Stellingen van Jeroen Paardekooper Overman behorende bij het proefschrift

Noonan and LEOPARD Syndrome in Zebrafish: Molecular Mechanisms and Cardiac Development

1. Shp2a and Shp2b are similar proteins which only differ functionally based on their temporal expression pattern (Chapter 4).
2. The altered association of Shp2 with proteins like Src and PZR is what drives the etiology of Noonan and LEOPARD syndromes (Chapter 6).
3. Enhancers and suppressors of Noonan- and LEOPARD syndromes rather than single gain-of-function mutations should be studied to further gain insight into these diseases (Chapters 5, 6 and 8).
4. LRP-1 modulated ERK signaling should be further investigated in light of Noonan and LEOPARD syndromes (Chapter 8).
5. Zebrafish is a versatile model organism to study phosphatases.
6. Mass spectrometry based phosphoproteomics in zebrafish is a useful tool to identify physiologically relevant mechanisms of disease.
7. Enzyme localization is equally important as enzyme activity.
8. Tissue specific regulation of downstream proteins contributes to the diverse outcomes of disease in different tissues.
9. Science communication to lay people should be a compulsory part of the PhD curriculum.
10. Science would benefit from more tenured jobs for post-doc researchers without having to aim for a group leader position

Stellingen van Monica Bonetti behorende bij het proefschrift

Noonan and LEOPARD Syndrome in Zebrafish: Molecular Mechanisms and Cardiac Development

1. Noonan and LEOPARD Shp2 cause hypo- and hyperphosphorylation of Fer and PZR, respectively, compared to WT- Shp2 (Chapter 5 and 6).
2. Downregulation of Fer cooperates with Noonan and LEOPARD-Shp2 to induce developmental defects (Chapter 5).
3. Noonan-like syndrome can be caused by extracellular cues (Chapter 8).
4. Congenital heart defects are the main cause of death for Noonan and LEOPARD patients (Chapter 7).
5. The impairment of the left/right axis determination is frequently associated with congenital heart malformations.
6. Zebrafish is a useful tool to study the function of essential genes.
7. Cell movements during gastrulation are important for correct zebrafish cardiac development.
8. Future investigation of gastrulation mechanisms should be based on the development of sensitive and quantitative techniques to quantitatively characterize defective cell movements.
9. Confocal microscopy, which enables the reconstruction of three-dimensional structures from the obtained images, has improved the study of cellular movements and shape changes as well as morphological studies of a wide spectrum of cells and tissues.
10. In science, the *best* method is the one that is *good enough* to solve an experimental problem.