JOINT SEMINAR

Spatiotemporal Architecture of Brain Tumors

By

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Abstract

Precision medicine in cancer proposes that genomic characterization of tumors can inform personalized targeted therapies. This proposition, however, is complicated by spatial heterogeneity and rapid evolution. Glioblastoma (GBM) constitutes the most common and aggressive primary brain tumor. To better understand how GBM evolves and the role of clonal heterogeneity, the team analyzed multi-sector or longitudinal genomic and transcriptomic data from hundreds of samples. The branching pattern together with estimates of evolutionary rates suggest that the relapse associated clone typically preexisted years before diagnosis. Using bulk and single-cell data, they found that samples from the same tumor mass share genomic and expression signatures, while geographically separated multifocal tumors and/or long-term recurrent tumors are seeded from different clones. Chemical screening of patient-derived glioma cells shows that therapeutic response is associated to genetic similarity, and multifocal tumors enriched with \textit{PIK3CA} mutations have a heterogeneous drug response pattern. Importantly, they show that targeting truncal events is more efficacious in reducing tumor burden. In summary, this work demonstrates that evolutionary inference from integrated genomic analysis in multi-sector biopsies can inform targeted therapeutic interventions for GBM patients.

All are Welcome!