Friday
January 29, 2021
17:00 (CET)

Computational and Quantitative Biology Lecture Series

The seminar will be held on line using TEAMS. Please register at https://bit.ly/39EH9WB
You will receive an invite with the link to the seminar.

Classification and precision therapy of glioblastoma

The overarching theme of our research program is the dissection of the role of proteins and networks (master regulators) that drive phenotypic states in normal and cancer cells of the brain. We use global and unbiased approaches to identify the genetic and transcriptional drivers of an obscure but incredibly important aberrant phenotype in brain tumors, the mesenchymal transformation of human high-grade glioma. This phenotype endows one of the most lethal types of human cancer (the glioblastoma multiforme, GBM) with extremely aggressive features such as the ability to invade the normal brain and form new blood vessels. In recent work we have identified and validated two transcription factors (Stat3 and C/EBP-beta) that, on their own, are necessary and sufficient to maintain the mesenchymal signature of high-grade glioma.

The dissection of transcriptional networks has provided us with invaluable information on the nature of the master regulators that control whole signatures of gene expression. However, cancer is a genetic disease and we recognized that the reconstruction of transcriptional networks should be integrated with the development of systems approaches aimed at identifying novel cancer-driving genetic alterations. The availability of massively parallel sequencing technologies has revolutionized the field of cancer genetics. By analyzing the whole transcriptome of human glioblastoma, we recently discovered that a subgroup of GBM patients is defined by the presence of gene fusions of FGFR and TACC genes in their tumors.

The identification of FGFR-TACC fusions in GBM patients and the elucidation of the mechanistic consequences triggered by the fusion proteins for development of brain tumors have allowed us to translate these findings to preclinical models of the disease and design clinical trials in GBM patients harboring FGFR-TACC fusions. This work provides the first example of an oncogenic and recurrent gene fusion in human GBM and leads our research towards the goal of personalized cancer translation.

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