Evolution of pancreatic cell types: a single cell transcriptomic approach

Director of Studies: Maria I. Arnone

Department of Biology and Evolution of Marine Organisms

Seat: Naples, Italy

Project Summary

One intriguing and still open fundamental question in biology is how different embryonic structures evolved in different animals. Among all the embryonic structures, the development of an internalized gastrointestinal system has represented a crucial evolutionary innovation, releasing multicellular organisms from body size constrains and facilitating the emergence of new complex body structures. Gut development occurs through similar mechanisms in bilateral animals involving the combined activity of orthologous transcription factors and signalling molecules. Two ParaHox genes, *pdx1* and *cdx*, have conserved fundamental functions in this process and their deregulation in humans can cause diseases as severe as diabetes and cancer. In particular, Pdx1 in vertebrates controls the specification of the pancreas and the maintenance of β-cells, as well as *insulin* transcription in these cells, resulting as causal factor in diabetes. Despite the evident conservation of *pdx1* expression in the gut of most deuterostomes and in vertebrate pancreatic-like cell types, the link between Pdx1 and *insulin* has never been documented outside vertebrates and the evolutionary origin of pancreatic cell types is completely unknown.

This project aims at reconstructing the evolutionary trajectory of pancreatic cell types in the deuterostome lineage. Through state of the art technologies such as single cell sequencing and gene perturbation approaches, we will identify pancreatic-like cell types in marine embryos belonging to different taxa and willattempt to decipher endocrine pancreatic function evolution through comparative analysis with known data in mammals. To this end, both comparative and functional genomics approaches will be applied to the following species: two echinoderms, the sea urchin *Strongylocentrotus purpuratus* and the sea star *Patiria miniata,* as representative of non-chordate deuterostomes, and the cephalochordate amphioxus *Branchyostoma lanceolatum,* as representative of a chordate non-vertebrate. Using functional genomics approaches we will for the first time compare at the single cell level the development of eligibly homologous structures between a vertebrate and an invertebrate, addressing the role of an organ identity gene, *pdx1,* on the origin of endocrine pancreatic functions. As an intermediate step of this study, the project will also generate for the first time a complete gene expression atlas of major cell types of the sea star larva and the first comprehensive atlas of pancreatic cell types described in a non-vertebrate chordate (the amphioxus).