

EFFECTS OF EPIDERMAL GROWTH FACTOR ON ADULT NEURAL STEM CELLS

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- I. Lindberg OR, Brederlau A, Jansson A, Nannmark U, Cooper-Kuhn C, Kuhn HG.
Characterization of epidermal growth factor-induced dysplasia in the adult rat subventricular zone. *Stem Cells and Development*. 2012 May 20;21(8):1356-66
- II. Lindberg OR, Brederlau A, Kuhn HG.
Epidermal growth factor-treatment of the adult brain subventricular zone leads to focal microglia accumulation and angiogenesis. *In manuscript*
- III. Lindberg OR*, Persson Å*, Brederlau A, Shabro A, Kuhn HG
EGF-Induced Expansion of Migratory Cells in the Rostral Migratory Stream. *PLoS One*. 2012;7(9):e46380.
- IV. Lindberg OR, Rosinski M, Kuhn HG.
Effects of Epidermal Growth Factor on Neural Stem Cells In Juvenile and Adult Rats After Postnatal Irradiation. *In manuscript*

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ABSTRACT

In the adult brain neural stem cells are present in two discrete regions; the hippocampus and the subventricular zone (SVZ). The environment surrounding the stem and progenitor cells, the neurogenic niche, is integral for proper stem cell development and proliferation. Manipulation of the neurogenic niche provides possibilities in regenerative therapy and modeling of diseases. Epidermal growth factor (EGF) is a growth factor involved in a plethora of developmental and homeostatic processes in the body. In the brain, EGF appears to play a role inducing lineage progression of stem cells to proliferative progenitor cells. Treatment with EGF leads to increased proliferation and expansion of the SVZ and focal hyperproliferative polyps are formed. However, neuroblasts development and neurogenesis are negatively affected.

The current thesis demonstrates how the EGF-induced polyps go through discrete stages of development. Polyps persistently recruit blood vessels and the angiogenic process is preceded by microglia accumulation and apoptosis.

The response of the SVZ to EGF is context dependent. Infusion into the juvenile brain yields a response distinct from the adult brain. Furthermore, prior postnatal whole brain irradiation alters certain aspects of EGF stimulation.

The rostral migratory stream (RMS) is the migratory path used by neuroblasts to reach the olfactory bulb where the cells become mature neurons. Upon EGF treatment the RMS responds in a fashion similar to the SVZ, with reduced numbers of neuroblasts and expansion of immature glial cells. Newly formed cells in the EGF-treated RMS express a unique combination of proteins and display migratory properties.

In summary, this thesis determines new pleiotropic effects of EGF on the SVZ and RMS neurogenic niches, depending on age, length of treatment, and prior radiation therapy. The local microenvironment of the EGF induced-polyps, promoting dysplasia, microglia accumulation, and angiogenesis, can provide important insight into future therapies and diseases modeling of stem cell-related diseases.

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