Abstract — MET Research Day 2025

Title: DNA methylation-based regulation and neuro-developmental trajectories of central nervous system tumors

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Abstract
Central nervous system (CNS) tumors are a diverse group of malignancies. They can be accurately diagnosed and subclassified by using only genome-wide DNA methylation patterns, and many tumor types are known to be driven via aberrant epigenetic regulation. Cell differentiation plays a crucial role in these tumors, with a lower differentiation state being linked to increased tumor aggressiveness. However, it is unknown why DNA methylation-based classification can precisely pinpoint CNS tumor subclasses and to what extent tumor-associated DNA methylation patterns are linked to differentiation states.
This project leverages publicly available DNA methylation data from 1098 normal samples, representing different brain locations and neuro-developmental stages, as well as 2682 CNS tumors, constituting more than 70 CNS tumor types. We identified a total of 1642 CpG sites exhibiting significant DNA methylation changes throughout steps in the normal neural developmental trajectories as well as 147 transcription factors, whose binding sites are enriched within the identified CpG sites. Preliminary data revealed drastic changes in DNA methylation taking place during the normal neural development, including a gradual decrease of DNA methylation in the astrocytic lineage.
Based on the DNA methylation status of 4942 neural and progenitor cell marker genes, which we clustered into 20 subgroups, we are currently comparing CNS tumors to stages of neural cell differentiation. Next, utilising gene regulatory networks, we aim to identify master regulators within each of the subgroups.
This project will uncover neural cell differentiation trajectories based on DNA methylation and their association with epigenetic oncogenic regulation of CNS tumors.