

ANNOUNCEMENT

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Penn Medicine Program Receives \$10 Million Renewal for Studying the Oldest Branch of the Immune System

PHILADELPHIA — The National Institute of Allergy and Infectious Diseases has awarded the [Perelman School of Medicine at the University of Pennsylvania](#) a five-year, \$10 million renewal of a program project to study the [oldest part of the human immune system called the complement system, or simply "complement."](#) Complement is a network of more than 50 proteins in the blood and on cell surfaces and is part of the innate immune system, in contrast to the adaptive system consisting of antibodies which can "learn" and adapt themselves on the fly to different antigens. The complement proteins quietly cruise the blood system, keeping a low profile until triggered into action.

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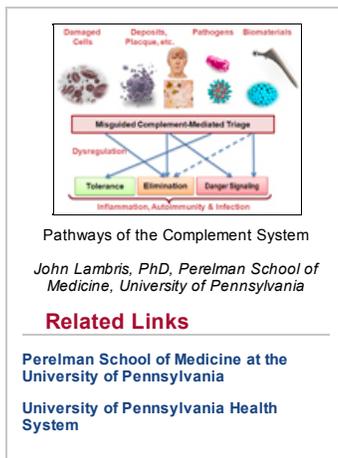
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[John Lambris, PhD](#), the Dr. Ralph and Sallie Weaver Professor of Research Medicine in the [Department of Pathology and Laboratory Medicine](#), has been studying the complement system for many years, and is the lead investigator on the renewed program project. Complement has been shown to contribute to a broad spectrum of immune, inflammatory, and age-related diseases. Lambris and colleagues are developing novel therapeutics to tame inappropriate complement activation and protect cell surfaces from an attack by this defense system.

Using small inhibitors of central complement components, engineered regulatory proteins, and protective cell coatings, they are demonstrating the benefit of therapeutic complement modulation in a variety of clinical situations, including organ transplantation, hemodialysis-related complications, and periodontitis. The latter disease is being investigated in collaboration with the Penn School of Dental Medicine, under the project leadership of **George Hajishengallis, DDS, PhD**. Although individual diseases have distinct triggers of complement activation, it is likely that there are common patterns of downstream immunomodulatory mechanisms that will

broaden our perception of complement's pathophysiological role and guide the development of complement therapeutics.

During the initial five years of the program project, the team unraveled several new mechanisms of complement and demonstrated surprising roles of this ancient system in cancer and liver regeneration. At the same time, the project produced an impressive arsenal of complement modulators, some of which already showed clinical.

"Although the value of inhibiting complement therapeutically has long been recognized, the availability of complement-directed drugs in the clinic is still very limited," says Lambris. The development and evaluation of a toolbox of complement inhibitors that block the system at various functional key steps will therefore be a centerpiece of the renewal.

"Although we have known about complement for over 100 years, it continues to surprise us, with discoveries of new functions that reach beyond microbial defense to include roles in immune surveillance, homeostasis, and development," says Lambris. "What's more, it is becoming evident that these functions rely on crosstalk with other bodily systems. However, complement-related diseases have often been studied in an isolated manner and without considering crosstalk."

This renewal will develop complement inhibitors by exploring the mechanisms of complement initiation, propagation, and immune crosstalk in inflammatory disorders and will evaluate the clinical potential of central and pathway-specific of these complement inhibitors.

Daniel Ricklin, PhD (Pathology and Laboratory Medicine), **Laura Dember, MD** (Renal Electrolyte and Hypertension Division), **Ali Naji, MD, PhD**, (Surgery), **Elizabeth Grice, PhD** (Dermatology), and **Evlambia Hajishengallis, DDS, PhD** (Dental Medicine), all from Penn are also co-principal investigators on the renewal.

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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 [Raymond and Ruth Perelman School of Medicine at the University](#)

[of Pennsylvania](#) (founded in 1765 as the nation's first medical school) and the [University of Pennsylvania Health System](#), which together form a \$4.3 billion enterprise.

The Perelman School of Medicine has been ranked among the top five medical schools in the United States for the past 17 years, according to U.S. News & World Report's survey of research-oriented medical schools. The School is consistently among the nation's top recipients of funding from the National Institutes of Health, with \$392 million awarded in the 2013 fiscal year.

The University of Pennsylvania Health System's patient care facilities include: The Hospital of the University of Pennsylvania – recognized as one of the nation's top "Honor Roll" hospitals by U.S. News & World Report; Penn Presbyterian Medical Center; Chester County Hospital; Penn Wissahickon Hospice; and Pennsylvania Hospital – the nation's first hospital, founded in 1751. Additional affiliated inpatient care facilities and services throughout the Philadelphia region include Chestnut Hill Hospital and Good Shepherd Penn Partners, a partnership between Good Shepherd Rehabilitation Network and Penn Medicine.

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