

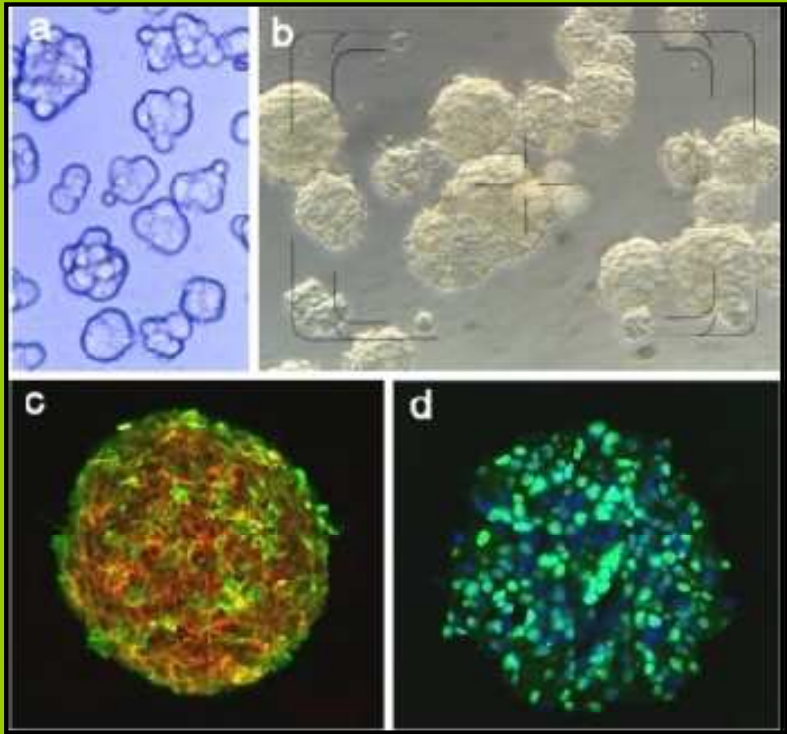
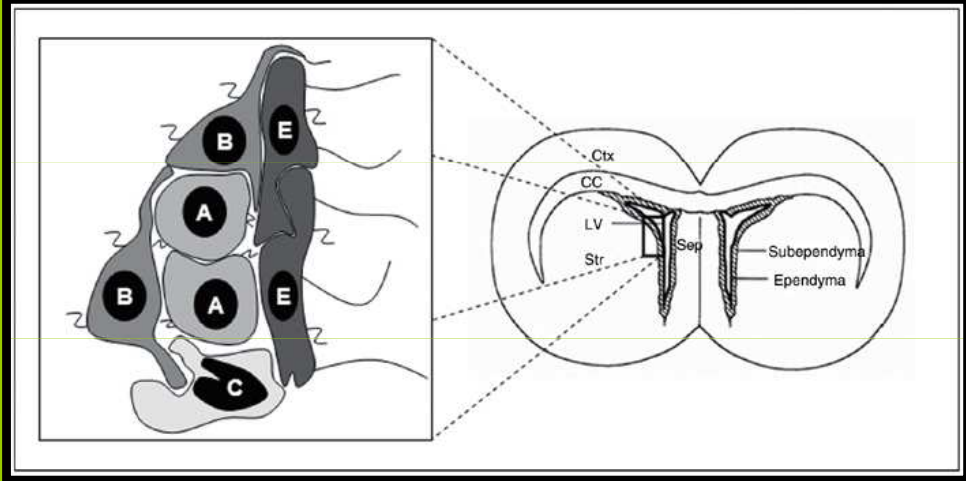
# Non-cell-autonomous action of STAT3 in maintenance of neural precursor cells in the mouse neocortex

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# Neurogeneze



Shh; Delta/Notch -> Hes  
Sox1, 2, 3; Emx2;  
Zic1; Pax6

radial  
glia\*  
*embryo*

**B**  
(NSC)

**E**  
(ependym)

*in vitro = neurosphere*  
EGF / FGF2 (*in vitro*)

