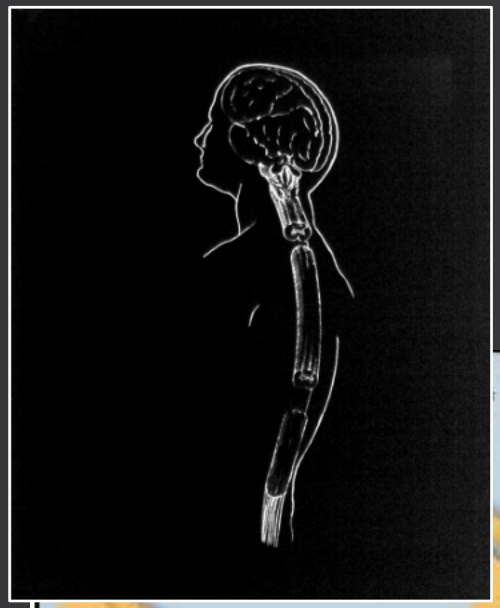
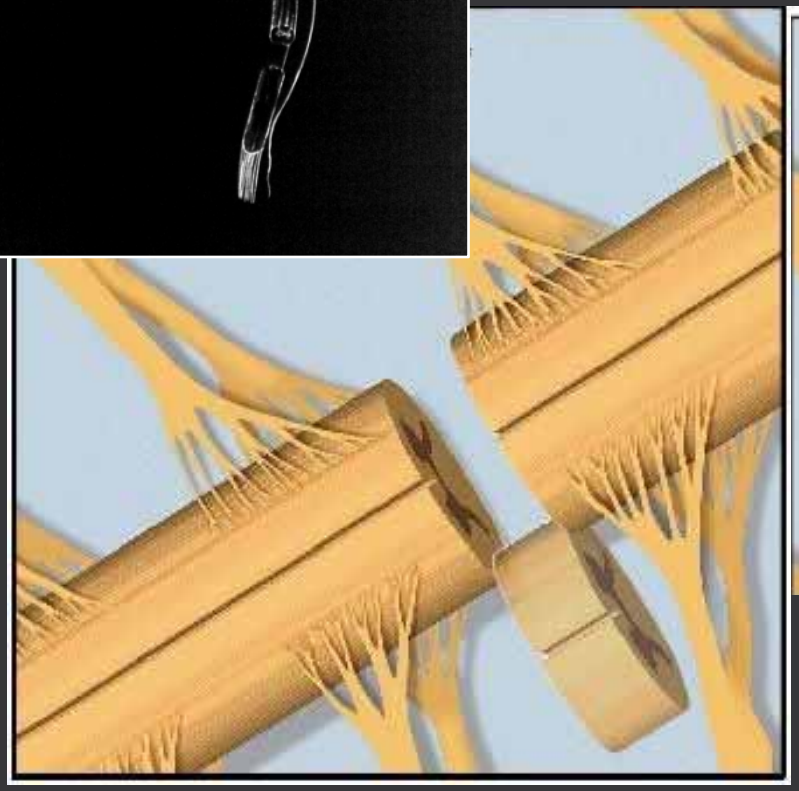
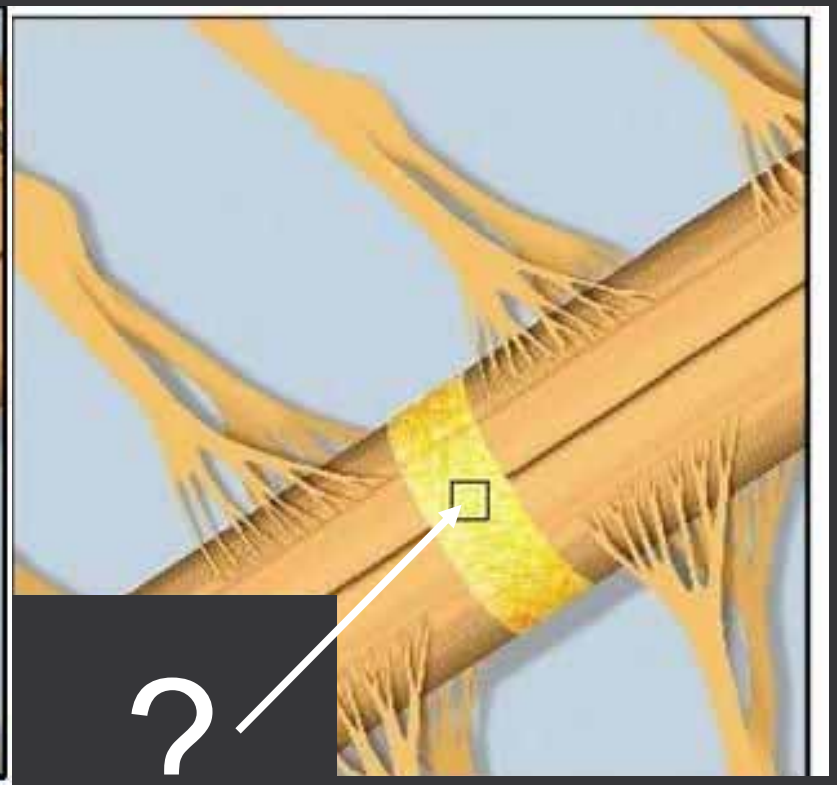
Lésions du SNC et biomatériaux

