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Abstracts

STEM-19. EGFR EXPRESSION CONFERS STEM CELL-LIKE PROPERTIES TO HUMAN NEURAL PROGENITORS AND GLIOMAS

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Activation of the epidermal growth factor receptor (EGFR) pathway is strongly implicated in the proliferation and migration of neural/glial progenitors and gliomas. EGFR is silenced after development but becomes aberrantly overexpressed in many low-grade and most high-grade gliomas, often in the absence of gene-amplification/activating mutations. The phenotype and functional characteristics of EGFR-expressing human brain cells are not well defined, as is the relationship of EGFR expression to gliomagenesis. We recently reported on the selective retention of EGFR expression in adult human subventricular zone (SVZ) glia. Notably, we also showed a strikingly similar epigenetic landscape at the wild-type EGFR promoter between germinal matrix/SVZ and EGFR-expressing gliomas. Here we undertook a detailed characterization of EGFR-expressing cells in the developing and adult human brain using warm postmortem material, and in human glioblastomas after fresh resection, hypothesizing that EGFR-positive cells harbor stem cell-like properties in vitro, which may implicate them in gliomagenesis. To better characterize the phenotype of human EGFR-expressing brain cells in vivo, we performed detailed confocal immunofluorescence analysis with markers for glial/neuronal lineage differentiation and proliferation. We found that during neural development, many EGFR-positive cells co-express markers of oligodendrocyte lineage, such as Olig2, similarly to most glioblastomas. We then analyzed the behavior of these cells in vitro. We used our novel, human-based protocol to isolate cells directly from fresh human samples, taking advantage of the inherent binding affinity of EGFR for its natural ligand, EGF. Intriguingly, we found that EGFR-positive, but not EGFR-negative, cells isolated from germinal matrix and from glioblastomas display stem-cell characteristics in culture, including self-renewal and trilineage differentiation. Our findings suggest that EGFR expression confers stem-cell-like properties to human progenitors and glioma cells, hint that its maintenance may play a role in gliomagenesis, and provide a novel isolation platform of functionally defined EGFR+ glioma populations for further molecular analyses.