

Supplementary Data

Meta-analysis of expression profiling data indicates need for combinatorial biomarkers in pediatric ulcerative colitis

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Table S1. Expression levels of receptors for predicted upstream regulators that were not differentially expressed

The Upstream regulators(UR)	The receptors of UR	NCBI Accession	GSE9686		GSE10616			
			q-value	logFC	q-value	logFC		
<i>TNF</i>	<i>TNFR1</i>	NM_001065	0.964449	-0.008	0.802000	-0.03		
	<i>TNFR2*</i>	NM_001066	0.000567	1.308	0.000056	1.32		
<i>OSM</i>	<i>OSMR*</i>	NM_003999	0.000004	2.28	0.000256	2.19		
	<i>OSM/EBI3/ IL-27B</i>	<i>gp130/IL6ST*</i>	NM_175767	0.004510	1.24	0.002669	1.64	
NM_002184			0.004750	1.232	0.002640	1.64		
NM_172248			0.000993	1.418	0.000547	1.45		
NM_172246			0.001640	1.67	0.000642	1.79		
<i>CSF2</i>	<i>CSF2RA*</i>	NM_006140	0.001820	1.672	0.000605	1.86		
		NM_172247	0.001820	1.742	0.000638	1.87		
		NM_172245	0.001780	1.674	0.000524	1.89		
		NM_172249	0.000954	1.249	0.001865	1.11		
		<i>VEGF/VEGFA</i>	<i>VEGFR3/FLT4</i>	NM_002020	0.135000	0.21	0.191192	0.25
				NM_182925	0.066300	-0.181	0.139729	-0.18
<i>IL1</i>	<i>VEGFR2/FLK1/KDR*</i>	NM_002253	0.000100	1.503	0.000453	1.88		
		<i>IL1R1</i>	NM_000877	0.003790	0.697	0.014902	0.64	
		<i>IL1R2</i>	NM_004633	0.611000	-0.208	0.925082	0.05	
<i>IL18</i>	<i>IL18R1*</i>	NM_173343	0.616000	-0.205	0.926827	0.05		
		NM_003855	0.000286	1.122	0.002777	1.12		
		NM_003853	0.005910	0.86	0.048610	0.71		
<i>PDGF BB/PDGF (complex)</i>	<i>PDGFRA*</i>	NM_006206	0.021700	1.634	0.018271	2.02		
		NM_002609	0.002460	1.128	0.048746	0.87		
		<i>PDGFRB</i>	NM_033016	0.106000	-0.246	0.008526	-0.52	
		NM_002608	0.150000	-0.24	0.048746	0.87		
<i>IL5</i>	<i>IL5RA</i>	NM_175728	0.297000	0.123	0.258163	0.14		
		NM_175725	0.318000	0.118	0.262857	0.14		
		NM_000564	0.532000	0.063	0.423365	0.09		
		NM_175726	0.530000	0.065	0.491669	0.08		
		NM_175727	0.926000	0.009	0.851207	-0.02		
<i>IL7/TSLP IL12 (complex)</i>	<i>IL7R</i>	NM_175724	0.990000	0.001	0.876582	-0.02		
		NM_002185	0.013300	1.534	0.053356	1.61		
		<i>IL12RB1</i>	NM_005535	0.997000	-4E-04	0.724499	-0.06	
		NM_153701	0.997000	-4E-04	0.000684	1.5		
		<i>IL12RB2*</i>	NM_001559	0.008480	0.368	0.037771	0.35	
<i>IFN/IFNA1/IFNA2/IFNA13/IFNB1 /IFNE/IFNK</i>	<i>IFNAR1</i>	NM_000629	0.019900	0.519	0.001944	0.72		
		<i>IFNAR2*</i>	NM_207585	0.000651	0.666	0.001634	0.75	
		NM_207584	0.000018	1.501	0.000164	1.52		
		NM_000874	0.000018	1.504	0.000168	1.52		
<i>CG IL21</i>	<i>LHCGR</i>	NM_000233	0.246000	-0.123	0.074687	-0.21		
		<i>IL21R*</i>	NM_021798	0.000114	1.297	0.002189	1.47	
		NM_181079	0.000119	1.299	0.002204	1.47		
<i>EGF/BTC</i>	<i>EGFR</i>	NM_181078	0.000123	1.299	0.002223	1.47		
		NM_201284	0.034400	-0.262	0.060171	-0.29		
		NM_005228	0.007750	-0.402	0.054154	-0.36		
		NM_201282	0.017100	-0.455	0.003126	-0.54		
<i>CCL5/CCL3</i>	<i>CCR1*</i>	NM_201283	0.023400	-0.306	0.032851	-0.36		
		<i>CCR3</i>	NM_001295	0.000850	2.092	0.000718	2.42	
		NM_001837	0.627000	-0.191	0.885801	-0.06		
		NM_178329	0.585000	-0.213	0.857326	-0.08		

