047128116	26828653	intronic	NA	NA	NA	NA	0.2625
IBD vs. Ctrl	rs1548478	1.61E-06	C	128407	0.040184125	26788153	intronic	NA	NA	NA	NA	0.4702
IBD vs. Ctrl	rs10266759	1.63E-06	A	128431	0.046366329	26855282	intronic	NA	NA	NA	NA	0.2527
IBD vs. Ctrl	rs7805778	1.64E-06	A	128432	0.045949403	26694926	intergenic	NPVF	0.1082079 45	0.01310842 7	0	0.2574
IBD vs. Ctrl	rs3757654	1.65E-06	A	128295	0.045642928	26711104	intronic	NPVF	0.1095317 04	0.01169563 2	0	0.258
IBD vs. Ctrl	rs3801866	1.76E-06	A	128425	0.040186857	26792512	intronic	NA	NA	NA	NA	0.4699

FIG. 1 (Continued)

PHENOTYPE	dbSNP	p_value	A1	n_miss	OR_Z_B	base_ pair_CH 7	snp_ location	cis_ eGENE	eqtl_beta	eqtl_p	priority	MAF
IBD vs. Ctrl	rs212853	1.80E-06	A	128442	0.040142242	26726320	intrinsic	NA	NA	NA	NA	0.4703
IBD vs. Ctrl	rs2023819	1.80E-06	A	128407	0.040142287	26798067	intrinsic	NA	NA	NA	NA	0.4701
Paneth-D1 phenotype	rs1526318	1.84E-06	A	296	9.336	27026223	intrinsic	NA	NA	NA	NA	0.001526
IBD vs. Ctrl	rs3801854	1.85E-06	G	128415	0.040097046	26812754	intrinsic	NA	NA	NA	NA	0.4692
IBD vs. Ctrl	rs3801822	1.86E-06	G	123876	0.046981606	26861201	intrinsic	NA	NA	NA	NA	0.2586
IBD vs. Ctrl	rs3801864	1.91E-06	A	128434	0.039901888	26794831	intrinsic	NA	NA	NA	NA	0.4694
IBD vs. Ctrl	rs3801836	1.91E-06	A	118503	0.047868577	26851400	intrinsic	NA	NA	NA	NA	0.2589
IBD vs. Ctrl	rs5012512	1.91E-06	C	128414	0.040043939	26812428	intrinsic	NA	NA	NA	NA	0.4714
IBD vs. Ctrl	rs2282906	1.96E-06	A	128387	0.039836217	26747964	intrinsic	NA	NA	NA	NA	0.4725
IBD vs. Ctrl	rs3801860	2.05E-06	A	128435	0.039922734	26800710	intrinsic	NA	NA	NA	NA	0.4705
IBD vs. Ctrl	rs727450	2.13E-06	G	128285	0.045083493	26787642	intrinsic	NA	NA	NA	NA	0.2633
IBD vs. Ctrl	rs7807640	2.15E-06	G	128435	0.039842694	26814394	intrinsic	NA	NA	NA	NA	0.4699
IBD vs. Ctrl	rs10227529	2.17E-06	A	121922	0.046922126	26886309	intrinsic	NA	NA	NA	NA	0.2534
IBD vs. Ctrl	rs11770043	2.19E-06	G	128416	0.039555215	26789814	intrinsic	NA	NA	NA	NA	0.4723
IBD vs. Ctrl	rs212837	2.24E-06	A	125453	0.04117104	26695215	intergenic	NPVF	0.0821950 54	0.03146251	0	0.3868
IBD vs. Ctrl	rs6461971	2.26E-06	G	128416	0.039757578	26814023	intrinsic	NA	NA	NA	NA	0.4714
IBD vs. Ctrl	rs212847	2.50E-06	G	128358	0.039580135	26722010	intrinsic	NA	NA	NA	NA	0.472
IBD vs. Ctrl	rs212849	2.51E-06	A	128385	0.039575327	26722643	intrinsic	NA	NA	NA	NA	0.4712
IBD vs. Ctrl	rs12668948	2.64E-06	G	128431	0.039492498	26744101	intrinsic	NA	NA	NA	NA	0.4708
IBD vs. Ctrl	rs212842	2.67E-06	A	128430	0.039472598	26711817	intrinsic	NA	NA	NA	NA	0.4644
IBD vs. Ctrl	rs7785689	2.71E-06	A	127957	0.045474693	26861609	intrinsic	NA	NA	NA	NA	0.2519
IBD vs. Ctrl	rs212846	3.12E-06	G	128416	0.039045125	26721613	intrinsic	NA	NA	NA	NA	0.473
IBD vs. Ctrl	rs989250	3.13E-06	G	125054	0.039929298	26803955	intrinsic	NA	NA	NA	NA	0.4642
IBD vs. Ctrl	rs3801814	3.30E-06	C	126670	0.04518497	26881302	intrinsic	NA	NA	NA	NA	0.2524

FIG. 1 (Continued)

PHENOTYPE	dbSNP	p_value	A1	n_miss	OR_Z_B	base_ pair_CH 7	snp_ location	cis_ eGENE	eqtl_beta	eqtl_p	priority	MAF
IBD vs. Ctrl	rs212852	3.34E-06	G	128393	0.038941113	26725984	intronic	NA	NA	NA	NA	0.4723
CD vs. Ctrl	rs2769364	3.65E-06	C	88338	- 0.049477687	26844468	intronic	NA	NA	NA	NA	0.4991
IBD vs. Ctrl	rs7802852	4.16E-06	G	126094	0.038964938	26787836	intronic	NA	NA	NA	NA	0.4701
IBD vs. Ctrl	rs212840	4.29E-06	A	122418	0.039523905	26701002	intergenic	NA	NA	NA	NA	0.4807
IBD vs. Ctrl	rs10261915	4.52E-06	G	126635	0.038852135	26814630	intronic	NA	NA	NA	NA	0.4696
CD vs. Ctrl	rs570840	5.27E-06	C	93123	- 0.046961637	26862139	intronic	NA	NA	NA	NA	0.4989
IBD vs. Ctrl	rs13186	5.32E-06	C	128389	0.038256604	26707657	UTR3	NFE2L3	0.0977858 55	0.03897937 3	0	0.4688
IBD vs. Ctrl	rs6964094	5.87E-06	NA	NA	0.045376582	26834380	intronic	NA	NA	NA	NA	#N/A
IBD vs. Ctrl	rs3801828	5.91E-06	A	122585	0.044640037	26855284	intronic	NA	NA	NA	NA	0.2635
IBD vs. Ctrl	rs3801839	6.20E-06	A	128260	- 0.038024936	26833021	intronic	NA	NA	NA	NA	0.4622
IBD vs. Ctrl	rs3801809	6.22E-06	A	123085	0.044846427	26895456	intronic	NA	NA	NA	NA	0.2529
IBD vs. Ctrl	rs55739485	6.66E-06	G	126594	0.043941926	26860741	intronic	NA	NA	NA	NA	0.2528
IBD vs. Ctrl	rs73061889	7.01E-06	C	126082	0.039930108	26799874	intronic	NA	NA	NA	NA	0.3512
Paneth-D1234 phenotype	rs1526318	7.06E-06	A	296	53.19	27026223	intronic	NA	NA	NA	NA	0.001526
IBD vs. Ctrl	rs73067472	7.20E-06	G	121903	0.044419434	26855959	intronic	NA	NA	NA	NA	0.2529
IBD vs. Ctrl	rs13229947	7.30E-06	A	128429	0.039580951	26767430	intronic	NA	NA	NA	NA	0.3419
CD vs. Ctrl	rs73077525	7.36E-06	C	93095	-0.06760096	26778568	intronic	NA	NA	NA	NA	0.1383
Paneth-D0 phenotype	rs1526318	7.48E-06	A	296	-53	27026223	intronic	NA	NA	NA	NA	0.001526
IBD vs. Ctrl	rs10256799	7.69E-06	G	123958	0.038179786	26818890	intronic	NA	NA	NA	NA	0.4881
CD vs. Ctrl	rs667841	8.08E-06	A	86708	- 0.047585389	26851231	intronic	NA	NA	NA	NA	0.4998
IBD vs. Ctrl	rs3801835	1.04E-05	A	116651	0.040529065	26852053	intronic	NA	NA	NA	NA	0.3797

FIG. 1 (Continued)

PHENOTYPE	dbSNP	p_value	A1	n_miss	OR_Z_B	base_ pair_CH 7	snp_ location	cis_ eGENE	eqtl_beta	eqtl_p	priority	MAF
IBD vs. Ctrl	rs10227898	1.05E-05	G	128417	0.038597726	26764618	intronic	JAZF1	- 0.0216838 55	0.02995406 6	0	0.3525
IBD vs. Ctrl	rs7782621	1.10E-05	G	128375	0.038518379	26790937	intronic	JAZF1	- 0.0216838 55	0.02995406 6	0	0.3518
IBD vs. Ctrl	rs1468203	1.21E-05	C	128433	0.038318414	26791287	intronic	JAZF1	- 0.0216838 55	0.02995406 6	0	0.3518
CD vs. Ctrl	rs17291131	1.22E-05	A	93782	-0.06695032	26729740	intronic	NA	NA	NA	NA	0.1203
IBD vs. Ctrl	rs7795074	1.25E-05	A	128433	0.038095696	26742154	intronic	JAZF1	- 0.0216838 55	0.02995406 6	0	0.3527
IBD vs. Ctrl	rs12532199	1.27E-05	G	128365	0.042356743	26854375	intronic	NA	NA	NA	NA	0.2527
IBD vs. Ctrl	rs1982995	1.43E-05	C	120804	0.043143237	26884135	intronic	NA	NA	NA	NA	0.2633
IBD vs. Ctrl	rs7802688	1.62E-05	A	128434	0.03777491	26785832	intronic	JAZF1	- 0.0216838 55	0.02995406 6	0	0.3514
IBD vs. Ctrl	rs56374720	1.63E-05	A	128433	0.037759945	26815776	intronic	JAZF1	- 0.0216838 55	0.02995406 6	0	0.352
IBD vs. Ctrl	rs11980739	1.66E-05	G	128430	0.037719621	26818164	intronic	JAZF1	- 0.0216838 55	0.02995406 6	0	0.3521
IBD vs. Ctrl	rs3801857	1.74E-05	A	128400	0.03763426	26811484	intronic	JAZF1	- 0.0216838 55	0.02995406 6	0	0.3519
IBD vs. Ctrl	rs484426	1.87E-05	G	127312	- 0.036145235	26853846	intronic	NA	NA	NA	NA	0.4703
IBD vs. Ctrl	rs1023712	1.87E-05	C	128419	0.037478852	26803163	intronic	JAZF1	- 0.0216838 55	0.02995406 6	0	0.3521

FIG. 1 (Continued)

PHENOTYPE	dbSNP	p_value	A1	n_miss	OR_Z_B	base_ pair_CH 7	snp_ location	cis_ eGENE	eqtl_beta	eqtl_p	priority	MAF
IBD vs. Ctrl	rs763616	2.04E-05	T	128394	0.037311811	26784600	intronic	JAZF1	- 0.0216838 55	0.02995406 6	0	0.3521
CD vs. Ctrl	rs73075509	2.09E-05	A	94077	- 0.064835474	26719824	intronic	NA	NA	NA	NA	0.1205
IBD vs. Ctrl	rs7803699	2.19E-05	G	128441	0.03718384	26814173	intronic	JAZF1	- 0.0216838 55	0.02995406 6	0	0.3513
IBD vs. Ctrl	rs73065521	2.89E-05	A	115449	0.042652009	26831409	intronic	NA	NA	NA	NA	0.2587
IBD vs. Ctrl	rs601106	2.90E-05	A	128417	- 0.035040695	26867957	intronic	NA	NA	NA	NA	0.4618
Paneth-D5 phenotype	rs117096549	3.21E-05	A	155	1.051	26759787	intronic	NA	NA	NA	NA	0.01017
Paneth-D5 phenotype	rs150740581	3.21E-05	G	155	1.051	26845629	intronic	NA	NA	NA	NA	0.01046
IBD vs. Ctrl	rs17372780	3.33E-05	C	128386	0.036326667	26804018	intronic	JAZF1	- 0.0216838 55	0.02995406 6	0	0.3518
IBD vs. Ctrl	rs1548479	3.33E-05	G	117740	0.036459643	26787664	intronic	NA	NA	NA	NA	0.4907
IBD vs. Ctrl	rs727449	4.74E-05	G	121887	0.036458201	26787577	intronic	NA	NA	NA	NA	0.3633
Paneth-D4 phenotype	rs17426587	5.53E-05	G	297	5.707	26960713	intronic	NA	NA	NA	NA	0.02208
Paneth-D4 phenotype	rs76373784	5.53E-05	A	297	5.707	27079239	intergenic	NA	NA	NA	NA	0.02165
IBD vs. Ctrl	rs6461961	5.71E-05	G	121910	0.034689032	26738984	intronic	NA	NA	NA	NA	0.4792
IBD vs. Ctrl	rs1123156	6.35E-05	A	123048	0.036087492	26817044	intronic	JAZF1	- 0.0216838 55	0.02995406 6	0	0.352
CD vs. Ctrl	rs3823928	8.50E-05	G	NA	0.070557754	26893317	intronic	NA	NA	NA	NA	0.2551

FIG. 1 (Continued)

PHENOTYPE	dbSNP	p_value	A1	n_miss	OR_Z_B	base_ pair_CH 7	snp_ location	cis_ eGENE	eqtl_beta	eqtl_p	priority	MAF
Paneth-D1 phenotype	rs799233	9.05E-05	G	297	3.886	27073660	intergenic	NA	NA	NA	NA	0.002567
MRUC vs non- MRUC	NA	9.85E-05	A	11022	-0.1417	26735911	intronic	NA	NA	NA	NA	#N/A
IBD vs. Ctrl	rs6970591	0.000110405	G	121876	0.03332746	26795244	intronic	NA	NA	NA	NA	0.4708
anti-TNF time to loss of response	rs77472965	0.000115445	G	243	3.8556	26783923	intronic	NA	NA	NA	NA	0.01671
MRUC vs non- MRUC	NA	0.0001211	A	11022	-0.1398	26744599	intronic	NA	NA	NA	NA	#N/A
MRUC vs non- MRUC	NA	0.0001241	A	11022	-0.1409	26711817	intronic	NA	NA	NA	NA	#N/A
MRUC vs non- MRUC	NA	0.0001265	A	11022	0.1394	26725389	intronic	NA	NA	NA	NA	#N/A
MRUC vs non- MRUC	NA	0.0001271	A	11022	-0.1396	26775626	intronic	NA	NA	NA	NA	#N/A
MRUC vs non- MRUC	NA	0.0001367	A	11022	0.1399	26740461	intronic	NA	NA	NA	NA	#N/A
CD vs. Ctrl	rs10486486	0.000145454	T	94090	0.040967145	26920621	intronic	NA	NA	NA	NA	0.351
MRUC vs non- MRUC	NA	0.0001469	A	11022	0.1381	26778732	intronic	NA	NA	NA	NA	#N/A
MRUC vs non- MRUC	NA	0.0001474	A	11022	0.138	26768482	intronic	NA	NA	NA	NA	#N/A
MRUC vs non- MRUC	NA	0.0001537	A	11022	0.1377	26734838	intronic	NA	NA	NA	NA	#N/A
MRUC vs non- MRUC	NA	0.0001602	A	11022	-0.1373	26754389	intronic	NA	NA	NA	NA	#N/A

