

MCB NOTES

FEBRUARY 2010



Squid uses bacterial light to avoid place on menu

Hawaiian monk seals looking for a tasty midnight snack of calamari have a hard time finding the little bobtail squid. From below, the squid become all but invisible by lighting up their undersides to blend in with the moonlight shining above. But how do squid make light?

Welcome to MCB Notes

It is my pleasure to welcome you to this first edition of the newly formatted MCB Notes. It is difficult to convey the full range of activities that occur in the department in a single issue, so I hope that this format will serve to highlight some worthy items from recent weeks. See our website link on the back page for more MCB news.

David Benson
Department Head

Spencer Nyholm, Assistant Professor in MCB, was awarded a \$616,483 grant from the National Science Foundation to find out how the squid acquire their ability to make light. Surprisingly, the light does not come from the squid, but from a population of a luminescent bacterium called *Vibrio fischeri* living in a light organ on the underside of its body. When a baby squid hatches from its egg it has no light-producing bacteria so it has to collect them from the seawater. During development, potentially hundreds of kinds of seawater bacteria could enter the new light organ, so the squid's immune system cells act as gatekeepers to help distinguish friend from foe. Nyholm's study aims to find out how those immune cells "learn" which bacteria are helpful *Vibrio fischeri* that will go on to be symbionts and which are potentially harmful and so must be eliminated.

"The symbiont is suppressing the immune system of the host so it does not recognize it," Nyholm explained. Learning about how the squid's immune cells distinguish microbial friend from foe will help us know how

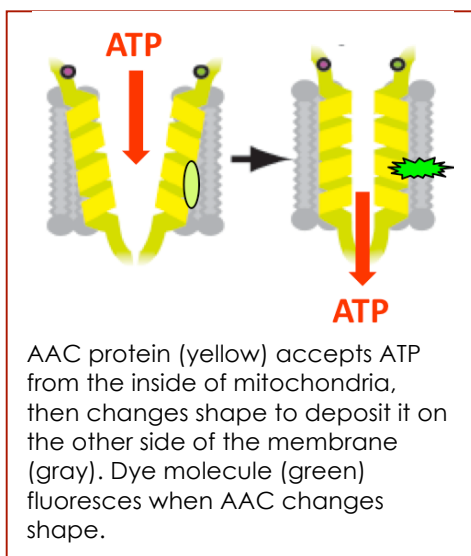
our immune system alerts us to the presence of pathogens among the helpful microbes in our intestinal tract.

To carry out his study Nyholm constructed a squid nursery in the basement of Torrey Life Sciences. In tanks containing some 800 gallons of seawater he nurtures twenty 4 cm long adult females and their offspring to provide the young squid he needs. He can raise up to 20,000 juvenile squid per year. "Bringing the ocean to Storrs is a challenge," he said. The squid "are extremely finicky eaters. We have to provide them with live shrimp. They like to hunt things that are their same size or bigger. They like a challenge, I suppose."

Vibrio fisheri and the squid live in a mutually beneficial or symbiotic relationship. Microbial symbioses are not unique to squid. We, too, live in symbiosis with bacteria, particularly those essential for digesting food. Our symbiotic bacteria do not make light, but they make a calamari snack a whole lot more digestible.

FIGHTING HEART DISEASE ONE AMINO ACID AT A TIME

Cardiovascular diseases including cardiomyopathy afflict one in three American adults according to the American Heart Association (AHA). One cause of cardiomyopathy (heart muscle disease) is a malfunctioning membrane protein of the energy generators or mitochondria inside heart muscle cells. MCB Assistant Professor **Nathan Alder** is exploring how this protein changes shape to help power heart muscle cells and how defects in the protein cause it to malfunction. Alder received a \$308,000 National Scientist Development Grant from the AHA to use fluorescent probes to study the ADP/ATP Carrier (AAC) protein as it exports ATP, the energy currency of a cell, out through the mitochondrial inner membrane.



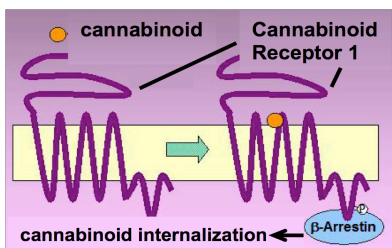
"The transporter itself has been implicated in a lot of different kinds of mitochondrial myopathies and cardiac myopathies"

The AAC protein acts like a funnel stuck in the mitochondrial membrane; moving ATP out of the mitochondrion by capturing ATP in the funnel mouth and changing its shape to release it on the other side. Alder attaches a fluorescent dye molecule, called a fluorophore, to selected amino acids that compose AAC and as AAC changes shape, the fluorophore may become exposed to different surroundings. In this new environment, the dye fluoresces a different color, allowing Alder to observe AAC's movement indirectly. "We are able to incorporate the fluorophore at several points along the growing polypeptide chain, get it imported into mitochondria and monitor the activity," Alder stated.

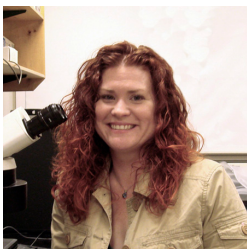
Alder incorporates his dyes at different amino acids on AAC including those that create a leaky AAC as in some inherited cardiomyopathies. "You create a situation where the inner membrane is no longer tight anymore and this has implications in apoptosis and heart disease." With this knowledge in hand, we can perhaps develop better treatments for the growing number of people afflicted by cardiomyopathic illnesses.



Associate Professor **Andrei Alexandrescu** has been awarded a \$290,000 grant from the American Diabetes Association to study how amylin, a hormone that regulates how much you eat, changes during Type 2 diabetes to kill insulin producing cells in the pancreas. Alexandrescu plans to study how amylin changes its shape under different conditions. Interactions among the amino acids that make up amylin are responsible for these varying structures and his work will shed light on which of these amino acids are responsible for the toxic form of amylin. These results may lead to the development of drugs that block the formation of these misshapen, toxic proteins. Type 2 diabetes is the most common form of diabetes in the US.



Rebecca Stadel, a postdoctoral research associate in Dr. Debra Kendall's lab, recently received an NIH National Research Service Award to study the process by which brain cells are affected by cannabinoids, compounds that are naturally produced in the brain and look chemically like the active ingredient in marijuana, otherwise known as cannabis. Stadel will examine how a brain cell protein, Cannabinoid Receptor One, interacts with the signaling protein β -Arrestin inside cells after binding a cannabinoid. Her work will allow us to better understand how brain cells signal the presence of cannabinoids and react to them. Ultimately, her work may lead to better drugs that mimic the desirable effects of cannabinoids while eliminating their undesirable side effects.



High-throughput DNA sequencing capacity continues to grow at UConn thanks in part to a recent NSF award to Associate Professors **Michael O'Neill** and **Rachel O'Neill** for the purchase of an Applied Biosystems SOLiD3 massively parallel DNA sequencer. The new sequencer joins other such instruments at the University's Center for Applied Genetics and Technology. The instrument will support the work of UConn researchers in developmental biology, ecology, evolutionary biology and cancer research. The \$407,672 grant will also provide opportunities for hands-on training and education in advanced genome sequencing methods for students in precollege and minority outreach programs.

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