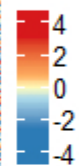Supplementary figure 1 A

Diagnosis
CD
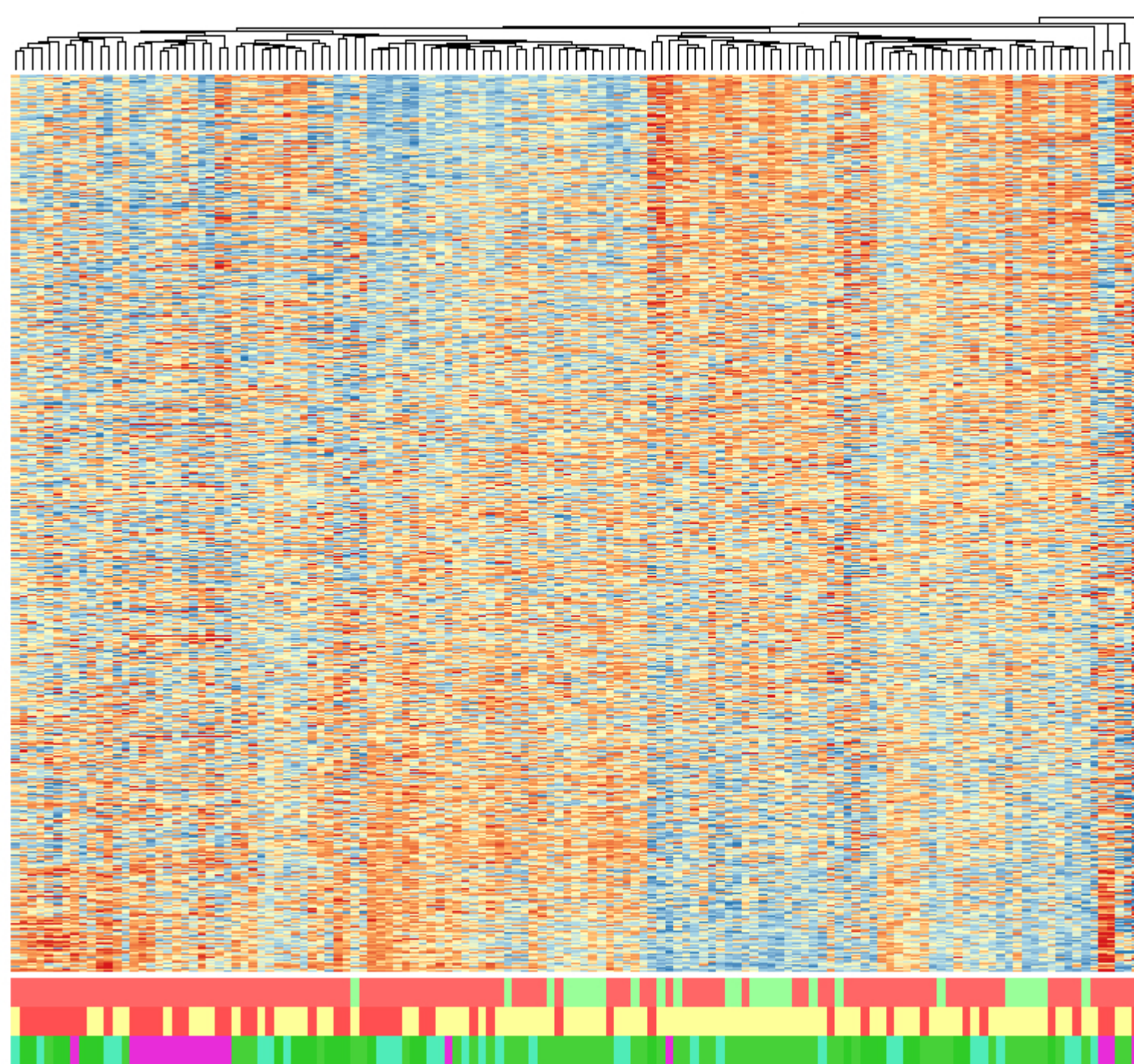Healthy control

Inflammation
Inflamed
Non-inflamed

Location
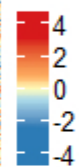Terminal ileum
Proximal colon
Distal colon
Rectum

Supplementary figure 1 B

Diagnosis
UC
Healthy control

Inflammation
Inflamed
Non-inflamed

Location
Terminal ileum
Proximal colon
Distal colon
Rectum

Supplementary figure 2

Supplementary figure 3

A — Top left: **UC - non-inflamed** (p= 0.832); Top right: **CD - Non-inflamed** (p= 0.175)

