PALADINS: PROTECTIVE APPROACHES LEVERAGING AD-APTIVE AND IN-NATE SYSTEMS

Transcriptomic Analysis Reveals Host Mirnas Correlated With Immune Gene Dysregulation During Fatal Disease Progression In The Ebola Virus Cynomolgus Macaque Disease Model

Charles Shoemaker USAMRIID

Ebola virus is a continuing threat to human populations causing a virulent hemorrhagic fever disease characterized by dysregulation of both the innate and adaptive host immune responses. Severe cases are distinguished by an early, elevated pro-inflammatory response followed by a pronounced lymphopenia with B and T cells unable to mount an effective anti-viral response. The precise mechanisms underlying the dysregulation of the host immune system are poorly understood. In recent years, focus on host-derived miRNAs showed these molecules to play an important role in the host gene regulation arsenal. Here, we describe an investigation of RNA biomarkers in the fatal Ebola virus disease (EVD) cynomolgus macaque model. We monitored both host mRNA and miRNA responses in whole blood longitudinally over the disease course in these NHPs. Analysis of the interactions between these classes of RNAs revealed several miRNA markers significantly correlated with downregulation of genes; specifically, those involved in dysregulated immune pathways associated with EVD. In particular, we noted strong interactions between the miRNAs hsa-miR-122-5p and hsa-miR-125b-5p with immunological genes regulating both B and T-cell activation. This promising set of biomarkers will be useful in future studies of severe EVD pathogenesis in both NHPs and humans and may serve as potential prognostic targets.

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