FIG. 1 (Continued)

PHENOTYPE	dbSNP	p_value	A1	n_miss	OR_Z_B	base_ pair_CH 7	snp_ location	cis_ eGENE	eqtl_beta	eqtl_p	priority	MAF
MRUC vs non-MRUC	NA	0.0001603	A	11022	0.1371	26793597	intronic	NA	NA	NA	NA	#N/A
CD vs. Ctrl	rs73067474	0.000164011	C	94086	- 0.058199662	26856632	intronic	NA	NA	NA	NA	0.1203
MRUC vs non-MRUC	NA	0.0001677	A	11022	0.1382	26747041	intronic	NA	NA	NA	NA	#N/A
CD vs. Ctrl	rs12530718	0.000169365	A	94080	0.040510182	26931205	intronic	NA	NA	NA	NA	0.3542
CD vs. Ctrl	rs73069529	0.000170257	A	94042	- 0.058395102	26889376	intronic	NA	NA	NA	NA	0.1187
MRUC vs non-MRUC	NA	0.0001703	A	11022	-0.1367	26770394	intronic	NA	NA	NA	NA	#N/A
MRUC vs non-MRUC	NA	0.0001798	A	11022	0.1375	26747064	intronic	NA	NA	NA	NA	#N/A
MRUC vs non-MRUC	NA	0.0001866	A	11022	0.1368	26707657	UTR3	NA	NA	NA	NA	#N/A
CD vs. Ctrl	rs6948657	0.000195236	A	NA	0.066537277	26855943	intronic	NA	NA	NA	NA	0.2546
IBD vs. Ctrl	rs188468488	0.000202798	G	128438	- 0.141223137	27109617	intergenic	NA	NA	NA	NA	0.01245
MRUC vs non-MRUC	NA	0.0002042	A	11022	-0.1363	26727362	intronic	NA	NA	NA	NA	#N/A
MRUC vs non-MRUC	NA	0.0002105	A	11022	-0.136	26726320	intronic	NA	NA	NA	NA	#N/A
IBD vs. Ctrl	rs475238	0.000210952	G	128414	- 0.030940809	26848278	intronic	NA	NA	NA	NA	0.4999
MRUC vs non-MRUC	NA	0.0002141	A	11022	0.1345	26787343	intronic	NA	NA	NA	NA	#N/A
CD vs. Ctrl	rs11770344	0.000217456	A	NA	- 0.058931343	26755001	intronic	NA	NA	NA	NA	0.445

FIG. 1 (Continued)

PHENOTYPE	dbSNP	p_value	A1	n_miss	OR_Z_B	base_ pair_CH 7	snp_ location	cis_ eGENE	eqtl_beta	eqtl_p	priority	MAF
CD vs. Ctrl	rs6962680	0.000223068	G	94083	0.039854169	26918106	intronic	NA	NA	NA	NA	0.3545
MRUC vs non-MRUC	NA	0.0002258	A	11022	-0.1353	26742148	intronic	NA	NA	NA	NA	#N/A
CD vs. Ctrl	rs3801832	0.000226925	A	NA	0.067420617	26852280	intronic	NA	NA	NA	NA	0.2612
MRUC vs non-MRUC	NA	0.0002309	A	11022	-0.1351	26775702	intronic	NA	NA	NA	NA	#N/A
MRUC vs non-MRUC	NA	0.000232	A	11022	0.135	26721613	intronic	NA	NA	NA	NA	#N/A
MRUC vs non-MRUC	NA	0.0002342	A	11022	0.135	26744101	intronic	NA	NA	NA	NA	#N/A
MRUC vs non-MRUC	NA	0.0002355	A	11022	-0.135	26722643	intronic	NA	NA	NA	NA	#N/A
MRUC vs non-MRUC	NA	0.0002383	A	11022	0.1349	26722010	intronic	NA	NA	NA	NA	#N/A
MRUC vs non-MRUC	NA	0.0002461	A	11022	0.1343	26793448	intronic	NA	NA	NA	NA	#N/A
MRUC vs non-MRUC	NA	0.0002503	A	11022	-0.1332	26799945	intronic	NA	NA	NA	NA	#N/A
MRUC vs non-MRUC	NA	0.0002586	A	11022	-0.1339	26747964	intronic	NA	NA	NA	NA	#N/A
PyodermaG	rs77339138	0.0002606	A	1421	3.273	27094255	intergenic	HOTAIRM1	0.3604290 ₂	0.00675335	0	0.05801
MRUC vs non-MRUC	NA	0.0002618	C	11022	-0.1339	26716458	intronic	NA	NA	NA	NA	#N/A
CD vs. Ctrl	rs17315929	0.000264421	A	NA	0.066349726	26864173	intronic	NA	NA	NA	NA	0.2621

FIG. 1 (Continued)

PHENOTYPE	dbSNP	p_value	A1	n_miss	OR_Z_B	base_ pair_CH 7	snp_ location	cis_ eGENE	eqtl_beta	eqtl_p	priority	MAF
MRUC vs non-MRUC	NA	0.0002707	A	11022	-0.1335	26762452	intronic	NA	NA	NA	NA	#N/A
MRUC vs non-MRUC	NA	0.0002707	A	11022	0.1335	26725984	intronic	NA	NA	NA	NA	#N/A
MRUC vs non-MRUC	NA	0.0002747	A	11022	0.1335	26730869	intronic	NA	NA	NA	NA	#N/A
MRUC vs non-MRUC	NA	0.0002752	A	11022	-0.1334	26792512	intronic	NA	NA	NA	NA	#N/A
MRUC vs non-MRUC	NA	0.0002767	A	11022	0.1334	26811306	intronic	NA	NA	NA	NA	#N/A
MRUC vs non-MRUC	NA	0.0002773	A	11022	0.1334	26815857	intronic	NA	NA	NA	NA	#N/A
MRUC vs non-MRUC	NA	0.0002773	A	11022	0.1334	26812669	intronic	NA	NA	NA	NA	#N/A
MRUC vs non-MRUC	NA	0.0002773	A	11022	0.1334	26815636	intronic	NA	NA	NA	NA	#N/A
MRUC vs non-MRUC	NA	0.0002777	A	11022	0.1333	26793064	intronic	NA	NA	NA	NA	#N/A
MRUC vs non-MRUC	NA	0.0002887	A	11022	0.133	26788153	intronic	NA	NA	NA	NA	#N/A
CD vs. Ctrl	rs73069538	0.000294111	G	92693	-0.056917783	26903237	intronic	NA	NA	NA	NA	0.1209
MRUC vs non-MRUC	NA	0.0002945	A	11022	0.1328	26800646	intronic	NA	NA	NA	NA	#N/A
MRUC vs non-MRUC	NA	0.0002946	A	11022	0.1328	26793094	intronic	NA	NA	NA	NA	#N/A

FIG. 1 (Continued)

PHENOTYPE	dbSNP	p_value	A1	n_miss	OR_Z_B	base_ pair_CH 7	snp_ location	cis_ eGENE	eqtl_beta	eqtl_p	priority	MAF
MRUC vs non-MRUC	NA	0.0002963	A	11022	0.1329	26816201	intronic	NA	NA	NA	NA	#N/A
MRUC vs non-MRUC	NA	0.0002984	A	11022	0.1328	26812754	intronic	NA	NA	NA	NA	#N/A
Paneth-D5 phenotype	rs17154322	0.0003028	G	155	0.5838	26714523	intronic	NA	NA	NA	NA	0.05105
Paneth-D5 phenotype	rs17154376	0.0003028	A	155	0.5838	26745464	intronic	NA	NA	NA	NA	0.05036
MRUC vs non-MRUC	NA	0.0003088	A	11022	-0.1325	26780199	intronic	NA	NA	NA	NA	#N/A
CD vs. Ctrl	rs513387	0.000311967	A	94086	-0.039367088	26823963	intronic	NA	NA	NA	NA	0.3249
MRUC vs non-MRUC	NA	0.0003125	A	11022	0.1322	26790969	intronic	NA	NA	NA	NA	#N/A
CD vs. Ctrl	rs55790519	0.00031304	C	94084	0.038808666	26927717	intronic	NA	NA	NA	NA	0.355
MRUC vs non-MRUC	NA	0.0003239	A	11022	0.132	26811840	intronic	NA	NA	NA	NA	#N/A
MRUC vs non-MRUC	NA	0.0003242	A	11022	-0.1319	26769702	intronic	NA	NA	NA	NA	#N/A
MRUC vs non-MRUC	NA	0.0003282	A	11022	0.1318	26793515	intronic	NA	NA	NA	NA	#N/A
MRUC vs non-MRUC	NA	0.0003283	A	11022	-0.1316	26793350	intronic	NA	NA	NA	NA	#N/A
MRUC vs non-MRUC	NA	0.0003288	A	11022	-0.1317	26800710	intronic	NA	NA	NA	NA	#N/A

FIG. 1 (Continued)

PHENOTYPE	dbSNP	p_value	A1	n_miss	OR_Z_B	base_ pair_CH 7	snp_ location	cis_ eGENE	eqtl_beta	eqtl_p	priority	MAF
MIRUC vs non-MIRUC	NA	0.0003294	A	11022	-0.1317	26798067	intronic	NA	NA	NA	NA	#N/A
MIRUC vs non-MIRUC	NA	0.000331	A	11022	-0.1305	26819774	intronic	NA	NA	NA	NA	#N/A
CD vs. Ctrl	rs73073796	0.000335215	A	86104	-0.055567818	26700439	intergenic	HOXA11, HOXA10, HOXA9	-0.0251998 0.03319054 , - 0.0784260 898118609 , - 0.1831879 51514832	0.03123705 95254648, 0.03319054 2567201, 0.04916874 54066987	0, 0, 0	0.1149
MIRUC vs non-MIRUC	NA	0.0003441	A	11022	0.1359	26777723	intronic	NA	NA	NA	NA	#N/A
MIRUC vs non-MIRUC	NA	0.0003482	A	11022	-0.1312	26794831	intronic	NA	NA	NA	NA	#N/A
Paneth-D3 phenotype	rs17154235	0.0003729	G	297	3.441	26692982	intergenic	NA	NA	NA	NA	0.02755
MIRUC vs non-MIRUC	NA	0.0003737	A	11022	0.1304	26789814	intronic	NA	NA	NA	NA	#N/A
IBD vs. Ctrl	rs503110	0.000382166	T	128433	-0.029637721	26857016	intronic	NA	NA	NA	NA	0.4998
CD vs. Ctrl	rs57135974	0.000387484	A	NA	0.064796568	26850699	intronic	NA	NA	NA	NA	0.2724
CD vs. Ctrl	rs1498922	0.000388623	G	94083	0.038212803	26932278	intronic	NA	NA	NA	NA	0.3549
CD vs. Ctrl	rs757129	0.000388789	C	94087	-0.037935957	26702506	intergenic	NA	NA	NA	NA	0.3632
MIRUC vs non-MIRUC	NA	0.0003986	A	11022	0.1298	26812428	intronic	NA	NA	NA	NA	#N/A

FIG. 1 (Continued)

PHENOTYPE	dbSNP	p_value	A1	n_miss	OR_Z_B	base_ pair_CH 7	snp_ location	cis_ eGENE	eqtl_beta	eqtl_p	priority	MAF
IBD vs. Ctrl	rs567124	0.000399802	A	124149	- 0.029968487	26845145	intronic	NA	NA	NA	NA	0.4873
OMPC UC vs. OMPC Ctrl	rs62457404	0.0004205	A	1273	2.763	27075533	intergenic	NA	NA	NA	NA	0.03729
MRUC vs non- MRUC	NA	0.0004207	A	11022	0.1295	26813025	intronic	NA	NA	NA	NA	#N/A
CD vs. Ctrl	rs17324488	0.000436986	G	94087	0.037881618	26933204	intronic	NA	NA	NA	NA	0.3544
CD vs. Ctrl	rs3934268	0.000459232	C	NA	0.063998847	26890572	intronic	NA	NA	NA	NA	0.2428
MRUC vs non- MRUC	NA	0.0004621	A	11022	0.1286	26811191	intronic	NA	NA	NA	NA	#N/A
IBD vs. Ctrl	rs757129	0.000472935	C	128424	- 0.030392548	26702506	intergenic	NA	NA	NA	NA	0.3632
MRUC vs non- MRUC	NA	0.0005117	A	11022	0.1278	26818890	intronic	NA	NA	NA	NA	#N/A
OMPC UC vs. OMPC Ctrl	rs17436757	0.0005426	G	1273	2.707	27049529	intergenic	NA	NA	NA	NA	0.03706
CD vs. Ctrl	rs2015649	0.000542883	G	NA	0.056365182	26780331	intronic	NA	NA	NA	NA	0.3655
MRUC vs non- MRUC	NA	0.0005453	A	11022	0.1269	26814394	intronic	NA	NA	NA	NA	#N/A
MRUC vs non- MRUC	NA	0.0005883	A	11022	0.1274	26816648	intronic	NA	NA	NA	NA	#N/A
MRUC vs non- MRUC	NA	0.0005919	A	11022	0.126	26814023	intronic	NA	NA	NA	NA	#N/A
OMPC UC vs. OMPC Ctrl	rs17437154	0.000592	A	1273	2.684	27125051	intergenic	NA	NA	NA	NA	0.03782
IGG Asca UC vs. IGA Asca Ctrl	rs17471095	0.0006016	C	1147	37.63	27024370	intronic	NA	NA	NA	NA	0.002623

FIG. 1 (Continued)

