Cell Host & Microbe, Volume 27

Supplemental Information

A Dynamic Immune Response

Shapes COVID-19 Progression

Eugenia Ziying Ong, Yvonne Fu Zi Chan, Wan Ying Leong, Natalie Mei Ying Lee, Shirin Kalimuddin, Salahudeen Mohamed Haja Mohideen, Kian Sing Chan, Anthony Tanoto Tan, Antonio Bertoletti, Eng Eong Ooi, and Jenny Guek Hong Low

Supplemental Information

А	Cluster 1				F
2 1		GO Biologica	l Pathways	-log FDR	L
	TLR and inflammatory		chronic inflammatory response (GO:00	02544)-	
	signaling (1)	regulation of t	oll-like receptor 4 signaling pathway (GO:00	34143)-	
	Outstand	negative n	egulation of interleukin-8 production (GO:00	32717)-	
	Cytokine signaling		on of tumor necrosis factor secretion (GO:19		
			of interleukin-6 biosynthetic process (GO:00		
	Cytolysis		regulation of granzyme B production (GO:00		
		regulation of acti	vation of membrane attack complex (GO:00		
				0 1 2 3	
C	Cluster 3				
U		GO Biologica	l Pathways	-log FDR	
			n assembly with MHC class II protein comple		
	Antigen	populo unigo	MHC protein complex assemb		
	presentation	regulati	on of T cell activation via T cell receptor con to MHC molecule on antigen presenting cell	(GO:2001188)	-
			dritic cell antigen processing and presentation		Г
	Leukocyte	positive re	gulation of T-helper 17 type immune response		L
	differentiation and activation		negative thymic T cell selection		
			positive regulation of monocyte differentiation sitive regulation of interferon-gamma secretion		
	Cytokine signaling	pos	interleukin-2-mediated signaling pathwa		
	Viral entry		positive regulation of viral entry into host of		
	,				6
					<u> </u>
E					
-				P _ ΙκΒα → D	egradation
IL1A		MyD88		+	-
	IL1R →	→ IRAK1/4	$ \longrightarrow $ IKK α		ranscription of ro-inflammatory
IL1B		TRAF6	ΤΑΒ		nediators like
					1B, TNFα, COX2
				NFKB IL	,,
	MYD8	8	IRAK1	IRAK4	
^{12.0} ך	MYD8	8	IRAK1 ^{8.5} 7		
	MYD8	8	8.5	IRAK4	
	MYD8	8		IRAK4	
	MYD8	8	8.5	IRAK4	
	MYD8	8	8.0-	IRAK4	
11.5- 11.0- 10.5- 10.0- 9.5	MYD8		8.0-	IRAK4 9.5 9.0 8.5- 8.0- 7.5	
11.5- 11.0- 10.5- 10.0- 9.5		11 12 13 17 18 19 20	8.5	IRAK4	2 13 17 18 19 20 onset
11.5- 11.0- 10.5- 10.0- 9.5- 3	46678610	11 12 13 17 18 19 20 rss onset	8.5 8.0 7.5 7.0 3 4 5 6 7 8 9 10 11 12 13 17 18 19 20 Days post Illness onset IKBKG/NEMO	IRAK4 9.5 9.6 8.6 7.5 7.5 7.5 9.6 9.6 9.6 9.6 9.6 9.6 9.6 9.6 9.6 9.6	2 13 17 18 19 20 onset
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Normalized log ₂ counts 11.0- 10.5- 9.5- 3	4 5 6 7 8 9 10 Days post illne	11 12 13 17 18 19 20 rss onset	8.5 8.0 7.5 7.0 3 4 5 6 7 8 9 10 11 12 13 1718 1920 Days post illness onset IKBKG/NEMO 8.5	IRAK4 9.5 9.0 9.5 9.0 9.5 9.5 9.5 9.5 9.5 9.5 9.5 9.5 9.5 9.5	2 13 17 18 19 20 onset