**C**  
(TA)

glia  
prekursor

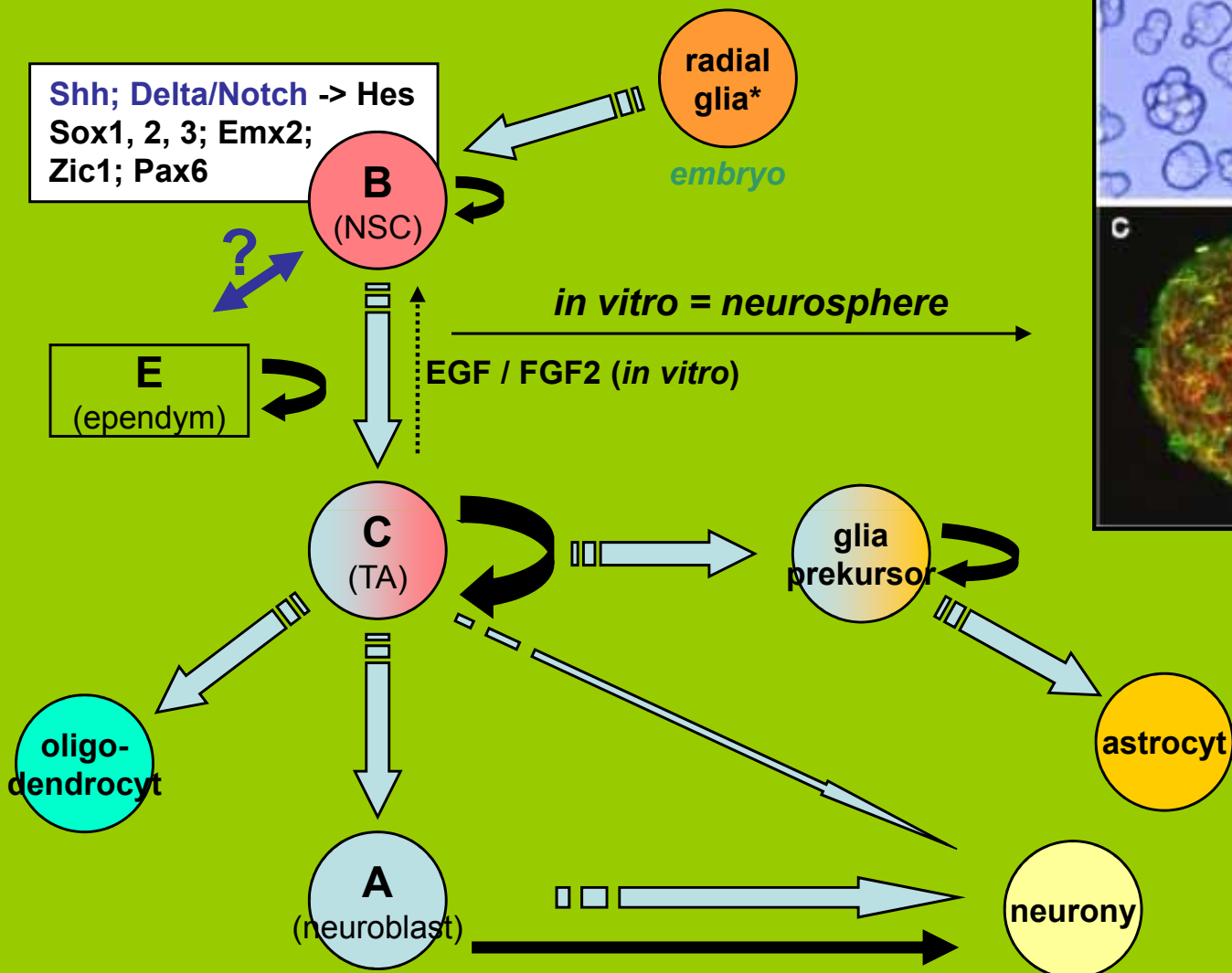
oligo-  
dendrocyt

astrocyt

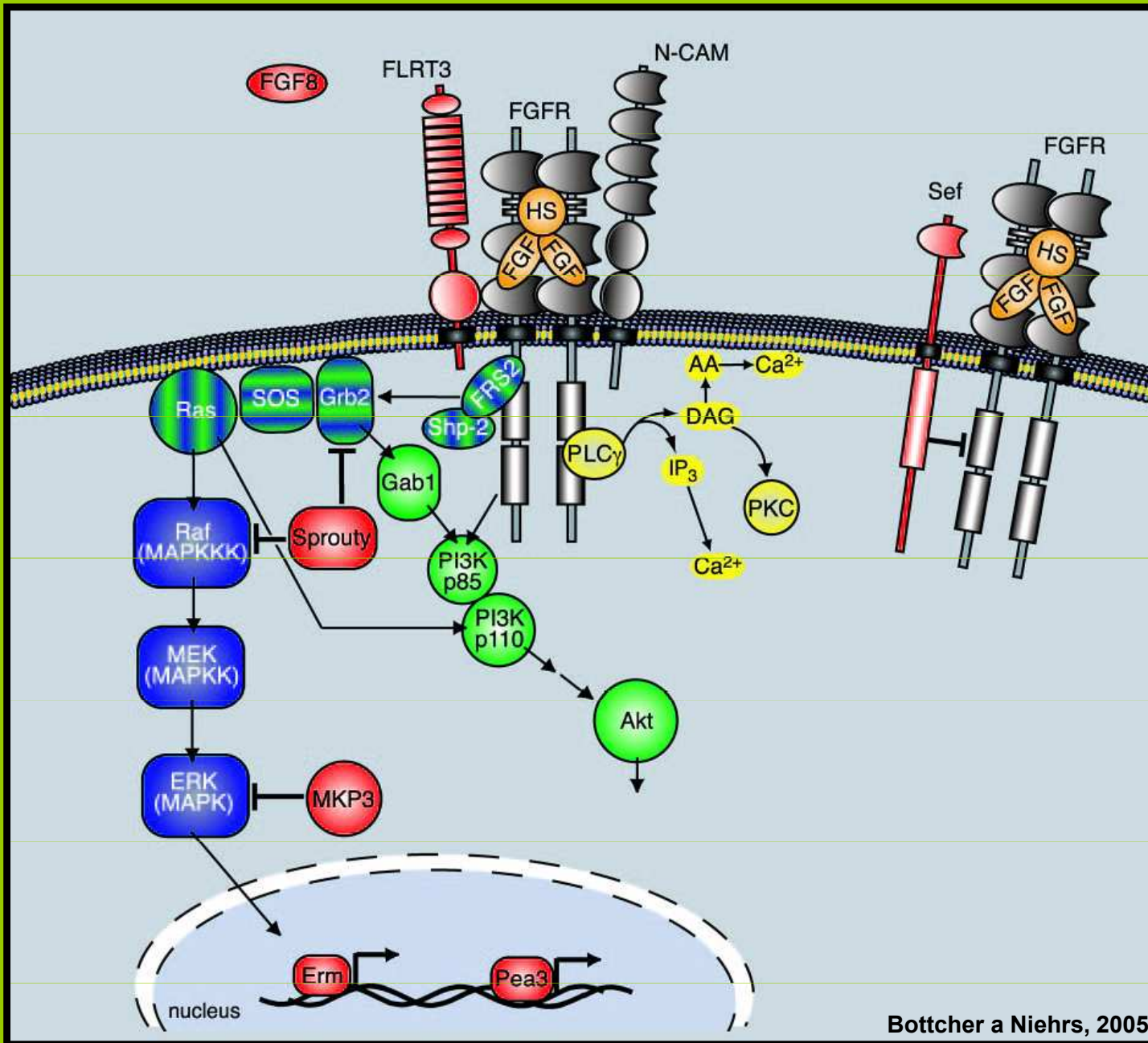
**A**  
(neuroblast)