<i>Fibrinogen</i>	<i>ITGB1</i> *	NM_002211	0.007160	0.684	0.001157	1.18	
		NM_033668	0.188000	0.21	0.014916	0.46	
		NM_033666	0.505000	0.053	0.432250	0.08	
<i>IL17F</i>	<i>ITGA5</i>	NM_002205	0.086000	0.322	0.548843	0.16	
		<i>ITGA2B</i>	NM_000419	0.421000	-0.075	0.055396	-0.24
		<i>IL-17RC</i>	NM_032732	0.013300	-0.288	0.009987	-0.42
<i>IL17F/IL17C</i>	<i>IL-17RA</i>	NM_153461	0.011800	-0.295	0.011586	-0.42	
		NM_153460	0.014400	-0.285	0.010955	-0.42	
		NM_014339	0.528000	0.064	0.614741	-0.06	
<i>SAA</i>	<i>CD36</i>	NM_001001547	0.938000	0.05	0.698807	0.28	
		NM_000072	0.938000	0.05	0.706475	0.27	
		NM_001001548	0.376000	0.518	0.068235	1.25	
<i>LTA/LT</i>	<i>LTBR</i>	NM_002342	0.007910	-0.34	0.090781	-0.25	
<i>IL27/EBI3</i>	<i>IL27RA</i> *	NM_004843	0.000514	1.029	0.004754	1.14	
<i>IFNL1</i>	<i>IL10RB</i>	NM_000628	0.009250	-0.409	0.077122	-0.34	
		<i>IFNLR1</i>	NM_170743	0.009320	-0.483	0.055396	-0.46
<i>Ap1</i>	<i>TAC1</i>	NM_012452	0.336000	0.181	0.198392	0.28	
<i>IL22</i>	<i>/BCMA/TNFRSF13B</i>	<i>IL22RA1</i>	NM_021258	0.270000	-0.3	0.687153	-0.14
		<i>IL22RA2</i>	NM_181310	0.018900	1.078	0.118424	0.78
		NM_181309	0.019000	1.077	0.117328	0.78	
<i>IL23</i>	<i>IL23R</i>	NM_052962	0.019300	1.069	0.115673	0.78	
		NM_144701	0.010100	-0.6	0.079804	-0.45	
		<i>CCL3</i>	<i>CCR4</i>	NM_005508	0.441000	-0.091	0.900976
<i>IL36A</i>	<i>IL1RL2</i>	NM_003854	0.003870	-0.439	0.003214	-0.51	
		<i>IL1RAP</i> *	NM_002182	0.048500	0.283	0.087739	0.33
		NM_134470	0.008990	0.415	0.009676	0.48	
<i>C5</i>	<i>C5AR1</i> *	NM_001736	0.000735	0.961	0.019548	0.78	
		<i>TGFBR1</i> *	NM_004612	0.001150	1.164	0.001091	1.38
		<i>TGFBR2</i> *	NM_001024847	0.003400	0.713	0.003924	0.9
<i>TSLP</i>	<i>CRLF2</i>	NM_003242	0.003470	0.712	0.004039	0.9	
		NM_022148	0.365000	-0.13	0.296690	-0.17	
		<i>IL17C</i>	<i>IL-17RE</i>	NM_153483	0.000649	-0.656	0.003525
<i>MIF</i>	<i>CXCR2</i> *	NM_153482	0.000687	-0.654	0.003553	-0.7	
		NM_153481	0.000667	-0.655	0.003468	-0.71	
		NM_153480	0.000709	-0.65	0.003707	-0.7	
		NM_144640	0.000800	-0.643	0.005108	-0.68	
		NM_001557	0.000031	2.744	0.001082	2.32	
		<i>CXCR4</i>	NM_001008540	0.121000	1.096	0.207240	1.13
		NM_003467	0.121000	1.097	0.206988	1.13	
		<i>CD74</i> *	NM_001025159	0.000539	1.64	0.000350	2.17
		NM_004355	0.000172	1.891	0.000345	2.29	
		NM_001025158	0.000172	1.892	0.000345	2.29	
<i>AP-1</i>	<i>CTLA4</i>	NM_005214	0.007710	1.078	0.063021	0.94	
		NM_001037631	0.007280	1.136	0.065263	0.98	
<i>PRL</i>	<i>PRLR</i>	NM_000949	0.052300	-0.172	0.094922	-0.2	
<i>AIMP1</i>	<i>FCER2</i>	NM_002002	0.884000	0.028	0.919485	-0.03	
<i>IGF2</i>	<i>IGF2R</i>	NM_000876	0.792000	-0.034	0.962755	-0.01	
<i>GHI</i>	<i>GHR</i>	NM_000163	0.238000	0.673	0.053277	1.08	
<i>LDL</i>	<i>LDLR</i>	NM_000527	0.649000	0.167	0.540602	-0.22	

