USZ Universitäts Spital Zürich

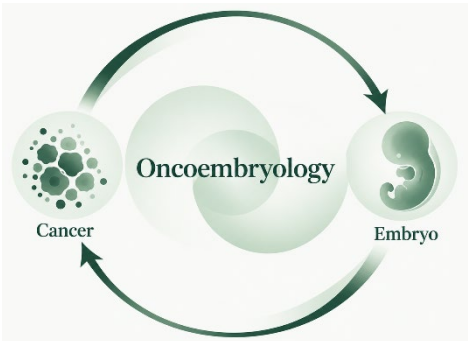
Department of Gastroenterology & Hepatology

Master's thesis project

Dissecting the regulators of oncoembryonic programs in colorectal cancer

Background Cancer cells often reactivate genetic programs that are normally restricted to embryonic development. These "oncoembryonic" programs provide cells with high plasticity and stem-like features, which in cancer contribute to tumor progression, metastasis and therapy resistance. Colorectal cancer (CRC) is among the most prevalent cancer types, in which we have found embryonic transcriptional programs re-emerged and drove aggressive behavior.

By directly comparing embryonic tissues with healthy adult colon and CRC, we identified core oncoembryonic cell states and transcriptional networks that are dormant in adult tissue yet reactivated in tumors. While these programs are now implicated in cancer biology, the regulatory logic that maintains or silences them in human cancer cells remains poorly understood. Understanding their regulation is essential for identifying vulnerabilities that could be exploited therapeutically.



Project aim
The goal of this Master's thesis is to identify and functionally characterize regulators of oncoembryonic programs in CRC using *in vitro* models and, where appropriate, complementary *in vivo* approaches.

Depending on the student's interests, background, and project progress, the project may include:

- Identification of regulators of oncoembryonic gene programs using CRISPR-based perturbation and chemical or pharmacological modulation
- Functional characterization of candidate regulators in human and mouse CRC organoids
- Analysis of cell-state changes using bulk and single-cell transcriptomic approaches
- Investigation of how oncoembryonic programs influence proliferation, differentiation, stress adaptation, and drug response *in vitro*

Techniques and training:
The student will gain hands-on experience with:

- Mammalian cell culture and colorectal cancer organoid models
- Molecular biology techniques, including cloning, qPCR, and protein analysis
- Functional perturbation approaches, including CRISPR/Cas-based and pharmacological strategies
- Transcriptomic data analysis, including bulk RNA-seq and potentially single-cell RNA-seq
- Microscopy and quantitative image analysis
- Depending on project progress and interest, exposure to epigenomic approaches and advanced computational analyses

Your profile:
We are looking for a motivated Master's student with a strong interest in cancer biology. The ideal candidate is curious, reliable, and willing to engage with experimentally challenging and open-ended biological questions. Previous experience with cell culture, molecular biology, organoids, or computational analysis is advantageous but not essential.

Host lab abd supervision: hosted in the lab of Prof. Dr. Michael Scharl & supervised by Dr. Hassan Fazilaty

Project period Projects start date is flexible.
Contact hassan.fazilaty@usz.ch

References

- Fazilaty, H., & Basler, K. Reactivation of embryonic genetic programs in tissue regeneration and disease. Nature Genetics, 2023
- Dalessi, T., et. Al., ... & Fazilaty, H. An oncoembryology approach uncovers SoxC-driven regulation of colon development and cancer. Biorxiv, 2024