

Molecular Comparison of Ulcerative Colitis Different in Age and Extent of Disease by Colon Biopsy mRNA Expression Profiling

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Disclosure: Janssen Research and Development



Adult vs. Pediatric UC – Data Compatibility

Data	Adult UC	Pediatric UC
	Simponi UC T17	GSE10616*
Data type	Colon biopsy	Colon biopsy
Platform (all in situ oligonucleotide)	Affymetrix HT HG U133+ PM array	Affymetrix HG U133 Plus 2
Total # of probes	54,715	54,675
Analysis	In-house	In-house
Analysis cutoff	$ FC > 2x$, adjust $p < 0.05$	$ FC > 2x$, adjust $p < 0.05$
Sample size	87 UC, 21 normal	10 UC, 11 normal
Disease profile	2253 probe sets	2129 probe sets

*Data extracted from Nature Genetics 2008

Top Ranked Canonical Pathways in Adult and Pediatric UC

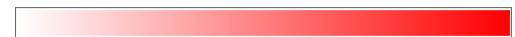
Canonical Pathway	Enrichment significance, -log(p-value*)	
	Pediatric UC (GSE10616)	Adult UC (C0524T17)
Hepatic Fibrosis / Hepatic Stellate Cell Activation	19.91	16.06
Granulocyte Adhesion and <u>Diapedesis</u>	18.50	25.49
<u>Agranulocyte</u> Adhesion and <u>Diapedesis</u>	15.74	22.96
Atherosclerosis Signaling	10.22	11.80
Inhibition of Matrix Metalloproteases	8.04	5.92
LPS/IL-1 Mediated Inhibition of RXR Function	7.99	7.33
Role of IL-17A in Psoriasis	7.91	9.23
Dendritic Cell Maturation	7.77	13.74
Altered T Cell and B Cell Signaling in RA	7.45	11.46
Differential Regulation of Cytokine Production in Intestinal Epithelial Cells by IL-17A and IL-17F	7.22	5.91
Role of Macrophages, Fibroblasts and Endothelial Cells in RA	6.87	11.71
TREM1 Signaling	5.27	13.45
Leukocyte Extravasation Signaling	5.26	10.85
B Cell Development	4.36	10.86

P-values based on Fisher's exact test

-log(p-value) < 1.3 considered significant enrichment (p-value < 0.05)

