CONCOMITANT CARDIAC PATHOLOGY WITH ENCEPHALITIS IN SIV-INFECTED ANIMALS WITH AIDS

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Kevin S. White[1], Joshua A. Walker[1], John Wang[2], Patrick Autissier[1], Andrew D. Miller[3], Rachel Burrack[4], Qingsheng Li[4], Woong Ki Kim[5], Kenneth C. Williams[1]

[1] Boston College, Department of Biology, Chestnut Hill, MA, USA, [2] Simon-Kucher & Partners, Boston, MA, USA, [3] Cornell University, College of Veterinary Medicine, Ithaca, NY, USA,
[4] Nebraska Center for Virology, School of Biological Sciences, University of Nebraska-Lincoln, Lincoln, NE, USA, [5] Eastern Virginia Medical School, Norfolk, VA, USA

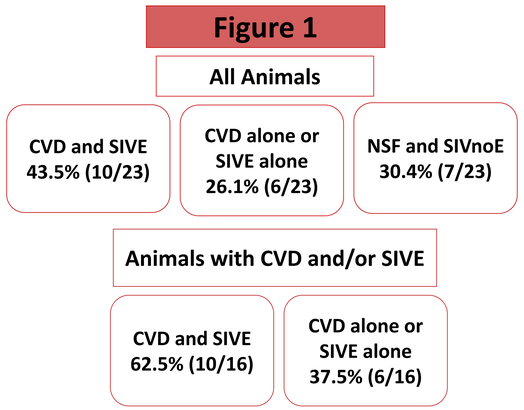
Background

Cardiovascular disease (CVD) and HIV-associated neurocognitive disease (HAND) are the most prevalent comorbidities among HIV-infected individuals on ART, and are possibly linked [1, 2]. Monocyte activation and macrophage accumulation in the heart and central nervous system (CNS) occur with CVD and HAND alone [3, 4], while the expansion of CD14+CD16+ monocytes, and the accumulation of macrophages correlate with cardiac inflammation and fibrosis, and SIV encephalitis (SIVE) [5-7]. Inhibiting monocyte and macrophage activation decreases cardiac and CNS pathologies [8-10. SIV-infection of perivascular CD163+ and CD206+ macrophages in the CNS is correlated with SIVE, but there are little to no SIV-RNA+ cells in the heart [11-13]. Galectins are β-galactoside-binding lectins produced in-part, by activated macrophages. Plasma galectins-3 and -9 are correlated with cardiovascular inflammation and fibrosis, and neurocognitive decline, respectively [14,15] but no studies have shown whether galectins-3 and -9 correlate with the development of CVD and SIVE together. **We asked whether CVD and SIVE co-develop with AIDS; if the number of monocytes and SIV-RNA+ macrophages, and plasma galectins-3 and -9 are increased and correlate with the co-development of CVD and SIVE.**

Materials & Methods

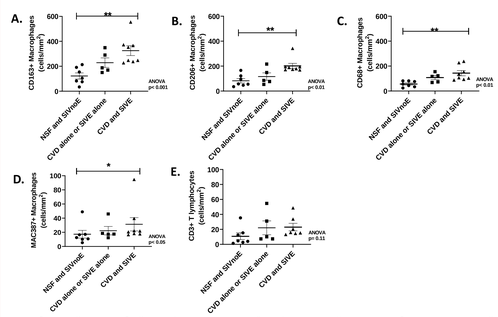
Study Design: We used twenty-three CD8+ T lymphocyte-depleted, SIV-infected macaques with AIDS. Animals were grouped by CVD and SIVE, CVD only or SIVE only, or no significant findings (NSF) and SIV no encephalitis (SIVnoE). **Single-label IHC:** The number of CD68+, CD163+, CD206+, and MAC387+ cardiac macrophages, CD3+ T-lymphocytes, and SIV-gp41+ productively infected cells were determined. **Cardiac collagen deposition (%)** was assessed with Massons Trichrome and the percent of collagen per tissue area was determined using ImageJ Analysis. **SIV-RNA *in situ* hybridization** was performed using the RNAscope ® 2.5 HD Assay-Red on three CNS cortical and one cardiac tissue per animal. **Absolute numbers of CD14+CD16+ monocytes** were determined by flow cytometric analysis on whole blood. **ELISA:** Terminal plasma IL-18, galectin-3, galectin-9, and soluble CD163 (sCD163) concentrations were measured according to the manufacturer's protocols. **Statistical Analysis:** One-way analysis of variance (ANOVA) with Dunn's multiple comparisons, and Spearman's r correlations were used with statistical significance accepted at $p < 0.05$.