B — Bottom left: **UC - inflamed** (p= 0.954); Bottom right: **CD - Inflamed** (p= 0.644)

Legend: Cluster 1, Cluster 2, Cluster 3. Axes: Estimate (y), Months (x).
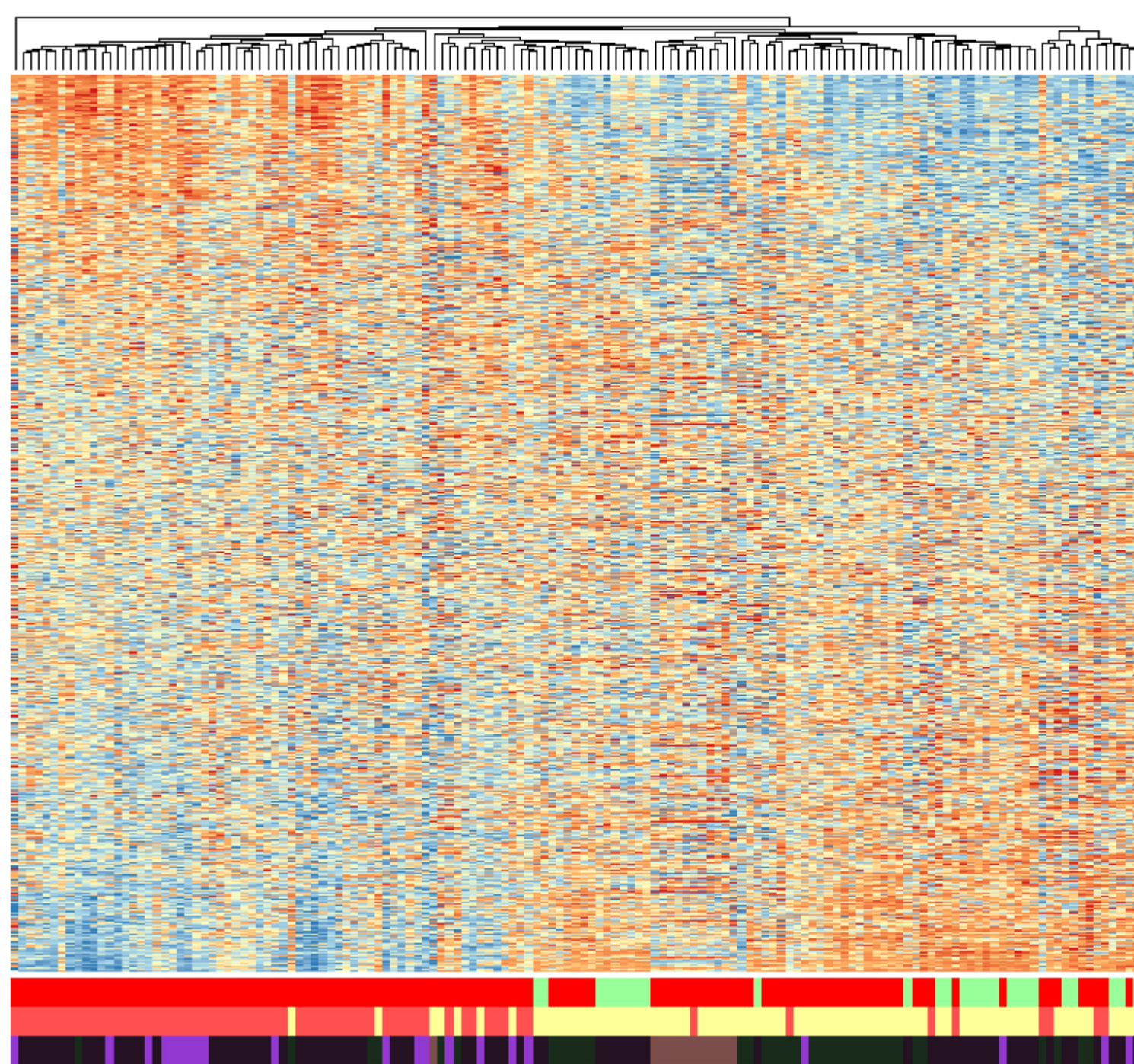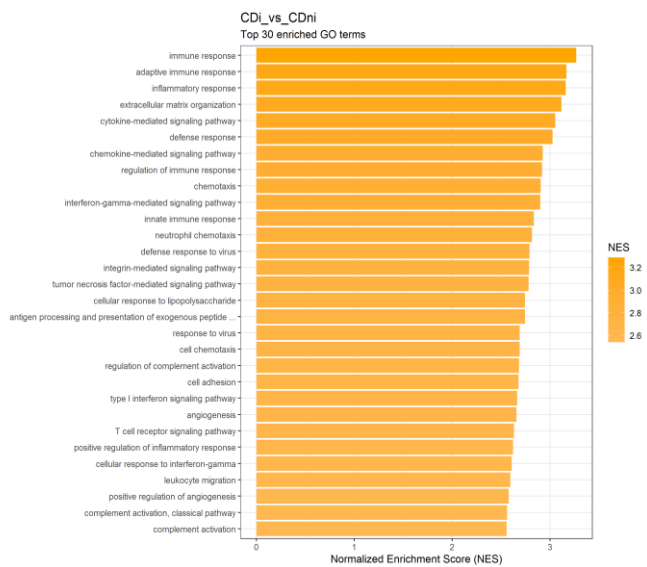
Supplementary figure 4 A