P. Menei
Dpt de neurochirurgie CHU d'Angers
INSERM U 646







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-Tubes polymériques creux

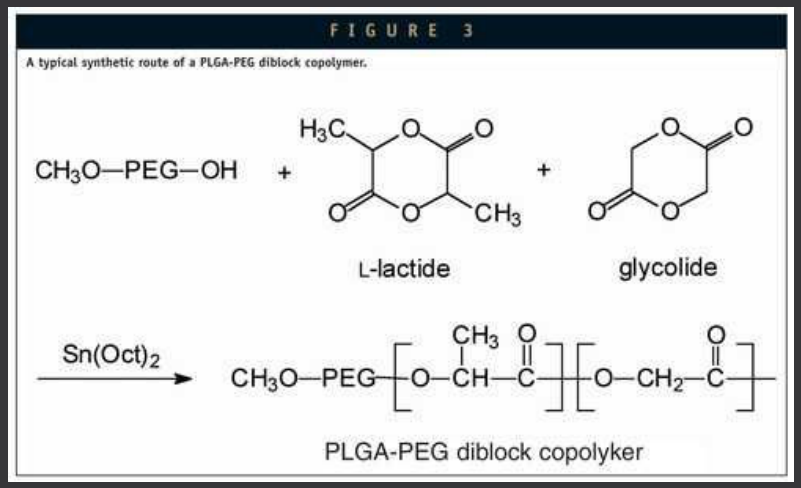
-Tubes polymériques pleins

-Hydrogels

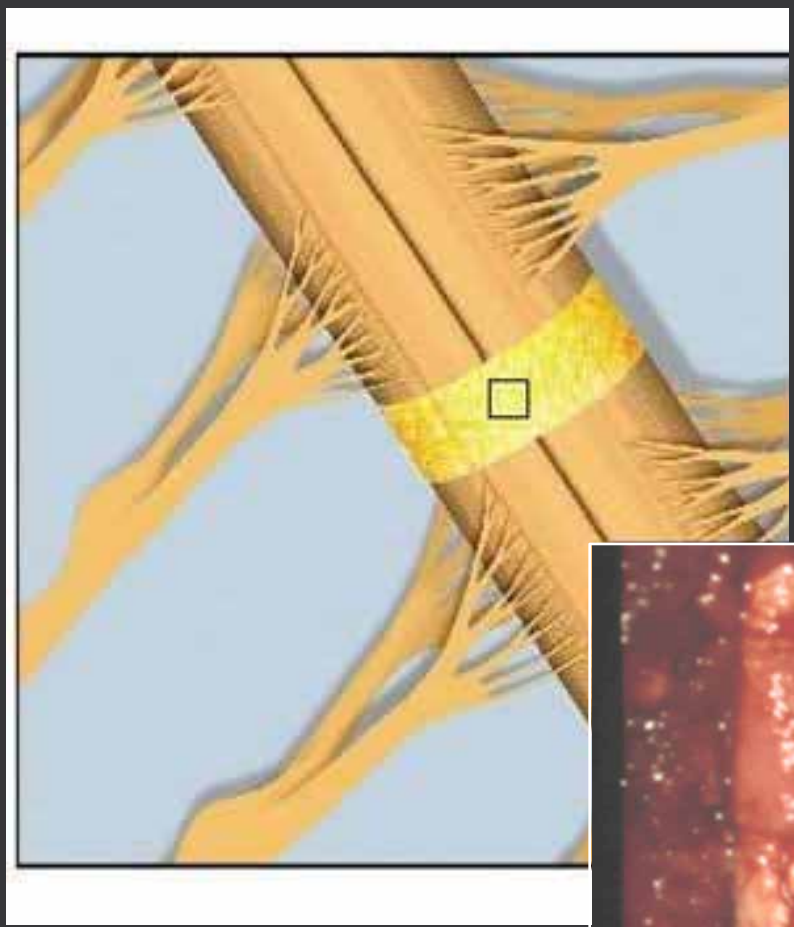
Tubes polymeriques creux

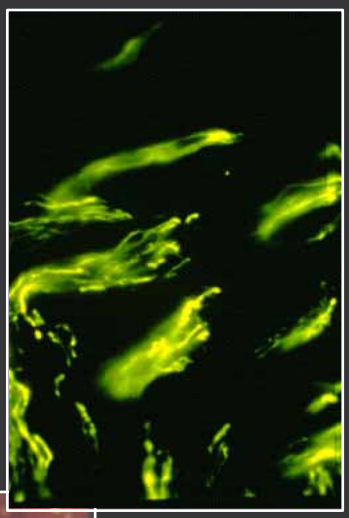
