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An Immunohistochemical Analysis of Free Radical Stress in the Heart of the HIV-1 Transgenic Rat

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It has been suggested that HIV infection is now a treatable disease and transmission rates have the possibility of approaching zero with current medications (1). Even if true, it must be remembered that approximately 1 million people are living with HIV infection in the United States (1). While current treatment results in viral expression levels below detection, there still exist cells which produce low levels of virus and viral proteins. It is believed that these viral reservoirs are what contribute to the noninfectious comorbidities that are now a challenge to HIV health care. Comorbidities such as cardiovascular disease, central nervous system disease, kidney disease, hepatic disease and cancers can decrease the quality of life. In other cases these comorbidities can be fatal, particularly as the patient ages. It is also important to note, that Minority Health Care Disparities can play an important role in contributing to the severities of the HIV comorbidities. This is because minority communities can have an increased risk for cardiovascular disease and/or Kidney disease. This situation can cause more severe symptoms. The present treatments for comorbidities are limited, but treatments for HIV comorbidities must now be a part of HIV health care programs. In addition, the pathophysiology of these diseases are for the most part unknown and may well have many contributing factors. Evidence suggests that the chronic viral reservoirs produce low levels of the different viral proteins. HIV Proteins such as GP-120, TAT and Nef have been demonstrated to be toxic to cells and produce an array of cellular abnormalities. In view of the health impact of these comorbidities, further research is justified in this area. For example, a model system would be a noted improvement for the study of HIV comorbidity pathology. We have developed the first HIV-1 Transgenic rat (HIV-1Tg) rat that chronically produces HIV -1 transgenes products (Gp-120, Tat and Nef) (2,3). It therefore is a model for the chronic condition of individuals on long term antiviral therapy. There has been growing evidence that demonstrates that these viral proteins can induce free radical damage (4). We initially identified in the human, primate and TG rat brain an increased amount of nitrotyrosine by immunohistochemical staining (5,6). This approach, demonstrated the histological location of the free radical production in the brain. But as the TG rats displayed symptoms consistent with several of the comorbidities, other tissues were examined such as the heart and kidney (7). We have identified HIV – TG proteins in cells found in the heart (GP-120, Tat and Nef). These cells displayed lymphocyte shapes. Cardiac dendritic cells (CDCs) have been demonstrated to play an important role in cardiovascular disease and are capable of free radical production. Local production of HIV proteins by these infiltrating hematopoietic cells can lead to the production of reactive oxygen species by the dendritic cells. Nox2 is a protein capable of generating reactive oxygen species. It has also been demonstrated to be important in the microbicidal oxidase system of phagocytes. Immunocytochemical staining for Nox2 revealed many CDCs like cells in close association with cardiomyocytes and blood vesicles. These are places where cardiac pathology has been identifies with H&E staining in the HIV-1 Tg rat. Because of this close association of the CDCs with the cardiomyocytes, reactive oxygen species production adjacent to them can contribute to cardiomyocyte dysfunction and death. This provides a mechanism for the gradual remodeling of the cardiac tissue which is found in HIV cardiac comorbidity (9).

