



Supplementary Figure 1 Comparison of total number of antibodies in healthy controls, CD and UC at the bacterial species level. The number of proteins displayed on the microbial protein arrays for each species is shown in parenthesis. The statistical significance of the difference in seroprevalence between groups were calculated using Chi-squared test, * $P < 0.05$, ** $P < 0.01$.

Supplementary Table 1 Bacteria and viruses studied on the microbial protein arrays

	Strain	Phylum	Number of proteins
Bacteria	<i>Helicobacter pylori</i>	Proteobacteria	171
	<i>Staphylococcus aureus</i>	Firmicutes	101
	<i>Pseudomonas aeruginosa</i>	Proteobacteria	69
	<i>Fusobacterium varium</i>	Fusobacteria	58
	<i>Mycobacterium avium</i>	Actinobacteria	57
	<i>Streptococcus gallolyticus</i>	Firmicutes	46
	<i>Streptococcus pneumoniae</i>	Firmicutes	46
	<i>Fusobacterium nucleatum</i>	Fusobacteria	42
	<i>Acinetobacter calcoaceticus</i>	Proteobacteria	38
	<i>Phocaeicola vulgatus</i>	Bacteroidetes	36
	<i>Klebsiella oxytoca</i>	Proteobacteria	33
	<i>Acinetobacter baumannii</i>	Proteobacteria	27
	<i>Haemophilus influenzae</i>	Proteobacteria	24
	<i>Proteus mirabilis</i>	Proteobacteria	23
	<i>Streptococcus pyogenes</i>	Firmicutes	23
	<i>Lactiplantibacillus plantarum</i>	Firmicutes	22
	<i>Bacillus anthracis</i>	Firmicutes	21
	<i>Escherichia coli</i>	Proteobacteria	20
	<i>Shigella flexneri</i>	Proteobacteria	19
	<i>Citrobacter koseri</i>	Proteobacteria	19
	<i>Roseburia intestinalis</i>	Firmicutes	18
	<i>Bacteroides fragilis</i>	Bacteroidetes	16
	<i>Neisseria meningitidis</i>	Proteobacteria	16
	<i>Gemella haemolysans</i>	Firmicutes	15
	<i>Cutibacterium granulorum</i>	Actinobacteria	14
	<i>Desulfovibrio desulfuricans</i>	Proteobacteria	13
	<i>Vibrio cholerae</i>	Proteobacteria	13
	<i>Parvimonas micra</i>	Firmicutes	12
	<i>Enterococcus faecalis</i>	Firmicutes	12

	Porphyromonas gingivalis	Bacteroidetes	12
	Veillonella parvula	Firmicutes	11
	Clostridioides difficile	Firmicutes	11
	Corynebacterium tuberculostearicum	Actinobacteria	11
	Streptococcus agalactiae	Firmicutes	10
	Klebsiella pneumoniae	Proteobacteria	10
	Akkermansia muciniphila	Verrucomicrobia	10
	Mycobacterium tuberculosis	Actinobacteria	9
	Campylobacter jejuni	Proteobacteria	8
	Eubacterium rectale	Firmicutes	8
	Ruminococcus albus	Firmicutes	8
	Prevotella copri	Bacteroidetes	8
	Leptotrichia buccalis	Fusobacteria	7
	Dorea formicigenerans	Firmicutes	5
	Alloiococcus otitis	Firmicutes	5
	Anaerococcus prevotii	Firmicutes	4
	Peptostreptococcus anaerobius	Firmicutes	4
	Bifidobacterium adolescentis	Actinobacteria	3
	Faecalibacterium prausnitzii	Firmicutes	2
	Collinsella aerofaciens	Actinobacteria	2
	Lachnospiraceae bacterium A4	Firmicutes	1
Viruses	Human gammaherpesvirus 4	Peploviricota	62
	Human alphaherpesvirus 1	Peploviricota	56
	Human betaherpesvirus 5	Peploviricota	42
	Human papillomavirus	Cossaviricota	35
	Human alphaherpesvirus 3	Peploviricota	33
	Human mastadenovirus C	Preplasmiviricota	25
	Vaccinia virus	Nucleocytoviricota	25
	Influenza A virus	Negarnaviricota	20
	Enterovirus C	Pisuviricota	10
	Coxsackievirus B4	Pisuviricota	9
	Rhinovirus B14	Pisuviricota	9