* Positive logFC and q-value < 0.05

Table S2. Expression levels of receptors to predicted upstream regulators that were differentially expressed

The Upstream regulators(UR)	The receptors of UR	NCBI Accession	GSE9686		GSE10616	
			q-value	logFC	q-value	logFC
<i>IL1B/IL1A</i>	<i>IL1R1</i>	NM_000877	0.01490168	0.638078	0.05192	0.5047544
	<i>IL1R2</i>	NM_004633	0.92508222	0.04612376	0.73942	-0.1604044
<i>IFNG</i>	<i>IFNGR1*</i>	NM_000416	0.00203069	0.64796339	0.03232	0.4309898
	<i>IFNGR2</i>	NM_005534	0.02734678	-0.35199119	0.01784	-0.3421646
<i>TGFBI</i>	<i>TGFBR1</i>	NM_032811	0.07843288	-0.39924435	0.22272	-0.2552363
	<i>TGFBR4</i>	NM_030900	0.00012386	-1.21207349	0.00818	-0.9596834
		NM_199122	0.00012923	-1.20612685	0.00804	-0.957314
<i>IL17A</i>		NM_004749	0.00014338	-1.19615166	0.00813	-0.9598502
	<i>IL17RA</i>	NM_014339	0.61474102	-0.05812228	0.57487	-0.0549465
	<i>IL17RB</i>	NM_018725	0.00320971	-1.21518581	0.01276	-0.9942018
		NM_172234	0.00321339	-1.2161327	0.01276	-0.9952967
	<i>IL17RC</i>	NM_153460	0.01095515	-0.41716286	0.05786	-0.2613939
		NM_153461	0.01158635	-0.41533981	0.054	-0.2678711
		NM_032732	0.00998736	-0.42431466	0.05242	-0.2668482
<i>IL17A</i>	<i>IL17RD</i>	NM_017563	0.01572808	-0.3488694	0.018	-0.3839925
	<i>IL17RE</i>	NM_153481	0.00346814	-0.70505616	0.00379	-0.7338211
		NM_153480	0.00370663	-0.70220352	0.00379	-0.7303083
		NM_153483	0.00352486	-0.70017927	0.00379	-0.734637
<i>IL6</i>		NM_144640	0.00510833	-0.67756985	0.00379	-0.7237509
	<i>IL6R</i>	NM_181359	0.03256818	-0.42177306	0.04104	-0.369827
		NM_000565	0.03400864	-0.41762472	0.04261	-0.3632954

* Positive logFC and q-value < 0.05

Table S3. Pathways that overlapped between expression profiling data from three studies of colonic biopsies and whole blood cells from pediatric ulcerative colitis (z-score > 2 and P value < 0.05)

Positive canonical pathway	Activation z-score			P-value		
	GSE9686	GSE10616	GSE119600	GSE9686	GSE10616	GSE119600
Tec Kinase Signaling	3.81	2.714	3.244	0.002344	0.012882	0.000004
IL-8 Signaling	3.666	3.349	2.885	0.006166	0.011749	0.0002
TREM1 Signaling	3.317	3.651	3.528	0.00003	0.003236	0.000004
Role of Pattern Recognition Receptors in Recognition of Bacteria and Viruses	3.28	2.746	2.6	0.022909	0.012882	0.039811
Production of Nitric Oxide and Reactive Oxygen Species in Macrophages	3.13	3.048	3.464	0.012303	0.00302	0.001072
Leukocyte Extravasation Signaling	2.951	2.63	2.714	0.00000	0.00000	0.012303
Acute Phase Response Signaling	2.898	2.263	3.28	0.006918	0.00138	0.016218
Neuroinflammation Signaling Pathway	2.866	2.36	3.447	0.00912	0.001148	0.013183

Table S4. List of differentially expressed predicted upstream regulators in whole blood cells

