Primate adult cortical cell autotransplantation, where do these cells come from?

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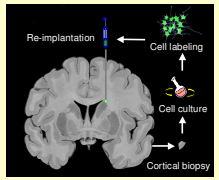
NEUROSCIENCE ATLANTA 2006

Session 719.10
Board C8

INTRODUCTION

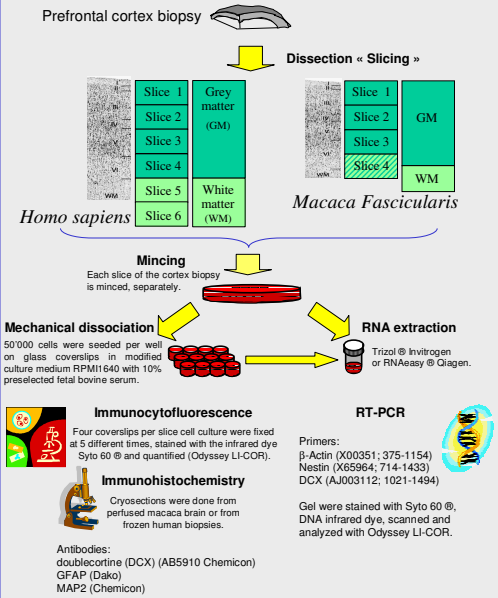
Restoring function of the central nervous system is a challenging task since, unlike most of the organs, the mature brain and spinal cord have a limited ability for self-repair. We have recently demonstrated that adult cortical cell autograft represent an attractive restoration alternative to bypass the caveats of fetal grafting(1). However, until now, the origin of the nestin positive cells obtained in culture from the cortical biopsies was not identified.



autologous cell transplantation.

We studied the expression of doublecortine, migrant neuroblast marker, in adult brain and in our adult cortical cell cultures.

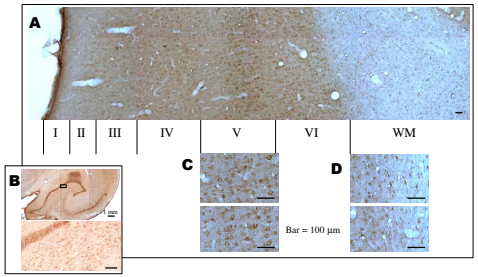
METHODS



Expression of Doublecortine in primate cortex:

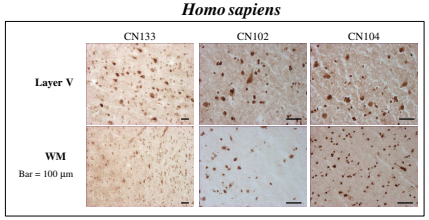
Immunohistochemistry revealed the expression of DCX in cortical structure in non-human and human primate brain:

Macaca fascicularis



As in the subgranular neurogenesis zone in the dentate gyrus (**B**), DCX-positive cells are present in Layer V of grey matter (**A, C**), they have a great nucleus and long processes. DCX-positive cells are also present in the white matter just near grey matter (**A, D**).

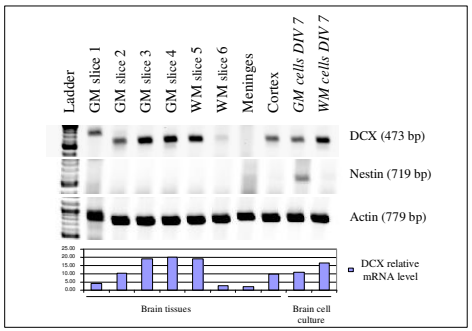
Homo sapiens



In human brain tissues, DCX-positive cells are also present in Layer V of GM and in the WM.

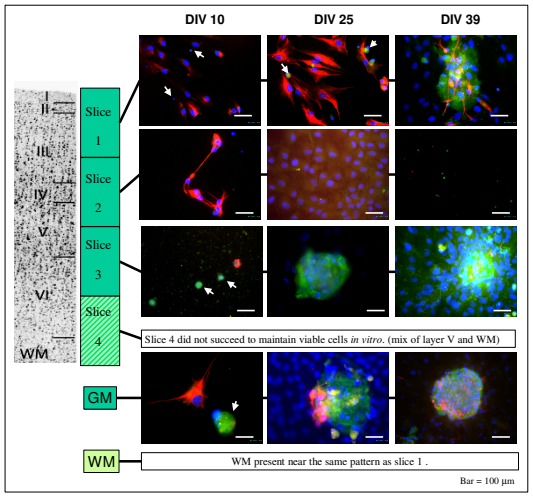
Note that DCX-positive cells are greater in GM that in WM

RT-PCR done for β-Actin, Nestin and DCX confirmed that DCX mRNA is expressed in the adult primate cortex but not nestin and DCX is expressed in the first cells obtained *in vitro* (DIV7).

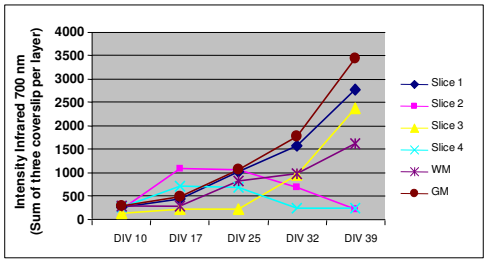


Cell culture from slices of *Macaca fascicularis* cortex:

Immunocytofluorescence revealed the presence of DCX-positive cells (white arrow) since the beginning of the culture. (slice 1, slice 3, GM and WM).
Note that DCX-positive cells from GM fraction and slice 3 are larger than slice 1 and WM ones.

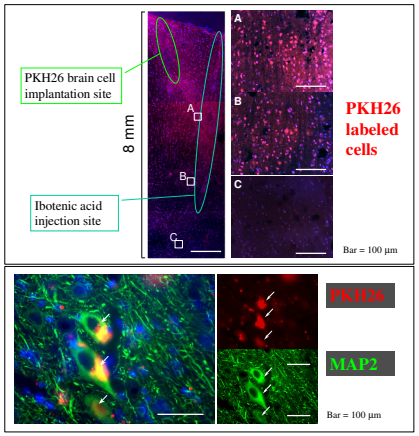


Syto60 ® cell quantification and immunocytofluorescence observation show that only cultures from slices 1 and 3 with DCX-positive cells survive overtime such as GM and WM fraction ones.



Autotransplantation of GM cells

For autotransplantation, grey matter cells were cultured in suspension under slow agitation. After labeling with viable fluorescent dye PKH26 (Sigma), frontal GM cortical cells were re-planted in ibotenic acid lesion in donor motor cortex.



Three months after reimplantation, PKH26 labeled cells (red) are detectable in the lesioned area. Immunohistofluorescence revealed that PKH26 labeled cells (red) express the neuronal marker MAP2.

SUMMARY

- DCX is expressed into the layer V of the primate cortex such as in zones of neurogenesis.
- Only slice culture with DCX-positive cells survive overtime.
- After re-implantation, adult grey matter cortical cells survive overtime, migrate surrounding the lesioned area and express the neuronal marker MAP2.

Hypothesis:

These DCX-positive cells could be at the origin of the adult cortical cells that were shown like being able to be used for the autotransplantation strategies in neurosurgery application.

References:

1 - Brunet et al., 2002, *Laboratory Investigation* 82 : 809-812.
2 - Brunet et al., 2003, *Cryobiology* 47:2 : 179-183.
3 - Brunet et al., 2005, *Experimental Neurology* 196(1) : 195-198.

Supported by
FNRS (3100AO-103924 to JB, JFB & ER),
Fondation LEENAARDS, ZWAHLEN Funds

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