Using human transcriptomics to identify infectious disease agents

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Host-Pathogen Genomics





RESEARCH



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Global gene expression profiling identifies new therapeutic targets in acute Kawasaki disease

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А	Inregulated Canonical Pathway	-Log10 (E		
		GLM	Z test	B
	IL-10 Signaling	7.35	9.72	U
	Role of Pattern Recognition Receptors in Recognition of Bacteria and Viruses	6.17	7.47	
	TREM1 Signaling	5.45	11.05	
	IL-8 Signaling	5.31	7.24	
	Granulocyte Adhesion and Diapedesis	5.20	5.91	
	Role of Macrophages, Fibroblasts and Endothelial Cells in Rheumatoid Arthritis	4.87	8.29	
	Gαi Signaling	4.85	5.56	
	Acute Phase Response Signaling	4.26	7.76	
	Hepatic Fibrosis / Hepatic Stellate Cell Activation	4.18	7.99	
	iNOS Signaling	4.03	6.00	
	Toll-like Receptor Signaling	4.03	7.02	
	Production of Nitric Oxide and Reactive Oxygen Species in Macrophages	3.45	7.71	
	Leukocyte Extravasation Signaling	3.43	5.67	
	IL-6 Signaling	3.29	7.82	
	NF-кВ Signaling	3.13	6.82	

EIF2 Signaling	42.50	41.83
Regulation of eIF4 and p70S6K Signaling	15.01	13.10
mTOR Signaling	14.18	15.15
B Cell Development	5.07	7.59
Antigen Presentation Pathway	3.51	8.04
Role of NFAT in Regulation of the Immune Response	3.08	12.34
Altered T Cell and B Cell Signaling in Rheumatoid Arthritis	3.00	4.89
iCOS-iCOSL Signaling in T Helper Cells	2.58	16.85
p70S6K Signaling	2.37	1.91
Cytotoxic T Lymphocyte-mediated Apoptosis of Target Cells	2.24	8.53
OX40 Signaling Pathway	2.14	9.03
Histamine Biosynthesis	2.05	1.51
Nur77 Signaling in T Lymphocytes	1.89	9.08
Calcium-induced T Lymphocyte Apoptosis	1.75	14.91
Allograft Rejection Signaling	1.43	6.64

Gene network analysis





Module-trait relationships

MEmagenta		0.12 (0.1)	0.018 (0.8)	0.006 (0.9)	0.049 (0.5)	0.047 (0.5)	- 1
MEblack		0.065 (0.4)	0.15 (0.03)	-0.042 (0.6)	-0.047 (0.5)	-0.022 (0.8)	
MEbrown		0.11 (0.1)	0.056 (0.4)	-0.012 (0.9)	-0.071 (0.3)	-0.029 (0.7)	
MEgreenyellow		0.081 (0.3)	0.14 (0.05)	-0.032 (0.7)	-0.029 (0.7)	-0.007 (0.9)	-0.5
MEpink		0.14 (0.06)	0.052 (0.5)	0.0036 (1)	-0.029 (0.7)	0.0047 (0.9)	
MEcyan		0.032 (0.7)	-0.28 (1e-04)	-0.07 (0.3)	0.13 (0.07)	-0.007 (0.9)	
MEblue		-0.22 (0.002)	-0.12 (0.1)	-0.092 (0.2)	-0.0022 (1)	0.0046 (0.9)	-0
MEsalmon		0.017 (0.8)	0.17 (0.02)	0.016 (0.8)	-0.0022 (1)	0.041 (0.6)	
MEmidnightblue		-0.45 (8e-11)	-0.1 (0.2)	-0.1 (0.2)	0.15 (0.03)	0.0083 (0.9)	
MEtan		-0.23 (0.002)	-0.0019 (1)	-0.016 (0.8)	-0.01 (0.9)	-0.024 (0.7)	- - 0.
MEgreen		0.0095 (0.9)	0.018 (0.8)	0.058 (0.4)	0.0017 (1)	-0.072 (0.3)	
MEturquoise		0.079 (0.3)	-0.044 (0.5)	0.12 (0.1)	0.019 (0.8)	-0.064 (0.4)	
MEgrey		0.1 (0.2)	0.019 (0.8)	-0.03 (0.7)	0.0021 (1)	0.033 (0.7)	- −1
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		•	4	thnic 9	-		

The IL 1 pathway is unusually active in KD











Figure S5: Performance of the 59-transcript 1 s.e elastic net signature by illness day at sample

collection in validation set



Days from onset

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ORIGINAL ARTICLE

Diagnosis of Childhood Tuberculosis and Host RNA Expression in Africa

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TB diagnosis by Host response array

Table 3. Diagnostic performance of the TB/OD disease risk score and the Xpert MTB/RIF ® in the Kenyan validation cohort.

	DRS based on the 51 transcript TB vs OD signature	Xpert MTB/RIF®*						
TB vs. Other Diseases – HIV + &HIV- combined								
	89.0	77.1						
Area under ROC curve (95% CI)	(82.3 - 94.9)	(69.9-85.7)						
	82.9	54.3						
Sensitivity, % (95% CI)	(68.6 - 94.3)	(37.1 - 68.6)						
	83.6	100 .0						
Specificity, % (95% CI)	(74.6 - 92.7)	(100.0 - 100.0)						
Culture Negative TB vs. Other Diseases – HIV + & HIV- combined								
	70.2	53.4						
Area under ROC curve (95% CI)	(58.7 - 79.7)	(50.0 - 57.9)						
	43.2	6.8						
Sensitivity, % (95% CI)	(27.3 - 56.8)	(0 – 13.6)						
	83.6	100. 0						
Specificity, % (95% CI)	(72.7 - 92.7)	(100.0 - 100.0)						
	TB vs. O Area under ROC curve (95% Cl) Sensitivity, % (95% Cl) Specificity, % (95% Cl) Culture Negative Area under ROC curve (95% Cl) Sensitivity, % (95% Cl) Specificity, % (95% Cl)	DRS based on the 51 transcript TB vs OD signature TB vs. Other Diseases – HIV + &HIV- combined 89.0 Area under ROC curve (95% CI) (82.3 - 94.9) 82.9 Sensitivity, % (95% CI) (68.6 - 94.3) 83.6 Specificity, % (95% CI) Culture Negative TB vs. Other Diseases – HIV + &HIV- co 70.2 Area under ROC curve (95% CI) (58.7 - 79.7) 43.2 Sensitivity, % (95% CI) (27.3 - 56.8) 83.6 Specificity, % (95% CI) (72.7 - 92.7)						

Are we missing a lot of TB diagnosis ?



Host-Pathogen Genomics