neurony

\*radiální glie – embryo  
a časně postnatálně

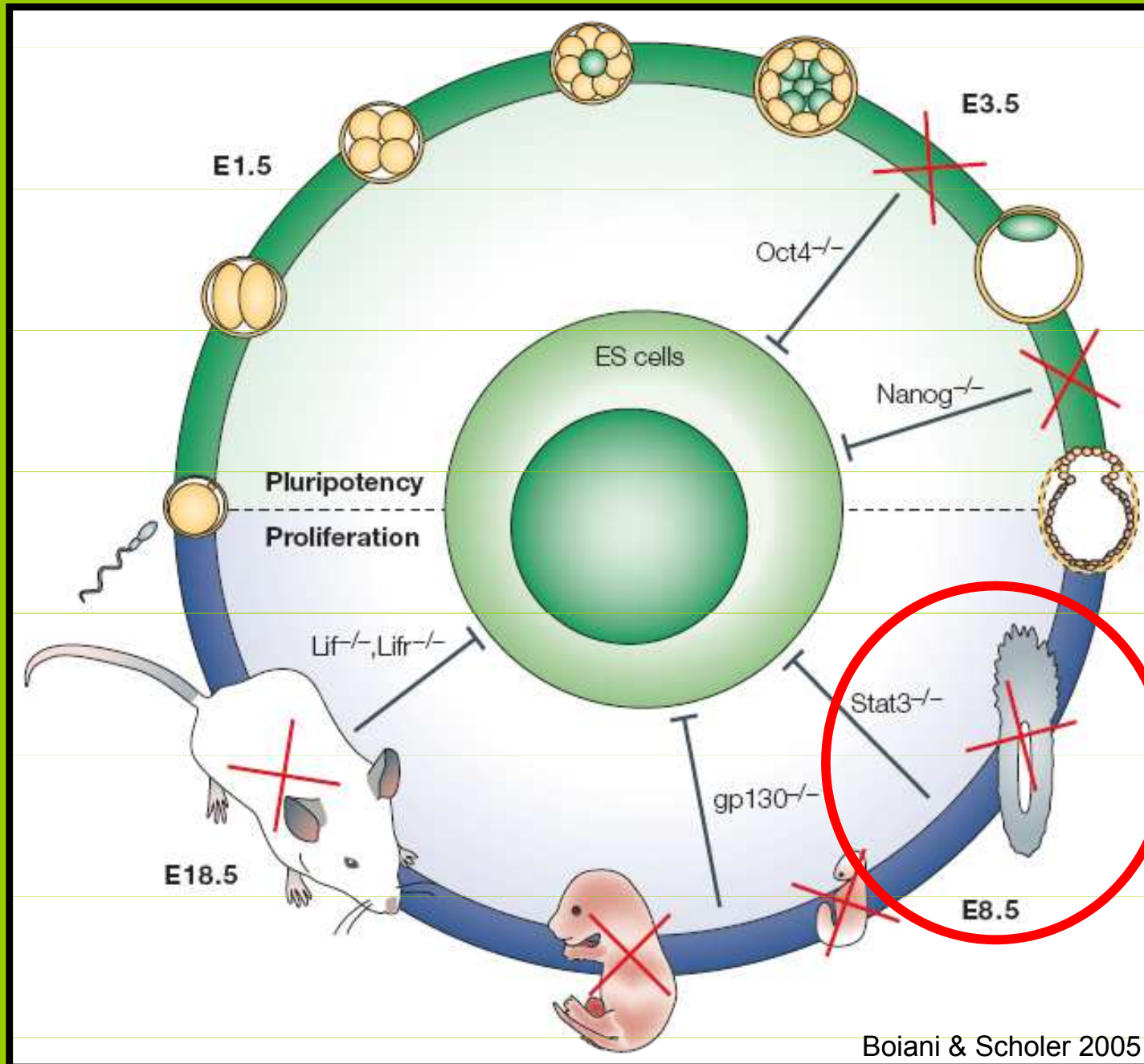


# Signální dráha FGFs (Fibroblastové růstové faktory)



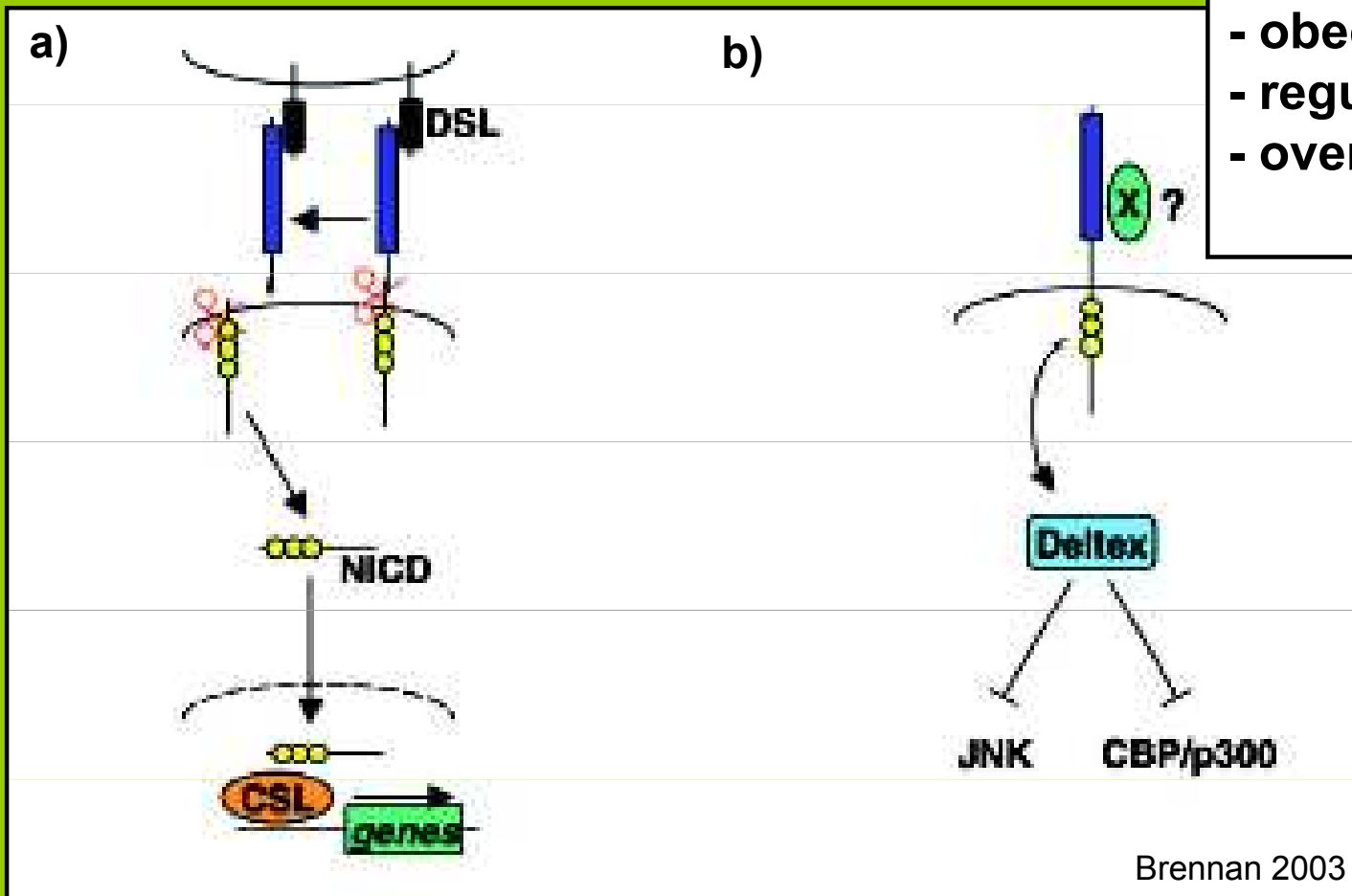






Boiani & Scholer 2005

## Signální dráha Notch



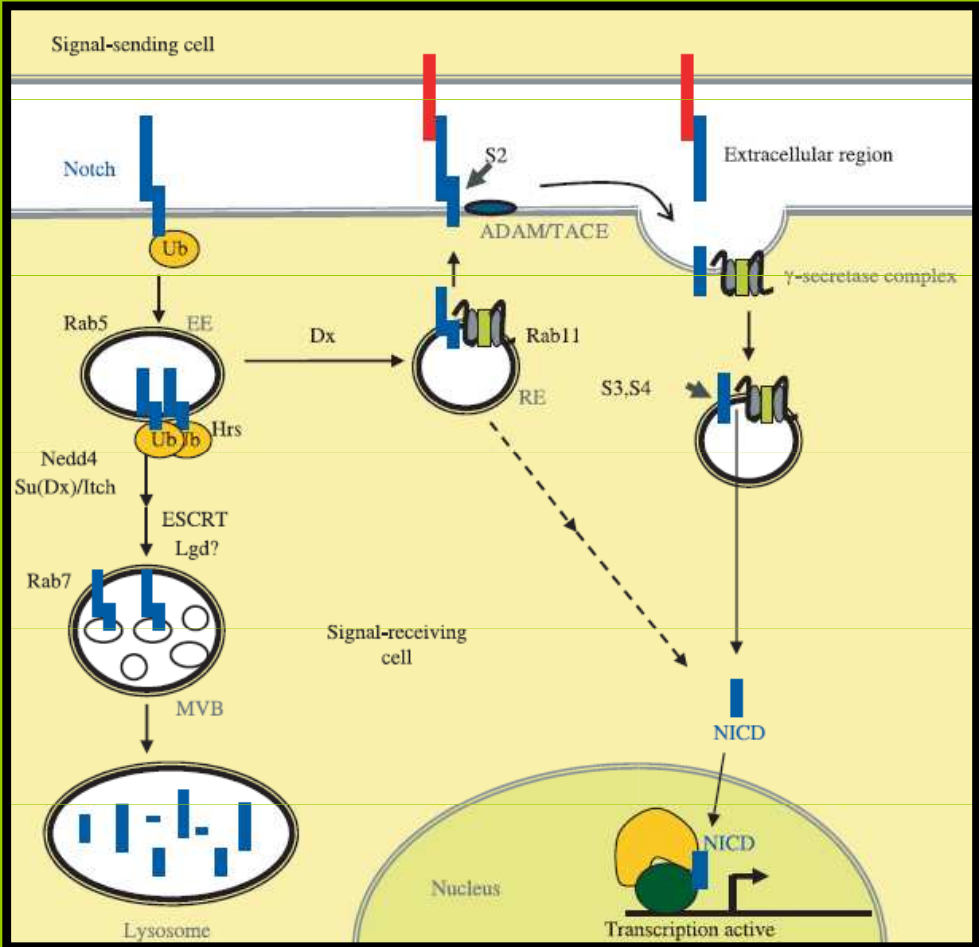
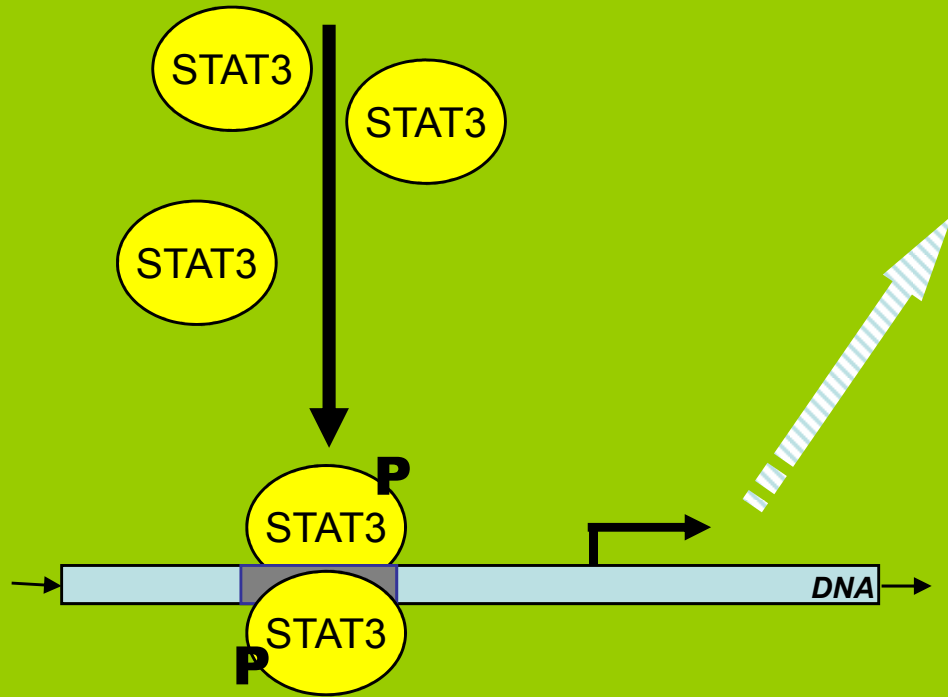
- obecně regulace diferenciace
- regulace NSC
- overexprese u nádorů