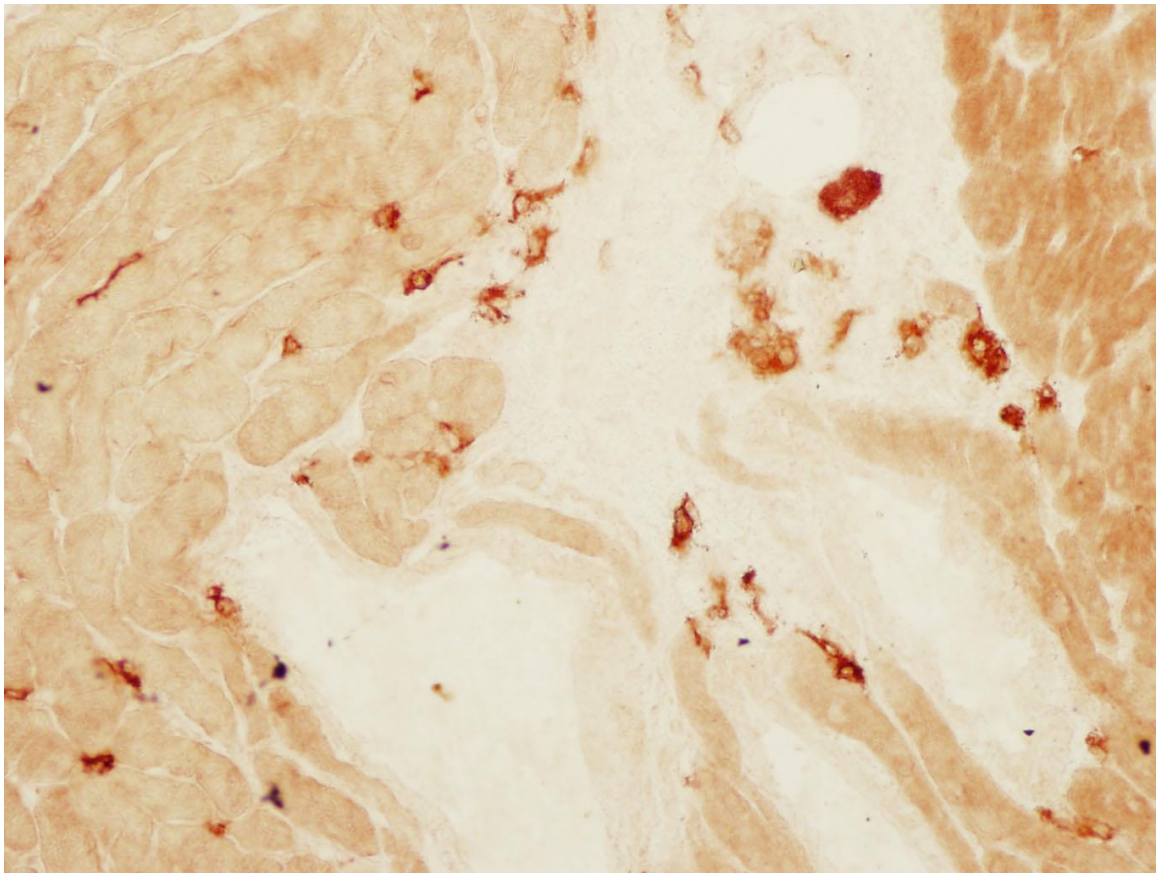

Figure 1. Immunohistochemical staining for Nox2. The ABC method with a red chromogen is used. A variety of morphologic shapes can be identified. Both lymphocyte shape and dendritic cells are evident.

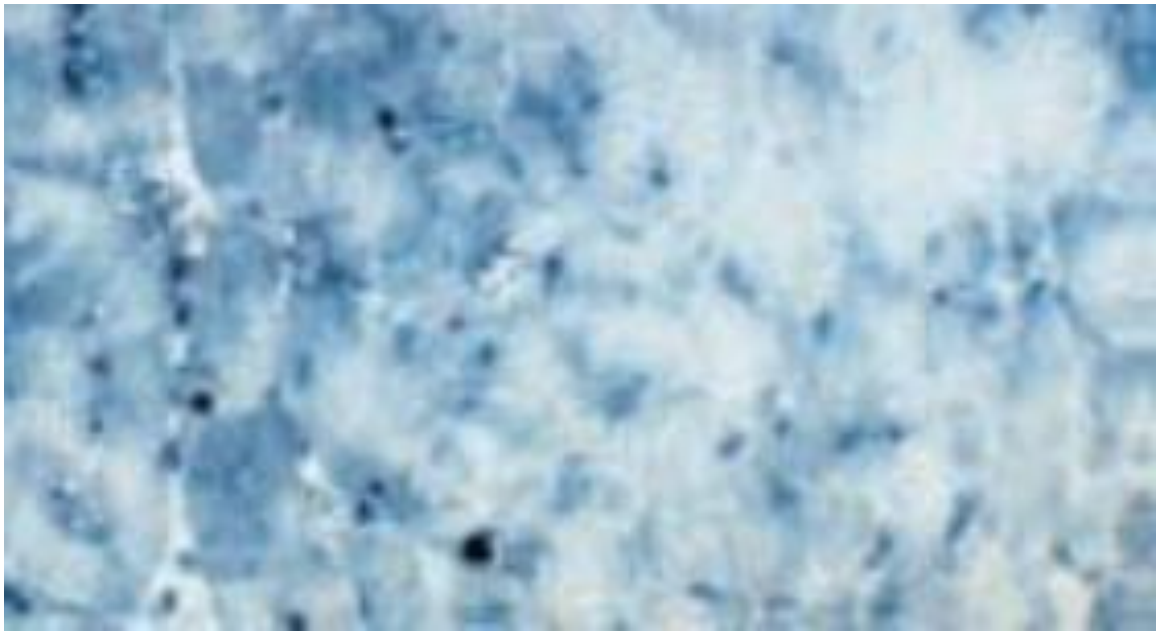

Figure 2. Immunohistochemical staining for GP-120. The ABC method with a blue chromogen is used. Lymphocyte shaped cells are evident.

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