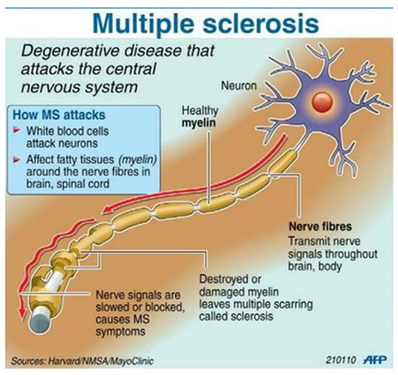
Therapeutic approach for Multiple Sclerosis using a bioeletronic cell implant

Audouard E, Rousselot L, Piguet F and Cartier N
NeuroGenCell, Institut du Cerveau et de la Moelle Epinière, INSERM U1127, Paris, France

I. Introduction

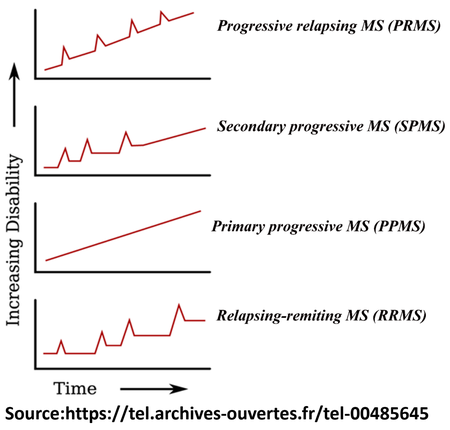


Multiple sclerosis (MS) is a chronic inflammatory disease of the central nervous system (CNS) , characterized by demyelinating lesions of nerve fibers in CNS.

2 million people worldwide are affected by MS.

The most common form of MS is relapsing-remitting form, characterized by unpredictable attacks that may or may not leave permanent deficits followed by periods of remission.

To date, there is no cure but only treatments that prevent flare-ups in recurrent forms.
Indeed, beta interferon injection (IFNβ) several times per week remains a therapy of choice for the treatment of MS.
However, these repeated injections are associated with inflammatory reactions at the injection site.



Source:https://tel.archives-ouvertes.fr/tel-00485645

It is therefore essential to develop innovative methods for taking medication.

Here, we evaluated a new approach based on optogenetic implants to control IFNβ protein delivery in MS patients.

II. What is the aim of optogenerapy project?

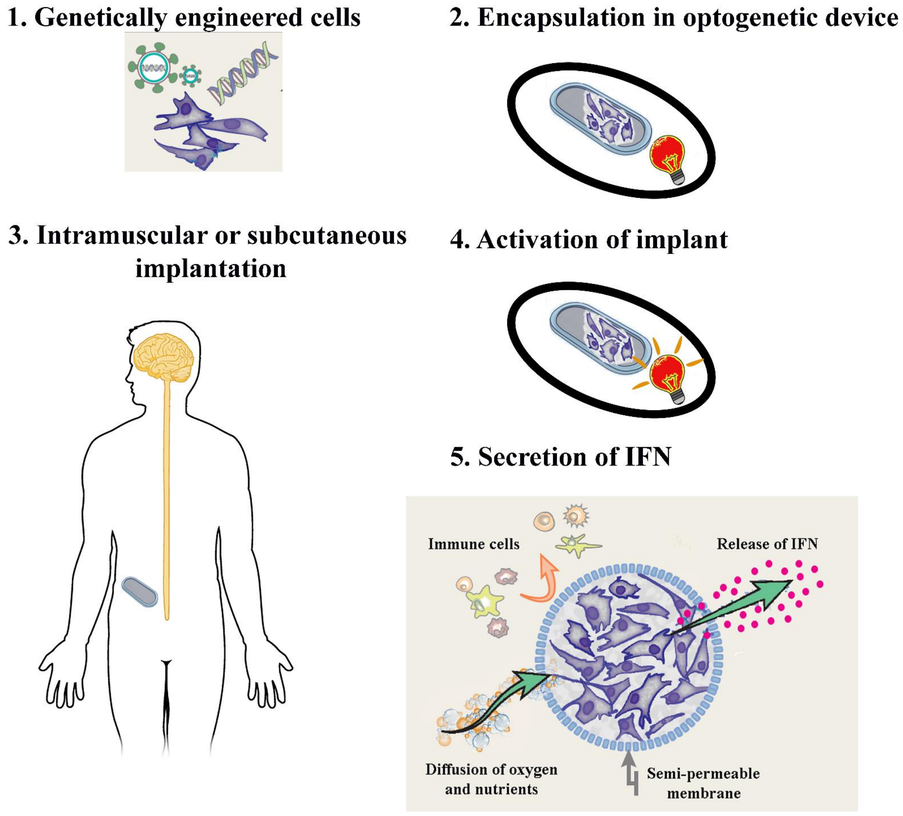


Figure1: Optogenerapy approach is based on subcutaneous implantation of genetically engineered cells encapsulated in a semi-permeable membrane that enables diffusion of small molecules.