- a) klasická dráha signální transdukce Notch, po navázání ligandu (DSL rodina = Delta, Serrate, Lag-2; Jagged) dojde k odštěpení extracelulární části receptoru a následně i intracelulární (NICD – Notch intracellular domain), ta translokuje do jádra a v dimeru s CSL (= CBF1 – Cp binding factor 1) aktivuje transkripci.
- b) dráha snad aktivovaná dosud neznámým faktorem, kdy dochází k aktivaci proteinu Deltax, který pak inhibuje JNK a CBP/p300 aktivitu.

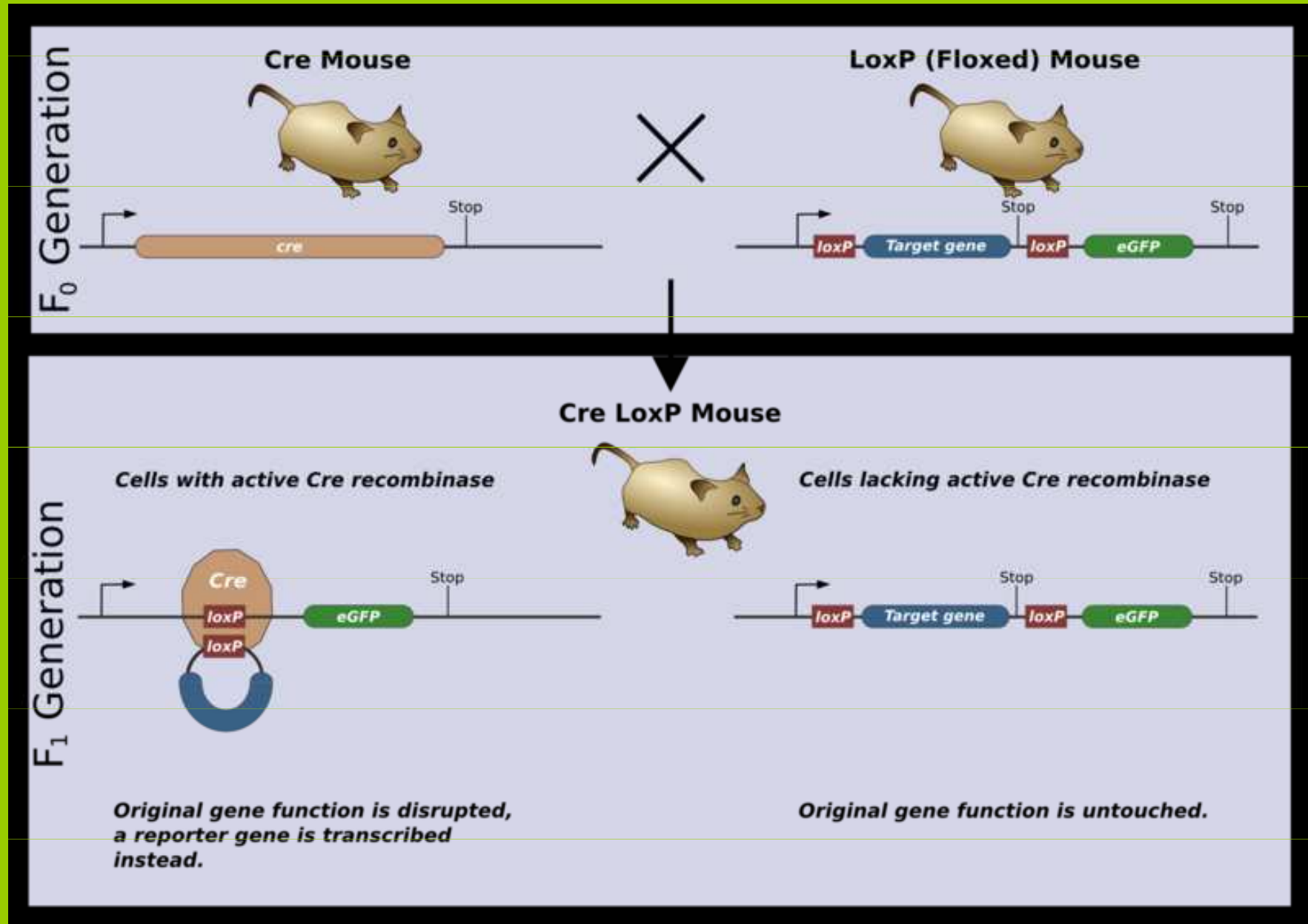
# STAT3 x NOTCH

## AKTIVACE

(LIF/LIFR/gp130->JAK2->)

