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Primary Research Interest:	Neurology
Description of Research:	<p>The research consists of the following aims: In aim 1, we will analyze the brains of HIV transgenic rats produced on wild-type and nude rat backgrounds (the latter to model the severe immunodeficient state) for associations between levels of immune activation and expression of markers of cellular and mitochondrial metabolism in the brains of the animals. In aim 2 we will analyze the mechanisms that underlies these associations using primary rat astrocytes in culture. We will also whether specific drug therapy can suppress the inflammation observed and improve the metabolic parameters of interest. In aim 3, the drugs that show effects in vitro will be studies in the animal models in vivo to see whether they can suppress the neurological and pathological abnormalities that have been previously observed in these animals.</p>
Relevance to VA:	<p>The Veterans Healthcare Administration (VHA) treats more than 26,000 individuals with HIV infection, making it the largest provider of care to HIV-infected individuals in the U.S. Neurological complications occur in HIV infection, with 40% at risk for developing HIV-related neurocognitive impairment (NCI). Therefore, many HIV-infected Veterans are at risk for NCI. An important factor underlying the development of NCI is that infected cells in the brain release inflammation that can cause neurological damage and dysfunction. Astrocytes, which make up the largest percentage of cells in the brain, produce many of these factors when infected by HIV. Utilizing an animal model of HIV infection, we will determine whether specific drug therapy, by decreasing astrocyte activation, can suppress or reverse the evidence of brain damage that can be seen in the model. These studies are important because, in humans, NCI overall responds poorly to treatment with currently available antiretroviral drugs. Therefore, information obtained from these studies will provide important clues for developing effective treatments for individuals, including Veterans, with HIV-related NCI.</p>