Penn Medicine News

February 15, 2011

CONTACT: Karen Kreeger
215-349-5658
karen.kreeger@uphs.upenn.edu

Penn Medicine
University of Pennsylvania School of Medicine
University of Pennsylvania Health System

This release is available online at
http://www.uphs.upenn.edu/news/News_Releases/2011/02/macular-degeneration-complement-inhibitors/

Penn Researcher Receives $2 million from NIH to Test Macular Degeneration Drug

PHILADELPHIA - **John Lambris, PhD**, the Dr. Ralph and Sallie Weaver Professor of Research Medicine in the Department of Pathology and Laboratory Medicine at the University of Pennsylvania School of Medicine, has been awarded a $2 million grant from the National Eye Institute to test a new class of drugs called complement inhibitors in a primate model of age-related macular degeneration (AMD).

The complement system is an evolutionarily ancient branch of the immune response. One of its key functions is to mark both bacterial and dying host cells for elimination by the body's cellular cleanup services; yet dysregulated complement has also been implicated in at least 30 diseases, including stroke, myocardial infarction, and AMD.

Complement inhibitors, discovered in the Lambris lab, were licensed by Louisville, KY-based Potentia Pharmaceuticals and are about to enter a Phase II clinical trial for the same disease (to be conducted by Alcon Inc.).

While the clinical trial will focus on wet AMD - the more serious form of the condition -- the animal studies covered by the grant will primarily focus on the efficacy and prevention mechanisms of newly discovered complement inhibitors in the early- and late-onset forms of dry AMD found in monkeys at the Tsukuba Primate Research Center at Tsukuba City, Japan and the SICONBREC primate facility in the Philippines, respectively.

The macula lutea is an oval-shaped yellow spot near the center of the retina and is the site of the progressive destruction of the macula that is the hallmark of AMD. It is only found in the eyes of humans, primates, and some birds, says Lambris, so the animal model of macular degeneration, developed by co-investigator Dr. T. Iwata at the National Institute of Sensory Organs in Japan, represents one of the closest disease models for human AMD. It offers a unique opportunity to study the effect of complement activity and inhibition on the development and progression of AMD, the major cause of blindness in elderly people in the US. "This is our life's opportunity to test complement inhibitors on disease progression in a clinically relevant animal model of AMD," adds Lambris.

For the last 10 years, researchers have shown that activation of the complement system has been associated with AMD. A genome-wide association study in an American population with dominantly dry-type AMD revealed a strong association with single nucleotide polymorphisms (SNPs) of complement genes. The lipid-proteins clumps that make up drusen - small, yellow or white deposits in the retina of the eye or on the optic nerve head and one of the most common early signs of AMD -- contain a plethora of active complement molecules in both humans and non-human primates.

These findings, says Lambris, have led his lab to consider the possibility of suppressing complement cascade in

the subretinal tissue to delay or reverse the onset of AMD. To test this hypothesis, they are using analogs of an inhibitor called Compstatin in a non-human primate model with early-onset macular degeneration that develops drusen in less than two years after birth. Their preliminary results showed drusen disappearance six months after injecting Compstatin into the eye.

Despite years of research on the molecular correlation between complement activation and disease progression in AMD, many aspects are still unresolved. Dr. Lambris, in collaboration with Penn Resesarch Assistant Professor **Daniel Ricklin, PhD**, and **Joshua Dunaief, MD, PhD**, associate professor of Opthalmology, devoted another part of the grant to a systematic molecular analysis of complement components in patients with AMD. Together, the studies proposed in the awarded grant are designed to shed more light into the etiology of this severe and abundant disease, and may well pave the way to introduce therapeutic options that interfere with disease progression much earlier than currently available drugs.

Editors' note:
Dr. Lambris holds several patents on Compstatin and clinical use of complement inhibitors. He is also the founder of Anosos Biotherapeutics, which develops complement therapeutics for various diseases. Anosos was established using PENN's UPSTART program: http://www.upenn.edu/pennnews/news/penn-s-center-technology-transfer-unveils-upstart-company-formation-program

###

Penn Medicine *is one of the world's leading academic medical centers, dedicated to the related missions of medical education, biomedical research, and excellence in patient care. Penn Medicine consists of the University of Pennsylvania School of Medicine (founded in 1765 as the nation's first medical school) and the University of Pennsylvania Health System, which together form a $4 billion enterprise.*

Penn's School of Medicine is currently ranked #2 in U.S. News & World Report's survey of research-oriented medical schools and among the top 10 schools for primary care. The School is consistently among the nation's top recipients of funding from the National Institutes of Health, with $507.6 million awarded in the 2010 fiscal year.

The University of Pennsylvania Health System's patient care facilities include: The Hospital of the University of Pennsylvania â€“ recognized as one of the nation's top 10 hospitals by U.S. News & World Report; Penn Presbyterian Medical Center; and Pennsylvania Hospital – the nation's first hospital, founded in 1751. Penn Medicine also includes additional patient care facilities and services throughout the Philadelphia region.

Penn Medicine is committed to improving lives and health through a variety of community-based programs and activities. In fiscal year 2010, Penn Medicine provided $788 million to benefit our community.