Human respirovirus 1	Negarnaviricota	7
Human metapneumovirus	Negarnaviricota	6
Rotavirus	Duplornaviricota	6
Mumps orthorubulavirus	Negarnaviricota	5
Measles morbillivirus	Negarnaviricota	5
Human respiratory syncytial virus B	Negarnaviricota	5
Rubella virus	Kitrinoviricota	4
Human parvovirus B19	Cossaviricota	4
Hepatitis B virus	Artverviricota	3
Sindbis virus	Kitrinoviricota	2
Semliki Forest virus	Kitrinoviricota	2
Chikungunya virus	Kitrinoviricota	2
Yellow fever virus	Kitrinoviricota	2
Human coronavirus OC43	Pisuviricota	2
Human coronavirus 229E	Pisuviricota	2
Tioman virus	Negarnaviricota	2
Macaca mulatta polyomavirus 1	Cossaviricota	2
Human polyomavirus 1	Cossaviricota	2
JC polyomavirus	Cossaviricota	2
Human bocavirus 1	Cossaviricota	2
Human endogenous retrovirus	Artverviricota	2
Small anellovirus 1	Unclassified phylum	2

Supplementary Table 2 Sensitivities in discovery, validation, and the entire set at 96% specificity for validated IgG antibodies with higher prevalence in healthy controls relative to CD patients

	Antigen	Protein name	Organism	Discovery	Validation	Entire
Bacteria	HP_1564	ABC transporter substrate-binding protein	<i>H. pylori</i>	14	16	16
	SACOL0985	MAP domain-containing protein	<i>S. aureus</i>	16	14	14
	AUO97_RS08350	Hypothetical protein	<i>A. baumannii</i>	14	14	13
	SACOL1164	Complement convertase inhibitor	<i>S. aureus</i>	14	16	14
	SPy_2009	Ecb LPXTG-anchored fibronectin-binding protein FbpA	<i>S. pyogenes</i>	38	22	24
	HI_0162	Hypothetical protein	<i>H. influenzae</i>	18	16	16
	PA_exoT	T3SS effector bifunctional cytotoxin	<i>P. aeruginosa</i>	14	14	13
	AB185_RS23245	exoenzyme T				
	AB185_RS19385	Type VI secretion system effector Hcp	<i>K. oxytoca</i>	18	18	19
		Hcp family type VI secretion system effector	<i>K. oxytoca</i>	20	16	19
Virus	null	Capsid protein, partial	Rhinovirus B14	14	22	17
	null	Nucleocapsid protein	Human coronavirus	32	16	18

Supplementary Table 3 Sensitivities in discovery, validation, and the entire set at 96% specificity for validated IgG antibodies with higher prevalence in healthy controls relative to UC patients

Antigen	Protein name	Organism	Discover y	Validatio n	Entir e
	Extracellular matrix				
SACOL0858	protein-binding	<i>S. aureus</i>	20	14	11
	adhesin Emp				
	LPXTG-anchored				
SACOL1140	heme-scavenging	<i>S. aureus</i>	16	20	16
	protein IsdA				
	Phosphatidylinosito				
SACOL0078	l-specific	<i>S. aureus</i>	14	20	16
	phospholipase C				
	MAP domain-				
SACOL2197	containing protein	<i>S. aureus</i>	16	16	14
	Peptidoglycan-				
PMI_RS02875	associated	<i>P. mirabilis</i>	14	16	15
	lipoprotein Pal				
	Lytic				
	transglycosylase				
SPy_2191	domain-containing	<i>S. pyogenes</i>	16	22	20
	protein				
	CAMP factor pore-				
SPy_cfa	forming toxin Cfa	<i>S. pyogenes</i>	18	20	16
	Outer membrane				
HI_0256	protein assembly	<i>H. influenzae</i>	18	18	15
	factor BamC				
	Cell envelope				
HI_null	integrity protein	<i>H. influenzae</i>	14	18	15
	TolA				
	Hypothetical				
HI_0162	protein	<i>H. influenzae</i>	16	20	18

