



MCB NOTES

NOVEMBER 2016

Microbes of the feathered work together

Increasingly the human microbiome is in the news. We hear that a body's microbiome, all the microbes both in and on a living body, might affect our weight, play a role in health aging, and affect our immune responses. All plants and animals have microbiomes, too, and while much research has been directed to the medical and agricultural aspects of microbiome

functions, much less has been done to understand how microbiomes shape life in the natural world. Newly arrived MCB **Assistant Professor Sarah Hird** seeks to address a part of this gap in our knowledge as she launches her research program to examine how a host's microbiome affects the evolution of the host and how the host affects the evolution of its microbiome.

Hird's background studying animal and bird diversification provides her with a unique perspective on studies of microbiome evolution. Questions basic to studies of animal evolution have not been asked about microbial evolution. Hird wants to ask such questions. "What contribution does each specific bacterial taxonomic rank

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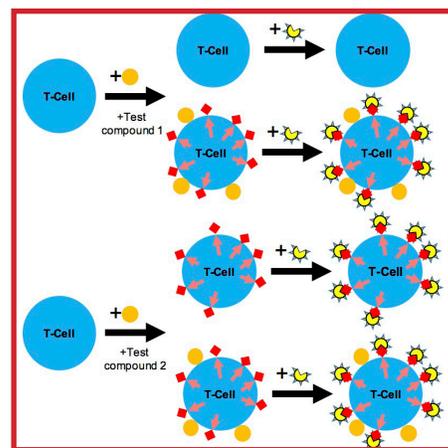
Helping our bodies to heal themselves

you receive an organ transplant, your immune system will fight this foreign tissue. If your own cells become cancerous, your immune system may fail to adequately recognize and kill those cells. Chemicals have long been used to treat these conditions, but in recent years, successful treatments have been conducted by reducing or enhancing the function of the patient's immune system, so that their bodies can better participate in its treatment.

Recently funded research in **Professor Adam Zweifach's** laboratory seeks a means to more rapidly search for new drugs to modulate the function of the human immune system. While doing so, he wants to learn more about the underlying functions of the components of the immune system.

The \$950,000 project (\$799,000 of which comes to UConn), funded by the NIH National Institute of Allergy and Infectious Diseases, **Continued on page 2**

Your body's immune system stands guard against infectious invaders, but sometimes it fails to work in your body's best interests. If



Zweifach's assay. Beads (yellow) added to T-cells (blue) stimulate surface protein (red) production that is detected with fluorescent antibodies (yellow). Test compound 1 is desirable because it stimulates cells only after beads adhere.

MCB Factoid

In the first quarter of FY 2017, MCB faculty received 6 new research awards totaling over \$4.5 million.

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page 3:

- Cell Bio PhD student Velle captures 3rd place in UConn Three Minute Thesis competition
- Supercomputer time awarded to Prof. May and Dr. Nangia
- Biochem PhD students Hesler and Daman receive Beckman Coulter Award
- Stony Brook's Dr. Hunnan was Khairallah Symposium speaker

Bird microbiomes

contribute to the variation (among the bacteria) that we see? Which bacteria are interacting and how do they correlate with each other?" she asks.



Hird's recent research has focused on the microbiomes of wild birds, particularly neotropical birds in Costa Rica and Peru. She published a study reporting measures of the numbers of different bacterial groups (phyla) in the guts of 59 species of birds. She used sophisticated statistical and bioinformatic tests of those data to determine which taxonomic and ecological properties of those birds had the largest influence on the distributions of those bacterial phyla in their guts. She wanted to "see whether all the microbiomes from a specific species (of bird) look most similar or do the microbiomes of birds collected at one specific place look more similar." She also examined whether diet, foraging strategy, age and other characters had an effect on the microbiomes' composition.

"The short answer was that bird species and the higher taxonomic orders like a bird order," make their microbiome communities look most similar, according to Hird. However, at least in this study, "ecology of the bird also matters to structuring these communities. Geographic space does not seem to matter," she says.

"Diet seems to be important for structuring gut communities."

"Diet seems to be important for structuring gut communities," Hird says. In birds, the effect of diet seems to be less than it is in mammals, perhaps because they don't tend to restrict their diets to plant- or animal-based foods. Birds have lots of overlapping dietary components. Some eat

seeds as well as insects, even hummingbirds eat some bugs to add more protein to their diet.

Hird is looking to bring some of her research closer to home, to examine microbiomes in wild birds in Connecticut. There are potential practical applications for her work, too. The avian flu virus, for example, is common among wild ducks, but does not cause major disease in ducks, as it can in humans. The virus' presence, however, correlates with a different bacterial microbiome from that of uninfected ducks, for unknown reasons. It could be that ducks Your body's immune system stands guard against infectious invaders, but sometimes it fails to work in your body's best interests. If you receive an organ transplant, your immune system will fight this foreign tissue. If your own cells become cancerous, your immune system may fail to adequately recognize and kill those cells. Chemicals have long been used to treat these conditions, but in recent years, successful treatments have been conducted by reducing or enhancing the function of the patient's immune system, so that their bodies can better participate in its treatment.

