

A microscopic image showing several myelinated axons. The axons are arranged in a bundle, with some showing clear, multi-layered myelin sheaths. The central part of the image is overlaid with text. The background is dark, making the lighter-colored axons and myelin stand out.

Myelination Defects and Recovery in Mouse
Models of Myelin Deficiency:
Histopathological Analysis and Assessment by a
Noninvasive *in vivo* Imaging

Research group

Biopathology of Myelin & *in Vivo* Imaging

- Said Ghandour, PhD, CNRS
- Jérôme Steibel, PhD, ULP
- Laura-Adela Harsan, PhD
- Jérôme de Seze MD, PhD, ULP
- Rémy Sapin, PhD ULP
- Arnaud Agin, PhD, ULP
- Blandine Guignard IE-ULP
- Chan Dao Lam TCN-ULP
- Frédéric Blanc, MD, PhD student
- Irina Petkova PhD student

Approaches:

-Animal models for myelin diseases

- transgenic mouse models (CNS, PNS)
- genetic mutant mice (jimmy mouse)
- chemical intoxication induced demyelination in adult mice

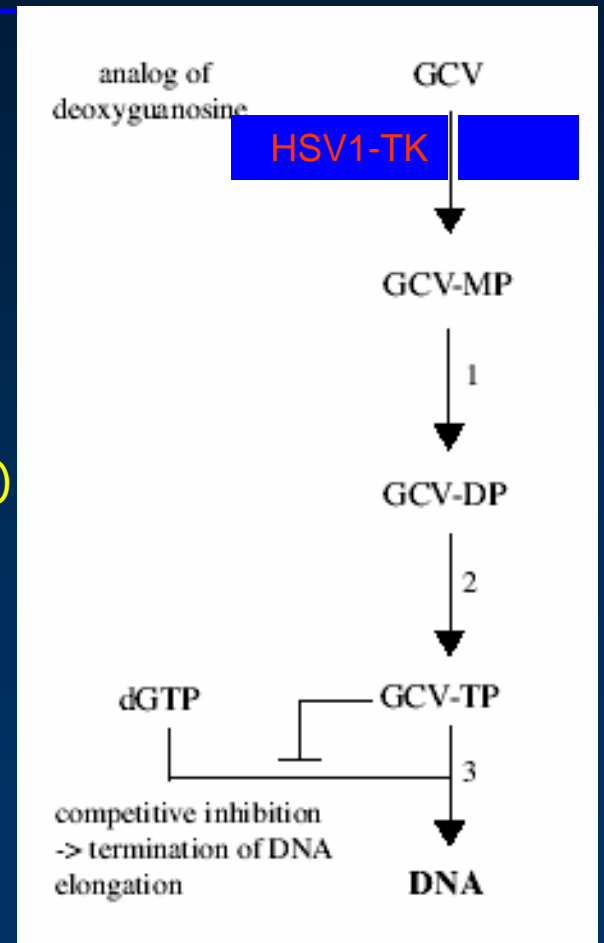
-Noninvasive myelin imaging and quantification

- MRI (DT-MRI)
- SPECT

Generation and characterization of « Oligo-TTK » transgenic mouse

Properties of HSV1-TK gene

- Inducible toxicity
- Specific phosphorylation of nucleoside analogue (ACV, GCV)
- High affinity to GCV at low concentration



Action of HSV1-TK/GCV

Phenotype of the Oligo-TTK GCV- treated mice

- Treatment with ganciclovir
50 $\mu\text{g/g}$ of body weight
- injection:
 - ▶ P1-P28 daily injection

Phenotype:

