

RalA in biology and therapy of MPNST in correlation to cancer stem cells

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Abstract For the last 20 years, cellular biologists have been focusing on the role of Ras signaling pathway in neurofibromatosis 1(NF1) and its lethal derivation, malignant peripheral nerve sheath tumors (MPNST). While our team has worked on the influence of Ras pathway on responsiveness of MPNST cells to therapy, we introduced a novel cell signaling pathway down-stream of Ras, i.e. *Ral pathway*, as an important regulator of the biological features of MPNST with potentials for being targeted for treatment of this malignancy. We have also showed that RalA is overactivated in the cancer stem cell (CSC) fraction of MPNST tumors establishing this pathway to harbor potentials for targeting MPNST CSCs. In summary our preliminary data shed light on following facts:

- 1- RalA signaling pathway is overactivated in differentiated MPNST cells and human tissues.
- 2- RalA overactivation is a characteristic of MPNST cancer stem cells.
- 3- RalA inhibition hinders the malignant phenotype of MPNST cells.
- 4- Disruption of RalA signaling results in loss of viability and invasion of MPNST cells.

In this presentation, we further evaluate the mechanism of RalA overactivation and in-vivo potentials of its inhibition as a therapeutic strategy for MPNST.

Approval Confirm

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Summary