0.0

25.5



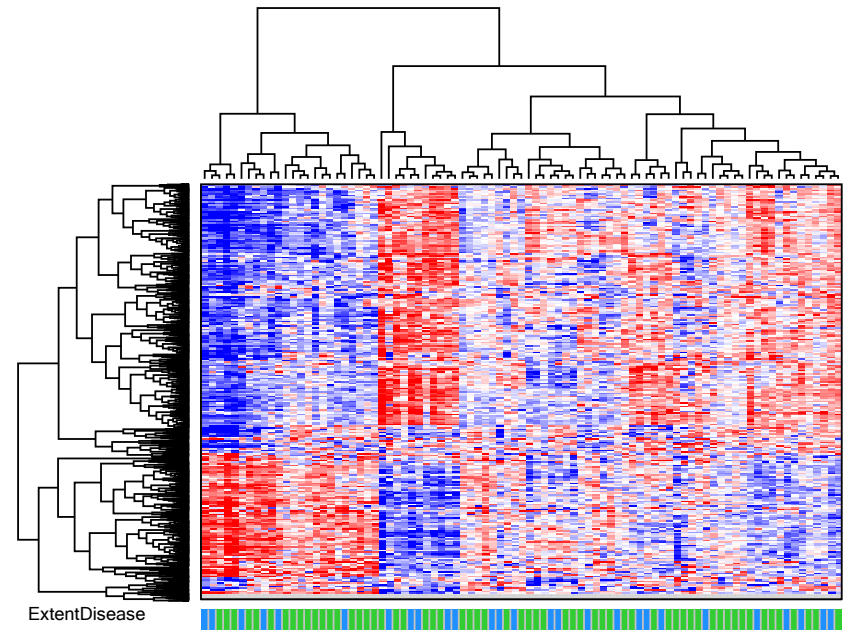
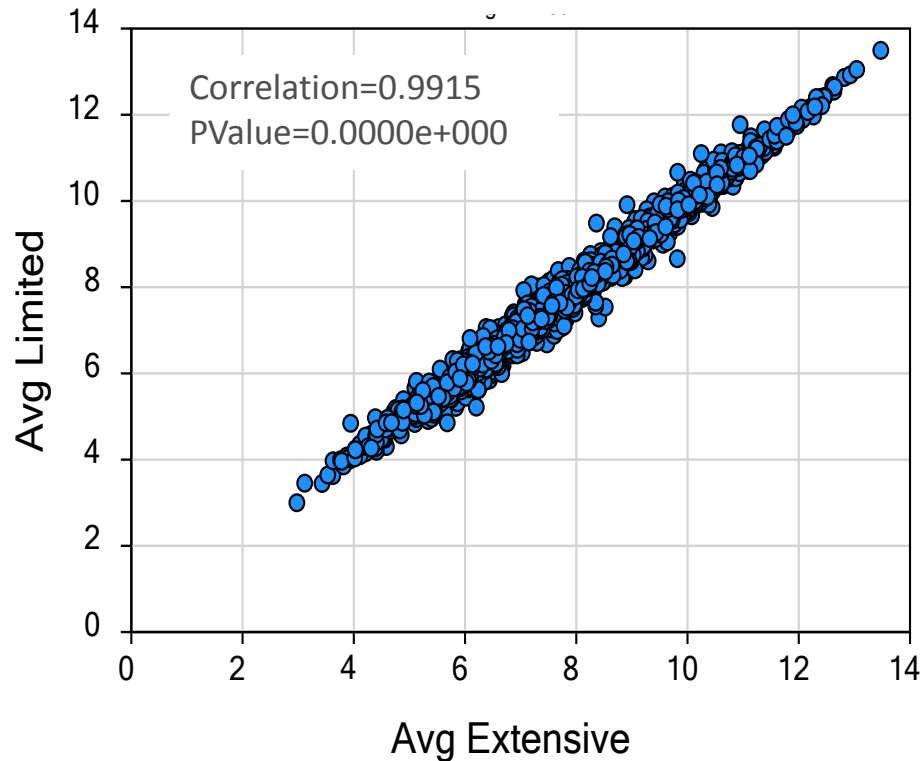
Common Upstream Expression Molecules Observed in Adult and Pediatric UC

Upstream regulators	Activation z-score	
	Pediatric UC (GSE10616)	Adult UC (C0524T17)
lipopolysaccharide	11.27	12.84
IL1B	9.48	10.38
TNF	9.17	11.36
NFkB (complex)	8.15	9.21
IFNG	7.78	10.07
phorbol myristate acetate	7.76	8.62
CSF2	7.60	7.59
IL1A	7.59	8.09
SB203580	-7.39	-7.64
poly rI:rC-RNA	7.37	8.61
IL6	7.37	7.62