supplementary figure 4B

Supplementary figure 4C

Figure Legends to the supplementary figures

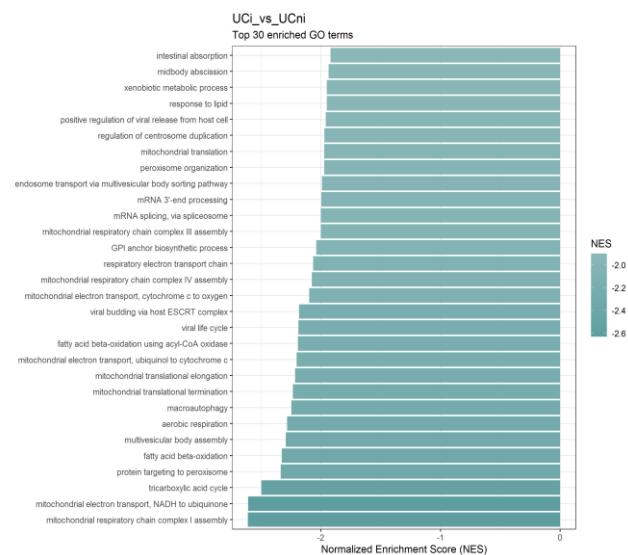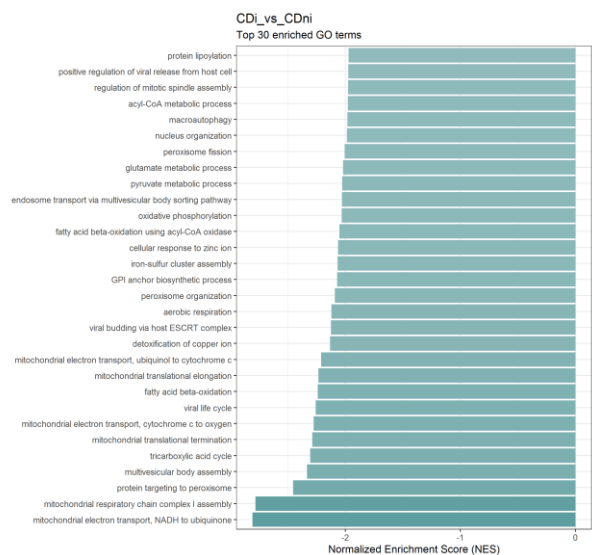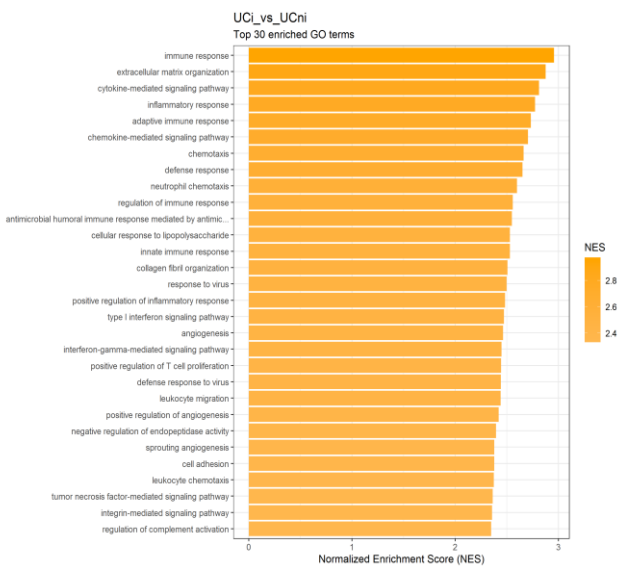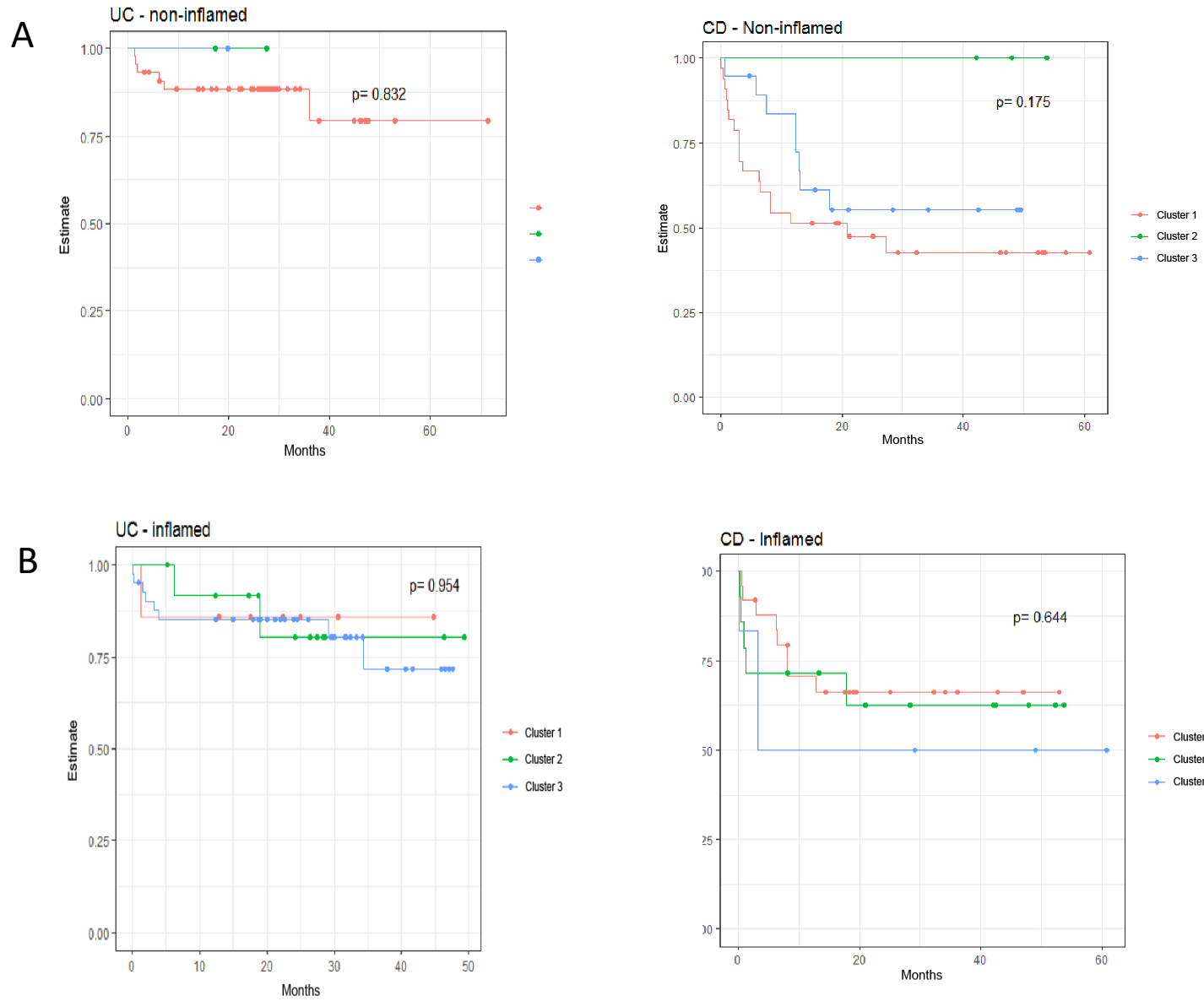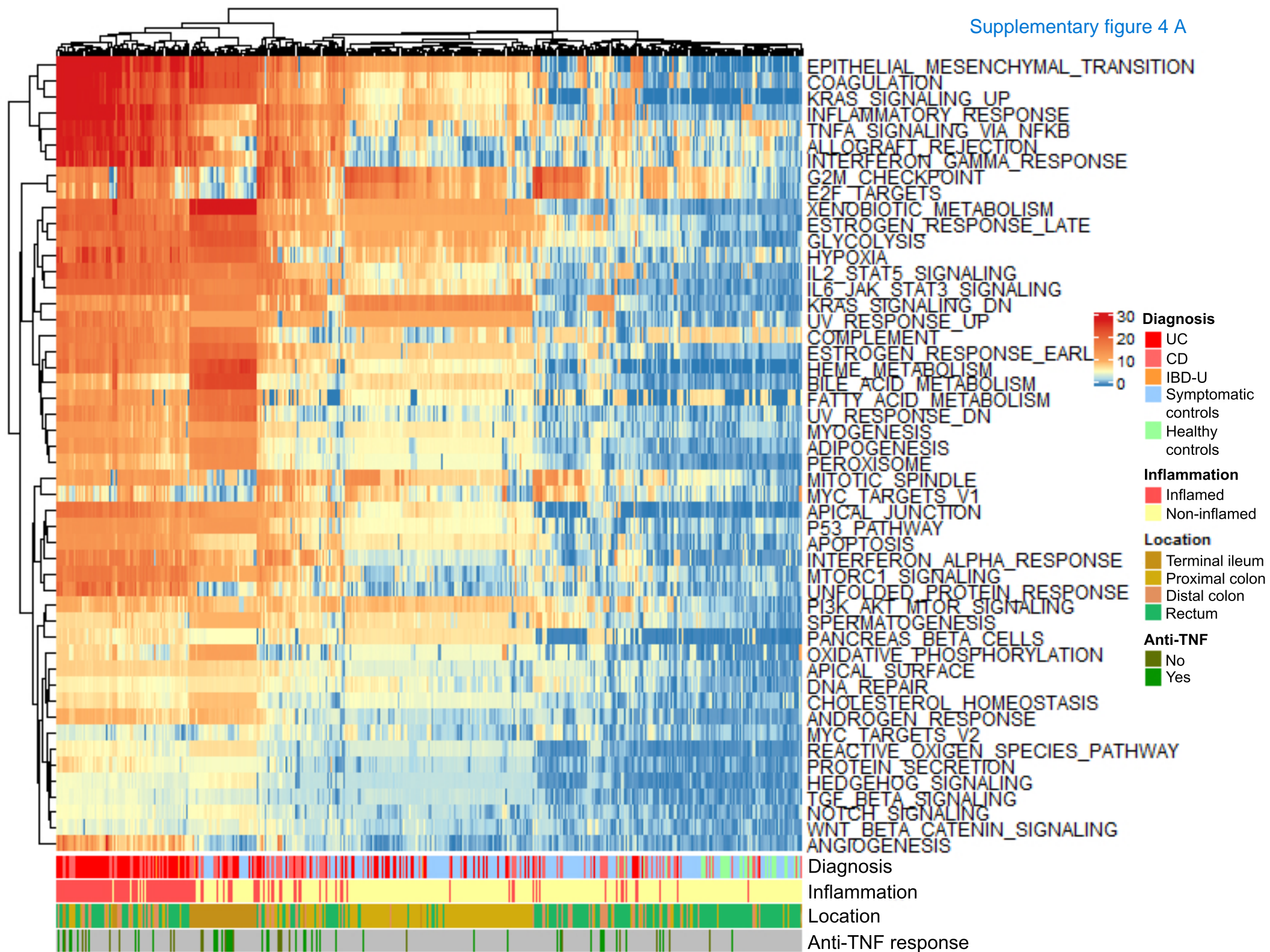