

**Supplemental Table 1** Genetic loci linked to CD and/or UC. Most gene deserts associated with CD and/or UC with no immediate candidate genes have been omitted from the table. Please note that at multiple associated genetic loci genetically (or functionally) 'causal' genes have not been identified yet, and the most likely candidates are presented as suggested in the original reports.

Chr	putative gene	Gene name	CD	UC	Reference
1p13	<i>PTPN22</i>	protein tyrosine phosphatase, non-receptor type 22 (lymphoid)	yes		(1)
1p31	<i>IL23R</i>	interleukin 23 receptor	yes	yes	(2)
1p36	<i>PLA2G2E</i>	phospholipase A2, group IIE		yes	(3)
1q21	<i>ECM1</i>	extracellular matrix protein 1		yes	(4)
1q23	<i>ITLN1</i>	intelectin 1 (galactofuranose binding)	yes		(1)
1q32	<i>IL10</i>	interleukin 10		yes	(5)
1q44	<i>NLRP3</i>	NLR family, pyrin domain containing 3	yes		(6)
2p16	<i>PUS10</i>	pseudouridylate synthase 10	yes	yes	(1, 3)
2q11	<i>IL18RAP</i>	interleukin 18 receptor accessory protein	yes	yes	(1, 7)
2q35	<i>ARPC2</i>	actin related protein 2/3 complex, subunit 2, 34kDa		yes	(5)
2q37	<i>ATG16L1</i>	ATG16 autophagy related 16-like 1	yes		(8)
3p12	<i>CADM2</i>	cell adhesion molecule 2		yes	(5)
3p21	<i>MST1</i>	macrophage stimulating 1 (hepatocyte growth factor-like)	yes	yes	(1, 4)
3p21	<i>BSN</i>	bassoon (presynaptic cytomatrix protein)	yes	yes	(9, 10)
4p13	<i>PHOX2B</i>	paired-like homeobox 2b	yes		(11)
5p13	<i>desert (PTGER4)</i>	prostaglandin E receptor 4 (subtype EP4)	yes	yes	(3, 12)
5q13	<i>S100Z</i>	S100 calcium binding protein Z		yes	(5)
5q31	<i>SLC22A5</i>	solute carrier family 22 (organic cation/carnitine transporter), member 5	yes		(13)
5q33	<i>IRGM</i>	immunity-related GTPase family, M	yes		(1)
5q33	<i>IL12B</i>	interleukin 12B	yes	yes	(10, 14)
6p21	<i>BTNL2</i>	butyrophilin-like 2 (MHC class II associated)	yes	yes	(5)
6p21	HLA	major histocompatibility complex	yes	yes	
6p22	<i>CDKAL1</i>	CDK5 regulatory subunit associated protein 1-like 1	yes		(1)
6q23	<i>TNFAIP3</i>	tumor necrosis factor, alpha-induced protein 3 (A20)	yes		(9)
6q27	<i>CCR6</i>	chemokine (C-C motif) receptor 6	yes		(1)
7q32	<i>IRF5</i>	interferon regulatory factor 5	yes	yes	(15)
9p24	<i>JAK2</i>	Janus kinase 2	yes	yes	(1, 7)
9q32	<i>TNFSF15</i>	tumor necrosis factor (ligand) superfamily, member 15	yes		(1)
9q33	<i>TLR4</i>	toll-like receptor 4	yes		(16)
9q34	<i>CARD9</i>	caspase recruitment domain family, member 9	yes	yes	(17)

