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 that can be accurately diagnosed and subclassified using genome-wide DNA methylation patterns alone. 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 works so well and to what extent tumor-associated DNA methylation patterns are linked to differentiation states.
This project leverages publicly available DNA methylation data from 2682 CNS tumors as well as 1098 normal samples representing different locations and neuro-developmental stages. The goal is to determine how DNA methylation is altered along the cell differentiation trajectories and how the differentiation-related patterns are represented in different CNS tumor types. We identified a total of 1642 CpG sites exhibiting changes throughout the normal neural development and identified transcription factors, whose binding sites are influenced by these alterations. Preliminary data revealed drastic changes taking place during the development, including a gradual decrease of DNA methylation in the astrocytic lineage.
Based on the DNA methylation dynamics of 4942 neural and progenitor cell marker genes, which were clustered to 20 subgroups, we are currently analyzing CNS tumors in the context of neural cell differentiation. Next, we will identify key transcription factors that are affected by the DNA methylation, to better understand DNA methylation driven regulation in these malignancies.