PHENOTYPE	dbSNP	p_value	A1	n_miss	OR_Z_B	base_ pair_CH 7	snp_ location	cis_ eGENE	eqtl_beta	eqtl_p	priority	MAF
MRUC vs non-MRUC	NA	0.0006151	A	11022	0.13	26776874	intronic	NA	NA	NA	NA	#N/A
OMPC UC vs. OMPC Ctrl	rs624448205	0.0006264	A	1273	2.676	26922612	intronic	NA	NA	NA	NA	0.03656
OMPC UC vs. OMPC Ctrl	rs624448207	0.0006264	A	1273	2.676	26926450	intronic	NA	NA	NA	NA	0.03657
Paneth-D3 phenotype	rs17436229	0.0006378	A	297	2.882	26959526	intronic	NA	NA	NA	NA	0.0319
MRUC vs non-MRUC	NA	0.0006743	A	11022	0.129	26776999	intronic	NA	NA	NA	NA	#N/A
MRUC vs non-MRUC	NA	0.0006911	A	11022	0.1288	26777849	intronic	NA	NA	NA	NA	#N/A
IBD vs. Ctrl	rs2769365	0.000711691	C	115505	- 0.029766543	26844616	intronic	NA	NA	NA	NA	0.4996
IBD vs. Ctrl	rs622011	0.000718234	G	128293	- 0.028245117	26855739	intronic	NA	NA	NA	NA	0.4996
OMPC UC vs. OMPC Ctrl	rs17448968	0.0007614	A	1273	2.627	27120334	intergenic	NA	NA	NA	NA	0.03807
L1_ileal	rs3801840	0.0007626	G	2162	1.305	26832986	intronic	NA	NA	NA	NA	0.2525
OMPC UC vs. OMPC Ctrl	rs62454370	0.0007943	A	1273	2.576	27098999	intergenic	NA	NA	NA	NA	0.03734
CD vs. Ctrl	rs1464969	0.000830338	C	94060	0.060046174	27026154	intronic	EVX1, NFE2L3	0.3943595 48260561, - 0.1041700 15067281	0.00410984 700729187, 0.03839726 97067958	0, 0	0.0819
IBD vs. Ctrl	rs471536	0.000839983	A	116383	- 0.029327903	26848685	intronic	NA	NA	NA	NA	0.4945

FIG. 1 (Continued)

PHENOTYPE	dbSNP	p_value	A1	n_miss	OR_Z_B	base_ pair_CH 7	snp_ location	cis_ eGENE	eqtl_beta	eqtl_p	priority	MAF
OMPC UC vs. OMPC Ctrl	rs79205492	0.0008469	G	1273	2.605	26936195	intronic	NA	NA	NA	NA	0.03734
OMPC UC vs. OMPC Ctrl	rs17426751	0.0008469	A	1273	2.605	26986060	intronic	NA	NA	NA	NA	0.03734
OMPC UC vs. OMPC Ctrl	rs17426772	0.0008469	G	1273	2.605	26991230	intronic	NA	NA	NA	NA	0.03734
L1_ileal	rs73069539	0.0008908	A	2162	1.305	26903661	intronic	HIBADH, HOXA11-AS	- 0.1186890 17417339, 0.04990810 0.0941114 404455934	0.04652407 2405745, 0.04990810 58041685	0, 0	0.2472
L1_ileal	rs10486485	0.0008966	A	2162	1.304	26900356	intronic	HIBADH, HOXA11-AS	- 0.1186890 17417339, 0.04990810 0.0941114 404455934	0.04652407 2405745, 0.04990810 58041685	0, 0	0.2478
L1_ileal	rs3801803	0.0008966	G	2162	1.304	26901740	intronic	HIBADH, HOXA11-AS	- 0.1186890 17417339, 0.04990810 0.0941114 404455934	0.04652407 2405745, 0.04990810 58041685	0, 0	0.2481
Perianal CD+ vs. Perianal CD-	NA	0.0009045	A	10738	1.219	26960847	intronic	NA	NA	NA	NA	#N/A
anti-TNF time to loss of response	rs17154461	0.000917639	A	243	3.31463	26800393	intronic	NA	NA	NA	NA	0.001501

FIG. 1 (Continued)

PHENOTYPE	dbSNP	p_value	A1	n_miss	OR_Z_B	base_ pair_CH 7	snp_ location	cis_ eGENE	eqtl_beta	eqtl_p	priority	MAF
OMPC UC vs. OMPC Ctrl	rs1560621	0.0009244	C	1273	2.583	26923382	intronic	NA	NA	NA	NA	0.03725
Paneth-D4 phenotype	rs1526318	0.0009529	A	296	15.9	27026223	intronic	NA	NA	NA	NA	0.001526
CD vs. Ctrl	rs10231161	0.000952934	C	NA	0.053663037	26710565	intronic	NA	NA	NA	NA	0.4581
MRUC vs non- MRUC	NA	0.0009532	A	11022	-0.1253	26774969	intronic	NA	NA	NA	NA	#N/A
OMPC UC vs. OMPC Ctrl	rs62454369	0.001064	A	1273	2.582	27098804	intergenic	NA	NA	NA	NA	0.03656
Surgery	rs6461964	0.001105	A	1032	0.744	26775702	intronic	NA	NA	NA	NA	0.4754
Paneth-D5 phenotype	rs3915203	0.001207	A	155	0.4794	27098702	intergenic	JAZF1	0.0429871 98	0.04054375 2	0	0.05144
Perianal CD+ vs. Perianal CD-	NA	0.00122	A	10738	1.208	27118974	intergenic	NA	NA	NA	NA	#N/A
CD vs. Ctrl	rs2391359	0.00122565	G	NA	0.049502206	26790786	intronic	NA	NA	NA	NA	0.4639
L1_ileal	rs12536560	0.00128	G	2162	1.292	26822876	intronic	NA	NA	NA	NA	0.2492
L1_ileal	rs73065517	0.001295	G	2160	1.292	26830555	intronic	NA	NA	NA	NA	0.2501
UC vs. Ctrl	rs188468488	0.001296973	G	95391	- 0.159105557	27109617	intergenic	NA	NA	NA	NA	0.01245
MRUC vs non- MRUC	NA	0.001298	A	11022	-0.1229	26827627	intronic	NA	NA	NA	NA	#N/A
CD vs. Ctrl	rs2712244	0.00130178	A	94065	0.035141152	26975932	intronic	NA	NA	NA	NA	0.3276
MRUC vs non- MRUC	NA	0.001329	A	11022	0.1226	26819917	intronic	NA	NA	NA	NA	#N/A
CD vs. Ctrl	rs2462910	0.001330787	A	94099	0.034910221	26969253	intronic	SNX10	0.0921909 76	0.04036737 8	0	0.3302

FIG. 1 (Continued)

PHENOTYPE	dbSNP	p_value	A1	n_miss	OR_Z_B	base_ pair_CH 7	snp_ location	cis_ eGENE	eqtl_beta	eqtl_p	priority	MAF
L1_ileal	rs17323934	0.001332	G	2162	1.293	26904330	UTR5	HIBADH, HOXA11-AS	- 0.1186890 17417339, 0.04990810 0.0941114 404455934	0.04652407 2405745, 0.04990810 58041685	0, 0	0.2438
L1_ileal	rs73069540	0.001332	A	2162	1.293	26904770	intronic	HIBADH, HOXA11-AS	- 0.1186890 17417339, 0.04990810 0.0941114 404455934	0.04652407 2405745, 0.04990810 58041685	0, 0	0.2438
L1_ileal	rs73069541	0.001332	G	2162	1.293	26904928	intronic	HIBADH, HOXA11-AS	- 0.1186890 17417339, 0.04990810 0.0941114 404455934	0.04652407 2405745, 0.04990810 58041685	0, 0	0.244
L1_ileal	rs3823938	0.001357	G	2162	1.287	26853741	intronic	NA	NA	NA	NA	0.2534
CD vs. Ctrl	rs10270187	0.001363911	C	89743	0.038094899	26885885	intronic	NA	NA	NA	NA	0.259
L1_ileal	rs10267950	0.001374	A	2162	1.29	26826757	intronic	NA	NA	NA	NA	0.2493
L1_ileal	rs10272303	0.001374	G	2162	1.29	26827815	intronic	NA	NA	NA	NA	0.2502
L1_ileal	rs1327988	0.001374	G	2162	1.29	26828965	intronic	NA	NA	NA	NA	0.2502
L1_ileal	rs3801844	0.001374	G	2162	1.29	26829759	intronic	NA	NA	NA	NA	0.2502
L1_ileal	rs3801843	0.001374	G	2162	1.29	26830201	intronic	NA	NA	NA	NA	0.2502
L1_ileal	rs3801842	0.001374	A	2162	1.29	26830263	intronic	NA	NA	NA	NA	0.2502
L1_ileal	rs1327989	0.001374	A	2162	1.29	26833563	intronic	NA	NA	NA	NA	0.2501
L1_ileal	rs10276471	0.001374	G	2162	1.29	26837940	intronic	NA	NA	NA	NA	0.2501
L1_ileal	rs3801850	0.001385	G	2162	1.289	26820577	intronic	NA	NA	NA	NA	0.2509

FIG. 1 (Continued)

PHENOTYPE	dbSNP	p_value	A1	n_miss	OR_Z_B	base_ pair_CH 7	snp_ location	cis_ eGENE	eqtl_beta	eqtl_p	priority	MAF
L1_ileal	rs3801822	0.001433	G	2160	1.289	26861201	intronic	NA	NA	NA	NA	0.2586
L1_ileal	rs10256250	0.001434	A	2160	1.288	26895080	intronic	NA	NA	NA	NA	0.2529
CD vs. Ctrl	rs17290728	0.001442919	C	94099	0.053138882	26712415	intronic	HNRNPA2B 1, HOXA11- AS	- 0.2523455 62761614, 0.1389458 52400567	0.00659779 123391432, 0.03950337 31354039	0, 0	0.1126
MRUC vs non- MRUC	NA	0.001449	A	11022	0.1178	26787836	intronic	NA	NA	NA	NA	#N/A
MRUC vs non- MRUC	NA	0.001502	A	11022	-0.1211	26835945	intronic	NA	NA	NA	NA	#N/A
CD vs. Ctrl	rs2712245	0.001507015	C	94081	0.034785673	26989211	intronic	NA	NA	NA	NA	0.3253
Surgery	rs6978504	0.001535	C	1032	0.7332	26695880	intergenic	JAZF1	- 0.0210221 26	0.04438306 4	0	0.3505
CD vs. Ctrl	rs213531	0.001562795	G	91200	- 0.033447084	26920494	intronic	NA	NA	NA	NA	0.4703
IBD vs. Ctrl	rs570840	0.001565502	C	127206	- 0.026505144	26862139	intronic	NA	NA	NA	NA	0.4989
L1_ileal	rs73065504	0.001569	G	2162	1.286	26825984	intronic	NA	NA	NA	NA	0.2497
CD vs. Ctrl	rs2960785	0.001587126	A	94094	-0.03240108	26952139	intronic	HOXA11-AS	- 0.0867804 19	0.04160811 7	0	0.4551
IBD vs. Ctrl	rs10486486	0.001587421	T	128426	0.027944567	26920621	intronic	NA	NA	NA	NA	0.351
IBD vs. Ctrl	rs73077525	0.001592965	C	127346	- 0.038256383	26778568	intronic	NA	NA	NA	NA	0.1383
L1_ileal	rs6972378	0.001624	G	2160	1.284	26753074	intronic	NPVF	0.1119454 61	0.00957578 4	0	0.2635
L1_ileal	rs10236221	0.001654	T	2161	1.283	26884671	intronic	NA	NA	NA	NA	0.2526

FIG. 1 (Continued)

PHENOTYPE	dbSNP	p_value	A1	n_miss	OR_Z_B	base_ pair_CH 7	snp_ location	cis_ eGENE	eqtl_beta	eqtl_p	priority	MAF
IBD vs. Ctrl	rs73069529	0.001654273	A	128361	- 0.039403598	26889376	intronic	NA	NA	NA	NA	0.1187
MRUC vs non-MRUC	NA	0.001658	A	11022	0.1201	26820850	intronic	NA	NA	NA	NA	#N/A
OMPC UC vs. OMPC Ctrl	rs62446164	0.001659	A	1273	2.519	26953819	intronic	NA	NA	NA	NA	0.03561
Paneth-D5 phenotype	rs17436215	0.001665	A	155	1.117	26958977	intronic	NA	NA	NA	NA	0.006975
L1_ileal	rs10486478	0.001673	A	2162	1.287	26819465	intronic	NA	NA	NA	NA	0.2502
L1_ileal	rs12532199	0.001692	G	2160	1.283	26854375	intronic	NA	NA	NA	NA	0.2527
CD vs. Ctrl	rs212839	0.001694773	C	93992	- 0.034972861	26700230	intergenic	NA	NA	NA	NA	0.3197
L1_ileal	rs10270187	0.001703	C	2162	1.282	26885885	intronic	NA	NA	NA	NA	0.259
L1_ileal	rs6951065	0.001717	G	2162	1.283	26756162	intronic	NPVF	0.1119454 61	0.00957578 4	0	0.2634
L1_ileal	rs6964817	0.001717	C	2162	1.283	26756424	intronic	NPVF	0.1119454 61	0.00957578 4	0	0.2628
CD vs. Ctrl	rs2693662	0.001718237	A	94066	0.034380722	26989564	intronic	NA	NA	NA	NA	0.325
L1_ileal	rs7785832	0.001743	G	2161	1.282	26852760	intronic	NA	NA	NA	NA	0.2529
MRUC vs non-MRUC	NA	0.001748	C	11022	0.1168	26702506	intergenic	NA	NA	NA	NA	#N/A
L1_ileal	rs4722644	0.001797	A	2162	1.281	26845386	intronic	NA	NA	NA	NA	0.2529
L1_ileal	rs12333525	0.001797	A	2162	1.281	26847762	intronic	NA	NA	NA	NA	0.2529
L1_ileal	rs73067443	0.001797	G	2162	1.281	26851074	intronic	NA	NA	NA	NA	0.2529
L1_ileal	rs3801837	0.001797	G	2162	1.281	26851361	intronic	NA	NA	NA	NA	0.2529
L1_ileal	rs3801836	0.001797	A	2162	1.281	26851400	intronic	NA	NA	NA	NA	0.2589
L1_ileal	rs17315334	0.001797	A	2162	1.281	26852860	intronic	NA	NA	NA	NA	0.2529
L1_ileal	rs73067456	0.001797	A	2162	1.281	26852998	intronic	NA	NA	NA	NA	0.2528

FIG. 1 (Continued)

