University of Basel

DBM Basel
Department of Biomedicine

MASTER THESIS PROJECT:

The basis for developmental robustness against disease in a mouse model for Fibrodysplasia Ossificans Progressiva.

Developmental Genetics
Prof. 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

Embryonic development is a marvel of biological complexity as gene expression, cellular development and differentiation are seamlessly integrated across tissue, organ and the organism as a whole. Despite the susceptibility to molecular and cellular disturbances, an intrinsic robustness within embryos often prevails, shielding developmental processes from genetic perturbations. Our research has unveiled fascinating insights into the molecular basis of developmental robustness and we are now applying this knowledge to explore the underlying mechanisms of developmental robustness in congenital diseases, an emerging field of significant biomedical interest. Fibrodysplasia Ossificans Progressiva (FOP) is a rare human condition characterized by abnormal bone formation triggered by the R206H mutation in the ACVR1 receptor which leads to excessive BMP signaling. Intriguingly, the manifestation of FOP occurs postnatally despite embryonic activity of the receptor and the goal of this project is to uncover why embryos seem unaffected by the condition.

Project Aims

The entry point for the proposed master›s project stems from the observation that the BMP antagonists are significantly upregulated in the limb buds of a mouse model for the FOP disease. This suggests that BMP antagonism during embryogenesis may counteract the excessive BMP signaling caused by the ACVR1R206H mutation.

Aim1: By investigating cellular and molecular changes in FOP mutant limb buds from the earliest stages, we aim to identify the compensatory mechanisms that protect the embryo from disease manifestation.

Aim2: The effects of excessive BMP signaling on FOP disease progression in the absence of BMP antagonism will be investigated genetically. Cellular, molecular, and phenotypic alterations will be analysed in embryos. Elucidating the mechanisms that enable embryos to evade or delay the onset of disease symptoms will be relevant for identifying potential therapeutic strategies for FOP.
This project encourages student interaction with several group members.

Methodologies

Over approximately 9 months, the research project will immerse the student in a diverse array of molecular and cellular techniques. These include mouse genetics to investigate gene interplay affecting disease onset, phenotypic studies on cartilage and bone formation and the isolation and 3D culturing of limb mesenchymal progenitors from both wild type and FOP model for comparative analysis of molecular and cellular differentiation. Advanced techniques such as fluorescent RNA in situ hybridization (HCR) and immunofluorescence will enable detailed cellular studies.

This project provides the student with a valuable combination of scientific methodology, analytical thinking, and innovative research skills. Participation in research seminars, journal clubs, and the master thesis writing process will strengthen their ability to effectively communicate scientific findings in English, offering an enriching educational and research experience.
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