Neurogenesis after Brain Ischemia

Introduction
- There are two neurogenic regions in the normal adult mammalian brain under physiological conditions: the Subventricular Zone (SVZ) of the lateral ventricle, and the Subgranular Zone (SGZ) of the hippocampus.
- Both regions maintain a population of neural stem cells (NSCs) and neuronal progenitors (NPCs).
- Brain ischemia alters the normal pattern of adult neurogenesis to stimulate cell proliferation within the SVZ and SGZ as well as migration of newly born, immature neurons to areas of damage.

Objective
- A better understanding of endogenous neurogenesis in the SVZ and SGZ, both in the intact and injured brain, in order to develop useful therapies for brain repair after ischemic injury or neurodegeneration.

Methodology
- Different sources of information have been used, such as PubMed (papers and reviews), scientific books and lectures offered by experts.
- A final selection of 32 out of 50 papers was done.
- Selection criteria was based on the journal impact, the date of publication and the relation with the main topic of the review.

Neurogenesis in the Subventricular Zone
- In the SVZ there are three main type of cells: type-A (neuroblasts), type-B (astrocyte-like cells) and type-C (transient amplifying cells).
- Neuroblasts migrate in chain towards the olfactory bulb (OB) eneased by type-B cells undergoing a tangential migration in the rostral migratory stream (RMS).
- Once in the OB, they mature and differentiate into granule and periglomerular interneurons.
- The RMS pathway is the single largest area for cell proliferation in the adult human brain discovered to date.

Stroke-induced neurogenesis in the Subventricular Zone
- Stroke increases cell proliferation and reduces migration from the SVZ to the OB. It also redirects some neuroblasts to migrate in chains in close association with astrocytes toward the ischemic area.

Neurogenesis in the Subgranular Zone
- The primary progenitors of the SGZ are radial glia-like cells that give rise to transient-amplifying progenitors.
- The progeny disperse and migrate a short distance into the dentate granule cell (DGC) layer where they mainly differentiate into mature granule neurons. A small number of these cells also differentiate into astrocytes or radial glia-like cells.
- Neurogenesis in this system remains local and decreases with age due to a disturbed survival of newborn cells.

Stroke-induced neurogenesis in the Subgranular Zone
- Ischemic insult leads to an increased proliferation of stem cells in the SGZ.
- After a stroke, neuroblasts migrate and integrate into the DGC layer following a time course of neuronal maturation similar to that in normal conditions.
- Most hippocampal progenitor cells give rise to DGC neurons, but some subpopulations migrate into the dentate hilus and become astrocytes.

Conclusions
- Persistence of NSCs in the adult healthy brain raise the possibility of using endogenous or transplantable NSCs and NPCs as regenerative therapies to replace neurons lost after ischemic insults.

References
- Curtis MA, Low VF, Faull RL. Dev Neurobiol 2012;72(7):990-1005
- Dhina K. Cell Mol Life Sci 2011 May;58(9):1545-1565
- AL et al., 2006
- AL et al., 2003 and Vescovi AL et al., 2006
- Vescovi AL et al., 2003 and Faull RL.