Evolution of the TRH neuropeptide pathway and its growth regulation function in echinoderms

Director of Studies: Maria I. Arnone

Department of Biology and Evolution of Marine Animals

Project Summary

In mammals, the Thyrotropin-Releasing Hormone (TRH) has a central role on regulation of metabolism and growth by stimulating the secretion of the TSH from the pituitary gland. In non-mammalian vertebrates, e.g. amphibians and fish, TRH also regulate growth by stimulating the release of Growth hormone and prolactin from the pituitary gland, while it has little or no effect on the secretion of TSH. The role of TRH so far remains poorly investigated in invertebrates.

Recent work in the Arnone's lab addressed the role of a sea urchin TRH neuropeptide (SpTRH) in *Strongylocentrotus purpuratus* larvae. SpTRH is produced by two Go-opsin expressing photoreceptor cells bilaterally distributed at each the side of the larval apical organ. Preliminary data shows that TRH protein production is regulated by light/dark cycle and feeding/starving conditions. Furthermore, knock-down experiments of the SpTRH precursor appear to inhibit the post embryonic arm growth.

This project has two main goals (i) a deep analysis of the role of TRH neuropeptide pathway during larval growth in two model sea urchin species, *S. purpuratus* and *Paracentrotus lividus*, and (ii) the evolution of the TRH neuropeptide pathway in echinoderms. The project will involve leading-edge gene function experiments including loss of function experiments using morpholino antisense oligonucleotides and CRISPR/Cas9 gene editing approaches; phenotypic plasticity, feeding- and photo-behavior measurements in various light/dark cycle and feeding/starving conditions in normal versus perturbed TRH neuropeptide pathway conditions; immunohistochemistry and drug treatments to study of the interplay between the TRH neuropeptide pathway and the serotonergic and dopaminergic systems. Thanks to the collaboration with the University of Sidney the project will also involve several Australian echinoderm species, including the sea urchins, *Heliocidaris tuberculata*, *H. erythrogramma*, and the sea stars, *Patirella regularis* and *Parvulastra exigua*.

It has been suggested that the TRH pathway originated before the divergence of protostomes and deuterostomes and that the ancestral role of this neuropeptide is on the control of postembryonic growth and reproduction. Therefore, the results of the proposed project will allow assessing, for the first time, the role of TRH in a non-chordate deuterostome and will concur in validating the hypothesis of an ancestral role of TRH on postembryonic growth regulation. Moreover, given the importance for studying the impact of climate change of the Australian echinoderm species used within this project for evolutionary purposes, we also expect that our results will be of relevance for climate adaptation studies.