WWTF Project LS20-034

Decoding cellular senescence in glioblastoma (GlioAge)

Abstract

Glioblastoma is an aggressive type of brain cancer that is prevalent and fatal in the elderly. Patients with glioblastoma are at increased risk of Alzheimer's disease, and recent evidence suggests that senescent glial cells, key mediators of brain aging, contribute to both diseases. There is strong enthusiasm about the potential of senolytic therapies for diseases of old age. However, we currently lack coherent models of how senescent cells drive tumor evolution, or how they respond to therapies. The proposed project aims to dissect senescent cell states in glioblastoma and to evaluate their impact on tumor fitness and neuronal loss. We hypothesize that senescent cell states in glioblastoma recapitulate important transcriptional programs of non-tumor glial cells, including their ability to promote neuronal degeneration. Newly established single-cell multi-omics technology provides a unique opportunity to test this hypothesis directly in patient samples. We will investigate single-cell epigenomes and transcriptomes to uncover the cellular plasticity of senescent phenotypes and to infer the underlying gene regulatory networks, which we will validate by CRISPR single-cell sequencing. Collectively, these experiments will provide fundamental insights into the role of senescence in the progression of glioblastoma and its contribution to cognitive decline, while also advancing a promising new therapeutic approach for this lethal cancer.

Scientific disciplines:
301904 - Cancer research (40%) | 301402 - Neurobiology (30%) | 106014 - Genomics (30%)

Keywords:
Glioblastoma, Senescence, Neurodegeneration, Ageing, Single-cell, Multi-omics

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Status: Ongoing (01.10.2021 - 30.09.2024) 36 months

Funding volume: EUR 898,970

Further links about the involved persons and regarding the project you can find at
https://archiv.wwtf.at/programmes/life_sciences/LS20-034