Targeted Project / AY 2025 -2026

Epigenetic regulation of cellular plasticity during brain development

Project Reference: TRG-SAN-OB

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BBSRC DTP main strategic theme: Transformative technologies

BBSRC DTP secondary strategic theme: Bioscience for an integrated understanding of health

Project outline:

Cellular plasticity, the ability of cells to change states, commonly underlies development and cancer. This project aims to resolve the epigenetic mechanisms that control cellular plasticity during normal brain development and identify how they are deregulated in brain cancer using state-of-the-art multi-omic profiling technologies. Recent advances in single cell and spatial epigenomic profiling, such as ATAC-seq, CUT&Tag and DbiT-seq, enable the precise mapping of chromatin accessibility and transcription factor-enhancer interactions in a cell type- and spatially-resolved manner. The prospective student would apply these methods in conjunction with deep learning based computational models to infer gene regulatory networks (GRNs) underlying cellular plasticity. First, the student would focus on resolving GRNs that control glial cell differentiation in the prenatal and pediatric human brain, leveraging large-scale datasets that have been generated in the Bayraktar lab. Second, the student would investigate how these differentiation mechanisms are corrupted in brain cancer, focusing on a type of glial-lineage derived tumour called IDH-mutant astrocytomas. These brain tumours develop slowly in adults and can be remarkably captured during their transformation from benign low grade tumours to high grade tumours with increased lethality. We hypothesise that epigenomic alterations of glial differentiation mechanisms play a critical role in this transformation. To effectively characterise the role of epigenetic regulation in astrocytoma transformation, it will be crucial to identify and characterise the activity of key transcriptional regulators that modulate grade transitions and contrast them to normal developmental mechanisms. By dissecting epigenetic regulation and mapping them in the spatial context of tissues, we aim to identify the key molecular drivers and cell extrinsic signals governing glial differentiation and astrocytoma transformation. This work will enrich our mechanistic understanding of cell identity during brain development and contrast these mechanisms to brain cancer. The project's interdisciplinary nature, encompassing bioinformatic and wet-lab techniques, will provide the student with a unique training environment.