

Elevations in TNF- α and IL-18 are Associated with Increased Risk of Probable Cytomegalovirus Tissue Invasive Disease in Solid Organ Transplant Recipients

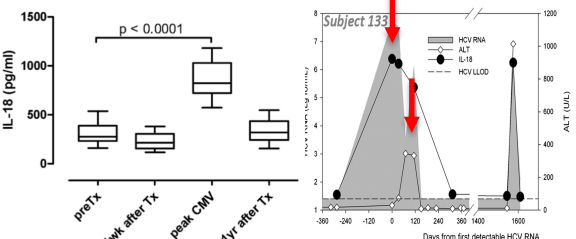
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Background

IL-18 is elevated during CMV viremia in D+/R- kidney recipients and precedes ALT elevations in acute HCV infection^{7,8}



Methods

275 SOT recipients with a positive CMV VL over 8 month period

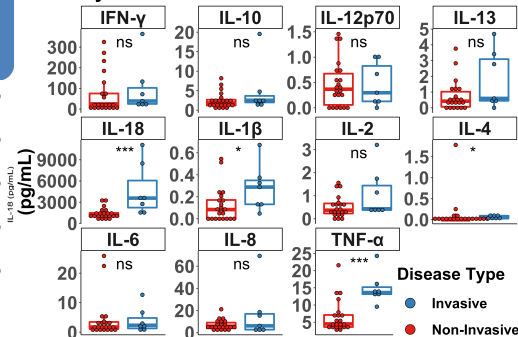
44 adults with at least two specimens

29 with CMV DNAemia

IL-18 and 10 other cytokines measured

Table 1	CMV DNAemia Alone	Probable Tissue Invasive Disease
n (%)	22 (76.9)	7 (24.1)
Age (mean (SD))	57.7 (10.8)	59.9 (6.6)
Male (%)	14 (63.6)	5 (71.4)
Graft Type (%)		
Kidney	12 (54.5)	3 (42.9)
Liver	4 (18.2)	2 (28.6)
Heart	1 (4.5)	1 (14.3)
Lung	5 (22.7)	1 (14.3)
CMV R-	7 (31.8)	5 (71.4)
Prior history of CMV Disease (%)	11 (50.0)	0 (0.0)
ALC at first positive CMV (mean(SD))	1179 (1371)	923 (1113)
Months since Transplant (mean (SD))	33.4 (40.7)	43.8 (68.7)
Current Immunosuppressives (%)		
Tacrolimus	21 (95.5)	7 (100.0)
Mycophenolate	13 (59.1)	7 (100.0)
Prednisone	19 (86.4)	7 (100.0)

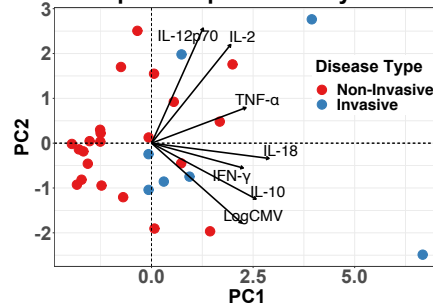
Cytokines at Peak CMV VL



n = 29; Wilcoxon-Mann-Whitney test
****, ***, **, * ns p < 0.0001, 0.001, 0.01, 0.05, or > 0.05

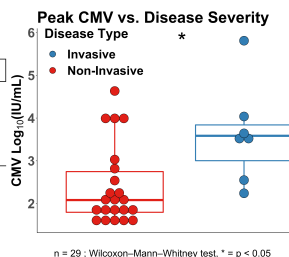
IL-18, IL-1 β , and TNF- α were significantly elevated in those with probable invasive disease

Principal Component Analysis



Results

CMV VL higher in invasive disease



n = 29; Wilcoxon-Mann-Whitney test, * p < 0.05

Increases in IL-18, TNF- α , and CMV VL at peak CMV VL in blood were associated with increased odds of probable tissue invasive disease in unadjusted logistic regression. When adjusted for graft type and recipient serostatus, elevations in IL-18 and TNF- α remained significantly associated with increased odds of probable invasive disease.

*Adjusted for Graft Type and Recipient Serostatus

Adjusted Odds Ratio		95% CI	P value
TNF- α (pg/mL)	1.43	1.07-1.92	0.02
IL-18 (500 pg/mL)	2.00	1.06-3.75	0.03
CMV Log10(IU/mL)	3.17	0.97-10.22	0.06

Conclusions

IL-18 and TNF- α may be non-invasive markers to distinguish tissue invasive CMV disease from DNAemia in SOT recipients

References

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