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TITLE

CO-EXPRESSION GENE MODULES ANALYSIS IN RESPONSE TO ATTENUATED CERCARIA VACCINE REVEALS A CRITICAL ROLE FOR NK CELLS IN PROTECTION AGAINST S. MANSONI

AUTHORS

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ABSTRACT

Background: Schistosomiasis affects nearly 240 million people, with 779 million at risk. Developing a vaccine would greatly enhance current control measures and elimination efforts. However, despite decades of research, an effective vaccine for schistosomiasis remains elusive. The Radiation-attenuated (RA) cercarial vaccine remains the best model for eliciting high levels of protection. We have recently explored this model in mice to identify potentially protective pathways by examining gene expression patterns in peripheral blood mononuclear cells (PBMC) using Gene Set Enrichment Analysis (GSEA). **Aims:** In this study, we reanalyzed transcriptomic data from PBMCs obtained from vaccinated (n = 12) and infected (n = 12) C57BL/6 mice at three time points (Days 7 and 17 after infection or vaccination, and Day 7 post-challenge), as well as from unmanipulated animals (n = 12). Additionally, we generated new data from PBMCs collected 35 days post-infection. **Methods:** Deconvolution analysis was performed to estimate immune cell composition by CIBERSORTx. Gene co-expression networks and Over Representation Analysis (ORA) were performed using the CEMiTool package. Protein-protein interaction networks were constructed using STRING and the hub proteins for each module were identified using Cytoscape. **Results:** Co-expression network analysis identified a module (M2) associated with the infection process, grouping genes related to a Th2 immune response, and a second module (M6) associated with the vaccination process, displaying pathways related to a Th1 response, CD8+ T cells and NK cells. Within each module, five hub proteins were identified based on protein-protein interaction networks. The M2 infection module revealed *Chil3*, *Il4*, *Cx3cr1*, *Emr1* and *Ccl2* as hubs, while module M6, associated with vaccination, disclosed *Prf1*, *Klrc1*, *IFN-γ*, *Ncr1* and *Tbx21* as hub proteins. **Conclusion:** Our data highlight the potential involvement of NK cells in bolstering the response to the RA vaccine via IFN-γ production regulated by the T-bet transcription factor (*Tbx21*). These findings may provide a basis for predicting favorable outcomes in the development of a vaccine against schistosomiasis.

KEYWORDS

Co-expression Network; Radiation-attenuated Vaccine; Hub-genes

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