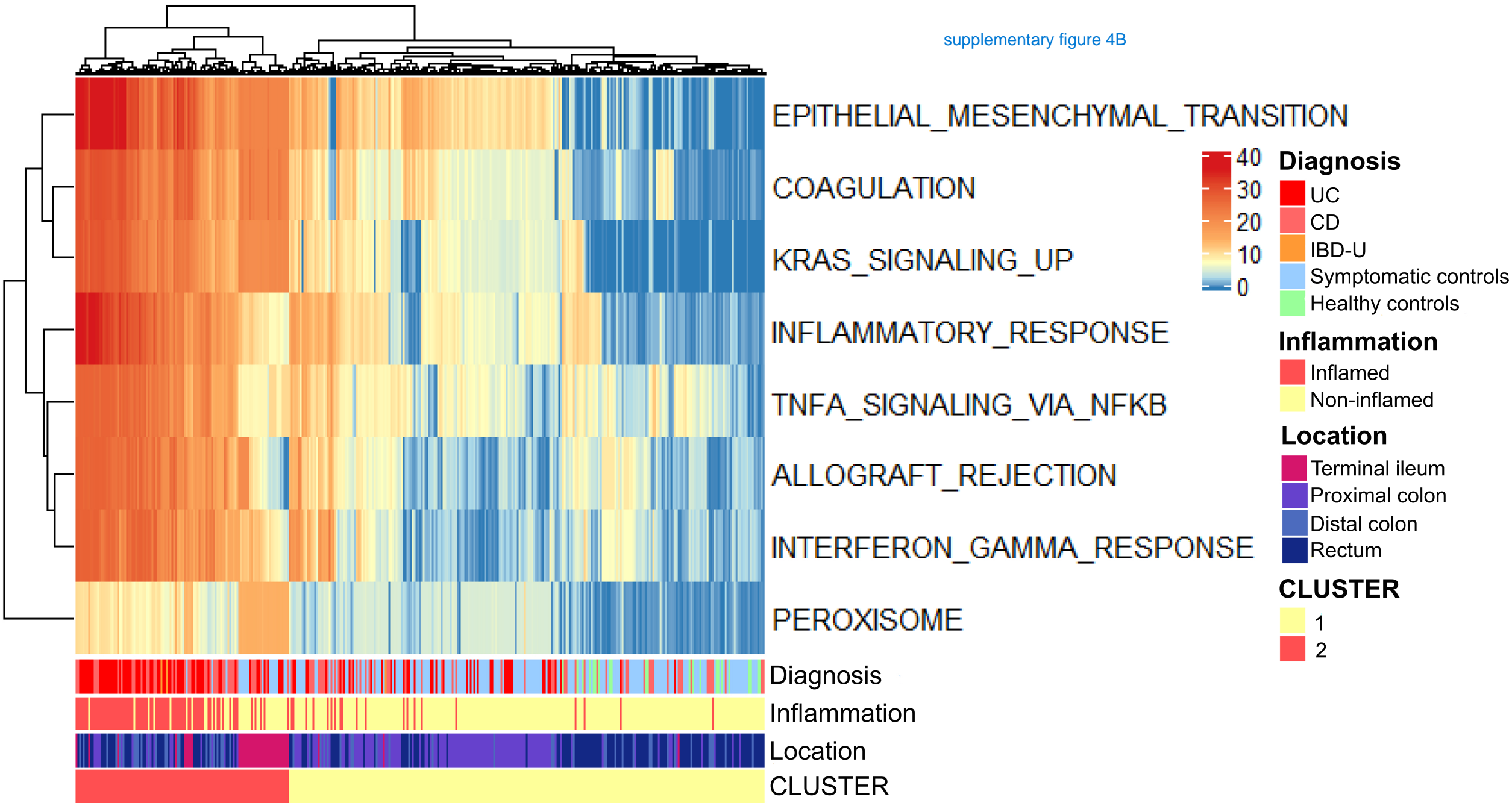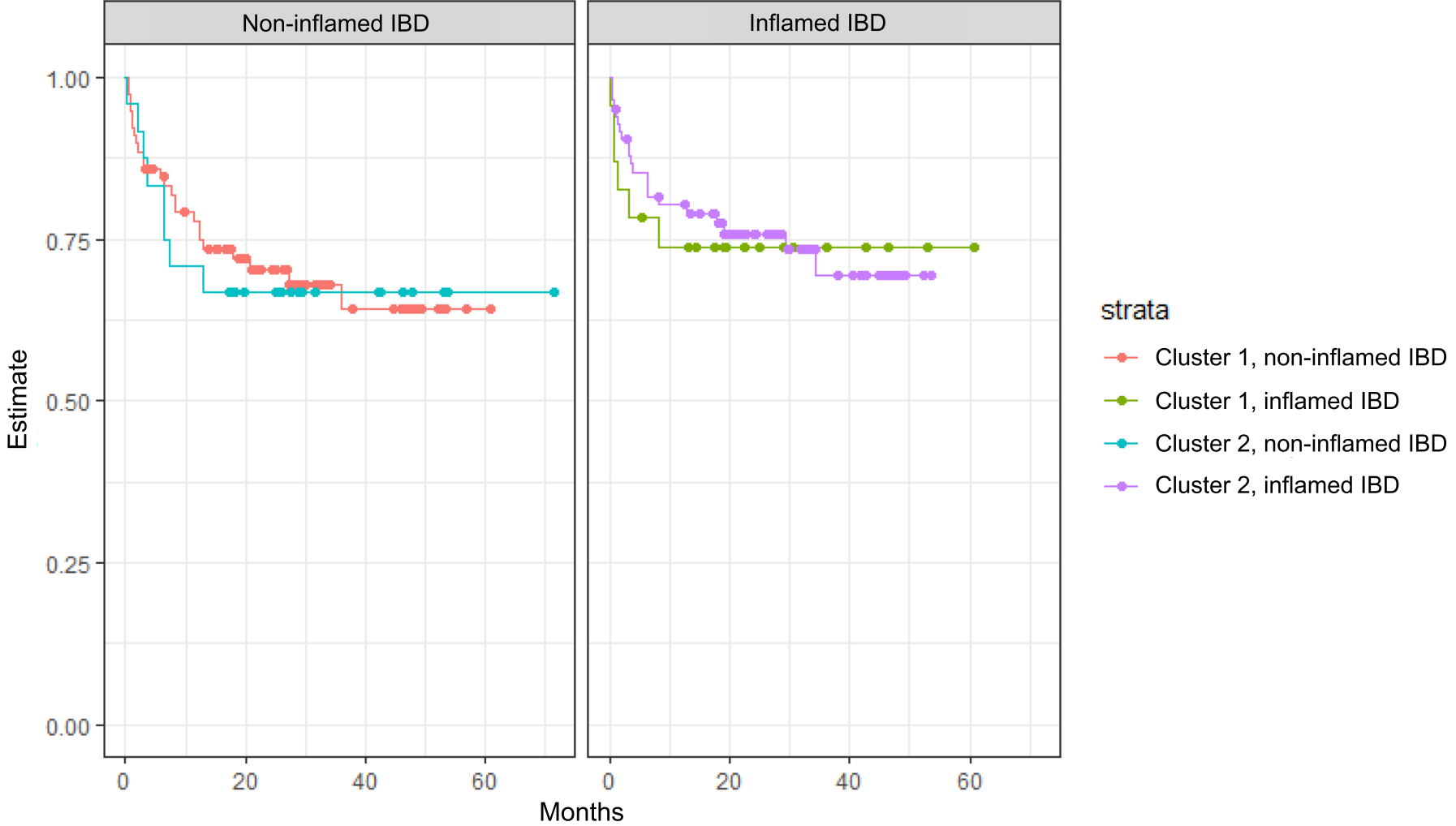**SUPPL. FIGURE 1:** Samples and raw data. Overview of sample collection. Hierarchical clustering of 40K probes in UC **(A)** and CD **(B)**. **Abbreviatons: CD: Crohn`s disease. UC: ulcerative colitis.**

