What is adult neurogenesis → generation of new neurons

**Multipotent** Stem Cells

[Diagram showing stem cells differentiating into neural cells, cardiac muscle, blood cells, and other cell types.]

Source: http://www.stemcellresearchfoundation.org  Fred Gage, Repair Yourself
New neural stem cells in rodent and human brain

Physiological situation
Adult neurogenesis
Pathological situation

Ischemia, Huntington, Alzheimer
- Stimulation of the adult neurogenesis
- Production and migration newborn neurons in the injured brain area

Neurodevelopmental mechanisms / neurodegenerative mechanisms
- Proteins involved in neurodegenerative disorders
  ⇋ protein involved in developmental or neuronal processes
  \(\alpha\)-Synuclein, Huntingtin, Presenilin..

Situation in Prion diseases???
- PrP function => unclear, but associated with neurogenesis
Maintains function of the brain and/or propagation of the disease in the brain.

**Objective of research project**
- Status of the adult neurogenesis
- Role of the adult neural stem cells
- Therapeutic strategies

**Adult neurogenesis during the course of infection**

- **Animal models**
  - prion infection of mice
  - Kinetics brain collection

- **Analysis**
  - Immunochemistry
  - Proliferation
  - Differentiation, migration
  - Cell death
  - Prions
  - Prion accumulation
  - In situ: Prions
  - In vitro: Isolation and culture of stem cells, Proliferation, Differentiation, Cell survival, Prion protein

- **Spatio-temporal windows of adult neurogenesis fluctuations**
  - i. no modification
  - ii. Neurogenesis is blocked
  - iii. Neurogenesis is stimulated
In situ analysis: comparison between the accumulation of prions and the localization of adult neural stem cells

- Immunohistochemistry

In situ

Prion accumulation

Neural stem cells

Cell culture analysis: are stem cells modified by the disease

- Proliferation of stem cells
- Differentiation

Culture of stem cells

Stem cells
Nestin

astrocytes
GFAP

Neurons
Tuj1
Therapeutic strategies based on the involvement of adult neurogenesis

- **i. No modification**
- **ii. Adult neurogenesis is stimulated, and then blocked**
- **iii. Adult neurogenesis is stimulated and plays a pathologic role**

- ✓ Understand the mechanism of stimulation / blockade
- ✓ Find ways to stimulate / block neurogenesis
- ✓ Find ways to cure stem cells and/or use them to deliver anti-prion molecules

*Use of therapeutic Lentivirus:* to express Dominant negative Prion, to express growth factor to stimulated neurogenesis

> Use of Stem cell grafted to replace deficient stem cells, to deliver molecules

Adapted from Vescovi et al. *Nature Reviews* 6, 425–436