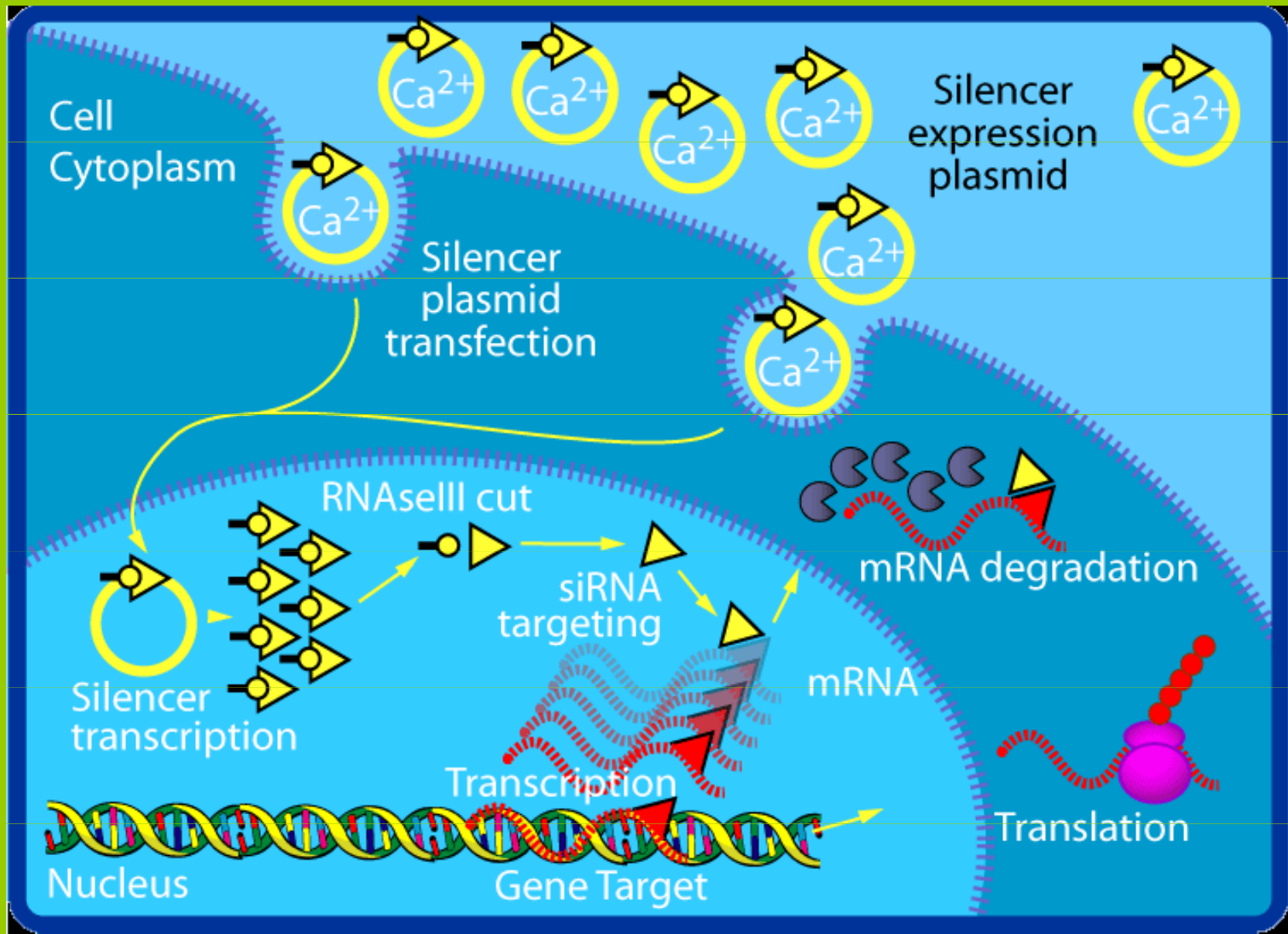


# Kondiciovaní mutanti – Cre / LoxP system



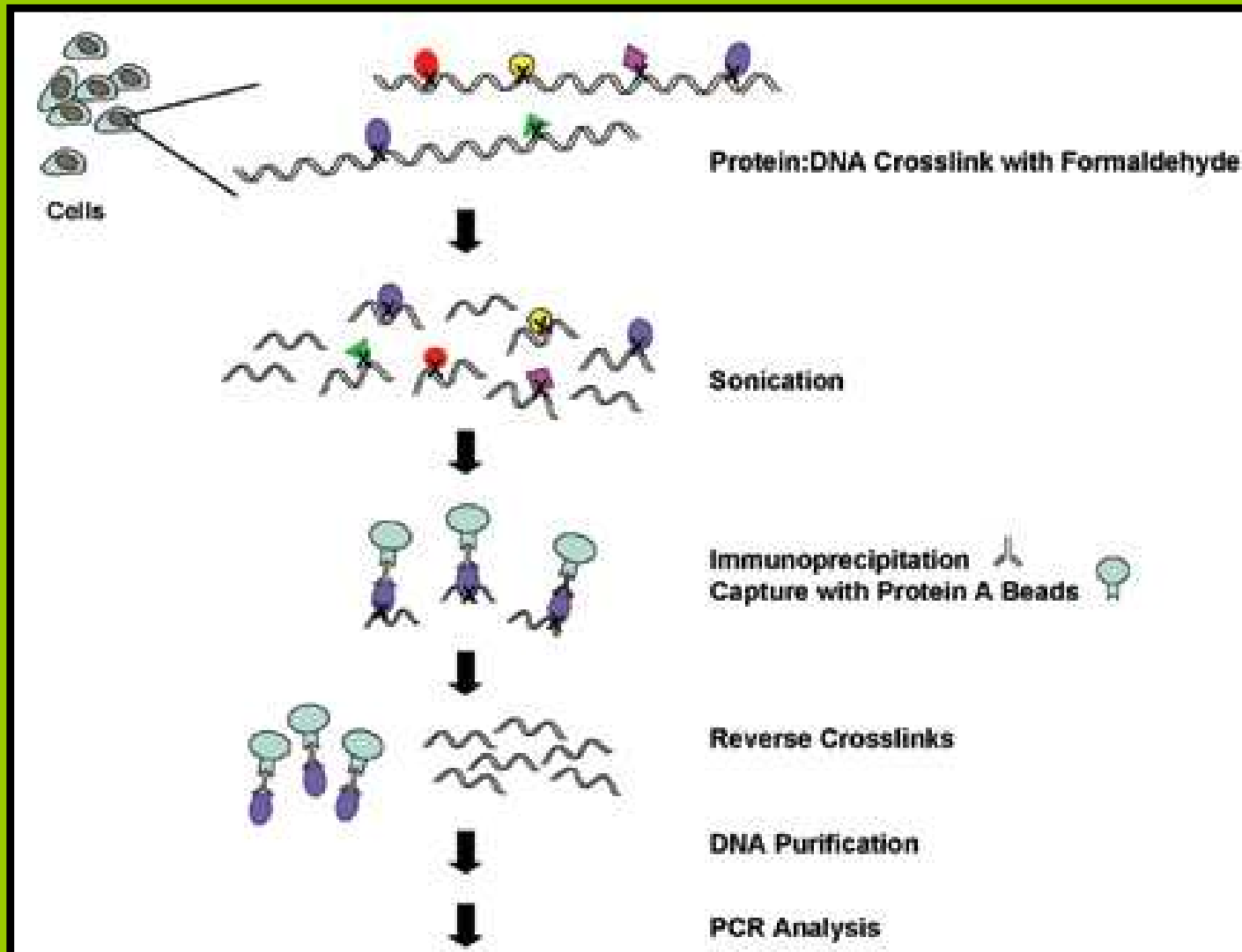


# siRNA technologie



# Imunoprecipitace chromatinu

Chip – chromatin immunoprecipitation

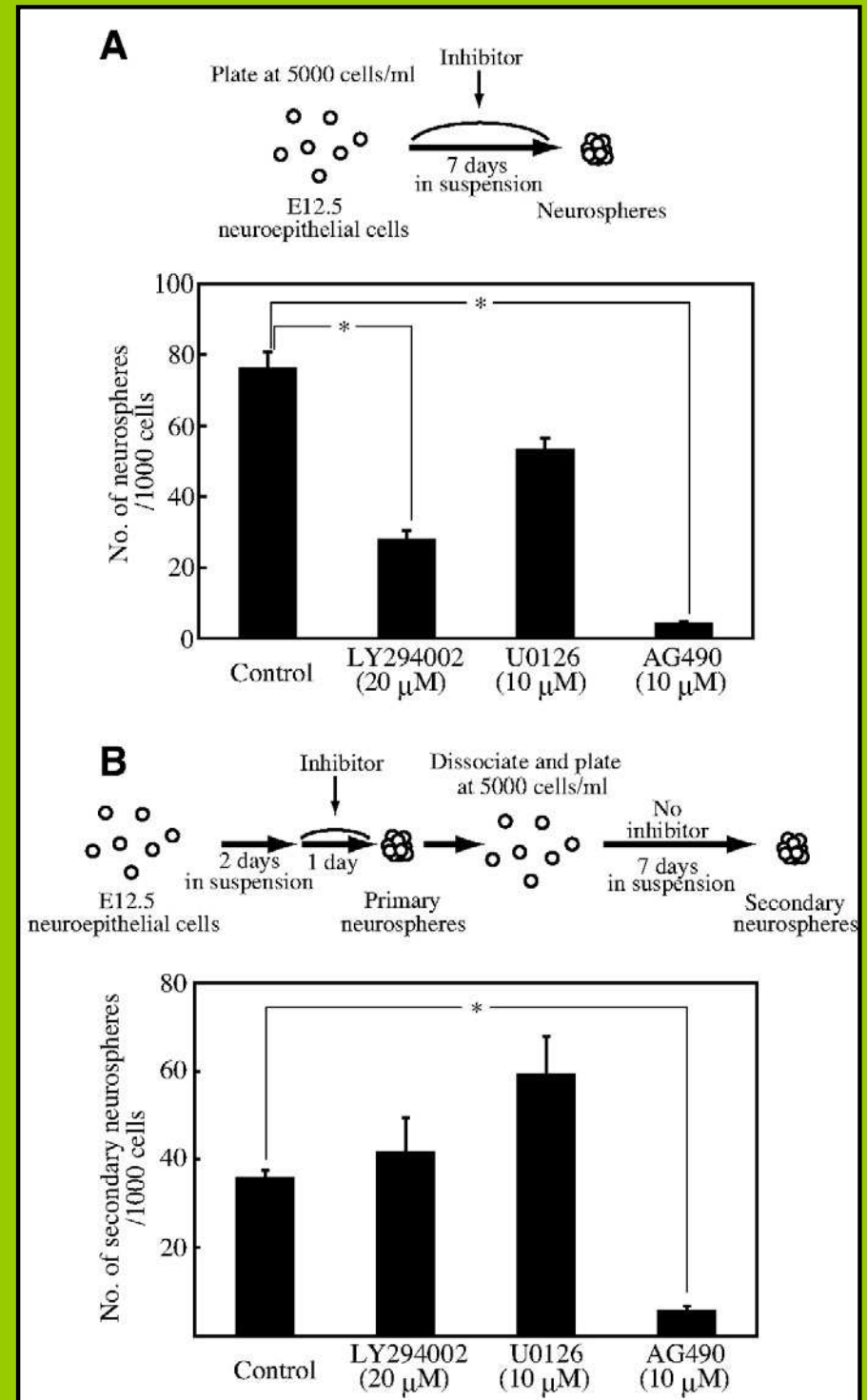


