

RESEARCH

Interferon-gamma to improve macrophage functions against *Mycobacterium avium* complex infection in HIV-infected patients

Primary Investigator: Janak Koirala, MD, MPH

*Researcher: Lori Koch, BS, CCRP
Funding Agency: American Lung Association of Illinois*

With the use of antiretroviral drugs, there has been a remarkable decrease in mortality and morbidity in HIV infected patients from AIDS and opportunistic infections. Antiretroviral drugs are substances that stop or suppress the activity of a retrovirus, a virus that copies its genome into the DNA of the host cells. A significant number of patients live with advanced HIV disease and remain at risk for various opportunistic infections.

This laboratory-based study was designed to determine and compare the effects of different cytokines, which are products of cells in the body, on the functions of macrophages and other white blood cells that contribute to the immune response and help fight infection. Two of these cytokines are known as interleukin 12 and interferon gamma, which are both thought to be important in the immune response, especially with regard to HIV infection. Previous studies have suggested that a decreased macrophage response to infection may be the result of a defect in the production pathways of these cytokines.

The short-term goal of this project is to elucidate the defects in the interleukin 12 and interferon gamma pathway and to evaluate the ability of these cytokines to improve the killing functions of immune cells against infective organisms.

The general focus of this research is to explore ways to improve immune function. These and similar studies may contribute to the devel-

opment of new treatments, allowing HIV infected patients to more effectively fight infections.

Estrogen Replacement and Synaptic Density

*Primary Investigator: Robert G. Struble, Ph.D.
Funding Agency: Illinois Department of Public Health*

This project will determine the effects of the estrous cycle and continuous estrogen replacement on neuronal and glial biomarkers and determine if the same effects found in the olfactory bulb are found in the cerebellum.

Hormone replacement therapy (HRT) decreases the risk of dementia in several chronic neurological diseases such as Alzheimer and Parkinson disease. However, recent clinical trials suggest that unopposed HRT may not improve cognitive function in individuals with dementia.

This project hypothesizes that continuous estrogen, the treatment paradigm used in many human clinical trials, may cause loss of estrogen efficacy by down-regulating the brain estrogen receptor. The project will determine if continuous, unopposed estrogen regulates the estrogen receptor and glial biomarkers, such as apolipoprotein E, in parallel with loss of synaptic density in the olfactory bulb. The project then will determine if similar changes occur in the cerebellum, a structure substantially different from the olfactory bulb but with the same estrogen receptors.

Understanding how estrogen can improve synaptic connectivity may be critical in designing rational therapeutic application of HRT in neurological disease.

Together, these studies will clarify how some treatment regimens for HRT might be ineffective in improving cognitive function. The project's

goals are to clarify how HRT might improve brain synaptic connections and be better used to obtain a positive clinical response.

Study of Macrophage DNASE1-like III deficiency and its treatment in SLE mice

Primary Investigator Michael C. Schneider, M.D.

Funding Agency: Lupus Research Institute, Inc.

Two independent mouse models of systemic lupus erythematosus (SLE) or lupus, an autoimmune disorder, are defective in the activity of the macrophage-secreted DNASE1L3 enzyme. This is the main enzyme barrier to the artificial entry of DNA into cells.

The study aims to determine whether a deficiency of activity of this enzyme or mutations in the DNASE1L3 gene are present in the human disease. In addition, the project will determine whether increasing the levels of enzyme in blood prevents or changes the course of SLE in the mouse models. If so, this enzyme is a strong candidate for use as a therapy into a treatment of this disease.

For more information about these projects, contact the Office of Research and Faculty Affairs at 217-545-7936.