- Tremors
- Ataxia
- Growth deficiency

14 days old mice



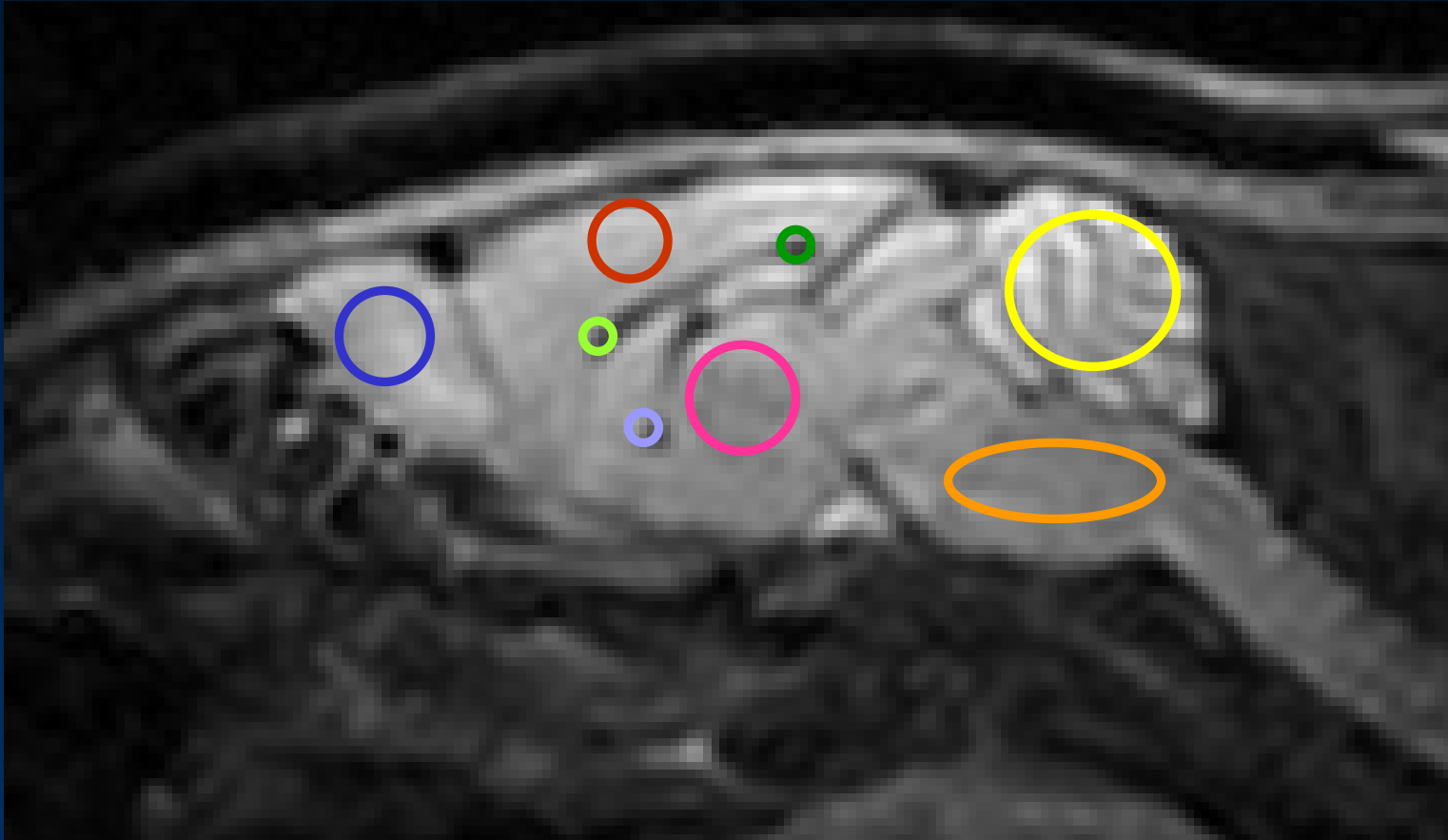
Myelin abnormalities assessment in the CNS by MRI

- Good anatomical resolution
- Contrast between white and gray matter
- Noninvasive imaging

Objectives

- ▶ Quantification of myelin modifications in transgenic & mutant mice.
- ▶ Correlation with histopathological findings.

METHODOLOGY



3 regions of white matter

genu of corpus callosum (GCC)

splenium of corpus callosum (SCC)

anterior commissure (CA)

3 mixed regions (white and gray matters)

Cerebellum (CB)

Brain stem

Olfactory bulb (OB)