Upstream Regulator	Log FC	Activation z-score
<i>VEGF</i>		3.946
<i>HGF</i>		3.674
<i>TGFB1</i>		3.455
<i>OSM</i>	0.406	3.056
<i>AR</i>		2.705
<i>IL6</i>		2.616
<i>EGF</i>		2.525
<i>LIF</i>		2.472
<i>EDNRA</i>		2.449
<i>Nr1h</i>		2.449
<i>INHBA</i>		2.444
<i>FGF2</i>		2.383
<i>26s Proteasome</i>		2.368
<i>CSF1</i>		2.324
<i>CSF3</i>		2.305
<i>PDGF BB</i>		2.282
<i>IGF1</i>		2.247
<i>LRP6</i>		2.216
<i>PGR</i>		2.169
<i>SELP</i>		2.121
<i>FGF8</i>		2.111

Table S5. List of potential biomarkers for ulcerative colitis in whole blood cells

Gene symbol	NCBI Accession	GSE119600 UC (Log FC)
<i>FGFBP2</i>	NM_031950	-0.796
<i>IL32</i>	NM_001012631	-0.686
<i>MUC6</i>	NM_005961	-0.678
<i>LGALS3</i>	NM_001357678	-0.512
<i>PII6</i> *	NM_001199159	-0.508
<i>ADM</i>	NM_001124	0.515
<i>PROK2</i>	NM_001126128	0.522
<i>COL18A1</i>	NM_030582	0.539
<i>F5</i>	NM_000130	0.624
<i>JCHAIN</i>	NM_144646	1.09
<i>MZB1</i> *,#	NM_016459	1.1
<i>MMP9</i>	NM_004994	1.25

*Indicates new potential biomarkers in blood; # Indicates new potential biomarkers in colon.