*Hypotéza:*

*FGF2 udržuje neurální kmenové buňky*

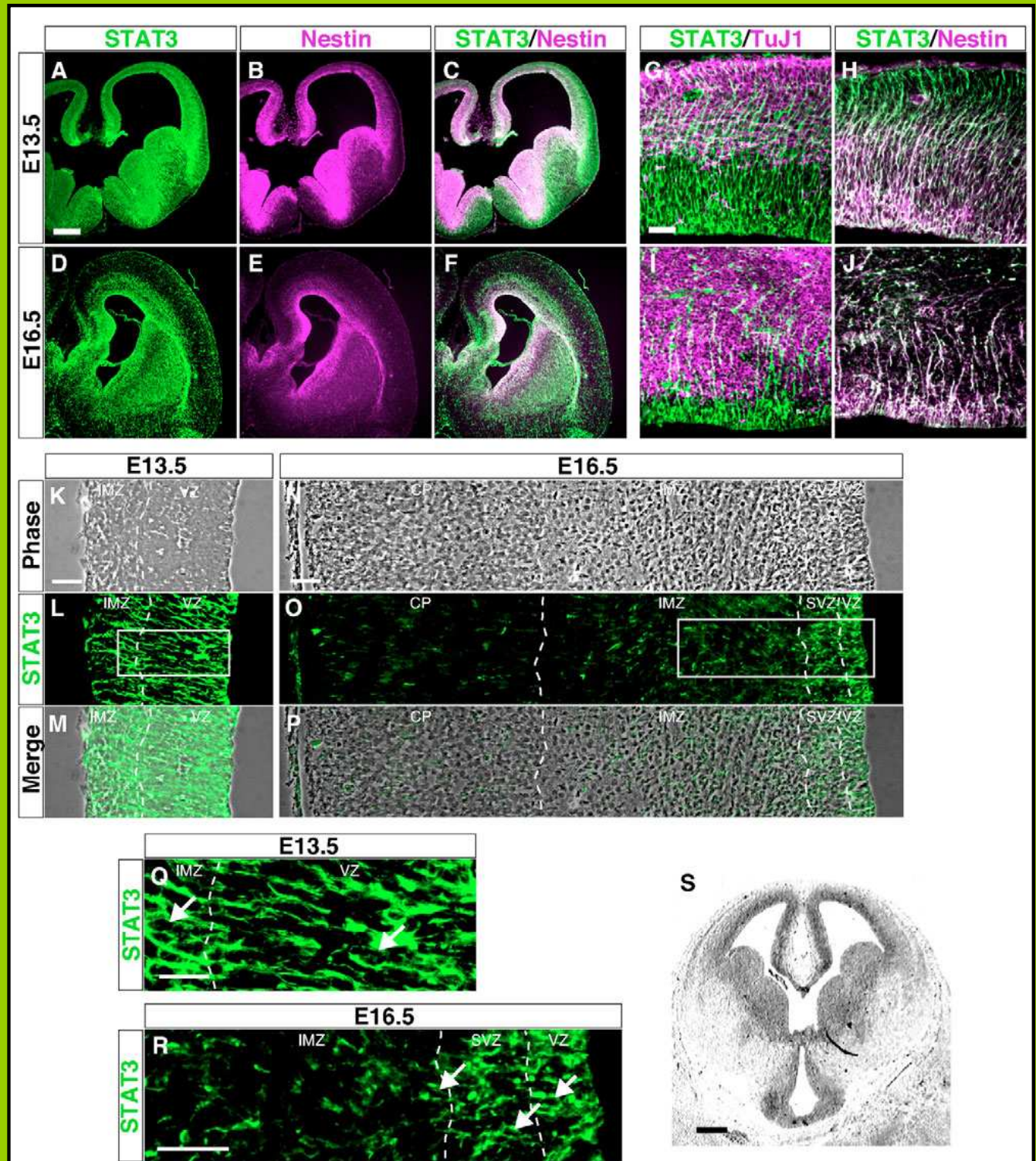
- **která z aktivovaných signálních drah je za to odpovědná???**
- **je působení této dráhy přímé (autonomní) nebo nepřímé (neautonomní)**