Chr	putative gene	Gene name	CD	UC	Reference
10p11	<i>CCNY</i>	cyclin Y	yes	yes	(9, 10)
10q21	<i>ZNF365</i>	zinc finger protein 365	yes		(1)
10q23	<i>DLG5</i>	discs, large homolog 5	yes		(18)
10q24	<i>NKX2-3</i>	NK2 transcription factor related, locus 3	yes	yes	(1, 10)
10q26	<i>DMBT1</i>	deleted in malignant brain tumors 1	yes		(19)
11p15	<i>NELL1</i>	NEL-like 1	yes	yes	(20)
11q13	<i>C11orf30</i>	chromosome 11 open reading frame 30	yes		(1)
12q12	<i>LRRK2, MUC19</i>	leucine-rich repeat kinase 2	yes		(1)
12q15	<i>IFNG</i>	interferon, gamma		yes	(7)
15q13	<i>HERC2</i>	hect domain and RLD 2	yes	yes	(9, 10)
16q12	<i>NOD2</i>	nucleotide-binding oligomerization domain containing 2	yes		(21-23)
16q24	<i>FAM92B</i>	family with sequence similarity 92, member B	yes		(11)
17q21	<i>STAT3</i>	signal transducer and activator of transcription 3	yes	yes	(1, 10)
17q21	<i>ORMDL3</i>	ORM1-like 3	yes		(1)
18p11	<i>PTPN2</i>	protein tyrosine phosphatase, non-receptor type 2	yes		(9, 10)
20q13	<i>TNFRSF6B</i>	tumor necrosis factor receptor superfamily, member 6b, decoy	yes	yes	(24)
21q22	<i>ICOSLG</i>	inducible T-cell co-stimulator ligand	yes		(1)
21q22	<i>PSMG1</i>	proteasome (prosome, macropain) assembly chaperone 1	yes	yes	(24)
22q12	<i>XPB1</i>	X-box binding protein 1	yes	yes	(25)
22q12	<i>NCF4</i>	neutrophil cytosolic factor 4, 40kDa	yes		(11)

**Supplemental Table 2.** Efficacy of classical therapeutics and biological agents in clinical trials of Crohn's disease and ulcerative colitis. Shown is the success or failure of therapeutics in patients with active disease (AD) or for maintenance of remission (M). The type of clinical trial is indicated (P, phase; MA, meta-analysis; RCT, randomized controlled trial). 5-ASA, 5-aminosalicylic acid; 6-MP, 6-mercaptopurin; CTLA-4, cytotoxic T-lymphocyte antigen 4; CRP, C-reactive protein; GM-CSF, granulocyte macrophage colony-stimulating factor; ICAM-1, intercellular adhesion molecule 1; mAbs, monoclonal antibodies; MAPK, mitogen-activated protein kinase; mTOR, mammalian target of rapamycin; PPAR, peroxisome proliferator-activated receptor; rhIL-10, recombinant human IL-10.

		Crohn's disease		Ulcerative colitis		
	drug	Mechanism	success	failure	success	failure
Classical therapeutics	<b>5-ASA / sulfasalazine</b>	PPAR $\gamma$ agonist and other mechanisms	Mild to moderate AD (MA) (26-28)		Mild to moderate AD + M (MA) (29, 30)	
	<b>Corticosteroids</b>	Various mechanisms	AD (MA) (31, 32)		AD (RCT) (33-35)	
	<b>Azathioprine/ 6-MP</b>	Purine synthesis inhibitor	M (MA) (36)		AD + M (P2 RCT) (37, 38)	
	<b>Methotrexate</b>	Antimetabolite	AD + M (MA/P2 RCT) (39, 40)			
	<b>Cyclosporine</b>	Calcineurin inhibitor		AD (MA) (41)	AD (P2 RCT) (42, 43)	
	<b>Tacrolimus</b>	Calcineurin inhibitor			AD (P2 RCT) (44)	
	<b>Antibiotics</b>	Modulation of the microbial flora	AD (MA) (45)		AD (MA) (46)	
cytokine targeting	<b>Infliximab</b>	Anti-TNF $\alpha$ antibody	AD + M (P3 RCT) (47-50)		AD (P3 RCT) (51)	
	<b>Adalimumab</b>	Anti-TNF $\alpha$ antibody	AD + M (P3 RCT) (52-54)			
	<b>Certolizumab</b>	Anti-TNF $\alpha$ antibody	AD + M (P3 RCT) (55, 56)			
	<b>Fontolizumab</b>	Anti-IFN $\gamma$ antibody		AD (P2 RCT) (57, 58)		
	<b>ABT-874</b>	Anti-IL-12/IL-23p40	AD (P2 RCT) (59)			
	<b>Ustekinumab (CNTO 1275)</b>	Anti-IL-12/IL-23p40	AD (P2 RCT) (60)			