Immune enhancement

is a follow-up study on a previously funded project that designed a high-throughput screen for immune-suppressing small molecules. Two new compounds were discovered that blocked the activation of



T-cells, a form of white blood cells that play key roles in recognizing and, sometimes, destroying foreign cells. That study continues as an effort to understand how these newly discovered compounds interact with T-cells.

The new study will modify the earlier assay to now look for small molecules that enhance the immune system, again through interactions with T-cells. The desired molecules should further enhance the activities of T-cells that are already activated to recognize and kill cancerous cells.

The assay is designed to rapidly search through thousands of small molecules contained in a library of molecules maintained by the Broad Institute at MIT and Harvard University. The screening process involves use of a multiplex high-throughput flow cytometer that is overseen by Prof. Zweifach's collaborator, Dr. Larry Sklar, at the University of New Mexico Center for Molecular Discovery. "The goal of this project is to see if we can identify compounds that enhance the activity of activated T-cells or other immune cells, but that don't themselves activate the T-cells," says Zweifach.

In the assay, T-cells are first activated with small beads that cause the T-cells to excrete specific proteins to their cell surfaces. An insufficient number of beads are used so that some cells do not bind any beads. Those cells that have bound beads are then detected by adding a fluorescent antibody that binds to their surface proteins, thus making activated cells distinguishable from unactivated cells in the flow cytometer. If a test molecule causes cells to fluorescence only after the cells have bound beads and are activated, then those are the compounds of interest. 384 samples can be screened in 15 minutes using the sophisticated flow cytometers at the Center.

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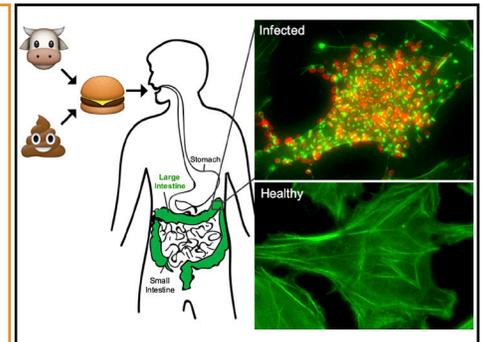
Though new immune-enhancing compounds will likely be found in Zweifach's study, the project is not only designed to discover pharmaceutically useful compounds. The project goal is create a method of screening that others can use for this purpose, but at the same time to discover new information about how our immune system functions. For example, Zweifach points out that, "Most immune cells use similar enough signaling mechanisms hooked up to different things so that if a compound is active in our cells, then we can test it on other kinds of immune cells that would be harder to screen." Thus his discoveries could allow examination of similar immune-enhancing effects on other cells of the immune system.

Advances in immunotherapies are sure to appear, and with those, advances in our understanding of how our bodies stave off diseases and disorders. Supporting those advances is the job of researchers like Zweifach, who use their knowledge of immune functions to streamline basic research and therapeutic efforts.

MORE NOTES



Cell Biology grad student scores 3rd place in 3-Minute Thesis contest. Katrina Velle, Cell Biology PhD student in Prof. Campellone's laboratory, was awarded 3rd place in the 2016 3 Minute Thesis Live Competition on the UConn campus. The 3MT competition awards senior graduate students from all disciplines who can present their thesis topic to a general audience in 3 minutes or less. UConn sends a video of its first place finisher to the international 3MT competition. Velle's talk was entitled "Surfing on Pedestals: How Pathogenic E. coli Spreads Infection."



Supercomputer time awarded to May. Prof. Eric May and his postdoctoral associate **Shivangi Nangia** received an allocation on the Anton2 supercomputer at the Pittsburgh Supercomputing Center. The allocation will allow them to analyze viral protein-membrane interactions over timescales which are not feasible on standard supercomputing environments.



Students win Beckman Coulter award. Stephen Hesler (PhD, Biochemistry) and **Tyler Daman** (PhD, Biochemistry) of the Cole and Robinson labs, respectively, are this year's recipients of the Beckman Coulter award. The award enabled them to attend the prestigious Advanced Analytical Ultracentrifugation Workshop and Symposium in Danbury, CT Oct. 13-19. Hesler researches fundamental aspects of an important protein of the innate immune response. Daman examines the intrinsically disordered features of nucleostemin, a nucleolus protein that regulates cell differentiation.



Khairallah Symposium featured Dr. Hannun. The 2016 Khairallah Symposium was held on Nov. 1. The Lamia and Edward A. Khairallah Fund for Scholarship supports this ongoing symposium series and MCB graduate students. This year's guest speaker was **Dr. Yasuf Hannun**, Director, Stony Brook Cancer Center, Vice Dean for Cancer Medicine, and Joel Strum Kenny Professor in Cancer Research at the Department of Biochemistry and Cell Biology, Stony Brook University. His seminar was entitled "Neutral Sphingomyelinase in the DNA Damage Response."

Writer: Prof. Kenneth Noll, MCB; kenneth.noll@uconn.edu

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