PHENOTYPE	dbSNP	p_value	A1	n_miss	OR_Z_B	base_ pair_CH 7	snp_ location	cis_ eGENE	eqtl_beta	eqtl_p	priority	MAF
L1_ileal	rs3801831	0.001797	G	2162	1.281	26853470	intronic	NA	NA	NA	NA	0.2529
L1_ileal	rs3823936	0.001797	G	2162	1.281	26853830	intronic	NA	NA	NA	NA	0.2528
L1_ileal	rs3823931	0.001797	G	2162	1.281	26854026	intronic	NA	NA	NA	NA	0.2528
L1_ileal	rs10262414	0.001797	A	2162	1.281	26854266	intronic	NA	NA	NA	NA	0.2528
L1_ileal	rs3801829	0.001797	C	2162	1.281	26854996	intronic	NA	NA	NA	NA	0.2529
L1_ileal	rs6948584	0.001797	A	2162	1.281	26855732	intronic	NA	NA	NA	NA	0.2528
L1_ileal	rs3823930	0.001797	G	2162	1.281	26856525	intronic	NA	NA	NA	NA	0.2528
L1_ileal	rs3823929	0.001797	G	2162	1.281	26856600	intronic	NA	NA	NA	NA	0.253
L1_ileal	rs3801825	0.001797	T	2162	1.281	26856959	intronic	NA	NA	NA	NA	0.2529
L1_ileal	rs73067475	0.001797	A	2162	1.281	26857120	intronic	NA	NA	NA	NA	0.2528
L1_ileal	rs73067476	0.001797	G	2162	1.281	26857240	intronic	NA	NA	NA	NA	0.2528
L1_ileal	rs28404962	0.001797	G	2162	1.281	26860324	intronic	NA	NA	NA	NA	0.2529
L1_ileal	rs13438513	0.001797	C	2162	1.281	26860633	intronic	NA	NA	NA	NA	0.2528
L1_ileal	rs55739485	0.001797	G	2162	1.281	26860741	intronic	NA	NA	NA	NA	0.2528
L1_ileal	rs3801823	0.001797	G	2162	1.281	26861031	intronic	NA	NA	NA	NA	0.2528
L1_ileal	rs3801821	0.001797	A	2162	1.281	26861206	intronic	NA	NA	NA	NA	0.2528
L1_ileal	rs3801820	0.001797	G	2162	1.281	26861353	intronic	NA	NA	NA	NA	0.2528
L1_ileal	rs7785689	0.001797	A	2162	1.281	26861609	intronic	NA	NA	NA	NA	0.2519
L1_ileal	rs212848	0.0018	C	2162	1.281	26722155	intronic	NPVF	0.1119454 61	0.00957578 4	0	0.2643
L1_ileal	rs3801809	0.001807	A	2160	1.281	26895456	intronic	NA	NA	NA	NA	0.2529
IBD vs. Ctrl	rs12530718	0.001807863	A	128417	0.027570406	26931205	intronic	NA	NA	NA	NA	0.3542
L1_ileal	rs12536145	0.001809	T	2162	1.281	26894860	intronic	NA	NA	NA	NA	0.253
L1_ileal	rs10242572	0.001809	G	2162	1.281	26895065	intronic	NA	NA	NA	NA	0.2531
L1_ileal	rs3801807	0.001828	G	2162	1.28	26897439	intronic	NA	NA	NA	NA	0.2528
CD vs. Ctrl	rs12537323	0.001828604	A	NA	0.056541317	26854388	intronic	NA	NA	NA	NA	0.2549

FIG. 1 (Continued)

PHENOTYPE	dbSNP	p_value	A1	n_miss	OR_Z_B	base_ pair_CH 7	snp_ location	cis_ eGENE	eqtl_beta	eqtl_p	priority	MAF
L1_ileal	rs2189019	0.001867	G	2158	1.28	26798581	intronic	NA	NA	NA	NA	0.2635
L1_ileal	rs212850	0.001897	A	2162	1.28	26724279	intronic	NPVF	0.1119454 61	0.00957578 4	0	0.2642
L1_ileal	rs212856	0.001897	A	2162	1.28	26729205	intronic	NPVF	0.1119454 61	0.00957578 4	0	0.2643
L1_ileal	rs4719877	0.001897	A	2162	1.28	26736220	intronic	NPVF	0.1119454 61	0.00957578 4	0	0.2643
CD vs. Ctrl	rs774267	0.001903723	A	94052	- 0.031926511	26963514	intronic	HOXA11-AS	- 0.0913561 01	0.03421850 8	0	0.459
L1_ileal	rs3801813	0.001925	G	2162	1.279	26887069	intronic	NA	NA	NA	NA	0.2527
L1_ileal	rs17375272	0.001953	A	2162	1.279	26866497	intronic	NA	NA	NA	NA	0.2524
L1_ileal	rs10225700	0.001953	A	2162	1.279	26869880	intronic	NA	NA	NA	NA	0.2524
L1_ileal	rs10225904	0.001953	A	2162	1.279	26869888	intronic	NA	NA	NA	NA	0.2524
L1_ileal	rs12535784	0.001953	A	2162	1.279	26882067	intronic	NA	NA	NA	NA	0.2525
Surgery	rs13229947	0.001988	A	1032	0.7387	26767430	intronic	NA	NA	NA	NA	0.3419
OMPC UC vs. OMPC Ctrl	rs2301719	0.002001	A	1273	2.684	27070597	intergenic	NA	NA	NA	NA	0.03691
L1_ileal	rs3801812	0.002044	A	2162	1.277	26887615	intronic	NA	NA	NA	NA	0.2531
L1_ileal	rs10272603	0.002044	G	2162	1.277	26888277	intronic	NA	NA	NA	NA	0.2532
L1_ileal	rs17376018	0.002044	G	2162	1.277	26889862	intronic	NA	NA	NA	NA	0.2532
L1_ileal	rs2031811	0.002044	G	2162	1.277	26890672	intronic	NA	NA	NA	NA	0.2531
L1_ileal	rs7804620	0.002044	C	2162	1.277	26891831	intronic	NA	NA	NA	NA	0.2531
L1_ileal	rs10486483	0.002044	A	2162	1.277	26892440	intronic	NA	NA	NA	NA	0.2596
L1_ileal	rs12539719	0.002046	A	2162	1.278	26844852	intronic	NA	NA	NA	NA	0.2584
L1_ileal	rs3823934	0.002046	G	2162	1.278	26853934	intronic	NA	NA	NA	NA	0.2524
MRUC vs non- MRUC	NA	0.00206	A	11022	-0.1115	26857016	intronic	NA	NA	NA	NA	#N/A

FIG. 1 (Continued)

PHENOTYPE	dbSNP	p_value	A1	n_miss	OR_Z_B	base_ pair_CH 7	snp_ location	cis_ eGENE	eqtl_beta	eqtl_p	priority	MAF
PyodermaG	rs113248554	0.002071	A	1417	2.612	26823014	intronic	HOTAIRM1	0.2987379 04	0.01254707	0	0.08564
L1_ileal	rs73069507	0.002074	G	2162	1.277	26877536	intronic	NA	NA	NA	NA	0.2529
L1_ileal	rs73069510	0.002074	G	2162	1.277	26877567	intronic	NA	NA	NA	NA	0.2529
L1_ileal	rs3801816	0.002074	A	2162	1.277	26881177	intronic	NA	NA	NA	NA	0.2529
L1_ileal	rs3801815	0.002074	G	2162	1.277	26881292	intronic	NA	NA	NA	NA	0.253
Perianal CD+ vs. Perianal CD-	NA	0.002089	G	10738	0.8014	26714523	intronic	NA	NA	NA	NA	#N/A
L1_ileal	rs10281261	0.002096	A	2162	1.277	26789472	intronic	NA	NA	NA	NA	0.2639
L1_ileal	rs7457076	0.002096	G	2162	1.277	26793215	intronic	NA	NA	NA	NA	0.2639
L1_ileal	rs2189017	0.002096	A	2162	1.277	26795073	intronic	NA	NA	NA	NA	0.2639
L1_ileal	rs73061894	0.002096	G	2162	1.277	26802085	intronic	NA	NA	NA	NA	0.264
IBD vs. Ctrl	rs73069538	0.002096023	G	126677	- 0.038866084	26903237	intronic	NA	NA	NA	NA	0.1209
L1_ileal	rs12532796	0.002121	G	2161	1.277	26854828	intronic	NA	NA	NA	NA	0.2524
Surgery	rs1030648	0.002124	G	1032	0.7403	26802672	intronic	JAZF1	- 0.0216838 55	0.02995406 6	0	0.3526
IBD vs. Ctrl	rs78028110	0.002142962	A	128429	0.050610181	26784056	intronic	EVX1, KIAA0087	0.3013987 74811087, 0.0311722 0.02933705 066916883	0.02256077 80515621, 0.02933705 87330475	0, 0	0.07211
CD vs. Ctrl	rs2462908	0.002156739	A	92707	0.034688868	27127696	intergenic	SNX10	0.0877676 81	0.04810610 1	0	0.3165
OMPC UC vs. OMPC Ctrl	rs3801817	0.00216	A	1273	2.493	26880852	intronic	NA	NA	NA	NA	0.03495
Surgery	rs10227898	0.002167	G	1032	0.7412	26764618	intronic	JAZF1	- 0.0216838 55	0.02995406 6	0	0.3525

FIG. 1 (Continued)

PHENOTYPE	dbSNP	p_value	A1	n_miss	OR_Z_B	base_ pair_CH 7	snp_ location	cis_ eGENE	eqtl_beta	eqtl_p	priority	MAF
Surgery	rs10256799	0.002177	G	1031	0.7563	26818890	intronic	NA	NA	NA	NA	0.4881
L1_ileal	rs10272190	0.002177	A	2158	1.276	26887942	intronic	NA	NA	NA	NA	0.2532
IBD vs. Ctrl	rs17291131	0.002178897	A	127932	- 0.037835537	26729740	intronic	NA	NA	NA	NA	0.1203
Surgery	rs7795074	0.002186	A	1032	0.741	26742154	intronic	JAZF1	- 0.0216838 55	0.02995406 6	0	0.3527
L1_ileal	rs6461979	0.002189	G	2162	1.275	26888918	intronic	NA	NA	NA	NA	0.2522
L1_ileal	rs3213853	0.002192	G	2162	1.275	26893524	intronic	NA	NA	NA	NA	0.2533
L1_ileal	rs3801805	0.002192	G	2162	1.275	26897640	intronic	NA	NA	NA	NA	0.2535
L1_ileal	rs10266759	0.002223	A	2162	1.275	26855282	intronic	NA	NA	NA	NA	0.2527
L1_ileal	rs3801826	0.002223	A	2162	1.275	26856720	intronic	NA	NA	NA	NA	0.2526
L1_ileal	rs2106905	0.002229	A	2162	1.275	26766851	intronic	NA	NA	NA	NA	0.264
L1_ileal	rs4722630	0.002229	C	2162	1.275	26773364	intronic	NA	NA	NA	NA	0.264
IGG Asca UC vs. IGA Asca Ctrl	rs17471102	0.002289	G	1147	9.381	27028180	intronic	NA	NA	NA	NA	0.006314
IGG Asca UC vs. IGA Asca Ctrl	rs28357132	0.002289	G	1147	9.381	27123880	intergenic	NA	NA	NA	NA	0.00631
Surgery	rs2189016	0.002295	T	1032	0.7423	26785016	intronic	JAZF1	- 0.0216838 55	0.02995406 6	0	0.3514
Paneth-D2 phenotype	rs1526318	0.002311	A	296	22.37	27026223	intronic	NA	NA	NA	NA	0.001526
L1_ileal	rs73069533	0.002323	A	2162	1.274	26892325	intronic	NA	NA	NA	NA	0.2525
L1_ileal	rs76438067	0.002324	A	2162	1.277	26911904	intronic	NA	NA	NA	NA	0.2436
IBD vs. Ctrl	rs73067474	0.002326933	C	128422	- 0.037876825	26856632	intronic	NA	NA	NA	NA	0.1203
CD vs. Ctrl	rs10227553	0.002356503	C	94002	0.033118219	26997029	intronic	SNX10	0.0921909 76	0.04036737 8	0	0.3313

FIG. 1 (Continued)

PHENOTYPE	dbSNP	p_value	A1	n_miss	OR_Z_B	base_ pair_CH 7	snp_ location	cis_ eGENE	eqtl_beta	eqtl_p	priority	MAF
PyodermaG	rs1024453	0.002362	A	1415	2.591	26763002	intronic	HOTAIRM1 , HOXA3	0.3531020 16590976, 0.2389938 05558549	0.00281884 626161775, 0.04138231 74929522	0, 0	0.0855
L1_ileal	rs6461963	0.002362	G	2162	1.273	26772491	intronic	NA	NA	NA	NA	0.2641
CD vs. Ctrl	rs2428416	0.002363573	A	94091	0.033150857	27069689	intergenic	SNX10	0.0921909 76	0.04036737 8	0	0.3308
MRUC vs non- MRUC	NA	0.002368	A	11022	0.1102	26833021	intronic	NA	NA	NA	NA	#N/A
L1_ileal	rs7804356	0.002386	G	2143	1.273	26891665	intronic	NA	NA	NA	NA	0.2533
Surgery	rs12668948	0.002397	G	1032	0.7589	26744101	intronic	NA	NA	NA	NA	0.4708
L1_ileal	rs727450	0.002408	G	2162	1.272	26787642	intronic	NA	NA	NA	NA	0.2633
L1_ileal	rs7805778	0.002417	A	2162	1.276	26694926	intergenic	NPVF	0.1082079 45	0.01310842 7	0	0.2574
L1_ileal	rs212838	0.002423	A	2162	1.275	26698194	intergenic	NPVF	0.1082079 45	0.01310842 7	0	0.2572
Surgery	rs7802852	0.002424	G	1031	0.7594	26787836	intronic	NA	NA	NA	NA	0.4701
Surgery	rs212846	0.002463	G	1032	0.76	26721613	intronic	NA	NA	NA	NA	0.473
MRUC vs non- MRUC	NA	0.002529	A	11022	2.216	27050106	intergenic	NA	NA	NA	NA	#N/A
L1_ileal	rs6971397	0.00256	G	2162	1.271	26782564	intronic	NA	NA	NA	NA	0.2634
IBD vs. Ctrl	rs667841	0.002571107	A	120151	- 0.025999016	26851231	intronic	NA	NA	NA	NA	0.4998
Surgery	rs7802688	0.002573	A	1032	0.7445	26785832	intronic	JAZF1	- 0.0216838 55	0.02995406 6	0	0.3514
Surgery	rs212849	0.002587	A	1032	0.7606	26722643	intronic	NA	NA	NA	NA	0.4712
CD vs. Ctrl	rs10085721	0.002603399	T	94085	0.032113123	26819917	intronic	NA	NA	NA	NA	0.3684

FIG. 1 (Continued)

