University of Basel

Departement Biomedizin Basel

OPEN Master Thesis Project

Uncovering the common molecular basis for digit loss in congenital malformations and evolution.

Developmental Genetics
PD Dr. Aimée Zuniga and Prof. Rolf Zeller
Department Biomedicine, University of Basel
Mattenstrasse 28, 4058 Basel
For detailed information - please browse to: https://www.devgenbasel.com

Project

The coordinated development of an embryo is one of the most fascinating processes in biology as gene expression, cellular development and differentiation are integrated at the tissue, organ and whole organism level. Disruption of the underlying molecular and cellular processes invariably cause congenital malformations (disease) or lethality. However, our recent research has provided fascinating insights into the interplay of molecular robustness and plasticity, the latter being a driving force of evolutionary diversification. Digit formation is a fantastic model to study these processes as the majority of us humans have five fingers and toes (=robustness), but this basic bauplan can be changed by (genetic) alterations that (1) cause congenital loss or gain of digits, or (2) evolutionary changes that underlie the adaption of digits and the limb skeleton to fast running, digging, climbing, swimming and flying. We have generated mouse models for congenital digit loss and are currently studying the molecular and cellular that underlie congenital digit reduction. Digit loss also occurred during evolution of even-toed ungulate species (e.g. pigs and cows), whose skeleton is optimized for fast movement on diverse territories. Based on our findings in our mouse models we aim to gain insight into the common molecular and cellular events underlying evolutionary digit loss in pig embryos and developing chicken wings.

Aims

The proposed master project is based on the results of comparative single cell RNA-sequencing and takes advantage of our recent identification of previously unknown limb mesenchymal progenitor (LMP) populations that are changed at early stages in limb buds that form only 4 digits instead of 5. We expect the project to provide fascinating and fundamental insights into the origin of the stem/progenitor cells that give rise to different digits and the mechanism(s) that determine digit numbers in different species. Cellular and molecular alterations from early stages onward will provide insight into how digit numbers are determined and reveal similarities between congenital and evolutionary-relevant digit reduction - i.e. between evolution and disease - an emerging field of high biomedical interest. This project will allow the student to benefit from interactions with several group members.

Approaches and techniques

The ~9 month research project will familiarize the student with a variety of different molecular and cellular techniques including: genetic approaches to mark cell lineages (descendants of progenitors/stem cells) in mouse limb buds; isolation and 3D cultures of LMPs from wild-type and mutant limb buds to comparatively analyse their molecular and cellular differentiation potential. In these cultures, molecular pathways are triggered or inhibited by addition of signal agonists and antagonists respectively. Molecular and cellular changes in limb buds and LMPs in culture will be analysed using state-of-the-art fluorescent RNA in situ hybridisation (HCR) and immunofluorescence for proteins to detect changes at cellular resolution. Relevant changes will be quantitated by RT-qPCR (RNA) and/or Western blotting (protein). In addition, the project requires scientific and project-oriented planning and analysis skills, innovative and critical thinking. Presentation and scientific communication skills in English will be furthered as part of the weekly research seminars, journal clubs and writing of the master thesis.

This project can be started as agreed with the master student.

Interested? Then drop us an email to arrange for an interview and project discussion. We look forward to hear from you!

Contact: Aimée Zuniga: aimee.zuniga@unibas.ch