**Fig. 1.**  
**Inhibition of FGF2-dependent NPC**  
**maintenance by an inhibitor of JAK2**





**Fig. 2.**  
**Expression of STAT3**  
**in the embryonic**  
**mouse brain**



**Fig. 3.**  
**Requirement of STAT3 for maintenance**  
**of FGF2-sensitive NPC**

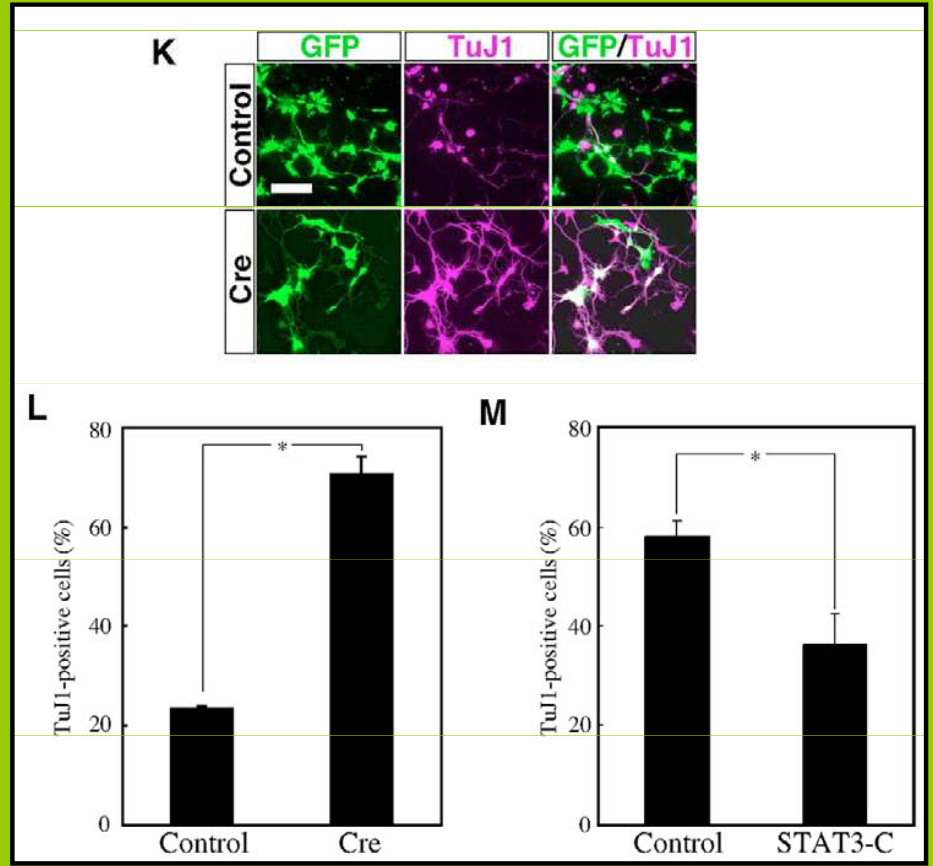
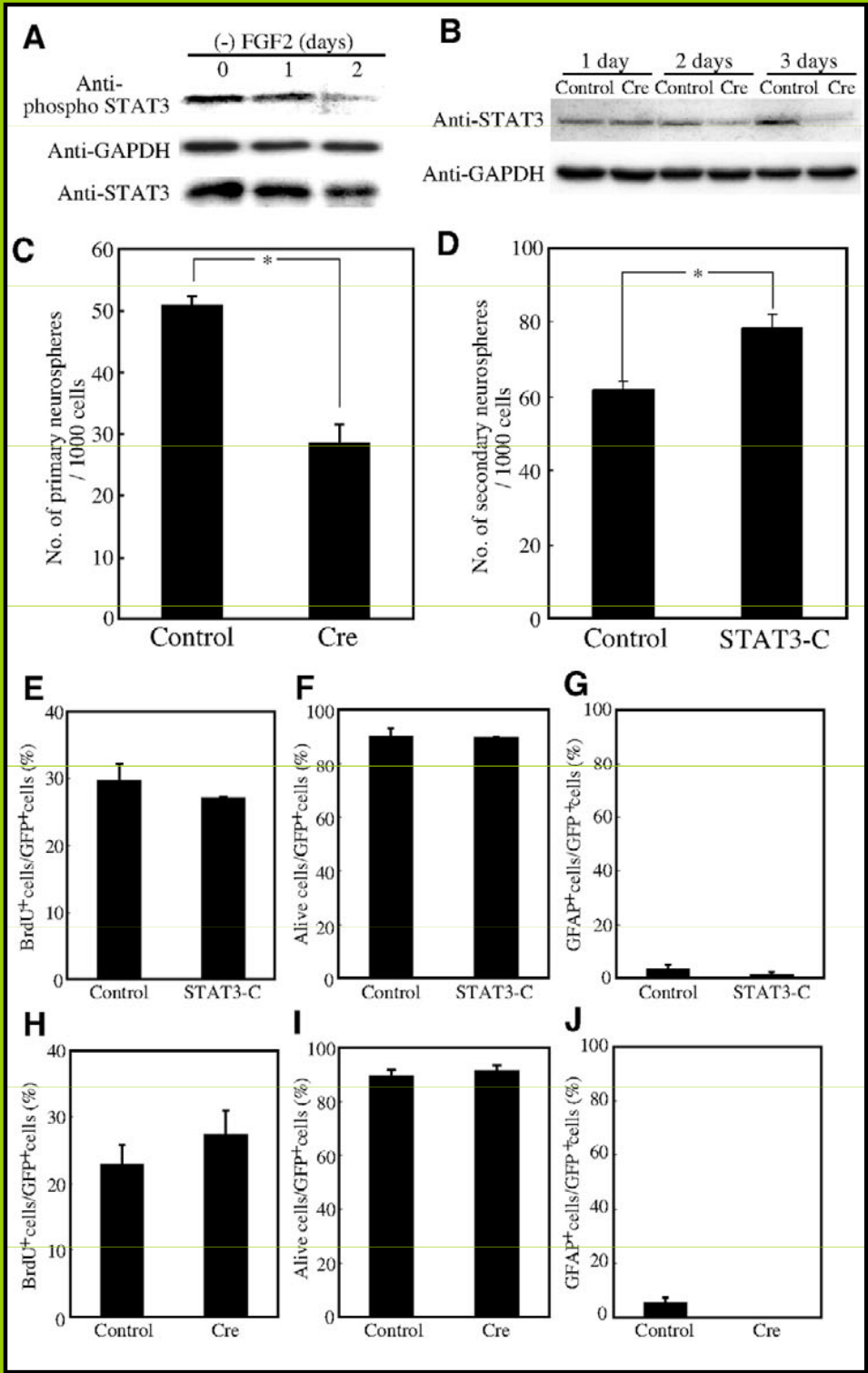
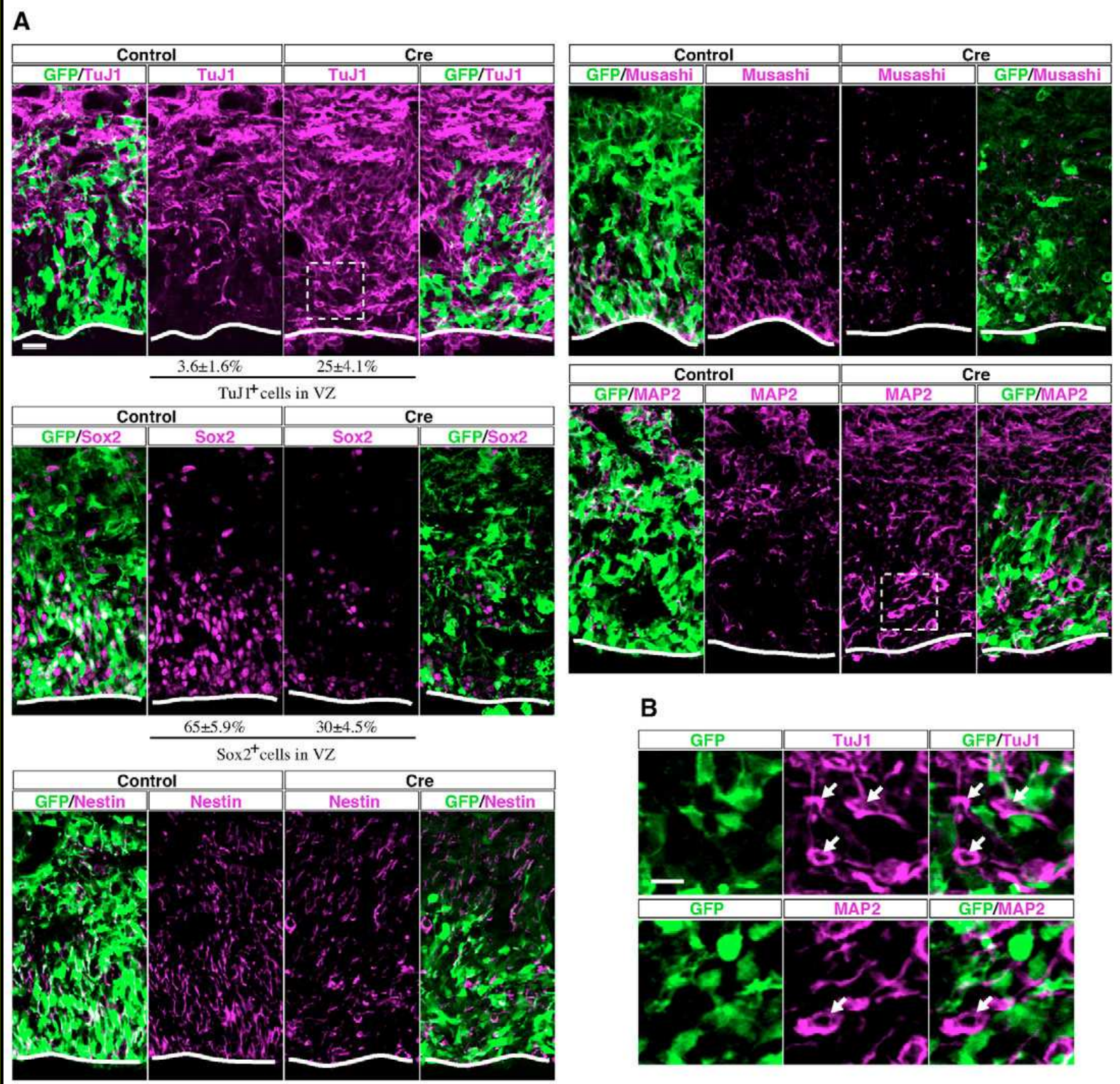
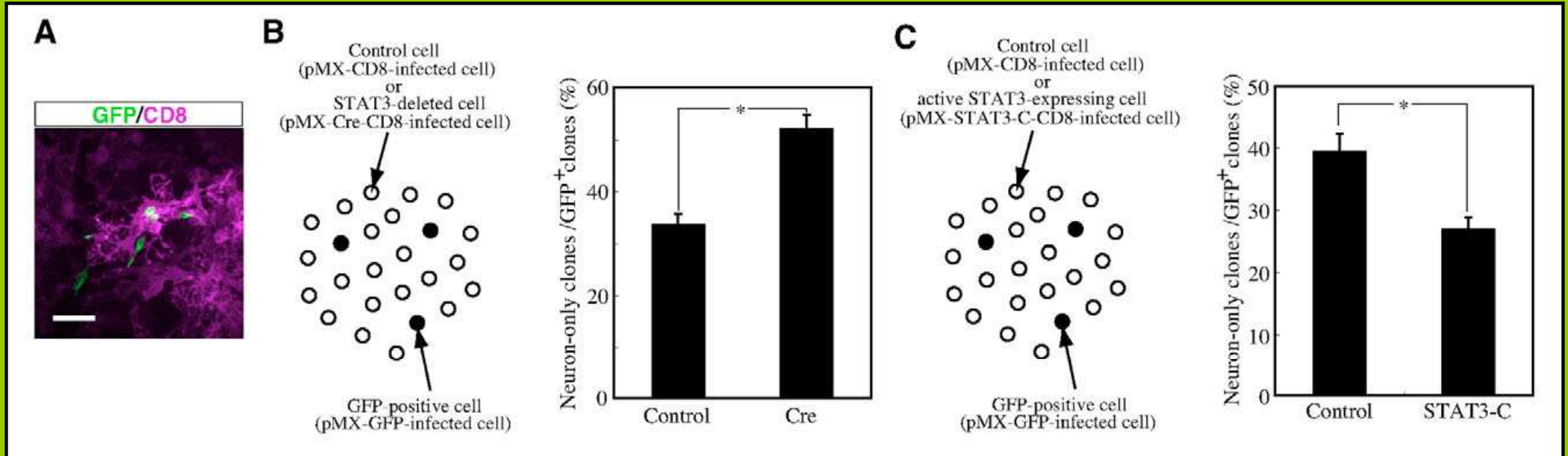