PHENOTYPE	dbSNP	p_value	A1	n_miss	OR_Z_B	base_ pair_CH 7	snp_ location	cis_ eGENE	eqtl_beta	eqtl_p	priority	MAF
L1_ileal	rs3801833	0.002621	A	2157	1.27	26852212	intronic	NA	NA	NA	NA	0.2528
MRUC Time to Colectomy <60 months vs >60 months	NA	0.002653	A	3931	-2.1769	27093427	intergenic	NA	NA	NA	NA	#N/A
Surgery	rs17372780	0.002656	C	1031	0.7452	26804018	intronic	JAZF1	- 0.0216838 55	0.02995406 6	0	0.3518
L1_ileal	rs3757654	0.002657	A	2161	1.273	26711104	intronic	NPVF	0.1095317 04	0.01169563 2	0	0.258
MRUC vs non- MRUC	NA	0.002683	A	11022	-0.109	26855739	intronic	NA	NA	NA	NA	#N/A
Surgery	rs212853	0.002729	A	1032	0.7618	26726320	intronic	NA	NA	NA	NA	0.4703
Surgery	rs212855	0.002729	A	1032	0.7618	26727362	intronic	NA	NA	NA	NA	0.4701
Surgery	rs2299102	0.002729	G	1032	0.7618	26747064	intronic	NA	NA	NA	NA	0.4708
IBD vs. Ctrl	rs1327988	0.002757116	G	128413	0.028860399	26828965	intronic	NA	NA	NA	NA	0.2502
IBD vs. Ctrl	rs10270187	0.002758405	C	124040	0.029179808	26885885	intronic	NA	NA	NA	NA	0.259
Perianal CD+ vs. Perianal CD-	NA	0.002761	C	10738	1.15	26712415	intronic	NA	NA	NA	NA	#N/A
Surgery	rs212858	0.002783	T	1032	0.7623	26730869	intronic	NA	NA	NA	NA	0.4701
Surgery	rs7803699	0.002784	G	1032	0.7471	26814173	intronic	JAZF1	- 0.0216838 55	0.02995406 6	0	0.3513
Surgery	rs763616	0.002789	T	1032	0.7466	26784600	intronic	JAZF1	- 0.0216838 55	0.02995406 6	0	0.3521
Surgery	rs1023712	0.002789	C	1032	0.7466	26803163	intronic	JAZF1	- 0.0216838 55	0.02995406 6	0	0.3521

FIG. 1 (Continued)

PHENOTYPE	dbSNP	p_value	A1	n_miss	OR_Z_B	base_ pair_CH 7	snp_ location	cis_ eGENE	eqtl_beta	eqtl_p	priority	MAF
Surgery	rs3801857	0.002789	A	1032	0.7466	26811484	intronic	JAZF1	- 0.0216838 55	0.02995406 6	0	0.3519
Surgery	rs1123156	0.002789	A	1032	0.7466	26817044	intronic	JAZF1	- 0.0216838 55	0.02995406 6	0	0.352
Surgery	rs11980739	0.002789	G	1032	0.7466	26818164	intronic	JAZF1	- 0.0216838 55	0.02995406 6	0	0.3521
IBD vs. Ctrl	rs6962680	0.002811677	G	128419	0.026389497	26918106	intronic	NA	NA	NA	NA	0.3545
Surgery	rs13186	0.002841	C	1032	0.7614	26707657	UTR3	NFE2L3	0.0977858 55	0.03897937 3	0	0.4688
PyodermaG	rs1024452	0.002847	A	1420	2.541	26763282	intronic	HOTAIRM1 , HOXA3	0.3531020 16590976, 0.2389938 05558549	0.00281884 626161775, 0.04138231 74929522	0, 0	0.08811
Paneth-D5 phenotype	rs34899291	0.002864	A	155	0.4259	27116185	intergenic	HOXA10, JAZF1	0.1018469 82683212, 0.0396480 477490366	0.02871331 00933085, 0.04096675 16622906	0, 0	0.06614
CD vs. Ctrl	rs2712246	0.002883551	G	94076	0.032367099	27023254	intronic	SNX10	0.0920098 76	0.03893039 9	0	0.3326
Surgery	rs212852	0.002889	G	1032	0.7637	26725984	intronic	NA	NA	NA	NA	0.4723
Surgery	rs2282906	0.002889	A	1032	0.7637	26747964	intronic	NA	NA	NA	NA	0.4725
L1_ileal	rs3801814	0.002939	C	2162	1.266	26881302	intronic	NA	NA	NA	NA	0.2524
PyodermaG	rs11982489	0.00296	G	1421	2.532	26722483	intronic	HOTAIRM1 , HOXA3	0.3531020 16590976, 0.2389938 05558549	0.00281884 626161775, 0.04138231 74929522	0, 0	0.0878

FIG. 1 (Continued)

PHENOTYPE	dbSNP	p_value	A1	n_miss	OR_Z_B	base_ pair_CH 7	snp_ location	cis_ eGENE	eqtl_beta	eqtl_p	priority	MAF
MRUC vs non-MRUC	NA	0.002992	A	11022	0.1074	26867957	intronic	NA	NA	NA	NA	#N/A
MRUC vs non-MRUC	NA	0.003015	C	11022	-0.1158	26801250	intronic	NA	NA	NA	NA	#N/A
CD vs. Ctrl	rs213514	0.003037775	A	94080	-0.030539495	26931894	intronic	NA	NA	NA	NA	0.4657
Surgery	rs212847	0.003048	G	1032	0.7646	26722010	intronic	NA	NA	NA	NA	0.472
Surgery	rs7782621	0.003062	G	1032	0.7484	26790937	intronic	JAZF1	-0.0216838 55	0.02995406 6	0	0.3518
Surgery	rs1468203	0.003062	C	1032	0.7484	26791287	intronic	JAZF1	-0.0216838 55	0.02995406 6	0	0.3518
CD vs. Ctrl	rs1327988	0.003105187	G	94078	0.03474509	26828965	intronic	NA	NA	NA	NA	0.2502
Surgery	rs7811764	0.003122	A	1032	0.765	26742148	intronic	NA	NA	NA	NA	0.4701
Surgery	rs56374720	0.003123	A	1032	0.7489	26815776	intronic	JAZF1	-0.0216838 55	0.02995406 6	0	0.352
CD vs. Ctrl	rs2465274	0.003198937	A	94097	0.032636414	27108127	intergenic	NA	NA	NA	NA	0.3156
PyodermaG	rs6967749	0.003211	G	1421	2.49	26713194	intronic	HOTAIRM1 , HOXA3	0.3531020 16590976, 0.2389938 0.04138231 05558549	0.00281884 626161775, 0.04138231 74929522	0, 0	0.08843
PyodermaG	rs1129771	0.003211	A	1421	2.49	26765596	exonic	HOTAIRM1 , HOXA3	0.3531020 16590976, 0.2389938 0.04138231 05558549	0.00281884 626161775, 0.04138231 74929522	0, 0	0.08817

FIG. 1 (Continued)

PHENOTYPE	dbSNP	p_value	A1	n_miss	OR_Z_B	base_ pair_CH 7	snp_ location	cis_ eGENE	eqtl_beta	eqtl_p	priority	MAF
PyodermaG	rs11976472	0.003211	C	1421	2.49	26765987	intronic	HOTAIRM1 , HOXA3	0.3531020 16590976, 0.2389938 05558549	0.00281884 626161775, 0.04138231 74929522	0, 0	0.08833
PyodermaG	rs11973332	0.003211	A	1421	2.49	26777367	intronic	HOTAIRM1 , HOXA3	0.3531020 16590976, 0.2389938 05558549	0.00281884 626161775, 0.04138231 74929522	0, 0	0.08818
PyodermaG	rs73683510	0.003211	C	1421	2.49	26792481	intronic	HOTAIRM1 , HOXA3	0.3531020 16590976, 0.2389938 05558549	0.00281884 626161775, 0.04138231 74929522	0, 0	0.08531
Surgery	rs4719879	0.003216	A	1032	0.7652	26780199	intronic	NA	NA	NA	NA	0.4709
Surgery	rs3801860	0.003216	A	1032	0.7652	26800710	intronic	NA	NA	NA	NA	0.4705
Surgery	rs7795313	0.003225	C	1032	1.31	26775626	intronic	NA	NA	NA	NA	0.4893
Surgery	rs5012512	0.00324	C	1032	0.7664	26812428	intronic	NA	NA	NA	NA	0.4714
Surgery	rs6461971	0.00324	G	1032	0.7664	26814023	intronic	NA	NA	NA	NA	0.4714
CD vs. Ctrl	rs2693659	0.003243526	A	94078	0.032084093	27093415	intergenic	SNX10	0.0920098 76	0.03893039 9	0	0.3326
Surgery	rs212842	0.003323	A	1032	0.7641	26711817	intronic	NA	NA	NA	NA	0.4644
MRUC vs non-MRUC	NA	0.003341	A	11022	0.1064	26897553	intronic	NA	NA	NA	NA	#N/A
PyodermaG	rs11978456	0.003376	G	1421	2.479	26764421	intronic	HOTAIRM1 , HOXA3	0.3531020 16590976, 0.2389938 05558549	0.00281884 626161775, 0.04138231 74929522	0, 0	0.08857

FIG. 1 (Continued)

PHENOTYPE	dbSNP	p_value	A1	n_miss	OR_Z_B	base_ pair_CH 7	snp_ location	cis_ eGENE	eqtl_beta	eqtl_p	priority	MAF
PyodermaG	rs7780206	0.003376	G	1421	2.479	26772774	intronic	HOTAIRM1 , HOXA3	0.3531020 16590976, 0.2389938 05558549	0.00281884 626161775, 0.04138231 74929522	0, 0	0.08579
Surgery	rs1548478	0.003413	C	1029	0.7671	26788153	intronic	NA	NA	NA	NA	0.4702
CD vs. Ctrl	rs213530	0.00342588	A	92682	-0.03052811	26920314	intronic	NA	NA	NA	NA	0.4664
Surgery	rs10261915	0.003451	G	1032	0.7673	26814630	intronic	NA	NA	NA	NA	0.4696
MIRUC vs non-MRUC	NA	0.003468	A	11022	0.1061	26845145	intronic	NA	NA	NA	NA	#N/A
CD vs. Ctrl	rs10256250	0.003471787	A	93174	0.034586712	26895080	intronic	NA	NA	NA	NA	0.2529
IBD vs. Ctrl	rs11770344	0.003474674	A	NA	- 0.035963152	26755001	intronic	NA	NA	NA	NA	0.445
CD vs. Ctrl	rs2693668	0.003497468	G	94097	0.031732454	27013433	intronic	SNX10	0.0920098 76	0.03893039 9	0	0.3316
Surgery	rs3801854	0.0035	G	1032	0.7676	26812754	intronic	NA	NA	NA	NA	0.4692
Surgery	rs3801853	0.0035	G	1032	0.7676	26813025	intronic	NA	NA	NA	NA	0.4692
Surgery	rs12700761	0.003524	G	1032	0.767	26793515	intronic	NA	NA	NA	NA	0.4706
Surgery	rs6970591	0.003524	G	1032	0.767	26795244	intronic	NA	NA	NA	NA	0.4708
IBD vs. Ctrl	rs17324488	0.003533153	G	128422	0.025777307	26933204	intronic	NA	NA	NA	NA	0.3544
IBD vs. Ctrl	rs1498922	0.003575731	G	128424	0.025732313	26932278	intronic	NA	NA	NA	NA	0.3549
Surgery	rs2237328	0.003608	T	1032	0.7685	26740461	intronic	NA	NA	NA	NA	0.4708
Surgery	rs58988613	0.003673	A	1032	0.7684	26769702	intronic	NA	NA	NA	NA	0.4706
Surgery	rs2023819	0.003673	A	1032	0.7684	26798067	intronic	NA	NA	NA	NA	0.4701
Surgery	rs891874	0.003673	G	1032	0.7684	26811191	intronic	NA	NA	NA	NA	0.4702
Surgery	rs2391360	0.003705	G	1032	0.7686	26816201	intronic	NA	NA	NA	NA	0.4699
Surgery	rs567124	0.003798	A	1028	1.294	26845145	intronic	NA	NA	NA	NA	0.4873

FIG. 1 (Continued)

PHENOTYPE	dbSNP	p_value	A1	n_miss	OR_Z_B	base_ pair_CH 7	snp_ location	cis_ eGENE	eqtl_beta	eqtl_p	priority	MAF
Perianal CD+ vs. Perianal CD-	NA	0.003806	A	10738	0.8117	26745464	intronic	NA	NA	NA	NA	#N/A
PyodermaG	rs11971098	0.00383	G	1421	2.473	26699061	intergenic	HOTAIRM1	0.3272394 97	0.00540630 4	0	0.08914
Surgery	rs3801864	0.003831	A	1032	0.7694	26794831	intronic	NA	NA	NA	NA	0.4694
Surgery	rs12700755	0.003855	A	1032	0.77	26762452	intronic	NA	NA	NA	NA	0.4711
IBD vs. Ctrl	rs73075509	0.003934043	A	128412	- 0.035418057	26719824	intronic	NA	NA	NA	NA	0.1205
IBD vs. Ctrl	rs55790519	0.003936871	C	128416	0.025466209	26927717	intronic	NA	NA	NA	NA	0.355
MRUC vs non- MRUC	NA	0.003944	A	11022	0.2926	26795244	intronic	NA	NA	NA	NA	#N/A
IBD vs. Ctrl	rs3801825	0.003970997	T	128440	0.027759065	26856959	intronic	NA	NA	NA	NA	0.2529
CD vs. Ctrl	rs10244751	0.003998661	A	92639	0.031777859	26950287	intronic	SNX10	0.0921909 76	0.04036737 8	0	0.3301
Surgery	rs7807640	0.004063	G	1032	0.7714	26814394	intronic	NA	NA	NA	NA	0.4699
Surgery	rs212844	0.004072	C	1032	0.7713	26716458	intronic	NA	NA	NA	NA	0.4716
CD vs. Ctrl	rs3801825	0.004095178	T	94098	0.033709719	26856959	intronic	NA	NA	NA	NA	0.2529
PyodermaG	rs7777645	0.004126	G	1421	2.408	26750913	intronic	HOTAIRM1 , HOXA3	0.3531020 16590976, 0.2389938 05558549	0.00281884 626161775, 0.04138231 74929522	0, 0	0.08892
Asca UC vs. Asca Ctrl	rs74471327	0.004131	A	1147	1.867	26936046	intronic	NA	NA	NA	NA	0.04567
Surgery	rs6973237	0.00416	C	1032	0.7713	26800646	intronic	NA	NA	NA	NA	0.47
Surgery	rs891875	0.00416	G	1032	0.7713	26811306	intronic	NA	NA	NA	NA	0.4699
Surgery	rs744611	0.00416	G	1032	0.7713	26811840	intronic	NA	NA	NA	NA	0.4698
Surgery	rs3801855	0.00416	G	1032	0.7713	26812669	intronic	NA	NA	NA	NA	0.47

