The Natural Sciences

BIOLOGICAL SCIENCES

Neurogenesis of Sea Anemones

The starlet sea anemone, *Nematostella vectensis*, is a species of small sea anemones that occupy an essential position in the tree of life. They are primitive animals with epithelial cells, neurons, stem cells, complex extra-cellular matrix and muscle fibers, and they have extensive regenerative ability. Although the *Nematostella* is a "primitive" animal, the sea anemone genome is more closely related to the human genome than the current invertebrate animals used to model human biology. Understanding the neuroregenerative properties of *Nematostella* is the current interest of biologist Michael Layden.

Layden's research focuses on understanding how the mechanisms that regulate regeneration of the anemone's nervous system may vary from mechanisms that generate the nervous system during development.

"Traditionally, people have looked at the process of neurogenesis during development (when a fertilized egg develops into an adult animal), but now the goal is to understand the same process during regeneration of adult bodies," says Layden, assistant professor of biological sciences. "There is a clear indication that when animals regenerate, the mechanisms are similar to those used during development. You don't reinvent the wheel to regenerate a limb, for example, but regeneration does not use the exact same molecular program as development. In order to understand the significance of differences observed between development and regeneration, you need to study them in the same animal."

Most current research on regeneration uses model systems that are not suited for investigating both animal regeneration and development. It is difficult to compare the neural development and neural regeneration directly because they are investigated in two different animals, says Layden. *Nematostella* is one of the few animal models that allow researchers to easily access and manipulate gene function during both development and regeneration. Understanding the similarities and differences in how developmental programs are redeployed during regeneration will provide researchers with critical clues needed to design better regenerative therapies for human neurological disorders.

Layden examines achaete-scute homologs (ash), a type of gene that regulates formation of a subset of the *Nematostella* nervous system during embryogenesis. He and his team disrupt this gene's function and analyze neural phenotypes at the *Nematastella*'s larval and juvenile polyp stages. In conjunction with this, he is improving methods

Michael Layden (above) examines the neuroregenerative properties of Nematostella.

to disrupt genetic function during regeneration. The goal is to assess whether this ash gene regulates formation of the same neurons that it does during development, regulates neural development using the exact same molecular program and/or regulates distinct neuron sub-types that are not regulated by this gene during development.

Using *Nematostella* allows researchers access to the neural processes in an invertebrate model that is inexpensive to study when probing regenerative properties. Layden can obtain thousands of embryos daily and his team can dissect anemones at any stage of their lives, including during regeneration. By examining sea anemones, he and his colleagues are laying the groundwork for future studies in vertebrates, such as zebrafish and mice.

Additionally, because *Nematostella* is a primitive animal, Layden's research will also provide insight about molecular programs that regulated formation of the ancestral nervous systems that gave rise to more complex nervous systems, such as the human brain.

CHEMISTRY

The Efficacy of pHLIP

Effective therapies for the treatment of cancer rely on the localized delivery of drugs. Targeted drugs attack the cancer while reducing the impact the drugs have on the rest of the body. A unique delivery peptide that can selectively target tumors in mice and translocate and release cargo molecules intracellularly based solely on the acid levels inherent to cancer cells is being investigated in the laboratory of Damien Thévenin.

Funded by the National Cancer Institute, the research by Thévenin's team investigates the efficacy of a pH-sensitive peptide to target and deliver the microtubule inhibitor monomethyl auristatin E (MMAE) to cancer cells and breast tumors. Many cancer-targeting therapies intended to improve the effectiveness and diminishing off-target cytotoxic effects have been developed and hold the promise of being therapeutic options for certain types of cancers. However, preclinical and clinical studies found that therapy strategies based on the targeting of specific proteins are significantly hampered by tumor heterogeneity, which can promote tumor evolution, leading to the loss of cell surface proteins and, eventually, to therapy resistance and disease progression. Moreover, targeted cancer biomarkers tend to be overexpressed in a tumor-associated, not tumor-specific, manner.

Acidity is a general hallmark of tumors. While normal tissue pH is