

## Oligodendroglioma Grant

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*Studying the step-wise transformation of neural stem cells into oligodendroglial cancer stem cells*

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### Abstract

The recent discovery of cancer stem cells in human glioblastoma, medulloblastoma and oligodendroglioma has sparked the pursuit of novel therapeutic approaches to more successfully overcome tumor recurrence. The "cancer stem cell hypothesis" claims that pathological adult stem cells, the cancer stem cells, give rise to a heterogeneous tumor and maintain it by aberrant differentiation and proliferation. The origin of cancer stem cells, however, has not been established yet. We recently isolated cancer stem cells (CSC) from a transgenic mouse model of oligodendroglial tumorigenesis as assessed by their multipotent and self-renewing capacities and their ability to form tumors in xenografts. Most importantly, we discovered that the neuronal stem cell population in transgenic mice already showed differentiation and proliferation abnormalities months before the actual tumor occurrence and we therefore referred to them as premalignant stem cells (aka PSC), supporting the hypothesis that CSC are derived from normal stem cells that undergo multiple and subsequent aberrations. We intend to identify and characterize the first changes in NSC that lead to their defective behavior and turn them into PSC, and test the hypothesis that CSC are derived from PSC