Fig. 4

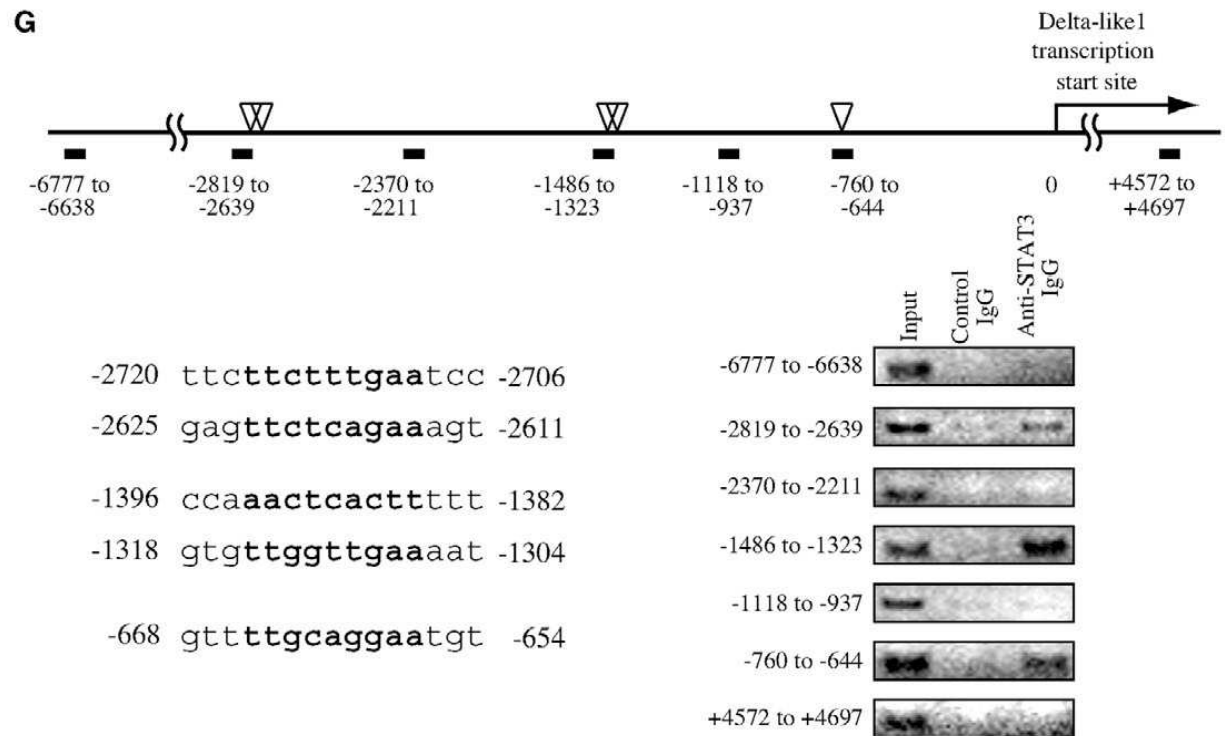
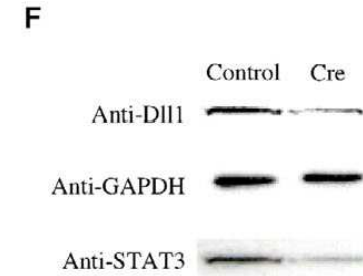
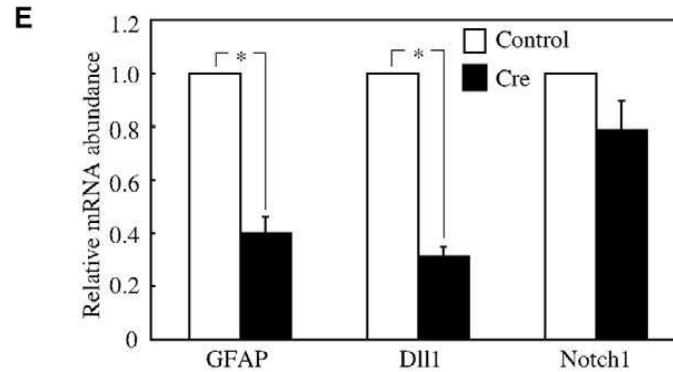
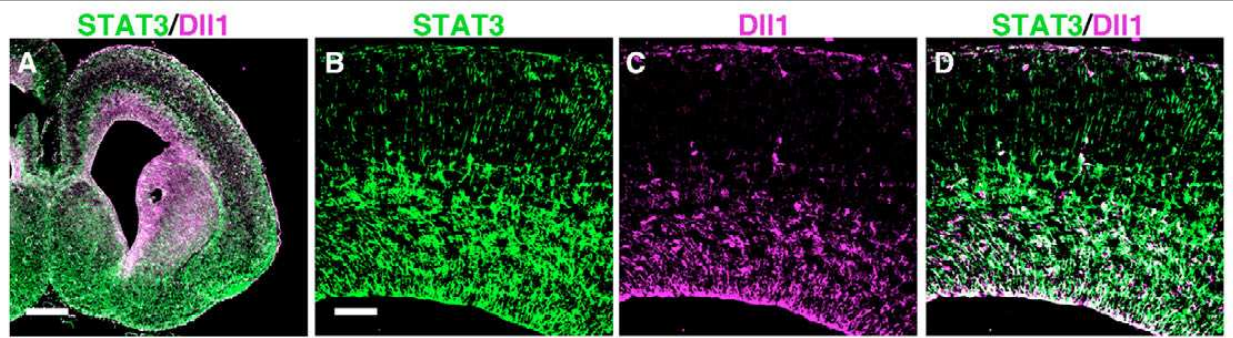


**Fig. 5. Inhibition of neurogenesis by STAT3 in a non-cell-autonomous manner**





**Fig. 6**  
**Regulation of DLL1**  
**expression by STAT3**



**Fig. 7. Requirement of Delta-Notch signaling for NPC maintenance by STAT3**