Figure 1



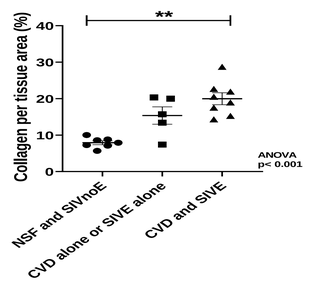
CVD and SIVE co-develop more frequently than CVD alone or SIVE alone, and NSF and SIVnoE in animals with AIDS. In animals with pathology, CVD and SIVE co-develops more frequently than CVD alone or SIVE alone.

Figure 2



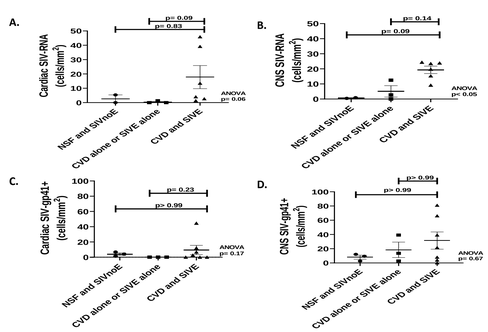
Animals with CVD and SIVE have increased numbers of CD163+, CD206+, CD68+, and MAC387+ cardiac macrophages compared to animals with CVD and SIVE alone, and NSF and SIVnoE.

Figure 3



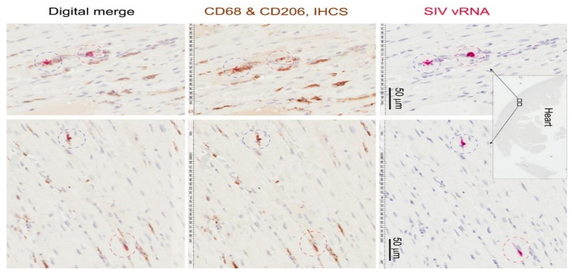
Animals with CVD and SIVE have an increased percentage of cardiac collagen deposition compared to animals with CVD or SIVE alone, and NSF and SIVnoE.

Figure 4



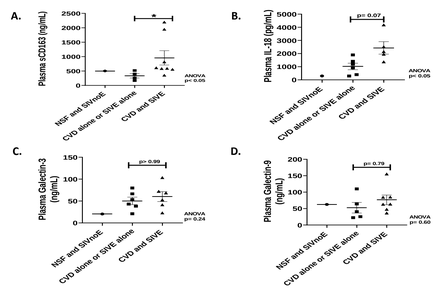
Animals with CVD and SIVE have a trend of increased numbers of SIV-RNA+ and SIV-gp41+ macrophages in cardiac tissues and the CNS compared to animals with CVD or SIVE alone, and NSF and SIVnoE.

Figure 5



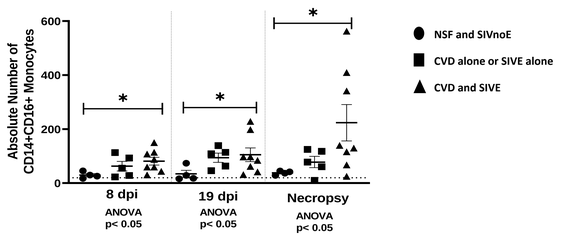
SIV-RNA+ cells are cardiac CD68+ and CD206+ macrophages.

Figure 6



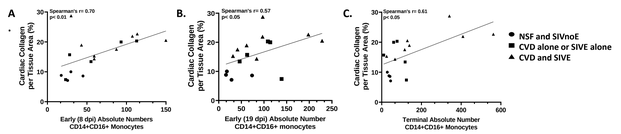
There are higher levels of sCD163, IL-18, galectin-3, and galectin-9, in animals with CVD and SIVE compared to animals with CVD alone or SIVE alone.

Figure 7



Animals with CVD and SIVE have increased numbers of CD14+CD16+ monocytes early (8 dpi and 19 dpi) and terminally compared to CVD or SIVE alone, and NSF and SIVnoE animals.

Figure 8



There is a positive correlation early and terminally of CD14+CD16+ monocytes and cardiac collagen deposition in all animals.

Conclusions

1. **In animals with AIDS, CVD and SIVE co-develop more frequently than CVD or SIVE alone, and NSF and SIVnoE.**
2. **There are more CD14+CD16+ monocytes and cardiac macrophages in animals with CVD and SIVE compared to CVD or SIVE alone.**
3. **SIV-RNA+ and SIV-gp41+ cells are more abundant in the CNS than the heart.**
4. **There are more SIV-RNA+ and SIV-gp41+ cells in the heart and CNS in animals with CVD and SIVE than CVD or SIVE alone.**
5. **The SIV-RNA+ cells in cardiac tissues are CD68+CD206+ macrophages.**
6. **Animals with CVD and SIVE have higher levels of plasma sCD163, IL-18, and galectins-3 and -9 compared to CVD or SIVE alone animals.**

Acknowledgements

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References

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