Supplementary Table S1. qRT-PCR primer list.

FXR F	5'-CTACCAGGATTTCAGACTTTGGAC-3'
FXR R	5'-GAACATAGCTTCAACCGCAGAC-3'
SHP F	5'-AGGGACCATCCTCTTCAACC-3'
SHP R	5'-TTCACACAGCACCCAGTGAG-3'
HRPT F	5'-ATTGTAATGACCAGTCAACAGGG-3'
HRPT R	5'-GCATTGTTTTGCCAGTGTCAA-3'
VILLIN F	5'-AGGGCAAGAGGAACGTGGT-3'
VILLIN R	5'-TCCCCTCGGTTGAAACTCTTC-3'
SI F	5'-GGAGATACACCAGAACAAGTAGTTCAA-3'
SI R	5'-AATCCAAGATTCCAATATGCTGG-3'
c-myc F	5'-CCACCACCAGCAGCGACT-3'
c-myc R	5'-CAGAAACAACATCGATTTCTTCCTC-3'
CCDN1 F	5'-CGTGGCCTCTAAGATGAAGGA-3'
CCDN1 R	5'-CGGTGTAGATGCACAGCTTCT-3'

Supplementary Table S2. Number of patients and hospitals.

Hospital	Patients
Academic Medical Centre Amsterdam	439
VU University Medical Centre Amsterdam	647
University Medical Centre Groningen	547
University Medical Centre Leiden	494
University Medical Centre St. Radboud, Nijmegen	148
University Medical Centre Utrecht	80
Total number of patients	**2355**

Supplementary Table S3. RS numbers and chromosomal locations of the SNPs in FXR.

	SNP number	Chromosomal location on chromosome 12 (dbSNP build 132)
Tagging SNPs	rs11837065*	100859733
	rs12313471	100864393
	rs11110390	100874901
	rs4764980	100885107
	rs11110395	100888664
	rs17030285*	100929963
	rs11610264	100932375
	rs10860603	100943948
	rs35739	100948515
Functional SNPs	-1G>T#	100887351
	518T>C#	100926058

*The rs11837065 and rs17030285 SNPs failed for technical reasons.

#The rs numbers of the functional SNPs are: rs56163822 (-1G>T) and rs61755050 (518T>C).

Supplementary Table S4. Association of genetic variants in FXR with the entire IBD cohort (patients with Crohn's disease and ulcerative colitis).

		IBD patients			Controls			p value*	OR	95% CI
		Allele counts			Allele counts					
		Minor	Major	MAF	Minor	Major	MAF			
-1G>T	A/C#	125	4461	0.027	36	1588	0.022	0.2674	1.21	0.84-1.76
518T>C	G/A	29	4545	0.006	6	1616	0.004	0.2227	1.52	0.65-3.57
rs12313471	G/A	277	4245	0.061	76	1548	0.047	**0.0317**	1.32	1.02-1.71
rs11110390	T/C	1473	3103	0.322	544	1070	0.337	0.2641	0.93	0.83-1.05
rs4764980	A/G	2271	2261	0.501	778	832	0.517	0.2179	1.07	0.96-1.20
rs11110395	T/G	156	3182	0.047	84	1538	0.052	0.4365	0.89	0.68-1.17
rs11610264	C/T	1343	3141	0.300	458	1160	0.283	0.2138	1.08	0.95-1.23
rs10860603	A/G	549	3687	0.130	214	1398	0.133	0.7492	0.97	0.82-1.15
rs35739	C/T	2033	2441	0.454	712	900	0.442	0.3790	1.05	0.94-1.18

OR = odds ratio; 95% CI = 95% confidence interval.

Minor allele / major allele; MAF = minor allele frequency

* Two-tailed P values were calculated by χ^2 analysis of allele counts

Significant p values are shown in bold.

Supplementary Table S5. Association of genetic variants in FXR with ulcerative colitis.

		UC patients			Controls			p value*	OR	95% CI
		Allele counts			Allele counts					
		Minor	Major	MAF	Minor	Major	MAF			
-1G>T	A/C#	58	2264	0.025	36	1588	0.022	0.5688	1.12	0.74-1.70
518T>C	G/A	10	2292	0.004	6	1616	0.004	0.7549	1.11	0.42-2.95
rs12313471	G/A	141	2155	0.061	76	1548	0.047	**0.0487**	1.32	1.00-1.76
rs11110390	T/C	719	1605	0.309	544	1070	0.337	0.0673	0.88	0.77-1.01
rs4764980	A/G	1182	1116	0.514	778	832	0.483	0.0554	1.13	1.00-1.29
rs11110395	T/G	58	1340	0.041	84	1538	0.052	0.1824	0.80	0.57-1.12
rs11610264	C/T	705	1585	0.308	458	1160	0.283	0.0949	1.13	0.98-1.29
rs10860603	A/G	283	1769	0.138	214	1398	0.133	0.6507	1.04	0.86-1.26
rs35739	C/T	1053	1227	0.462	712	900	0.442	0.2135	1.08	0.95-1.23

OR = odds ratio; 95% CI = 95% confidence interval

Minor allele / major allele; MAF = minor allele frequency

* Two-tailed P values were calculated by χ^2 analysis of allele counts

Significant p values are shown in bold.

Supplementary Table S6. Association of genetic variants in FXR with Crohn's disease.

