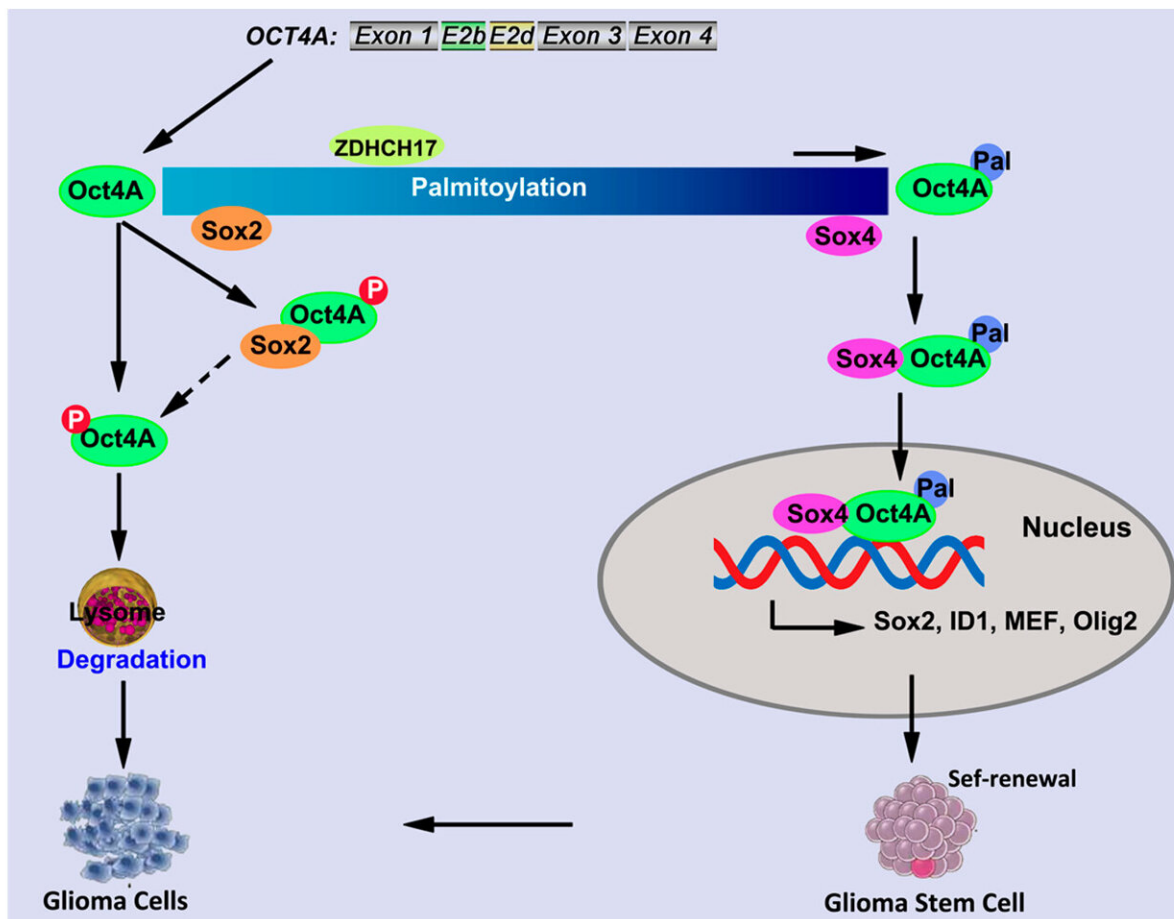


Key factor found in tumorigenicity of glioma stem cells

June 23 2022, by Zhang Nannan



Schematic illustration of the mechanism of Oct4A palmitoylation promotes tumorigenicity and stemness in human glioblastoma cells. Credit: Chen Xueran

Researchers led by Prof. Fang Zhiyou and Prof. Chen Xueran from the Hefei Institutes of Physical Science (HFIPS) of the Chinese Academy of Sciences (CAS), have found, for the first time, that Oct4A is the key factor in maintaining the tumorigenic activity of glioblastoma stem cells (GSCs). Palmitoylation mediated by ZDHHC17 is essential to prevent lysosomal degradation of Oct4A to maintain its protein stability and facilitate the formation of complexes between Sox4 and Oct4A.

Relevant results were published in *Neuro-Oncology*.

Glioblastoma (GBM) is the most common primary intracranial tumor in adults with the highest degree of malignancy. GSCs may be an important cause of the occurrence, resistance to radiotherapy and chemotherapy, and recurrence of GBM. Therefore, targeted therapy of GSCs may be a new strategy for the treatment of malignant [glioma](#).

Oct4, also known as Pou5f1, is a member of the POU transcription factor family. This gene has multiple different transcription start sites, which can form different mRNA subtypes and be translated into different protein subtypes, participating in the regulation of physiological development. Although it has been detected in advanced gliomas, its [biological function](#) and transcriptional machinery maintained by the stemness of Oct4 protein-mediated GSCs, has not been fully determined.

In this study, the researchers investigated the role of the transcription factor Oct4/POU5F1 in glioma, and discovered the novel role of palmitoylation in the function of the Oct4 splicing variant Oct4A in GBM.

As a result, three Oct4 variants are expressed in different types of brain tumors, and Oct4A is particularly important for maintaining tumorigenicity in GSCs. DNA hypomethylation up-regulated the

expression of OCT4 gene, which may be one of the main reasons for the up-regulation of stem cell-related gene expression in re-current gliomas.

Moreover, Oct4A palmitoylation, mediated by ZDHHC17, was found to be critical for preserving Oct4A from lysosome degradation, thereby maintaining protein levels in glioma cells in vitro. The researchers also reported that palmitoylated Oct4A interacted with Sox4. Competitive Oct4A palmitoylation inhibitors were tested as potential therapeutic compounds, and negatively affected the self-renewal ability and tumorigenicity of GSCs.

"These findings indicate that Oct4A plays a role in the tumorigenic activity of glioblastoma," said Chen Xueran, who conducted the research, "while Oct4A palmitoylation may be a candidate therapeutic target."

More information: Xueran Chen et al, Oct4A palmitoylation modulates tumorigenicity and stemness in human glioblastoma cells, *Neuro-Oncology* (2022). [DOI: 10.1093/neuonc/noac157](https://doi.org/10.1093/neuonc/noac157)

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