Cell-based therapy using miR-302-367 expressing cells represses glioblastoma development

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Glioblastomas are incurable primary brain tumors that affect patients of all ages. The aggressiveness of this cancer has been attributed in part to the persistence of treatment-resistant glioblastoma stem-like cells (GSC). We have demonstrated that microRNA cluster miR-302-367 has the potential to force GSC exit from stemness, promoting loss of stemness properties and tumorigenicity and revealing a great therapeutic interest. In our study we attempt to develop a cell-based therapy for miR-302-367 continuous delivery by taking advantage of the capability of glioma cells to secrete exosomes that enclose small RNA molecules. We engineered primary glioma cells to stably express the miR-302-367. Remarkably, these cells altered, in a paracrine manner, the expression of stemness markers, the proliferation and the tumorigenicity of neighboring glioblastoma cells. Further characterization of the secretome derived from miR-302-367 expressing cells showed that a large amount of miR-302-367 was enclosed in exosomes, which were internalized by the neighboring glioblastoma cells. This miR-302-367 cell-to-cell transfer resulted in the inhibition of its targets such as CXCR4/SDF1, SHH, cyclin D, cyclin A and E2F1. Orthotopic xenograft of miR-302-367-expressing cells together with glioblastoma stem-like cells efficiently altered initiation and tumor development in mice brain.

Biography

Thierry Virolle is a Research Director (permanent position) at Institut National de la Santé et de la Recherche Médicale (INSERM), Head of the Team Cancer Stem Cell Plasticity and Functional intra-tumor Heterogeneity at the Institute of Biologie Valrose (IBV). He is Co-Founder of the French National Sud Cancer Stem Cell Network, SUNRISE dedicated to the study of cancer stem cell. He is Doctor of Science (PhD) at Nice Sophia Antipolis University (2000), his researches focus on the regulation of the plasticity of glioblastoma cancer stem cells and its contribution in the genesis of functionally divergent tumor territories.

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