Extensive vs. Local Disease: Adult Patients

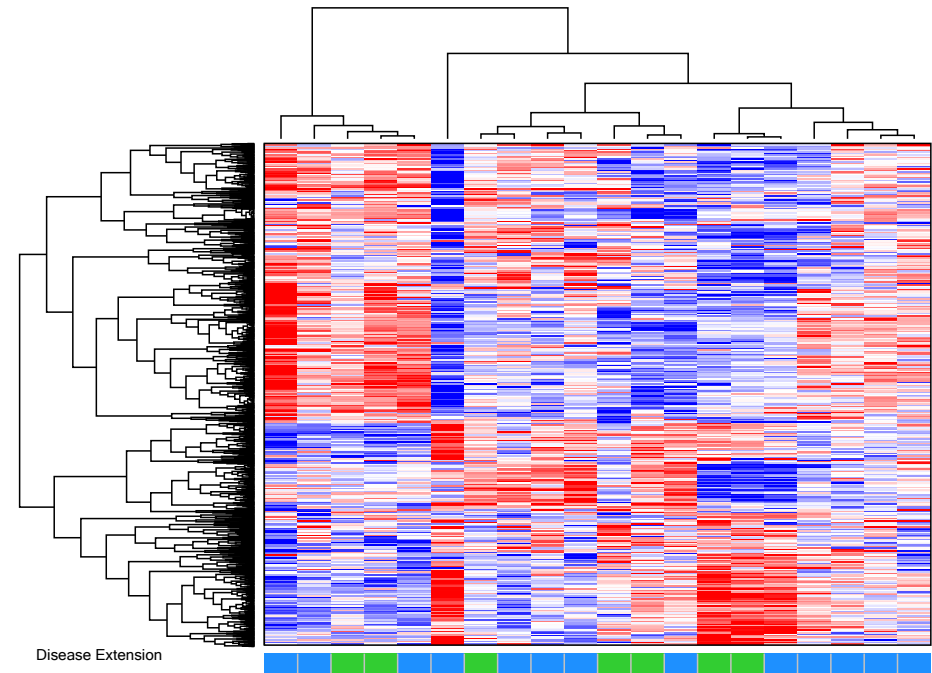
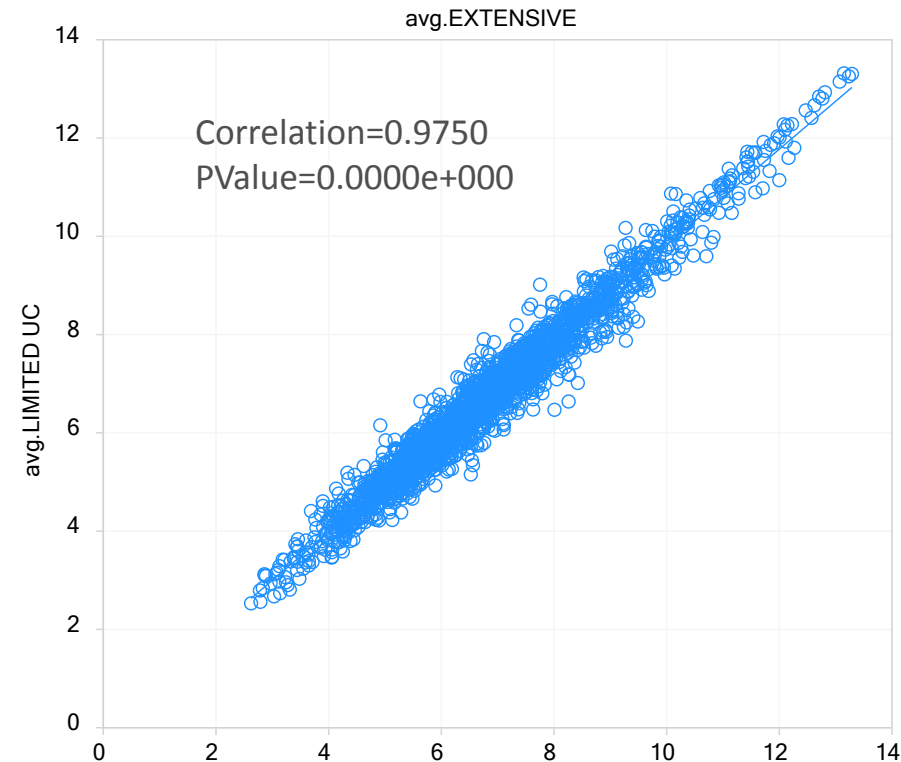
Dataset: C0154T17 ADULT ULCERATIVE COLITIS STUDY, BASELINE SAMPLES



- Disease profile in extensive UC is highly correlated with that in local disease
- Unsupervised clustering of the disease profile shows no segregation of extensive (n=27) vs. limited (n=60) UC in adult patients.

Extensive vs. Local Disease: Pediatric Subjects

Dataset: CNT0148UC01001 PEDIATRIC ULCERATIVE COLITIS STUDY, BASELINE SAMPLES



- Disease profile in extensive UC is highly correlated with that in local disease
- Unsupervised clustering of the disease profile shows no segregation of extensive (n=13) vs. limited (n=7) UC in adult patients.

Backup

Figure 2A

Top Canonical Pathways in Pediatric and Adult UC