		CD patients			Controls			p value*	OR	95% CI
		Allele counts			Allele counts					
		Minor	Major	MAF	Minor	Major	MAF			
-1G>T	A/C#	67	2197	0.030	36	1588	0.022	0.1550	1.33	0.88-2.00
518T>C	G/A	19	2253	0.008	6	1616	0.004	0.0725	2.05	0.84-4.99
rs12313471	G/A	136	2090	0.061	76	1548	0.047	0.0548	1.32	0.99-1.76
rs11110390	T/C	754	1498	0.335	544	1070	0.337	0.8845	1.01	0.88-1.16
rs4764980	A/G	1089	1145	0.487	778	832	0.483	0.7954	1.02	0.89-1.16
rs11110395	T/G	98	1842	0.051	84	1538	0.052	0.8636	1.03	0.72-1.31
rs11610264	C/T	638	1556	0.291	458	1160	0.283	0.6024	1.04	0.90-1.20
rs10860603	A/G	266	1918	0.122	214	1398	0.133	0.3153	0.91	0.75-1.10
rs35739	C/T	980	1214	0.447	712	900	0.442	0.7597	1.02	0.90-1.16

OR = odds ratio; 95% CI = 95% confidence interval

Minor allele / major allele; MAF = minor allele frequency

* Two-tailed P values were calculated by χ^2 analysis of allele counts

Supplementary Table S7. Association of genetic variants in FXR: subgroup analysis of patients with L1 Crohn's disease vs. Crohn's disease with other disease localization.

		CD L1 patients			CD patients			p value*	OR	95% CI
		Allele counts			Allele counts					
		Minor	Major	MAF	Minor	Major	MAF			
-1G>T	A/C#	15	483	0.030	49	1657	0.029	0.8701	1.10	0.61-1.96
518T>C	G/A	1	503	0.002	18	1690	0.011	0.0674	0.35	0.07-1.87
rs12313471	G/A	26	462	0.053	105	1575	0.062	0.4517	0.87	0.56-1.34
rs11110390	T/C	187	309	0.377	551	1147	0.324	**0.0294**	1.26	1.02-1.55
rs4764980	A/G	221	279	0.442	834	840	0.498	**0.0273**	0.80	0.65-0.98
rs11110395	T/G	26	400	0.061	71	1393	0.048	0.3021	1.30	0.82-2.06
rs11610264	C/T	138	348	0.284	486	1166	0.294	0.6625	0.95	0.76-1.19
rs10860603	A/G	48	436	0.099	211	1431	0.129	0.0830	0.76	0.54-1.05
rs35739	C/T	211	273	0.436	754	896	0.457	0.4139	0.92	0.75-1.13

OR = odds ratio; 95% CI = 95% confidence interval

Minor allele / major allele; MAF = minor allele frequency

* Two-tailed p values were calculated by χ^2 analysis of allele counts

Significant p values are shown in bold.

Supplementary Table S8. Association of genetic variants in FXR: subgroup analysis of patients with L2 Crohn's disease vs. Crohn's disease with other disease localization.

		CD L2 patients			CD patients			p value*	OR	95% CI
		Allele counts			Allele counts					
		Minor	Major	MAF	Minor	Major	MAF			
-1G>T	A/C#	17	561	0.029	47	1579	0.029	0.9503	1.05	0.60-1.84
518T>C	G/A	3	573	0.005	16	1620	0.010	0.3065	0.66	0.21-2.11
rs12313471	G/A	28	538	0.049	103	1499	0.064	0.2032	0.77	0.51-1.19
rs11110390	T/C	184	388	0.322	554	1068	0.342	0.3870	0.92	0.75-1.12
rs4764980	A/G	275	293	0.484	780	826	0.486	0.9502	0.99	0.82-1.20
rs11110395	T/G	30	472	0.060	67	1321	0.048	0.3174	1.27	0.82-1.98
rs11610264	C/T	173	395	0.305	451	1119	0.287	0.4366	1.09	0.88-1.34
rs10860603	A/G	59	489	0.108	200	1378	0.127	0.2394	0.84	0.62-1.14
rs35739	C/T	258	304	0.459	707	865	0.450	0.7029	1.04	0.86-1.26

OR = odds ratio; 95% CI = 95% confidence interval

Minor allele / major allele; MAF = minor allele frequency

Two-tailed P values were calculated by χ^2 analysis of allele counts

Supplementary Table S9. Association of genetic variants in FXR: subgroup analysis of patients with L3 Crohn's disease vs. Crohn's disease with other disease localization.

		CD L3 patients			CD patients			p value*	OR	95% CI
		Allele counts			Allele counts					
		Minor	Major	MAF	Minor	Major	MAF			
-1G>T	A/C#	32	1096	0.028	32	1044	0.030	0.8481	0.95	0.58-1.56
518T>C	G/A	15	1117	0.013	4	1076	0.004	**0.0150**	3.08	1.08-8.83
rs12313471	G/A	77	1037	0.069	54	1000	0.051	0.0806	1.37	0.96-1.95
rs11110390	T/C	367	759	0.326	371	697	0.347	0.2879	0.91	0.76-1.08
rs4764980	A/G	559	547	0.505	496	572	0.464	0.0558	1.18	1.00-1.39
rs11110395	T/G	41	921	0.043	56	872	0.060	0.0808	0.70	0.46-1.05
rs11610264	C/T	313	771	0.289	311	743	0.295	0.7479	0.97	0.80-1.17
rs10860603	A/G	152	942	0.139	107	925	0.104	**0.0130**	1.39	1.07-1.81
rs35739	C/T	496	592	0.456	469	577	0.448	0.7276	1.03	0.87-1.22

(rs10860603, p=0.01, OR 1.39, 95% CI 1.07-1.81; Supplementary Table 9).

OR = odds ratio; 95% CI = 95% confidence interval

Minor allele / major allele; MAF = minor allele frequency

* Two-tailed P values were calculated by χ^2 analysis of allele counts

Significant p values are shown in bold.