Mechanisms of Activation / Inflammation and Impact on Pathogenesis

PE7 Social stress prior to SIV or SHIV infection associates with higher viral load and lower CD4 counts

G. Neigh[1,2,3], T. Hayes[3], R. Trible[3], T. Vanderford[3], D. Carnathan[3], C. Harrell[1], K. Easley[4], B. Cervasi[3], M. Paiardini[3], G. Silvestri[3]
[1]Emory University, Physiology, Atlanta, United States, [2]Emory University, Psychiatry & Behavioral Sciences, Atlanta, United States, [3]Yerkes National Primate Research Center, Atlanta, United States, [4]Emory University, Biostatistics, Atlanta, United States

Background: The tempo of disease progression in HIV-infected humans and SIV-infected macaques is quite variable among individuals, with high levels of virus replication and immune activation predicting shorter survival. Prolonged exposure to stress alters immune system function and shortens survival time in SIV-infected macaques. Macaques establish a relatively stable matriarchal hierarchy in which subordinate animals consistently demonstrate elevated markers of chronic stress compared to dominant ones. In the current study we tested the hypothesis that stress history, as dictated by the subject's social rank prior to study assignment, predicts plasma viral load (PVL) and disease progression during chronic SIV infection.

Methods: All macaques originated from social groups housed at Yerkes National Primate Research Center with established rank systems. Retrospective individual animal meta-analysis was conducted on PVL and CD4 data across the acute and chronic phases of infection and the relative data were retrospectively compiled and analyzed. PVLs from five previous studies were measured by RTPCR as copies of SIV RNA/ml of plasma. From blood absolute $CD4^+$ T-cell counts and Ki-67 expression were measured by flow cytometry.

Results: Sixty-two infected macaques were stratified based on the pre-infection social rank and evaluated longitudinally. In the acute phase of infection, neither virus replication nor absolute $CD4^+$ T-cell count were predicted by social rank prior to study assignment ($p>0.05$). However, in chronic phases of infection, social rank prior to study assignment influenced the level of virus replication and absolute CD4 count ($p< 0.05$). In the chronic phase of infection plasma PVL from subordinate subjects was elevated compared to that from dominant/mid ranks (mean 5.806 log10 vs. 4.213 log10 copies/ml), and absolute CD4 counts were significantly decreased in subordinate subjects compared to dominant/mid subjects (mean 348 vs. 513 cells/ul blood). Finally, CD4 Ki-67 expression increased from the acute to chronic phase more in subordinate animals compared to dominant/mid animals.

Conclusions: These data demonstrate that social history prior to SIV/SHIV infection influences PVL and CD4 count in chronic disease, with increased exposure to stress being associated with higher levels of virus replication, increased depletion of $CD4^+$ T-cells, and greater increases in activation of $CD4^+$ T-cells.