FIG. 1 (Continued)

PHENOTYPE	dbSNP	p_value	A1	n_miss	OR_Z_B	base_ pair_CH 7	snp_ location	cis_ eGENE	eqtl_beta	eqtl_p	priority	MAF
Surgery	rs4345466	0.00416	G	1032	0.7713	26815636	intronic	NA	NA	NA	NA	0.4699
Surgery	rs10951149	0.00416	G	1032	0.7713	26815857	intronic	NA	NA	NA	NA	0.4699
Surgery	rs1123158	0.00416	G	1032	0.7713	26816648	intronic	NA	NA	NA	NA	0.47
Surgery	rs11770043	0.004217	G	1032	0.7718	26789814	intronic	NA	NA	NA	NA	0.4723
Surgery	rs12700759	0.004217	A	1032	0.7718	26793350	intronic	NA	NA	NA	NA	0.4723
anti-TNF time to loss of response	rs17154461	0.00423278	A	344	2.86027	26800393	intronic	NA	NA	NA	NA	0.001501
CD vs. Ctrl	rs74471327	0.004248026	A	94099	0.070120372	26936046	intronic	NA	NA	NA	NA	0.04567
MRUC vs non- MRUC	NA	0.004358	A	11022	0.1127	26738984	intronic	NA	NA	NA	NA	#N/A
CD vs. Ctrl	rs2462904	0.004455136	G	94089	0.030901076	26966326	intronic	SNX10	0.0921909 76	0.04036737 8	0	0.3334
Surgery	rs687254	0.004485	G	1032	1.297	26819774	intronic	NA	NA	NA	NA	0.4863
CD vs. Ctrl	rs2253415	0.004507368	G	94094	0.030922119	27034947	upstream	SNX10	0.0921909 76	0.04036737 8	0	0.3331
PyodermaG	rs7809419	0.004511	G	1421	2.417	26811564	intronic	HOTAIRM1	0.3307590 01	0.00385504 1	0	0.09361
CD vs. Ctrl	rs2712234	0.004517263	G	94075	0.031582437	27126324	intergenic	SNX10	0.0877676 81	0.04810610 1	0	0.3223
I2 CD vs. I2 Ctrl	rs117032411	0.004524	A	1792	1.757	26989363	intronic	NA	NA	NA	NA	0.02847
L3 B1 vs non-IBD ctrl	rs757129	0.004534	C	3327	1.22	26702506	intergenic	NA	NA	NA	NA	0.3632
Surgery	rs12700758	0.00455	G	1032	0.7731	26790969	intronic	NA	NA	NA	NA	0.47
Surgery	rs3801866	0.00455	A	1032	0.7731	26792512	intronic	NA	NA	NA	NA	0.4699
Surgery	rs11773029	0.00455	G	1032	0.7731	26793064	intronic	NA	NA	NA	NA	0.47
Surgery	rs11773050	0.00455	G	1032	0.7731	26793094	intronic	NA	NA	NA	NA	0.47
Surgery	rs12700760	0.00455	T	1032	0.7731	26793448	intronic	NA	NA	NA	NA	0.4703

FIG. 1 (Continued)

PHENOTYPE	dbSNP	p_value	A1	n_miss	OR_Z_B	base_ pair_CH 7	snp_ location	cis_ eGENE	eqtl_beta	eqtl_p	priority	MAF
Paneth-D2 phenotype	rs17436222	0.004579	G	297	14.85	26959067	intronic	NA	NA	NA	NA	0.00494
IBD vs. Ctrl	rs12536560	0.004579652	G	128008	0.027406116	26822876	intronic	NA	NA	NA	NA	0.2492
IBD vs. Ctrl	rs2769364	0.004629916	C	121885	- 0.024378799	26844468	intronic	NA	NA	NA	NA	0.4991
IBD vs. Ctrl	rs116887315	0.004656103	G	127377	- 0.098198802	26695781	intergenic	NA	NA	NA	NA	0.02003
MRUC Time to Colectomy <60 months vs >60 months	NA	0.004739	A	3931	-0.1603	26819774	intronic	NA	NA	NA	NA	#N/A
CD vs. Ctrl	rs79497972	0.00481393	A	90933	0.213463355	26769022	intronic	NA	NA	NA	NA	0.003823
IBD vs. Ctrl	rs10256250	0.004840749	A	127508	0.02734569	26895080	intronic	NA	NA	NA	NA	0.2529
PyodermaG	rs73683496	0.004866	G	1421	2.372	26701494	intergenic	HOTAIRM1	0.3272394 97	0.00540630 4	0	0.0893
MRUC vs non-MRUC	NA	0.004874	A	11022	-0.1021	26848278	intronic	NA	NA	NA	NA	#N/A
IBD vs. Ctrl	rs6964817	0.004919904	C	127999	0.026682227	26756424	intronic	NPVF	0.1119454 61	0.00957578 4	0	0.2628
CD vs. Ctrl	rs79445145	0.004983428	G	94099	-0.05903858	26752960	intronic	NA	NA	NA	NA	0.05942
PyodermaG	rs73683491	0.00501	G	1421	2.365	26695578	intergenic	HOTAIRM1	0.3272394 97	0.00540630 4	0	0.0893
PyodermaG	rs11971041	0.00501	G	1421	2.365	26698848	intergenic	HOTAIRM1	0.3272394 97	0.00540630 4	0	0.08968
PyodermaG	rs7799519	0.00501	G	1421	2.365	26699295	intergenic	HOTAIRM1	0.3272394 97	0.00540630 4	0	0.08964

FIG. 1 (Continued)

PHENOTYPE	dbSNP	p_value	A1	n_miss	OR_Z_B	base_ pair_CH 7	snp_ location	cis_ eGENE	eqtl_beta	eqtl_p	priority	MAF
MRUC Time to Colectomy <60 months vs >60 months	NA	0.005041	A	3931	-0.1591	26735911	intronic	NA	NA	NA	NA	#N/A
Perianal CD+ vs. Perianal CD-	NA	0.005077	A	10738	1.187	26721827	intronic	NA	NA	NA	NA	#N/A
PDM	rs73075509	0.005083	A	2093	1.341	26719824	intronic	NA	NA	NA	NA	0.1205
PDM	rs17291131	0.005083	A	2093	1.341	26729740	intronic	NA	NA	NA	NA	0.1203
L3_ ileocolonic	rs73069539	0.005123	A	2162	0.8225	26903661	intronic	HIBADH, HOXA11-AS	- 0.1186890 17417339, 0.04990810 0.0941114 404455934	0.04652407 2405745, 0.04990810 58041685	0, 0	0.2472
CD vs. Ctrl	rs12536560	0.005160985	G	93836	0.032954254	26822876	intronic	NA	NA	NA	NA	0.2492
OMPC UC vs. OMPC Ctrl	rs62448202	0.005169	G	1273	2.27	26912774	intronic	NA	NA	NA	NA	0.03288
OMPC UC vs. OMPC Ctrl	rs62448203	0.005169	A	1273	2.27	26914277	intronic	NA	NA	NA	NA	0.03298
OMPC UC vs. OMPC Ctrl	rs62448204	0.005169	G	1273	2.27	26914634	intronic	NA	NA	NA	NA	0.03283
MRUC vs non- MRUC	NA	0.0053	A	11022	2.428	26942369	intronic	NA	NA	NA	NA	#N/A
MRUC time to colectomy	NA	0.005312	A	6326	-2.8842	26747337	intronic	NA	NA	NA	NA	#N/A
Surgery	rs7802771	0.005463	A	1032	1.288	26734838	intronic	NA	NA	NA	NA	0.4931

FIG. 1 (Continued)

PHENOTYPE	dbSNP	p_value	A1	n_miss	OR_Z_B	base_ pair_CH 7	snp_ location	cis_ eGENE	eqtl_beta	eqtl_p	priority	MAF
L2 B1 vs non-IBD ctrl	rs17154376	0.005483	A	3008	1.691	26745464	intronic	NA	NA	NA	NA	0.05036
MRUC vs non- MRUC	NA	0.005588	A	11022	2.413	27124817	intergenic	NA	NA	NA	NA	#N/A
L3_ileocolonic	rs3801840	0.005672	G	2162	0.8266	26832986	intronic	NA	NA	NA	NA	0.2525
CD vs. Ctrl	rs2712248	0.005688595	G	94093	0.030420291	27120689	intergenic	SNX10	0.0877676 81	0.04810610 1	0	0.3221
Surgery	rs622011	0.005798	G	1032	1.278	26855739	intronic	NA	NA	NA	NA	0.4996
Surgery	rs503110	0.005798	T	1032	1.278	26857016	intronic	NA	NA	NA	NA	0.4998
L3_ileocolonic	rs10236221	0.005827	T	2161	0.827	26884671	intronic	NA	NA	NA	NA	0.2526
Surgery	rs2769364	0.005834	C	1032	1.278	26844468	intronic	NA	NA	NA	NA	0.4991
MRUC vs non- MRUC	NA	0.00584	C	11022	-0.1085	26794980	intronic	NA	NA	NA	NA	#N/A
Surgery	rs475238	0.005841	G	1032	1.278	26848278	intronic	NA	NA	NA	NA	0.4999
CD vs. Ctrl	rs77900944	0.005920699	C	94094	- 0.066915549	26866982	intronic	NA	NA	NA	NA	0.04169
L3_ileocolonic	rs3801813	0.005922	G	2162	0.8273	26887069	intronic	NA	NA	NA	NA	0.2527
CD vs. Ctrl	rs6964817	0.0059337917	C	93827	0.031900281	26756424	intronic	NPVF	0.1119454 61	0.00957578 4	0	0.2628
CD vs. Ctrl	rs12539719	0.005982096	A	89813	0.032745505	26844852	intronic	NA	NA	NA	NA	0.2584
L3_ileocolonic	rs10486485	0.006048	A	2162	0.826	26900356	intronic	HIBADH, HOXA11-AS	- 0.1186890 17417339, 0.0941114 404455934	0.04652407 2405745, 0.04990810 58041685	0, 0	0.2478

FIG. 1 (Continued)

PHENOTYPE	dbSNP	p_value	A1	n_miss	OR_Z_B	base_ pair_CH 7	snp_ location	cis_ eGENE	eqtl_beta	eqtl_p	priority	MAF
L3_ileocolonic	rs3801803	0.006048	G	2162	0.826	26901740	intronic	HIBADH, HOXA11-AS	- 0.1186890 17417339, 0.04990810 0.0941114 404455934	0.04652407 2405745, 0.04990810 58041685	0, 0	0.2481
L3_ileocolonic	rs6461979	0.006051	G	2162	0.8276	26888918	intronic	NA	NA	NA	NA	0.2522
L3_ileocolonic	rs10270187	0.006076	C	2162	0.8278	26885885	intronic	NA	NA	NA	NA	0.259
IBD vs. Ctrl	rs10231161	0.006093546	C	NA	0.034474094	26710565	intronic	NA	NA	NA	NA	0.4581
Surgery	rs3801872	0.006097	C	1032	1.284	26744599	intronic	NA	NA	NA	NA	0.493
Surgery	rs2299101	0.006097	A	1032	1.284	26747041	intronic	NA	NA	NA	NA	0.4928
MRUC Time to Colectomy <60 months vs >60 months	NA	0.0061	A	3931	-0.3563	26866982	intronic	NA	NA	NA	NA	#N/A
Paneth-D2 phenotype	rs79445145	0.006104	G	297	3.926	26752960	intronic	NA	NA	NA	NA	0.05942
Surgery	rs212851	0.006114	A	1032	1.284	26725389	intronic	NA	NA	NA	NA	0.4928
anti-TNF time to loss of response	rs10280775	0.00622954	G	344	2.73545	26692741	intergenic	NA	NA	NA	NA	0.000819 5
anti-TNF time to loss of response	rs10273840	0.00622954	A	344	2.73545	26736943	intronic	NA	NA	NA	NA	0.000920 1
anti-TNF time to loss of response	rs12334046	0.00622954	A	344	2.73545	26784800	intronic	NA	NA	NA	NA	0.000737 6
anti-TNF time to loss of response	rs10486476	0.00622954	C	344	2.73545	26788223	intronic	NA	NA	NA	NA	0.000737 6

FIG. 1 (Continued)

PHENOTYPE	dbSNP	p_value	A1	n_miss	OR_Z_B	base_ pair_CH 7	snp_ location	cis_ eGENE	eqtl_beta	eqtl_p	priority	MAF
anti-TNF time to loss of response	rs10265721	0.00622954	A	344	2.73545	26789405	intronic	NA	NA	NA	NA	0.000819 5
anti-TNF time to loss of response	rs10231691	0.00622954	G	344	2.73545	26792305	intronic	NA	NA	NA	NA	0.000737 6
anti-TNF time to loss of response	rs10258711	0.00622954	G	344	2.73545	26803600	intronic	NA	NA	NA	NA	0.000737 6
anti-TNF time to loss of response	rs10258868	0.00622954	G	344	2.73545	26803724	intronic	NA	NA	NA	NA	0.000737 6
B2	rs1464969	0.006246	C	2170	1.409	27026154	intronic	EVX1, NFE2L3	0.3943595 48260561, - 0.1041700 15067281	0.00410984 700729187, 0.03839726 97067958	0, 0	0.0819
L3_ileocolonic	rs17323934	0.006296	G	2162	0.8266	26904330	UTR5	HIBADH, HOXA11-AS	- 0.1186890 17417339, 0.0941114 404455934	0.04652407 2405745, 0.04990810 58041685	0, 0	0.2438
L3_ileocolonic	rs73069540	0.006296	A	2162	0.8266	26904770	intronic	HIBADH, HOXA11-AS	- 0.1186890 17417339, 0.0941114 404455934	0.04652407 2405745, 0.04990810 58041685	0, 0	0.2438

FIG. 1 (Continued)

