

Molecular Regulation and Role of Placenta Growth Factor

*Primary Investigator: Donald S. Torry, Ph.D.
Funding agency: National Institute of Child Health and Human Development*

The development of adequate blood supply in the placenta is essential for a normal pregnancy, and evidence shows that a lack of adequate blood supply contributes to many obstetrical complications. Dr. Torry and his team of researchers currently are investigating a placenta growth factor (PlGF) and its receptor (flt1) as potential regulators of placenta function and blood flow during pregnancy.

Dr. Torry reasons that abnormal production of PlGF by the placenta would influence blood flow as well as placenta function, both of which contribute significantly to the success or failure of pregnancies. His team has found that human placental cells express the PlGF-specific receptor, flt-1, and that PlGF protects placental cells from undergoing premature death in culture.

Dr. Torry and his team also have found severely decreased PlGF serum levels in women diagnosed with preeclampsia, an obstetrical condition associated with increased cell death within the placenta. They discovered that a decrease in serum PlGF levels occurred very early in pregnant women who eventually developed preeclampsia — long before clinical signs and symptoms of the condition usually become evident.

It appears that in the pregnant preeclamptic uterus, regulators of PlGF gene expression prevent PlGF from functioning normally. Dr. Torry's recent evidence suggests that by culturing preeclamptic placental cells outside the body, scientists can remove the repressive factors, allowing PlGF to function normally. Under-

standing PlGF regulation could lead to new therapies to help minimize the negative outcomes of preeclampsia.

This work is performed in collaboration with Dr. Tuan Nguyen and colleagues in the OB/GYN Department.



Selective Potentiation of Calcium Currents in Cardiac Myocytes by Cocaine

*Primary Investigator: Louis S. Premkumar, Ph.D.
Funding agency: Illinois Department of Public Aid*

Cocaine use is a major health problem not only because of the dependence it causes, but also because it generates life-threatening cardiac arrhythmias following an overdose. Chronic cocaine use causes heart damage. In western countries, cardiovascular complications from cocaine abuse now account for the majority of drug-related emergency room visits and deaths.

Dr. Premkumar hypothesizes that cocaine directly enhances calcium flow through voltage-gated calcium channels, membranes essential for normal cell function. This leads to calcium overload. Studies suggest that channel blockers can prevent cocaine-induced cardiovascular events (including lethal ventricular fibrillation), and they have been suggested as an antidote to treat cardiac symptoms during cocaine intoxication. However, the specific role of voltage-gated calcium channels in cocaine-induced responses is not fully understood.

In this study, Dr. Premkumar has proposed to determine the type of calcium channel that cocaine enhances, and how it does so. He also will investigate the effect and functional consequences of the process. He then will correlate the findings

with the medical records of cocaine addicts and deaths related to cocaine use, especially the impact on the heart.

Findings from this study will provide a better understanding of cocaine action that may help in identifying cocaine-induced cardiovascular changes, leading to newer therapeutic strategies to deal with cocaine abuse and intoxication.



Sleep Deprivation and Recuperation in Aged Mice

*Primary Investigator: Linda A. Toth, DVM
Funding agency: Illinois Department of Public Aid*

Age-related changes in sleep and circadian rhythms contribute to sleep fragmentation, non-restorative sleep and inadequate amounts of sleep, which may have adverse consequences on health, particularly in young or elderly patient populations. However, the relationship between sleep and immune processes has received relatively little scientific study to date.

This project will develop a model system for evaluating the relationship between sleep loss and susceptibility to, or recuperation from, infectious disease (such as influenza infection) or inflammatory disease (such as immune-mediated hepatitis) in mice.

The long-term goals of this research are to identify genes that influence physiologic responses to sleep deprivation and to assess the health impact of disruptions in sleep.

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