		Crohn's disease		Ulcerative colitis		
	drug	Mechanism	success	failure	success	failure
	<b>STA-5326</b>	Small molecule inhibitor of IL-12/IL23	AD (P1/2a) (61)			
	<b>Atlizumab/ Tocilizumab</b>	Anti-IL-6R antibody	AD (P2 RCT) (62)			
	<b>rhIL-10</b>	IL-10		AD (P3 RCT) (63, 64)		AD (P2 RCT) (65)
	<b>Oprelvekin</b>	Recombinant IL-11		AD (P2 RCT) (66)		AD (RCT, terminated)
	<b>pegylated IFN-<math>\alpha</math>2b</b>	Interferon alpha				AD (P2 RCT) (67)
	<b>IFN-<math>\beta</math>1a</b>	Interferon beta		AD + MA (P2 RCT) (68)		AD (P2, MA) (69, 70)
	<b>RDP58</b>	Decapeptide disrupting the MyD88-IRAK-TRAF6 protein complex (?)			AD (P2 RCT) (71)	
anti-adhesion/anti-chemokine mAbs	<b>Natalizumab</b>	Anti- $\alpha$ 4 Integrin antibody	AD in patients with $\uparrow$ CRP, M for responders (P3 RCT) (72-74)			
	<b>MLN002, Vedolizumab</b>	Anti- $\alpha$ 4 $\beta$ 7 Integrin antibody	+/- in AD (P2 RCT) (75)		AD (P2 RCT) (76)	
	<b>Alicaforsen</b>	ICAM-1 antisense oligonucleotide		AD (P2 RCT) (77)		AD (P2 RCT) (78)
	<b>CCX282-B</b>	CCR9 antagonist	+/- in AD (P2) (79, 80)			
modulation of T cell responses	<b>Visilizumab</b>	Anti-CD3 antibody				terminated (no efficacy/inferior safety profile)
	<b>Basiliximab</b>	Anti-CD25 antibody				AD (P2 RCT) (81)
	<b>Daclizumab</b>	Anti-CD25 antibody				AD (P2 RCT) (82)
	<b>Ch5D12</b>	Anti-CD40 antibody	AD (P1/2a) (83)			
	<b>Hematopoietic stem cell transplantation</b>	Autologous and allogeneic stem cell transplantation	AD (uncontrolled trials) (84-87)			
	<b>Leukocytapheresis</b>	Leukocyte replacement with naive bone marrow-derived cells		AD (P2/3) (88)		

		Crohn's disease		Ulcerative colitis			
		drug	Mechanism	success	failure	success	failure
MAPK inhibitors	<b>Semapimod (CNI-1493)</b>		MAPK inhibitor	AD (P1) (89)			
	<b>Doramapimod (BIRB796)</b>		MAPK inhibitor		AD (P2 RCT) (90)		
growth factors	<b>Sargramostim</b>		GM-CSF		AD (P3 RCT) (91, 92)		
	<b>Somatotropin</b>		Human growth hormone	AD (P2) (93)			
	<b>Repifermin (KGF2)</b>		Keratinocyte growth factor				AD (P2 RCT) (94)
	<b>Epithelial growth factor</b>		Epithelial growth factor			AD (P2 RCT) (95)	
miscellaneous	<b>Rosiglitazone</b>		PPAR- $\gamma$ agonist			AD (P2 RCT) (96)	
	<b>Tetomilast (OPC-6535)</b>		Phosphodiesterase-4 inhibitor				AD (P2 RCT) (97)
	<b>Everolimus</b>		mTOR inhibitor		M (P2 RCT) (98)		
	<b>Kremezin (AST-120)</b>		Carbon adsorbent			AD (P1) (99)	
	<b>Thalidomide/ Lenalidomide</b>		unknown		AD (P2 RCT) (100, 101)		
	<b>Epanova</b>		Omega 3 fatty acid		M (P3 RCT) (102)		
	<b>Probiotics</b>				M (MA) (103)		AD (MA) (104)

## Supplementary References

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