SUPPL. FIGURE 2: Gene set enrichment analyses comparing inflamed and non-inflamed samples in **(A)** CD and **(B)** UC. The enriched GO terms are given as Normalized Enrichment Scores (NES) and the top 30 positive NES is demonstrated in top panel (orange) and the top 30 negative NES are demonstrated in bottom panel (blue). **Abbreviations: CDi: Inflamed CD. CDni: Non-inflamed CD. UCi: Inflamed UC. UCni: non-inflamed UC. NES: Normalised Enrichment Score.**

SUPPL. FIGURE 3: Predicting time for treatment escalation. **(A)** Differentially expressed genes were extracted from clusters of non-inflamed biopsies from UC (left) and CD (right). Kaplan Meier curves illustrating time until treatment escalation for the identified clusters. There were no significant differences in clinical outcome between patients affiliated to the three clusters (UC (p=0.832) and CD (p= 0.175)). **(B)** Differentially expressed genes were extracted from clusters of inflamed biopsies from UC (left) and CD (right). Kaplan Meier curves illustrating time until treatment escalation analyses for the identified clusters. There were no significant differences in clinical outcome between patients affiliated to the three clusters (UC(p=0.954) and CD (p= 0.644)). **Abbreviatons: CD: Crohn`s disease. UC: ulcerative colitis.**

SUPPL FIGURE 4: Pathway signature analysis. Hierarchical clustering of curated biological pathways. **(A)** 50 curated pathways giving 5 clusters. **(B)** The visually strongest signal of clustering in the black frame of figure (A), are defined into 2 clusters. **(C)** Kaplan Meyer curves of the 2 clusters in (B), related to time for treatment escalation for IBD-patients. Inflamed and non-inflamed samples from the clusters are analysed separately: Non-inflamed samples ("inflammation_status_c" for control/non-inflamed) to the left and inflamed samples (inflammation status_i" for inflammation) to the right. **Abbreviatons: CD: Crohn`s disease. UC: ulcerative colitis. IBD-U: IBD-unclassified.**

Suppl. table 1: Baseline characteristics for patients according to treatment escalation status.

