There’s a cliche in medicine that immunity is a double-edged sword. The same function that protects the body against viral or bacterial invaders can also cause harm when it goes into overdrive. “In immunity, nothing can be entirely beneficial,” said Dr. George Hajishengallis, the Thomas W. Evans Centennial Professor in the Department of Basic and Translational Sciences at Penn Dental Medicine. “Depending on context, you may want to inhibit or promote these processes.”

The downside of immunity — specifically, maladaptive trained innate immunity — took Dr. Hajishengallis to the National Institutes of Health earlier this year, when he was invited to be the keynote speaker at an NIH workshop. His talk was titled “Immunometabolic Crosstalk in Trained Immunity and Inflammation” and described a concept he’s working on with longtime collaborators in Germany that was also outlined this year in *Nature Reviews Immunology*. (Trained immunity is the property of cells in the innate immune system — such as neutrophils and monocytes and their progenitors — to memorize an infectious or inflammatory event and respond much faster and stronger to a similar challenge in the future.)

In periodontitis, a key research focus of Dr. Hajishengallis' laboratory, bacteria eventually move from the gums into the patient’s blood, causing the local inflammation to become systemic. When the patient’s bone marrow senses this inflammation, the immune system responds by producing more neutrophils and monocytes than a healthy patient would. This, explains Dr. Hajishengallis, is an example of maladaptive trained innate immunity, because instead of protecting the body, these hyperactive immune cells exacerbate inflammation. If left unchecked, this inflammation can worsen an existing condition, such as arthritis, or even instigate a new chronic inflammatory disease.

“When you become sick, it doesn’t matter [whether] that came from the mouth or came from another part of the body. It will affect your systemic health sooner or later.”

— DR. GEORGE HAJISHENGALLIS

Tracking the Downside of Immunity: An Oral-Systemic Health Connection

“When you become sick, it doesn’t matter [whether] that came from the mouth or came from another part of the body. It will affect your systemic health sooner or later.”

— DR. GEORGE HAJISHENGALLIS

bad cascade of events,” Dr. Hajishengallis says. “Besides common risk factors, this is another mechanism that could explain why we have comorbidities.”

Dr. Hajishengallis and his collaborators theorize that, in certain contexts, inhibiting maladaptive trained innate immunity, particularly in vulnerable populations, such as elderly patients, could provide a therapeutic approach to combating chronic inflammation. Blocking that ongoing inflammation, he explains, could in turn prove beneficial against a host of chronic inflammatory diseases.

This work is of particular interest to the NIH, Dr. Hajishengallis notes, because there is a growing effort to better understand the association between oral diseases and systemic health. Why, for instance, do people with periodontitis have increased risk for arthritis, cardiovascular disease, diabetes, or Alzheimer’s? One way to illuminate these associations, Dr. Hajishengallis explains, is through the study of maladaptive trained innate immunity.

“When you become sick, it doesn’t matter [whether] that came from the mouth or came from another part of the body,” he said. “It will affect your systemic health sooner or later.”

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BASIC & TRANSLATIONAL SCIENCES

NEWS/ACHIEVEMENTS

Dr. Calga Akay-Espinoza was awarded a Penn Center for AIDS Research pilot grant for a project titled HIV viral dynamics and host-cell gene expression profiles in human-induced pluripotent stem cell-derived myeloid cells.

SELECTED PUBLICATIONS

A selection of recently published work by department faculty (indicated in bold).


BATTLING RHEUMATOID ARTHRITIS

A new study led by Dr. George Hajishengallis shows that the protein DEL-1 could reduce the painful inflammation of RA in an animal model. See the following article:


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Dr. Marco Tizzano has joined the Department as an Associate Professor. His appointment to this tenure-track post was effective October 1.

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**BATTLING RHEUMATOID ARTHRITIS**

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Phosphatase Activity
Phosphatidylinositol-3,4,5-Triphosphate and Campylobacter jejuni Exhibits Potent

“then we can explain it by induction of maladaptive trained immunity in connection between maladaptive trained innate immunity and chronic their sights on the unfortunate side effects of trained innate immunity. could provide protection against cancer. Now, the partners have turned actually kill tumor cells — in other words, that trained innate immunity progenitor cells, which give rise to lines of differentiated blood cells for development

Dr. Hajishengallis and his team have been working closely with the laboratory of Triantafyllos Chavakis, faculty at the Institute for Clinical Chemistry and Laboratory Medicine at Technische Universität in Dresden, Germany, on this research. The partnership has yielded dozens of journal articles and research papers. “It’s a very prolific collaboration,” Dr. Hajishengallis said. “We consider them our sister lab.”

The earliest iteration of the collaboration, published in the journal Cell, showed that innate immune memory takes place in bone marrow progenitor cells, which give rise to lines of differentiated blood cells for months to come. The team later showed that trained neutrophils could actually kill tumor cells — in other words, that trained innate immunity could provide protection against cancer. Now, the partners have turned their sights on the unfortunate side effects of trained innate immunity.

The next step, Dr. Hajishengallis said, is to formally prove the connection between maladaptive trained innate immunity and chronic inflammation. To do this, the team will cause periodontitis in mice and monitor whether the infection makes the rodents more susceptible to other chronic inflammatory diseases. If a connection is found, he said, “then we can explain it by induction of maladaptive trained immunity in bone marrow progenitor cells.”

HIV & THE BRAIN
A study from the lab of Dr. Kelly Jordan-Sciutto details the mechanism by which HIV infection blocks the maturation process of brain cells that produce myelin, a fatty substance that insulates neurons. See the following article: