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RESEARCH COMMUNICATION

Inhibitor of differentiation 4 drives brain tumor-initiating cell genesis through cyclin E and notch signaling

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Cellular origins and genetic factors governing the genesis and maintenance of glioblastomas (GBM) are not well understood. Here, we report a pathogenetic role of the developmental regulator Id4 (inhibitor of differentiation 4) in GBM. In primary murine Ink4a/Arf^{-/-} astrocytes, and human glioma cells, we provide evidence that enforced Id4 can drive malignant transformation by stimulating increased cyclin E to produce a hyperproliferative profile and by increased Jagged1 expression with Notch1 activation to drive astrocytes into a neural stem-like cell state. Thus, Id4 plays an integral role in the transformation of astrocytes via its combined actions on two-key cell cycle and differentiation regulatory molecules.

[*Keywords:* Id4; Ink4a/Arf^{-/-} astrocyte; notch signaling; cyclin E; neural stem-like cells; glioblastoma]

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