III. Tools to study the biocompatibility of implants

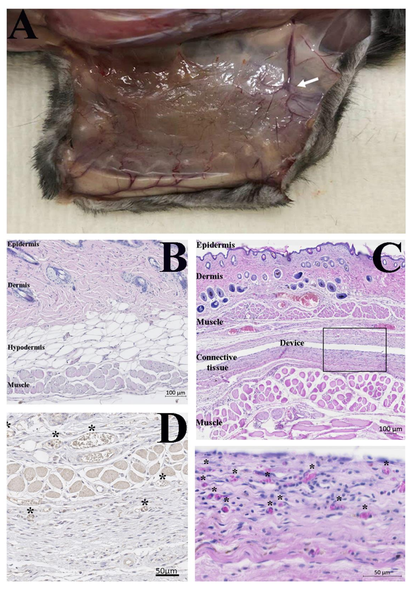
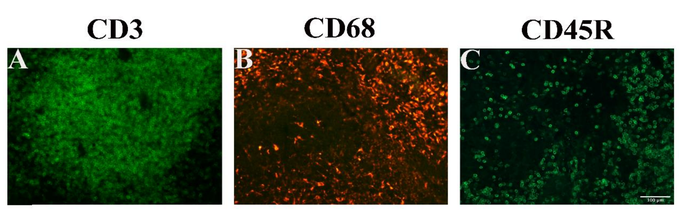


Figure2: Tools to study the neovascularization.
(A)Vascularization 1-month after implantation. (B-C) Hematoxylin-eosin staining on skin tissue. (D) Immunochemistry using anti-vWF antibody to visualise blood vessels.



D Evaluation of the local immunological effects of implantation:

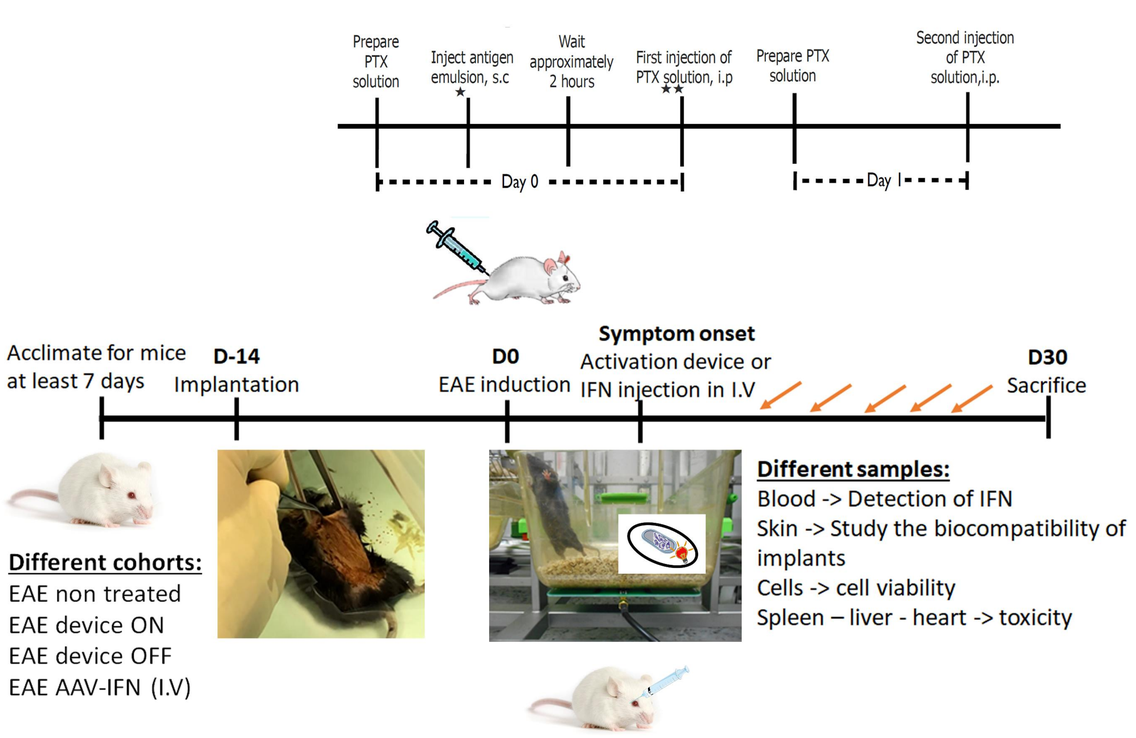
Inflammatory cell types:
Polymorphonuclear cells (HE)
Lymphocytes (CD3)
Plasma cells (CD 45R)
Macrophage (CD68)
Giant cells (HE and CD68)
Necrosis (HE)

The inflammation score criteria :
0 = no cell type detected
1 = rare; 1–5 cells/high-power fields (hpf) (except for giant cells, 1–2/hpf)
2 = 5–10 cells/hpf (except for giant cells, 3–5/hpf)
3 = heavy infiltrate
4 = packed

The final average irritating ranking was obtained from the average of overall scores.
Non irritant: 0 - 2.9
Slight irritant: 3 - 8.9
Moderate irritant: 9 - 15
Severe irritant: > 15

Figure3: Tools to study the inflammation after implantation.
Immunofluorescence against inflammatory cell type: anti-CD3 (A;T cells), anti-CD68 (B; macrophage and giant cells) and anti-CD45R (C;plasma cells). (D) Method to evaluate local immunological effects of implantation (Sarkanen et al, 2012).

IV. Validation of therapeutic efficacy in EAE model mice



Different cohorts:
EAE non treated
EAE device ON
EAE device OFF
EAE AAV-IFN (I.V)

Different samples:
Blood -> Detection of IFN
Skin -> Study the biocompatibility of implants
Cells -> cell viability
Spleen – liver - heart -> toxicity

V. Conclusions

The novelty of the approach relies on the control of the secretion of proteins for therapeutic purposes.
The therapeutic action associated with a fine dosage of therapy would prevent adverse immune responses such as pain and local irritation at the injection site.

VI. Acknowledgement

The Optogenerapy project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement N°720694.

Thank you to Cartier Team and ICM platforms

VII. Bibliography

Sarkanen et al, Bioactive acellular implant induces angiogenesis and adipogenesis and sustained soft tissue restoration *in Vivo. Tissue Engineering: Part A. 2012 Volume 18, 2568-80.*