Human microRNA responses predict cytomegalovirus replication following solid organ transplantation

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BACKGROUND
Homo sapiens mature microRNA-200b-3p and -200c-3p are predicted to bind to 3' UTR of mRNA encoding human cytomegalovirus (HCMV) immediate early protein 2 (IE2). We hypothesized that expression of these microRNAs pre-transplant could predict HCMV replication after solid organ transplantation (SOT).

METHODS
272 SOT recipients were HCMV-seropositive pre-transplant and were managed using pre-emptive therapy. Pre-transplant PBMCs were stimulated with HCMV followed by collection of RNA one day post-stimulation. MicroRNAs were quantified using real-time RT-PCR. Human foreskin fibroblasts were transfected with 200b-3p and 200c-3p and infected with HCMV one hour post-transfection. Protein was collected at 3- and 7-dpi and underwent immunoblotting for IE2.

RESULTS
Medians of 200b-3p and 200c-3p were significantly lower in recipients with HCMV replication (n = 144) (361.6 vs. 552.6, P = .035; 3586.8 vs. 12986.8 copies/µL, P = .03, respectively). Multivariate regression revealed that 200b-3p <100 copies/µL (OR: 0.53, P = .02), D-/R+ HCMV serostatus (OR: 0.55, P = .02) and graft rejection (OR: 1.86, P = .03) were independently associated with HCMV replication. Transfection with 200b-3p resulted in 2.7- and 2.5-fold decreased IE2 at 3- and 7-dpi, respectively, compared to mock cells.

CONCLUSIONS
MicroRNAs may play a biologically relevant role in controlling HCMV replication post-transplant.