	HI_1174	Outer membrane beta-barrel protein	<i>H. influenzae</i>	16	16	16
	PM_null	InlB B-repeat-containing protein	<i>P. micra</i>	14	20	14
	SP_1732	Stk1 family PASTA domain-containing Ser/Thr kinase	<i>S. pneumoniae</i>	24	32	24
	SP_2136	Choline-binding protein PcpA	<i>S. pneumoniae</i>	22	32	23
	SP_0785	Membrane-fusion protein	<i>S. pneumoniae</i>	16	32	19
	SP_0366	Oligopeptide ABC transporter, oligopeptide-binding protein AliA	<i>S. pneumoniae</i>	14	22	17
	SP_1923	Pneumolysin	<i>S. pneumoniae</i>	32	34	33
	SP_0377	Choline-binding protein CbpC	<i>S. pneumoniae</i>	20	28	22
	SACOL1869	Serine protease SplA	<i>S. aureus</i>	16	18	16
	AB185_RS2746 5	Peptidoglycan-associated lipoprotein Pal	<i>K. oxytoca</i>	16	14	15
	SACOL2291	CHAP domain-containing protein	<i>S. aureus</i>	24	18	15
	PVgp1	Capsid protein VP1	Enterovirus C	14	20	18
	null	Capsid protein, partial	Rhinovirus B14	14	24	18
Virus	null	Polyprotein	Rhinovirus B14	34	36	28
	null	Polyprotein	Coxsackievirus B4	22	24	18

N	Nucleoprotein	Human metapneumovirus	14	28	18
F	Fusion glycoprotein	Human metapneumovirus	16	24	20
null	Fusion protein	Human respiratory syncytial virus B	14	18	16
PA	Polymerase acidic protein	Influenza A virus	26	20	23
PVgp1	Genome polyprotein	Enterovirus C	20	32	28
NP	Nucleoprotein	Influenza A virus	14	20	17
M1	Matrix protein 1	Influenza A virus	22	32	25

Supplementary Table 4 Sensitivities in discovery, validation, and the entire set at 96% specificity for validated IgA antibodies with higher prevalence in healthy controls relative to CD patients (Top) and UC patients (Bottom)

	Antigen	Protein name	Organism	Discovery	Validation	Entire
Crohn's disease	SACOL2509	Fibronectin-binding protein FnbB	<i>S. aureus</i>	28	18	17
		Fibronectin-binding protein FnbA	<i>S. aureus</i>	18	22	19
Bacteria	SACOL2476	Staphylopine-dependent metal ABC transporter substrate-binding protein CntA	<i>S. aureus</i>	18	14	12
		LPXTG-anchored fibronectin-binding protein FbpA	<i>S. pyogenes</i>	30	20	21
	HI_null	Cell envelope integrity protein TolA	<i>H. influenzae</i>	18	18	17
	HI_oapA	Opacity-associated protein OapA	<i>H. influenzae</i>	16	14	15
	SP_1479	Polysaccharide deacetylase family protein	<i>S. pneumoniae</i>	18	20	20

Ulcerative colitis	SACOL1868	Serine protease SplB	<i>S. aureus</i>	18	14	13
	SACOL2509	Fibronectin-binding protein FnbB	<i>S. aureus</i>	22	18	18
Bacteria	HI_oapA	Opacity-associated protein OapA	<i>H. influenzae</i>	14	18	17
	SP_0366	Oligopeptide ABC transporter, oligopeptide-binding protein AliA	<i>S. pneumoniae</i>	16	16	13
	SP_0346	Capsular polysaccharide biosynthesis protein Cps4A	<i>S. pneumoniae</i>	20	16	18
	SP_0336	Penicillin-binding protein 2X	<i>S. pneumoniae</i>	14	16	15
	SP_1479	Polysaccharide deacetylase family protein	<i>S. pneumoniae</i>	18	18	14
	SP_0377	Choline-binding protein CbpC	<i>S. pneumoniae</i>	20	16	18
	SACOL2194	Hyaluronate lyase HysA	<i>S. aureus</i>	20	18	19