PHENOTYPE	dbSNP	p_value	A1	n_miss	OR_Z_B	base_ pair_CH 7	snp_ location	cis_ eGENE	eqtl_beta	eqtl_p	priority	MAF
L3_ileocolonic	rs73069541	0.006296	G	2162	0.8266	26904928	intronic	HIBADH, HOXA11-AS	- 0.1186890 17417339, 0.04990810 0.0941114 404455934	0.04652407 2405745, 0.04990810 58041685	0, 0	0.244
MRUC vs non- MRUC	NA	0.006323	A	11022	0.2764	26814630	intronic	NA	NA	NA	NA	#N/A
L3_ileocolonic	rs7804356	0.006332	G	2143	0.8279	26891665	intronic	NA	NA	NA	NA	0.2533
MRUC vs non- MRUC	NA	0.006364	A	11022	0.1078	26774325	intronic	NA	NA	NA	NA	#N/A
CD vs. Ctrl	rs2522826	0.006405243	A	94071	0.030099452	27115718	intergenic	NA	NA	NA	NA	0.321
IBD vs. Ctrl	rs73073796	0.006433633	A	118773	- 0.034207543	26700439	intergenic	HOXA11, HOXA10, HOXA9	- 0.0251998 053586744 , - 0.0784260 898118609 , - 0.1831879 51514832	0.03123705 95254648, 0.03319054 2567201, 0.04916874 54066987	0, 0, 0	0.1149
L3_ileocolonic	rs3801812	0.006471	A	2162	0.829	26887615	intronic	NA	NA	NA	NA	0.2531
L3_ileocolonic	rs10272603	0.006471	G	2162	0.829	26888277	intronic	NA	NA	NA	NA	0.2532
L3_ileocolonic	rs17376018	0.006471	G	2162	0.829	26889862	intronic	NA	NA	NA	NA	0.2532
L3_ileocolonic	rs2031811	0.006471	G	2162	0.829	26890672	intronic	NA	NA	NA	NA	0.2531
L3_ileocolonic	rs7804620	0.006471	C	2162	0.829	26891831	intronic	NA	NA	NA	NA	0.2531
L3_ileocolonic	rs10486483	0.006471	A	2162	0.829	26892440	intronic	NA	NA	NA	NA	0.2596
L2 B1 vs non-IBD ctrl	rs17154322	0.00649	G	3008	1.662	26714523	intronic	NA	NA	NA	NA	0.05105

FIG. 1 (Continued)

PHENOTYPE	dbSNP	p_value	A1	n_miss	OR_Z_B	base_ pair_CH 7	snp_ location	cis_ eGENE	eqtl_beta	eqtl_p	priority	MAF
PDM	rs17290008	0.006492	A	2093	1.328	26699976	intergenic	NA	NA	NA	NA	0.1208
Paneth-D4 phenotype	rs112802670	0.00656	G	297	4.249	26934754	intronic	NA	NA	NA	NA	0.01467
L3_ileocolonic	rs4722644	0.006574	A	2162	0.8291	26845386	intronic	NA	NA	NA	NA	0.2529
L3_ileocolonic	rs12333525	0.006574	A	2162	0.8291	26847762	intronic	NA	NA	NA	NA	0.2529
L3_ileocolonic	rs73067443	0.006574	G	2162	0.8291	26851074	intronic	NA	NA	NA	NA	0.2529
L3_ileocolonic	rs3801837	0.006574	G	2162	0.8291	26851361	intronic	NA	NA	NA	NA	0.2529
L3_ileocolonic	rs3801836	0.006574	A	2162	0.8291	26851400	intronic	NA	NA	NA	NA	0.2589
L3_ileocolonic	rs17315334	0.006574	A	2162	0.8291	26852860	intronic	NA	NA	NA	NA	0.2529
L3_ileocolonic	rs73067456	0.006574	A	2162	0.8291	26852998	intronic	NA	NA	NA	NA	0.2528
L3_ileocolonic	rs3801831	0.006574	G	2162	0.8291	26853470	intronic	NA	NA	NA	NA	0.2529
L3_ileocolonic	rs3823936	0.006574	G	2162	0.8291	26853830	intronic	NA	NA	NA	NA	0.2528
L3_ileocolonic	rs3823931	0.006574	G	2162	0.8291	26854026	intronic	NA	NA	NA	NA	0.2528
L3_ileocolonic	rs10262414	0.006574	A	2162	0.8291	26854266	intronic	NA	NA	NA	NA	0.2528
L3_ileocolonic	rs3801829	0.006574	C	2162	0.8291	26854996	intronic	NA	NA	NA	NA	0.2529
L3_ileocolonic	rs6948584	0.006574	A	2162	0.8291	26855732	intronic	NA	NA	NA	NA	0.2528
L3_ileocolonic	rs3823930	0.006574	G	2162	0.8291	26856525	intronic	NA	NA	NA	NA	0.2528
L3_ileocolonic	rs3823929	0.006574	G	2162	0.8291	26856600	intronic	NA	NA	NA	NA	0.253
L3_ileocolonic	rs3801825	0.006574	T	2162	0.8291	26856959	intronic	NA	NA	NA	NA	0.2529
L3_ileocolonic	rs73067475	0.006574	A	2162	0.8291	26857120	intronic	NA	NA	NA	NA	0.2528
L3_ileocolonic	rs73067476	0.006574	G	2162	0.8291	26857240	intronic	NA	NA	NA	NA	0.2528
L3_ileocolonic	rs28404962	0.006574	G	2162	0.8291	26860324	intronic	NA	NA	NA	NA	0.2529
L3_ileocolonic	rs13438513	0.006574	C	2162	0.8291	26860633	intronic	NA	NA	NA	NA	0.2528
L3_ileocolonic	rs55739485	0.006574	G	2162	0.8291	26860741	intronic	NA	NA	NA	NA	0.2528
L3_ileocolonic	rs3801823	0.006574	G	2162	0.8291	26861031	intronic	NA	NA	NA	NA	0.2528

FIG. 1 (Continued)

PHENOTYPE	dbSNP	p_value	A1	n_miss	OR_Z_B	base_ pair_CH 7	snp_ location	cis_ eGENE	eqtl_beta	eqtl_p	priority	MAF
L3_ileocolonic	rs3801821	0.006574	A	2162	0.8291	26861206	intronic	NA	NA	NA	NA	0.2528
L3_ileocolonic	rs3801820	0.006574	G	2162	0.8291	26861353	intronic	NA	NA	NA	NA	0.2528
L3_ileocolonic	rs7785689	0.006574	A	2162	0.8291	26861609	intronic	NA	NA	NA	NA	0.2519
MRUC Time to Colectomy <60 months vs >60 months	NA	0.006589	A	3931	0.1538	26778732	intronic	NA	NA	NA	NA	#N/A
Cbir UC vs. Cbir Ctrl	rs17464502	0.006608	A	1116	10.99	26991692	intronic	NA	NA	NA	NA	0.003977
L3_ileocolonic	rs73069533	0.006611	A	2162	0.8292	26892325	intronic	NA	NA	NA	NA	0.2525
L3_ileocolonic	rs12536145	0.006638	T	2162	0.8295	26894860	intronic	NA	NA	NA	NA	0.253
L3_ileocolonic	rs10242572	0.006638	G	2162	0.8295	26895065	intronic	NA	NA	NA	NA	0.2531
L3_ileocolonic	rs3801807	0.00664	G	2162	0.8295	26897439	intronic	NA	NA	NA	NA	0.2528
L3_ileocolonic	rs12532199	0.006643	G	2160	0.8293	26854375	intronic	NA	NA	NA	NA	0.2527
MRUC Time to Colectomy <60 months vs >60 months	NA	0.006653	A	3931	0.1554	26747041	intronic	NA	NA	NA	NA	#N/A
MRUC vs non- MRUC	NA	0.006707	A	11022	-0.1581	26932929	intronic	NA	NA	NA	NA	#N/A
Surgery	rs4722628	0.006709	C	1032	1.281	26735911	intronic	NA	NA	NA	NA	0.4922
L3_ileocolonic	rs12539719	0.006716	A	2162	0.8294	26844852	intronic	NA	NA	NA	NA	0.2584
L3_ileocolonic	rs3823934	0.006716	G	2162	0.8294	26853934	intronic	NA	NA	NA	NA	0.2524
L3_ileocolonic	rs3801822	0.006719	G	2160	0.8291	26861201	intronic	NA	NA	NA	NA	0.2586

FIG. 1 (Continued)

PHENOTYPE	dbSNP	p_value	A1	n_miss	OR_Z_B	base_ pair_CH 7	snp_ location	cis_ eGENE	eqtl_beta	eqtl_p	priority	MAF
MRUC Time to Colectomy <60 months vs >60 months	NA	0.006735	A	3931	0.162	26777723	intronic	NA	NA	NA	NA	#N/A
MRUC Time to Colectomy <60 months vs >60 months	NA	0.00677	A	3931	-0.1629	26835945	intronic	NA	NA	NA	NA	#N/A
L3_ileocolonic	rs10256250	0.006789	A	2160	0.8295	26895080	intronic	NA	NA	NA	NA	0.2529
MRUC Time to Colectomy <60 months vs >60 months	NA	0.006809	A	3931	-0.1533	26775626	intronic	NA	NA	NA	NA	#N/A
CD vs. Ctrl	rs2428430	0.006821196	A	89814	- 0.028295949	27064596	intergenic	NA	NA	NA	NA	0.4802
Surgery	rs212840	0.006836	A	1032	0.7813	26701002	intergenic	NA	NA	NA	NA	0.4807
CD vs. Ctrl	rs2522825	0.006869917	G	94066	0.029913807	27111994	intergenic	NA	NA	NA	NA	0.3176
L3_ileocolonic	rs7785832	0.006945	G	2161	0.8301	26852760	intronic	NA	NA	NA	NA	0.2529
Asca UC vs. Asca Ctrl	rs17436229	0.006972	A	1147	1.976	26959526	intronic	NA	NA	NA	NA	0.0319
MRUC Time to Colectomy <60 months vs >60 months	NA	0.006998	A	3931	0.1529	26725389	intronic	NA	NA	NA	NA	#N/A
L3_ileocolonic	rs12532796	0.007029	G	2161	0.8302	26854828	intronic	NA	NA	NA	NA	0.2524
L3_ileocolonic	rs3823938	0.007039	G	2162	0.8316	26853741	intronic	NA	NA	NA	NA	0.2534

FIG. 1 (Continued)

PHENOTYPE	dbSNP	p_value	A1	n_miss	OR_Z_B	base_ pair_CH 7	snp_ location	cis_ eGENE	eqtl_beta	eqtl_p	priority	MAF
MRUC Time to Colectomy <60 months vs >60 months	NA	0.007044	A	3931	-0.162	26827627	intronic	NA	NA	NA	NA	#N/A
Surgery	rs607099	0.007055	A	1032	1.266	26848159	intronic	NA	NA	NA	NA	0.4921
L3_ileocolonic	rs3213853	0.007068	G	2162	0.8307	26893524	intronic	NA	NA	NA	NA	0.2533
L3_ileocolonic	rs3801805	0.007068	G	2162	0.8307	26897640	intronic	NA	NA	NA	NA	0.2535
MRUC Time to Colectomy <60 months vs >60 months	NA	0.007113	A	3931	-0.1524	26770394	intronic	NA	NA	NA	NA	#N/A
IBD vs. Ctrl	rs213531	0.007137325	G	125153	- 0.023026367	26920494	intronic	NA	NA	NA	NA	0.4703
MRUC Time to Colectomy <60 months vs >60 months	NA	0.007177	A	3931	-0.1523	26799945	intronic	NA	NA	NA	NA	#N/A
PDM	rs213530	0.007191	A	2093	1.195	26920314	intronic	NA	NA	NA	NA	0.4664
anti-TNF time to loss of response	rs62447701	0.00730732	G	99	2.6825	26717752	intronic	NA	NA	NA	NA	0.02954
Ulcerative Colitis vs. non- IBD Controls	rs17154453	0.007308	G	6863	0.7462	26792957	intronic	NA	NA	NA	NA	0.05783
L3_ileocolonic	rs3801809	0.007343	A	2160	0.8314	26895456	intronic	NA	NA	NA	NA	0.2529
Surgery	rs3801806	0.007374	A	1032	1.27	26897553	intronic	NA	NA	NA	NA	0.4991
L3_ileocolonic	rs10266759	0.007409	A	2162	0.8314	26855282	intronic	NA	NA	NA	NA	0.2527

FIG. 1 (Continued)

PHENOTYPE	dbSNP	p_value	A1	n_miss	OR_Z_B	base_ pair_CH 7	snp_ location	cis_ eGENE	eqtl_beta	eqtl_p	priority	MAF
L3_ileocolonic	rs3801826	0.007409	A	2162	0.8314	26856720	intronic	NA	NA	NA	NA	0.2526
UC vs. Ctrl	rs116887315	0.00741354	G	94566	- 0.119011936	26695781	intergenic	NA	NA	NA	NA	0.02003
L3_ileocolonic	rs3801833	0.007454	A	2157	0.8314	26852212	intronic	NA	NA	NA	NA	0.2528
Surgery	rs12700754	0.007486	G	1032	1.276	26754389	intronic	NA	NA	NA	NA	0.4937
MRUC Time to Colectomy <60 months vs >60 months	NA	0.007551	A	3931	-0.1515	26744599	intronic	NA	NA	NA	NA	#N/A
CD vs. Ctrl	rs496173	0.007597592	G	NA	- 0.042889487	26883159	intronic	NA	NA	NA	NA	0.4591
L3_ileocolonic	rs17375272	0.007645	A	2162	0.832	26866497	intronic	NA	NA	NA	NA	0.2524
L3_ileocolonic	rs10225700	0.007645	A	2162	0.832	26869880	intronic	NA	NA	NA	NA	0.2524
L3_ileocolonic	rs10225904	0.007645	A	2162	0.832	26869888	intronic	NA	NA	NA	NA	0.2524
L3_ileocolonic	rs12535784	0.007645	A	2162	0.832	26882067	intronic	NA	NA	NA	NA	0.2525
IBD vs. Ctrl	rs2391359	0.007646432	G	NA	0.031691336	26790786	intronic	NA	NA	NA	NA	0.4639
Paneth-D4 phenotype	rs3801806	0.007683	A	297	1.079	26897553	intronic	NA	NA	NA	NA	0.4991
OMPC UC vs. OMPC Ctrl	rs7782107	0.007728	C	1273	2.182	26855888	intronic	NA	NA	NA	NA	0.03449
Paneth-D2 phenotype	rs117410660	0.007743	C	297	11.43	26750738	intronic	NA	NA	NA	NA	0.006683
Paneth-D2 phenotype	rs17426629	0.007743	A	297	11.43	26965878	intronic	NA	NA	NA	NA	0.005617
CD vs. Ctrl	rs12154908	0.007767345	A	88380	- 0.053183834	26787032	intronic	NA	NA	NA	NA	0.07656
L3_ileocolonic	rs73065517	0.007781	G	2160	0.8318	26830555	intronic	NA	NA	NA	NA	0.2501

FIG. 1 (Continued)