* including one patient who died without having escalated. Abbr.: **Abbreviations:** CD (Crohn's disease), CRP (C-reactive protein, mg/L), F-Calpro (fecal calprotectin mg/kg) IBD_U (inflammatory bowel disease unclassified), UC (ulcerative colitis)

Diagnosis		Escalation	No escalation
CD	N	31	34
	Age(mean)	24	32
	CRP median (quartiles)	16 (8 - 40)	5 (3 - 17)
	F-Calpro median (quartiles)	1900 (1406 - 2886)	531 (290 - 1224)
IBD_U	N	1	2
	Age (mean)	14	40
	CRP median (quartiles)	1 (1 - 1)	47 (47 - 47)
	F-Calpro median (quartiles)	-	612 (612 - 612)
UC	N	13	67*
	Age (mean)	28	38
	CRP median (quartiles)	19 (9 - 48)	4 (3 - 9)
	F-Calpro median (quartiles)	1433 (526 – 6000+)	1389 (556 - 3057)

Suppl. Table 2: Results from escalation analysis for candidate genes in Lee et al (2017). IBD refers to the combined UC+CD+IBD-U analysis. HR=Hazard ratio; CD (Crohn`s disease), FOXO3 (forkhead box O3), HLA-B (human leucocyte antigen B), IBD (inflammatory bowel disease); IGFBP1 (insulin-like growth factor binding protein 1), IGFBP3 (insulin-like growth factor binding protein 3), UC (ulcerative colitis)

Diagnosis	Inflammation	GeneName	SystematicName	HR (95% CI)	p-value
CD	Inflamed	FOXO3	NM_001455	0.90 (0.1 - 5.7)	0,913
CD	Inflamed	HLA-B	NM_005514	4.54 (1.0 - 21.0)	0,053
CD	Inflamed	HLA-B	ENST00000466304	0.86 (0.7 - 1.0)	0,097
CD	Inflamed	IGFBP1	NM_000596	3.30 (0.3 - 38.8)	0,342
CD	Inflamed	IGFBP3	NM_001013398	0.99 (0.5 - 2.0)	0,970
CD	Non-inflamed	FOXO3	NM_001455	0.92 (0.2 - 3.4)	0,906
CD	Non-inflamed	HLA-B	NM_005514	1.51 (0.6 - 3.6)	0,354
CD	Non-inflamed	HLA-B	ENST00000466304	0.83 (0.7 - 1.0)	0,087
CD	Non-inflamed	IGFBP1	NM_000596	0.13 (0.0 - 1.0)	0,045
CD	Non-inflamed	IGFBP3	NM_001013398	1.47 (0.8 - 2.6)	0,198
UC	Inflamed	FOXO3	NM_001455	1.36 (0.1 - 15.6)	0,803
UC	Inflamed	HLA-B	NM_005514	0.64 (0.1 - 3.1)	0,580
UC	Inflamed	HLA-B	ENST00000466304	0.87 (0.6 - 1.2)	0,443
UC	Inflamed	IGFBP1	NM_000596	8.60 (1.0 - 70.7)	0,045
UC	Inflamed	IGFBP3	NM_001013398	1.63 (0.9 - 3.1)	0,139
UC	Non-inflamed	FOXO3	NM_001455	1.54 (0.1 - 33.3)	0,782
UC	Non-inflamed	HLA-B	NM_005514	3.04 (0.3 - 26.4)	0,313
UC	Non-inflamed	HLA-B	ENST00000466304	1.76 (0.7 - 4.4)	0,227
UC	Non-inflamed	IGFBP1	NM_000596	0.50 (0.0 - 25.4)	0,728
UC	Non-inflamed	IGFBP3	NM_001013398	1.22 (0.3 - 5.1)	0,784
IBD	Inflamed	FOXO3	NM_001455	1.22 (0.3 - 5.0)	0,786
IBD	Inflamed	HLA-B	NM_005514	1.73 (0.6 - 5.0)	0,312
IBD	Inflamed	HLA-B	ENST00000466304	0.86 (0.7 - 1.0)	0,075
IBD	Inflamed	IGFBP1	NM_000596	3.36 (0.7 - 15.3)	0,116
IBD	Inflamed	IGFBP3	NM_001013398	1.22 (0.8 - 1.9)	0,366
IBD	Non-inflamed	FOXO3	NM_001455	1.51 (0.5 - 5.0)	0,498
IBD	Non-inflamed	HLA-B	NM_005514	1.91 (0.9 - 4.2)	0,112
IBD	Non-inflamed	HLA-B	ENST00000466304	0.96 (0.8 - 1.2)	0,756
IBD	Non-inflamed	IGFBP1	NM_000596	0.49 (0.1 - 2.5)	0,389
IBD	Non-inflamed	IGFBP3	NM_001013398	1.70 (1.0 - 3.0)	0,058