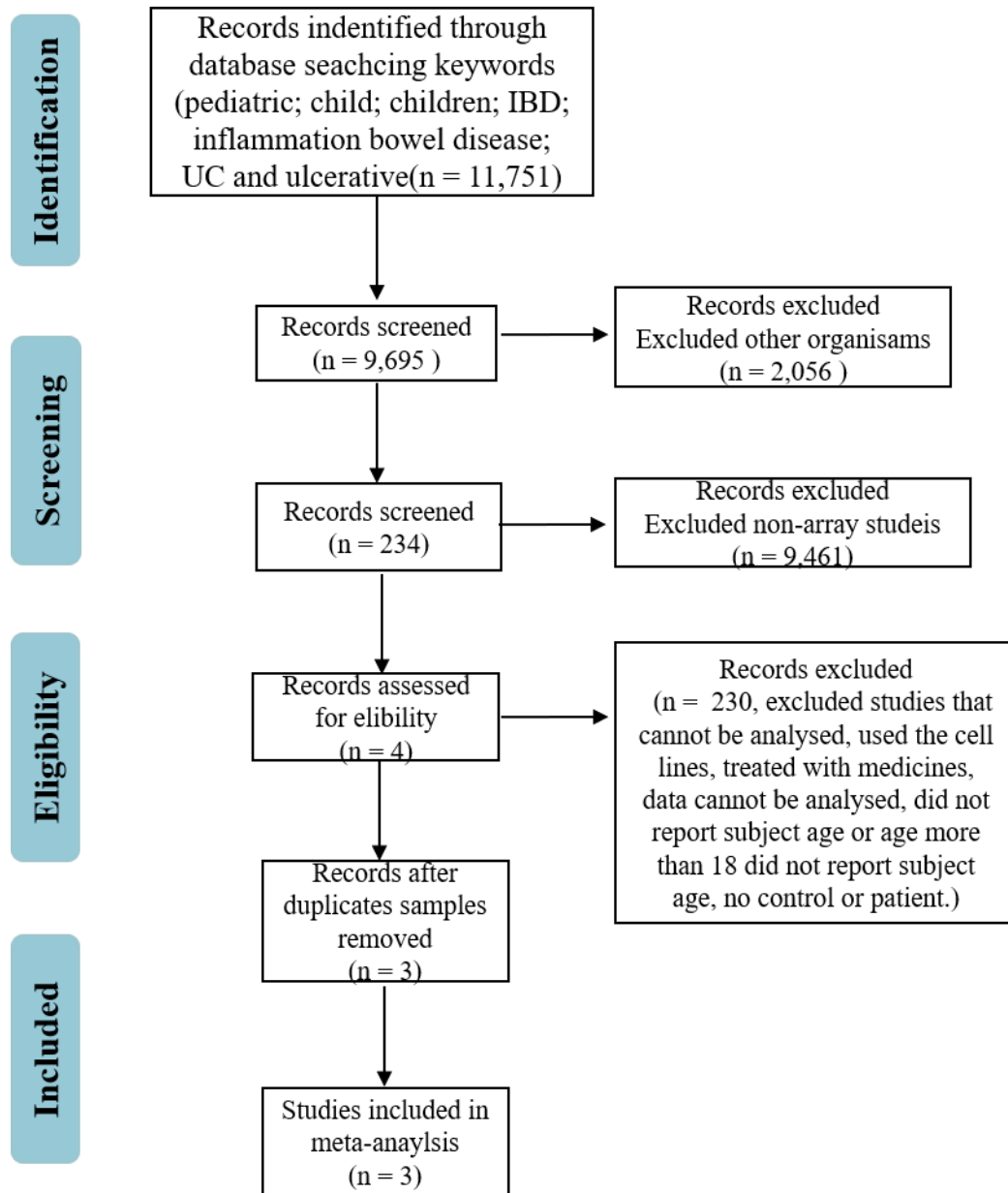


Figure S1. Summary of workflow used for the microarray meta-analysis

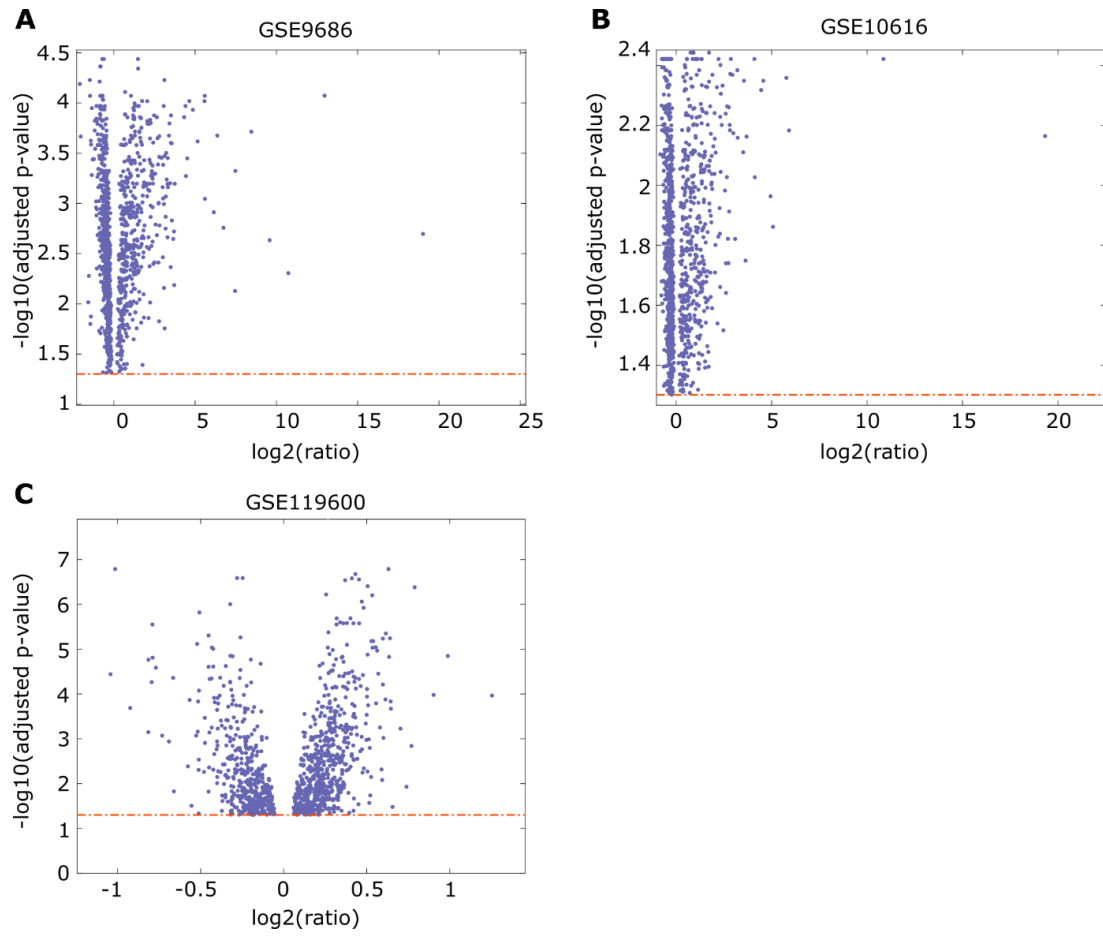


Figure S2. Volcano plots for three datasets

Volcano plots showing differentially expressed genes shared by all datasets. Red horizontal line denotes adjusted P-value cutoff of 0.05