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stinuo 6 010 9 0 10 0		11 12 13 1718 1920 ess onset F6	8.5 0.5 7.5 3 4 5 6 7 8 9 10 11 21 3 17 1920 Days post Illness onset IKBKG/NEMO 9.5 9.6 9.6 9.7 9.7 9.7 9.7 9.7 9.7 9.7 9.7	IRAK4 9.5 9.0 8.0 7.5 9.4 9.5 9.0 9.5 9.5 9.0 9.5 9.0 9.5 9.5 9.0 9.5 9.0 9.5 9.0 9.5 9.0 9.5 9.0 9.5 9.0 9.5 9.0 9.5 9.0 9.5 9.0 9.0 9.5 9.0 9.0 9.0 9.0 9.0 9.0 9.0 9.0 9.0 9.0	2 13 17 18 19 20 onset
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Normalized log, contrast Normalized log, counts Normalized log, counts Norm	1 5 6 7 8 5 10 Days positiline TRAI 1 5 6 7 8 10 1 5 6 7 8 10 1 5 6 7 8 10 1 5 7 8 10 1 5 7 8 10 1 5 7 8 10 1 5 7 8 10 1 5 7 8 10	11 12 13 17 18 19 20 ess onset 76 11 12 13 17 18 19 20 eess onset KKB	8.5 0.5 1.5 1.5 1.5 1.5 1.5 1.5 1.5 1	IRAK4 9.5 9.5 9.5 9.5 9.5 9.5 9.5 9.5 9.5 9.5	2 13 17 18 19 20 onset 2 13 17 18 19 20 onset 2 13 17 18 19 20 onset 50
Normalized tog, 200 Normalized tog, 200 Normal	1 5 6 7 8 9 10 Days positiline TRAI •	11 12 13 17 18 19 20 ess onset 76 11 12 13 17 18 19 20 eess onset KKB	^{8.6} ^{9.6} ^{1.6} 	IRAK4 9.5 9.5 9.5 9.5 9.5 9.5 9.5 9.5 9.5 9.5	2 13 17 18 19 20 onset 2 13 17 18 19 20 onset 2 13 17 18 19 20 onset 50
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Normalized tog, 200 Normalized tog, 200 Normal	1 5 6 7 8 9 10 Days positiline TRAI •	11 12 13 17 18 19 20 ess onset 76 11 12 13 17 18 19 20 eess onset KKB	A A A A A A A A A A A A A A	IRAK4 9.5 9.5 9.5 9.5 9.5 9.5 9.5 9.5 9.5 9.5	2 13 17 18 19 20 onset 2 13 17 18 19 20 onset 2 13 17 18 19 20 onset 50
Normalized tog, 200 Normalized tog, 200 Normal	1 5 6 7 8 9 10 Days positiline TRAI •	11 12 13 17 18 19 20 ess onset 76 11 12 13 17 18 19 20 eess onset KKB	A A A A A A A A A A A A A A	IRAK4 9.5 9.5 9.5 9.5 9.5 9.5 9.5 9.5 9.5 9.5	2 13 17 18 19 20 onset 2 13 17 18 19 20 onset 2 13 17 18 19 20 onset 50
Normalized log, counts Normalized log, counts	1 5 6 7 8 9 10 Days positiline TRAI •	11 12 13 17 18 19 20 ess onset 76 11 12 13 17 18 19 20 eess onset KKB	A A A A A A A A A A A A A A	IRAK4 9.5 9.5 9.5 9.5 9.5 9.5 9.5 9.5 9.5 9.5	2 13 17 18 19 20 onset 2 13 17 18 19 20 onset 2 13 17 18 19 20 onset 50
Normalized tog, 200 Normalized tog, 200 Normal	I 5 6 7 8 5 10 Days post illine TRAI I 5 6 7 8 10 I 5 6 7 8 6 10 I 5 6 7 8 6 10 Days post illine IKBKB/I I 5 6 7 8 6 Days post illine IKBKB/I I 5 7 8 6 Days post illine IKBKB/I I 5 6 7 8 I 8 6 7 8 9 I 8 6 7 8 9 I 9 0 10 10 Days post illine RELAI		A A A A A A A A A A A A A A	IRAK4 9.5 9.5 9.5 9.5 9.5 9.5 9.5 9.5 9.5 9.5	2 13 17 18 19 20 onset 2 13 17 18 19 20 onset 2 13 17 18 19 20 onset 50