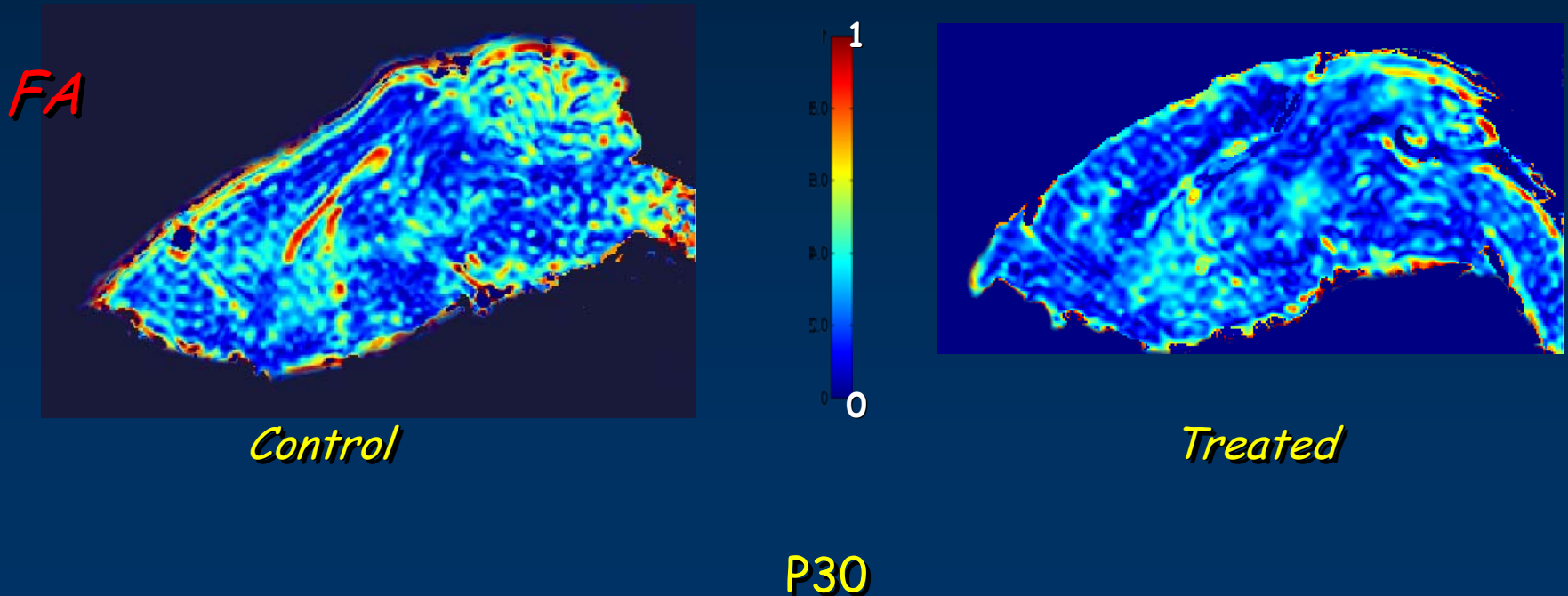
2 structures of gray matter

Cortex (C)

Thalamus (T)

Dysmyelination, P1-30

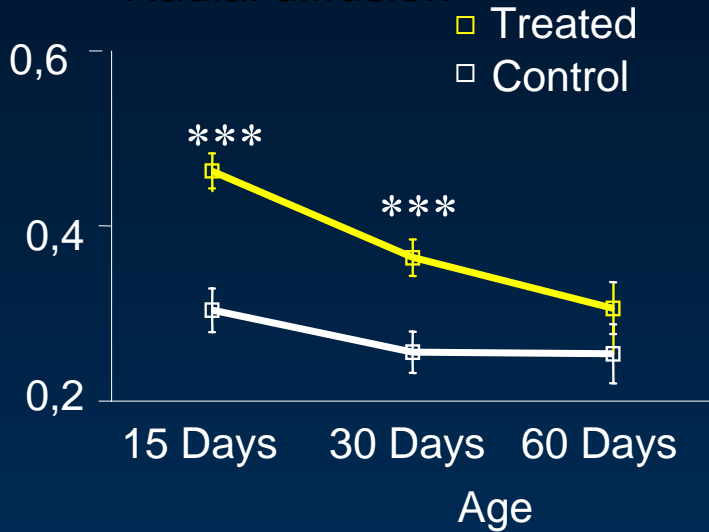
Fractional anisotropy maps at P30 in control and treated mice revealed a decreased anisotropy and an atrophy of corpus callosum and cerebellum in transgenic treated mice



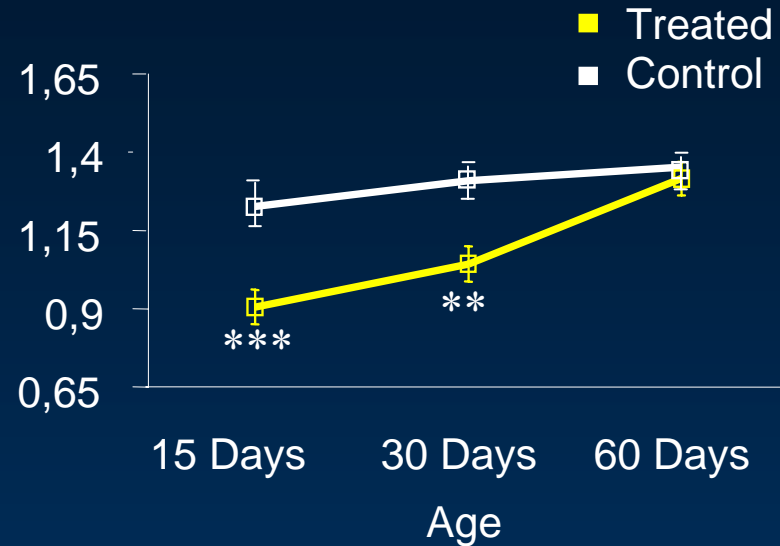
Remyelination dynamics

Genu of corpus callosum

Radial diffusion



Axial diffusion



Fractional anisotropy

