Development of the cardiac pacemaker system and how it controls heart rate

Summary

Development of specialized cells and structures in organs is regulated by spatially-restricted molecular pathways. Disruptions in these pathways can cause severe congenital malformations or functional defects such as in the heart. The heart is formed as a linear tube that transforms into a complex looped structure by growth and morphogenesis. Growth of the heart tube is mainly driven by the accretion of undifferentiated cells from the lateral plate mesoderm, the so-called second heart field. The cells that are added to the inflow pole of the heart tube will differentiate into pacemaker cells. Cardiac pacemaker cells generate an action potential by: spontaneous, rhythmic membrane depolarization, which triggers the neighboring working myocardium to contract. Although pacemaker cells are situated within, and coupled to, the surrounding cardiomyocytes, they retain a primitive myocardial identity even in the adult heart.

To study genetics of cardiac development in vivo we use the vertebrate zebrafish model. We have studied signaling pathways that regulate the accretion of second heart field cells to the linear heart tube. Our specific interest is in the pacemaker cells that are found at the inflow pole of the heart tube and we identified a central regulator required for their function. We have applied spatially resolved transcriptomics to identify novel spatially restricted pathways during development of the cardiac pacemaker cells and are applying functional genetics and optogenetic sensors to study their function and regulation by the autonomous nervous system.