Evolution of pancreatic cell types: a single cell transcriptomic approach

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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 evolutionary origin of pancreatic cell types is completely unknown.

To address these questions, the project aims at reconstructing the evolutionary trajectory of pancreatic cell types. Through stat-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 will attempt 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 three echinoderms, the sea urchins *Strongylocentrotus purpuratus,* for which a single cell atlas has been recently generated (DOI: 10.7554/eLife.70416) and *Paracentrotus lividus*, for which the genome at chromosome resolution has been recently released, and the sea star *Patiria miniata,* as representative of non-chordate deuterostomes. Using functional genomics approaches and algorithms (such as SAMap, doi: 10.7554/eLife.66747) enabling mapping of single-cell transcriptomes between phylogenetically remote species, the project will allow the comparison at the single cell level of the development of eligibly homologous structures in metazoans, addressing the role of an organ identity gene, *pdx1,* on the origin of endocrine pancreatic functions.