Functional theme	Pathway	Number
	-	of genes
Host Susceptibility	Virus-Host Interaction	14
	Angiotensin System	12
Interferon Response	ALPK1 Signaling	7
	DNA Sensing	44
	Glycan Sensing	38
	Inflammasomes Interferon	22
	Response Genes JAK-STAT	24
	Signaling	71
	MAPK Signaling	24
	NLR Signaling	95
	RNA Sensing	56
	TLR Signaling	76
	TNF Signaling	72
	Type I Interferon Signaling	68
	Type II Interferon Signaling	41
	Type III Interferon Signaling	10
Innate Immune Cell Activation	Chemokine Signaling	75
	Cytotoxicity	11
	Host Defense Peptides	15
	IL-1 Signaling	45
	IL-17 Signaling	20
	IL-2 Signaling	29
	IL-6 Signaling	16
	JAK-STAT Signaling	71
	MAPK Signaling	24
	Mononuclear Cell Migration	54
	Myeloid Activation	167
	Myeloid Inflammation	27
	NF-kappaB Signaling	75
	NK Activity	32
	NO Signaling	9
	Other Interleukin Signaling	77
	Oxidative Stress Response	44
	Phagocytosis	30
	PPAR Signaling	7
	TGF-beta Signaling	28
	TNF Signaling	72
Adaptive Immune Response	BCR Signaling	55
	Complement System	23
	Cytotoxicity	11
	IL-1 Signaling	45
	IL-17 Signaling	20
	IL-2 Signaling	29

Supplementary Table 1. Pathway annotations across the 5 functional themes of the nCounter Human Host Response panel.

	IL-6 Signaling	16
	Immune Exhaustion	17
	Immune Memory	9
	JAK-STAT Signaling	71
	Lymphocyte Trafficking	25
	MAPK Signaling	24
	MHC Class I Antigen Presentation	34
	MHC Class II Antigen Presentation	17
	Mononuclear Cell Migration	54
	NF-kappaB Signaling	75
	Other Interleukin Signaling	77
	T-cell Costimulation	28
	TCR Signaling	92
	TGF-beta Signaling	28
	TH1 Differentiation	19
	TH17 Differentiation	36
	TH2 Differentiation	18
	TH9 Differentiation	10
	TNF Signaling	72
	Treg Differentiation	14
Homeostasis	Apoptosis	27
	Angiotensin System	12
	Autophagy	15
	Coagulation	33
	HIF1A Signaling	21
	Leukotriene and Prostaglandin Inflammation	13
	Lysosome	27
	MAPK Signaling	24
	NO Signaling	9
	Oxidative Stress Response	44
	Proteotoxic Stress	28
	TGF-beta Signaling	28
	Tissue Stress	7
	TNE Signaling	70

Supplementary table 2: Response to biologic treatment at 3 months after therapy start

	Responders	Non-responders
Crohn's disease	2	2
Anti-TNF	0	2
Vedolizumab	1	0
Ustekinumab	1	0
Ulcerative colitis	15	5
Anti-TNF	13	3
Vedolizumab	2	1
Ustekinumab	0	0

discriminated according to treatment received

TNF, tumor necrosis factor

Supplementary figure 1



Supplementary figure 1: Gene expression analysis of active IBD patients according to response to biologic therapy. Inflamed colonic biopsies were sampled from UC and CD patients, before the beginning of biologic therapy and analyzed using NanoString nCounter Host Response panel for gene expression. Patients were grouped according to therapy response after 3 months from treatment start. Principal component analysis based on the full set of genes is shown between responders (n=17) and non responders (n=7). PC, principal component

Supplementary figure 2



Supplementary figure 2: Gene expression analysis of active IBD patients according to sampling location. Inflamed colonic biopsies were sampled from UC and CD patients with active disease and analyzed using NanoString nCounter Host Response panel for gene expression (776 genes). Principal component analysis based on the full set of genes is shown between samples collected from the rectum (n=8), sigmoid colon (n=9), left colon (n=4), transverse colon (n=2) and right colon (n=4). PC, principal component.

Supplementary figure 3



Supplementary figure 3: Gene expression analysis of UC patients with active disease, UC patients in remission and healthy subjects. Mucosal gene expression data in inflamed biopsies from UC patients in active disease, and sigmoid biopsies from UC patients in remission and healthy subjects were analyzed using the NanoString nCounter Host response panel, 776 genes. Principal component analysis based on the full set of genes is shown between UC active (n=20), UC remission (n=10) and healthy subjects (n=10).PC, principal component; UC, ulcerative colitis.