PHENOTYPE	dbSNP	p_value	A1	n_miss	OR_Z_B	base_ pair_CH 7	snp_ location	cis_ eGENE	eqtl_beta	eqtl_p	priority	MAF
Surgery	rs1548480	0.00788	A	1032	1.274	26787343	intronic	NA	NA	NA	NA	0.4936
MRUC vs non-MRUC	NA	0.007894	A	11022	-0.1119	26711104	intronic	NA	NA	NA	NA	#N/A
MRUC Time to Colectomy <60 months vs >60 months	NA	0.007949	A	3931	-0.1786	26844852	intronic	NA	NA	NA	NA	#N/A
CD vs. Ctrl	rs17471088	0.007974906	A	94080	0.029194256	27014440	intronic	NA	NA	NA	NA	0.3211
Surgery	rs11764558	0.008	A	1032	1.273	26778732	intronic	NA	NA	NA	NA	0.4929
IBD vs. Ctrl	rs34790403	0.008007661	C	128396	-0.05203689	26833283	intronic	NA	NA	NA	NA	0.04397
CD vs. Ctrl	rs188468488	0.008138107	G	94097	-0.121251065	27109617	intergenic	NA	NA	NA	NA	0.01245
Surgery	rs7784257	0.008143	G	1032	1.273	26799945	intronic	NA	NA	NA	NA	0.4933
MRUC Time to Colectomy <60 months vs >60 months	NA	0.008222	A	3931	0.1495	26793597	intronic	NA	NA	NA	NA	#N/A
L3_ileocolonic	rs73069507	0.008337	G	2162	0.8337	26877536	intronic	NA	NA	NA	NA	0.2529
L3_ileocolonic	rs73069510	0.008337	G	2162	0.8337	26877567	intronic	NA	NA	NA	NA	0.2529
L3_ileocolonic	rs3801816	0.008337	A	2162	0.8337	26881177	intronic	NA	NA	NA	NA	0.2529
L3_ileocolonic	rs3801815	0.008337	G	2162	0.8337	26881292	intronic	NA	NA	NA	NA	0.253
MRUC time to colectomy	NA	0.008339	A	6326	-0.1267	26844852	intronic	NA	NA	NA	NA	#N/A

FIG. 1 (Continued)

PHENOTYPE	dbSNP	p_value	A1	n_miss	OR_Z_B	base_ pair_CH 7	snp_ location	cis_ eGENE	eqtl_beta	eqtl_p	priority	MAF
MRUC Time to Colectomy <60 months vs >60 months	NA	0.008367	A	3931	0.1585	26820850	intronic	NA	NA	NA	NA	#N/A
MRUC time to colectomy	NA	0.008384	A	6326	0.9275	26958977	intronic	NA	NA	NA	NA	#N/A
B3	rs490366	0.008452	G	2170	1.228	26851805	intronic	HOXA3, NFE2L3	0.1553281 37530774, 0.1091601 0191584	0.03053671 93727985, 0.03484452 44134559	0, 0	0.2463
L3_ileocolonic	rs10267950	0.008453	A	2162	0.8335	26826757	intronic	NA	NA	NA	NA	0.2493
L3_ileocolonic	rs10272303	0.008453	G	2162	0.8335	26827815	intronic	NA	NA	NA	NA	0.2502
L3_ileocolonic	rs1327988	0.008453	G	2162	0.8335	26828965	intronic	NA	NA	NA	NA	0.2502
L3_ileocolonic	rs3801844	0.008453	G	2162	0.8335	26829759	intronic	NA	NA	NA	NA	0.2502
L3_ileocolonic	rs3801843	0.008453	G	2162	0.8335	26830201	intronic	NA	NA	NA	NA	0.2502
L3_ileocolonic	rs3801842	0.008453	A	2162	0.8335	26830263	intronic	NA	NA	NA	NA	0.2502
L3_ileocolonic	rs1327989	0.008453	A	2162	0.8335	26833563	intronic	NA	NA	NA	NA	0.2501
L3_ileocolonic	rs10276471	0.008453	G	2162	0.8335	26837940	intronic	NA	NA	NA	NA	0.2501
MRUC time to colectomy	NA	0.008469	A	6326	-0.2378	26817044	intronic	NA	NA	NA	NA	#N/A
MRUC vs non- MRUC	NA	0.008492	A	11022	-0.2672	26701002	intergenic	NA	NA	NA	NA	#N/A
MRUC Time to Colectomy <60 months vs >60 months	NA	0.008523	A	3931	-0.1489	26754389	intronic	NA	NA	NA	NA	#N/A

FIG. 1 (Continued)

PHENOTYPE	dbSNP	p_value	A1	n_miss	OR_Z_B	base_ pair_CH 7	snp_ location	cis_ eGENE	eqtl_beta	eqtl_p	priority	MAF
MIRUC Time to Colectomy <60 months vs >60 months	NA	0.008526	A	3931	0.1489	26787343	intronic	NA	NA	NA	NA	#N/A
L3_ileocolonic	rs3801850	0.008536	G	2162	0.8339	26820577	intronic	NA	NA	NA	NA	0.2509
IBD vs. Ctrl	rs774267	0.008550721	A	128379	- 0.022037803	26963514	intronic	HOXA11-AS	- 0.0913561 01	0.03421850 8	0	0.459
Paneth-D4 phenotype	rs622011	0.008561	G	297	1.057	26855739	intronic	NA	NA	NA	NA	0.4996
Paneth-D4 phenotype	rs503110	0.008561	T	297	1.057	26857016	intronic	NA	NA	NA	NA	0.4998
L3_ileocolonic	rs73065504	0.008634	G	2162	0.8337	26825984	intronic	NA	NA	NA	NA	0.2497
IBD vs. Ctrl	rs11762308	0.00865235	G	128429	- 0.036942617	26932929	intronic	HOTAIRM1 , HOXA7	- 0.2166372 08147244, - 0.1840119 6815672	0.04642287 12753543, 0.04844997 75871686	0, 0	0.1019
OMPC CD vs. OMPC Ctrl	rs187621319	0.008656	G	2281	4.509	26865161	intronic	NA	NA	NA	NA	0.00247
L3_ileocolonic	rs10272190	0.008717	A	2158	0.8345	26887942	intronic	NA	NA	NA	NA	0.2532
Asca UC vs. Asca Ctrl	rs17154376	0.008723	A	1147	1.721	26745464	intronic	NA	NA	NA	NA	0.05036
L3 B2a+B2b vs non-IBD ctrl	rs73069529	0.00878	A	1050	1.469	26889376	intronic	NA	NA	NA	NA	0.1187
Surgery	rs12700757	0.008785	G	1032	1.27	26770394	intronic	NA	NA	NA	NA	0.4921
Surgery	rs12700756	0.0088	A	1032	1.269	26768482	intronic	NA	NA	NA	NA	0.4949

FIG. 1 (Continued)

PHENOTYPE	dbSNP	p_value	A1	n_miss	OR_Z_B	base_ pair_CH 7	snp_ location	cis_ eGENE	eqtl_beta	eqtl_p	priority	MAF
MRUC Time to Colectomy <60 months vs >60 months	NA	0.008845	A	3931	-0.1775	26911904	intronic	NA	NA	NA	NA	#N/A
Paneth-D1234 phenotype	rs794445145	0.008848	G	297	6.08	26752960	intronic	NA	NA	NA	NA	0.05942
L1_ileal	rs78028110	0.008879	A	2162	1.417	26784056	intronic	EVX1, KIAA0087	0.3013987 74811087, 0.0311722 066916883	0.02256077 80515621, 0.02933705 87330475	0, 0	0.07211
Paneth-D4 phenotype	rs475238	0.008881	G	297	1.056	26848278	intronic	NA	NA	NA	NA	0.4999
Paneth-D4 phenotype	rs607099	0.008899	A	297	1.047	26848159	intronic	NA	NA	NA	NA	0.4921
Ulcerative Colitis vs. non- IBD Controls	rs17437175	0.008962	G	6864	0.7517	27130276	intergenic	JAZF1, HOXA9, HOXA7	0.0595691 447084118 , - 0.3226377 26865606, - 0.3096022 66535008	0.00590475 47611523, 0.01430261 56741274, 0.01791882 40116877	0, 0, 0	0.0584
IGG Asca UC vs. IGA Asca Ctrl	rs118063014	0.008975	T	1147	3.805	26820637	intronic	NA	NA	NA	NA	0.02286
MRUC vs non- MRUC	NA	0.009072	A	11022	0.5193	26783923	intronic	NA	NA	NA	NA	#N/A

FIG. 1 (Continued)

PHENOTYPE	dbSNP	p_value	A1	n_miss	OR_Z_B	base_ pair_CH 7	snp_ location	cis_ eGENE	eqtl_beta	eqtl_p	priority	MAF
MRUC Time to Colectomy <60 months vs >60 months	NA	0.009094	A	3931	0.1483	26734838	intronic	NA	NA	NA	NA	#N/A
MRUC Time to Colectomy <60 months vs >60 months	NA	0.009097	A	3931	0.1477	26768482	intronic	NA	NA	NA	NA	#N/A
MRUC time to colectomy	NA	0.009168	A	6326	0.1112	26777723	intronic	NA	NA	NA	NA	#N/A
MRUC Time to Colectomy <60 months vs >60 months	NA	0.009242	A	3931	0.1561	26819917	intronic	NA	NA	NA	NA	#N/A
MRUC vs non- MRUC	NA	0.009245	A	11022	-0.1069	26821320	intronic	NA	NA	NA	NA	#N/A
Paneth-D0 phenotype	rs79445145	0.009457	G	297	-6.022	26752960	intronic	NA	NA	NA	NA	0.05942
MRUC vs non- MRUC	NA	0.009467	A	11022	0.0981	26823963	intronic	NA	NA	NA	NA	#N/A
L3_ileocolonic	rs12536560	0.009497	G	2162	0.8358	26822876	intronic	NA	NA	NA	NA	0.2492
IBD vs. Ctrl	rs12539719	0.009566903	A	124139	0.025314244	26844852	intronic	NA	NA	NA	NA	0.2584
B3	rs1391805	0.009573	G	2170	1.224	26896236	intronic	HOXA3, NFE2L3	0.1553281 37530774, 0.1091601 0191584	0.03053671 93727985, 0.03484452 44134559	0, 0	0.2491

FIG. 1 (Continued)

PHENOTYPE	dbSNP	p_value	A1	n_miss	OR_Z_B	base_ pair_CH 7	snp_ location	cis_ eGENE	eqtl_beta	eqtl_p	priority	MAF
L3_ileocolonic	rs3801814	0.009607	C	2162	0.8365	26881302	intronic	NA	NA	NA	NA	0.2524
L3_ileocolonic	rs10486478	0.009624	A	2162	0.8348	26819465	intronic	NA	NA	NA	NA	0.2502
Surgery	rs12700762	0.009629	A	1032	1.266	26793597	intronic	NA	NA	NA	NA	0.4932
CD vs. Ctrl	rs11762308	0.009649811	G	94091	- 0.045076838	26932929	intronic	HOTAIRM1 , HOXA7	- 0.2166372 0.08147244, - 0.1840119 6815672	0.04642287 12753543, 0.04844997 75871686	0, 0	0.1019
i2 CD vs. i2 Ctrl	rs3801817	0.009652	A	1792	0.5902	26880852	intronic	NA	NA	NA	NA	0.03495
Paneth-D4 phenotype	rs2769364	0.009731	C	297	1.04	26844468	intronic	NA	NA	NA	NA	0.4991
Paneth-D4 phenotype	rs567124	0.009731	A	297	1.04	26845145	intronic	NA	NA	NA	NA	0.4873
MRUC Time to Colectomy <60 months vs >60 months	NA	0.009734	A	3931	0.1543	26776874	intronic	NA	NA	NA	NA	#N/A
IBD vs. Ctrl	rs212839	0.009792056	C	128292	- 0.023323518	26700230	intergenic	NA	NA	NA	NA	0.3197
MRUC Time to Colectomy <60 months vs >60 months	NA	0.009902	A	3931	0.154	26776999	intronic	NA	NA	NA	NA	#N/A
Ulcerative Colitis vs. non- IBD Controls	rs17290008	0.009926	A	6863	0.8235	26699976	intergenic	NA	NA	NA	NA	0.1208

FIG. 1 (Continued)

PHENOTYPE	dbSNP	p_value	A1	n_miss	OR_Z_B	base_ pair_CH 7	snp_ location	cis_ eGENE	eqtl_beta	eqtl_p	priority	MAF
MRUC Time to Colectomy <60 months vs >60 months	NA	0.009982	A	3931	-0.1937	27099624	intergenic	NA	NA	NA	NA	#N/A
anti-TNF time to loss of response	rs513387	0.00998769	A	99	2.57626	26823963	intronic	NA	NA	NA	NA	0.3249
L1 B1 vs non-IBD ctrl	rs78028110	0.009989	A	2906	1.764	26784056	intronic	EVX1, KIAA0087	0.3013987 74811087, 0.0311722 066916883	0.02256077 80515621, 0.02933705 87330475	0, 0	0.07211

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2020/017209

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - C07K 14/47; C12Q 1/6883 (2020.01)

CPC - C07K 14/4702; C12Q 2600/118; C12Q 2600/156; C12Q 2600/158 (2020.02)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

See Search History document

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

USPC - 435/6.11; 514/44A (keyword delimited)

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

See Search History document

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2018/0305459 A1 (CEDARS-SINAI MEDICAL CENTER) 25 October 2018 (25.10.2018) entire document	1-12, 15, 19
Y	WO 2017/185180 A1 (QU BIOLOGICS INC.) 02 November 2017 (02.11.2017) entire document	1-20
Y	US 2018/0142302 A1 (CEDARS-SINAI MEDICAL CENTER) 24 May 2018 (24.05.2018) entire document	4-6, 10-12, 17-20
Y	US 2012/0073585 A1 (ROTTER et al) 29 March 2012 (29.03.2012) entire document	5, 6, 11, 12
Y	US 2017/0233815 A1 (TIMMONS) 17 August 2017 (17.08.2017) entire document	13-16
A	MEDDENS et al. "Systematic analysis of chromatin interactions at disease associated loci links novel candidate genes to inflammatory bowel disease," Genome Biology, 30 November 2016 (30.11.2016), Vol. 17, Pgs. 1-15. entire document	1-20
A	NARZO et al. "Blood and Intestine eQTLs from an Anti-TNF-Resistant Crohn's Disease Cohort Inform IBD Genetic Association Loci," Clinical and Translational Gastroenterology, 23 June 2016 (23.06.2016), Vol. 7, No. 6, Pgs. 1-18. entire document	1-20
A	YE et al. "Genetic variation in IBD: progress, clues to pathogenesis and possible clinical utility," Expert Review of Clinical Immunology, 09 May 2016 (09.05.2016), Vol. 12, No. 10, Pgs. 1091-1107. entire document	1-20

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Date of the actual completion of the international search

16 April 2020

Date of mailing of the international search report

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