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O-ONC-44 - Functional role of PML and SOX9 in Glioblastoma Multiforme

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Resumen

Introduction and objectives: The patient poor survival in glioblastoma multiforme (GBM) is consequence of the presence of a population of therapy resistant glioblastoma stem cells. Recent molecular studies indicate that some proteins such as SOX9 or PML are enriched in this population and its activation an important event in their maintenance. Our group has shown that PML maintains glioblastoma stem cells through the expression of SOX9. Our objective is to determine impact of PML silencing in glioblastoma stem cell tumorigenic potential and address the effect of SOX9 expression restoration on this event.

Material and methods: We compared overall survival of mice in which control glioblastoma stem cells, PML downregulated, SOX9 restored in PML downregulated and SOX9 overexpressed cells were injected. Lentivirally transduced cells were injected using a stereotactic technique in an intracranial model using NOD-SCID mice. 1×10^5 was the number of stem cells injected in each group and 5 mice per condition were injected.

Results: The overall survival of the mice injected with control cells was 116 days. Decreased survival was observed in the SOX9 upregulation group. The overall survival of this group was 35 days. Survival was elongated when PML was downregulated, with an overall lifespan of 175 days. This extended survival was reduced when SOX9 expression was restored (133 days).

Conclusions: Understanding the mechanism by which PML and SOX9 participates in glioblastoma stem cell activity will facilitate development of therapeutic strategies. Their inhibition might be a novel therapeutic approach in GBM.

Key words: *Gliobastoma multiforme. Stem cells. SOX9. PML. Stereotactic injection.*