	GO Biological Pathways -log FDR
Cell migration	mononuclear cell migration (GO:0071674)-
B-cell proliferation	B cell proliferation (GO:0042100)-
	regulation of T-helper 2 cell cytokine production (GO:2000551)-
	positive regulation of interleukin-17 production (GO:0032740)-
Cvtokine and	positive regulation of interferon-gamma biosynthetic process (GO:0045078)-
chemokine signaling	paracrine signaling (GO:0038001)-
	type 2 immune response (GO:0042092)-
	response to erythropoietin (GO:0036017)-
	complement activation, alternative pathway (GO:0006957)-
Complement activation	regulation of complement-dependent cytotoxicity (GO:1903659)-
Organ development	glomerular mesangium development (GO:0072109)-
Organ development	metanephric mesangial cell differentiation (GO:0072209)
Response to	response to mycophenolic acid (GO:0071505)-
chemical stimulus	cellular response to mycophenolic acid (GO:0071506)
Cell adhesion	positive regulation of heterotypic cell-cell adhesion (GO:0034116)-
Lymphoid cell	lymphoid progenitor cell differentiation (GO:0002320)

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	GO Biological Pathways	-log FDR
TLR and inflammatory signaling (2)	lipopolysaccharide-mediated signaling pathway (GO:0031663)-	
	regulation of MyD88-independent toll-like receptor signaling pathway (GO:0034127)-	
	I-kappaB phosphorylation (GO:0007252)-	
	positive regulation of prostaglandin-E synthase activity (GO:2000363)-	
	positive regulation of interleukin-6 biosynthetic process (GO:0045410)-	
	interleukin-9-mediated signaling pathway (GO:0038113)-	
Cytokine signaling	response to interleukin-9 (GO:0071104)	
	response to interleukin-21 (GO:0098756)-	
	interleukin-21-mediated signaling pathway (GO:0038114)-	
	necroptotic signaling pathway (GO:0097527)-	
	positive regulation of apoptotic cell clearance (GO:2000427)	
Cell death	death-inducing signaling complex assembly (GO:0071550)-	
	positive regulation of apoptotic process involved in development (GO:1904747)-	
	negative regulation of macrophage apoptotic process (GO:2000110)-	
	regulation of calcidiol 1-monooxygenase activity (GO:0060558)-	
Cellular metabolism	arginine catabolic process to ornithine (GO:0019547)-	
T-cell activation	regulation of gamma-delta T cell activation (GO:0046643)-	
TGFb signaling	common-partner SMAD protein phosphorylation (GO:0007182)-	
Vesicle transport	vesicle fusion with endoplasmic reticulum-Golgi intermediate compartment (ERGIC) membrane (GO:1990668)	
Matrix metallopeptidase secretion	positive regulation of matrix metallopeptidase secretion (GO:1904466)	5 10 18 20

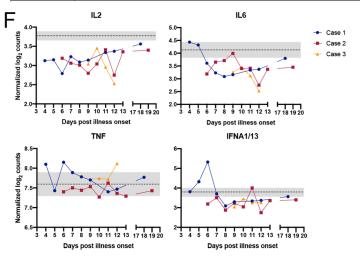


Figure S1. Gene expression and pathway analysis following NanoString profiling of immune genes in healthy controls and COVID-19 cases, related to Figure 2. (A-D) All genes included in gene cluster 1 (A), cluster 2 (B), cluster 3 (C) and cluster 4 (D) were analysed against PANTHER classification system using Gene Ontology (GO) Enrichment Analysis for biological processes. GO terms with > 40-fold enrichment following GO enrichment analysis were shortlisted, and summarization of redundant GO terms was performed using REViGO. Enriched representative GO terms (FDR<0.01) are shown for each gene cluster. (E) Flowchart depicting IL1R-mediated signaling cascade adapted from KEGG (hsa04064). Gene expression for signaling intermediates downstream of IL1R-mediated signaling are represented by normalized log2 counts. (F) Gene expression for pro-inflammatory cytokines in COVID-19 cases represented by normalized log2 counts. Dotted line and grey shaded area indicate mean gene expression \pm SD for healthy controls.