Naturel/synthétique

Non-biodégradable/biodégradable



NEURO-TUBE



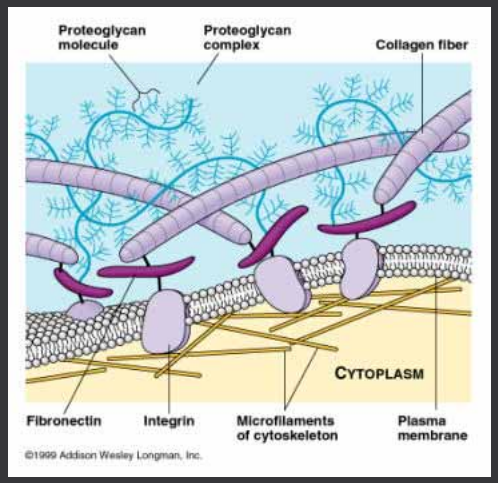


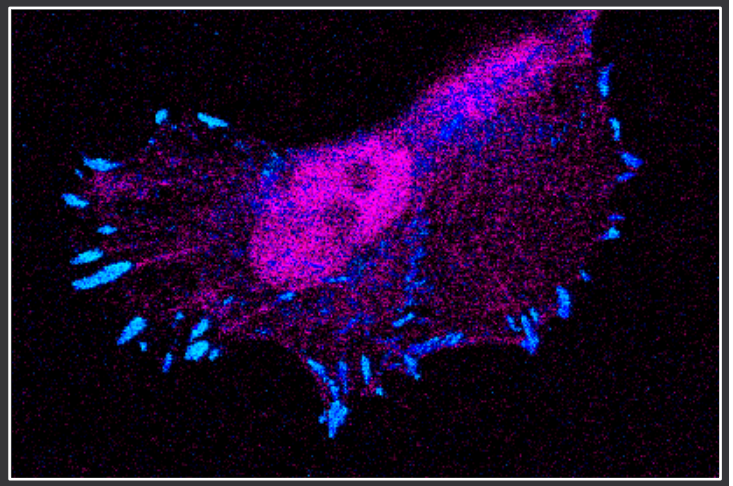
Tubes polymeriques « remplis »

-Matrice neutre

-Matrice avec facteurs neurotrophiques

-Matrice avec cellules « conductrices »





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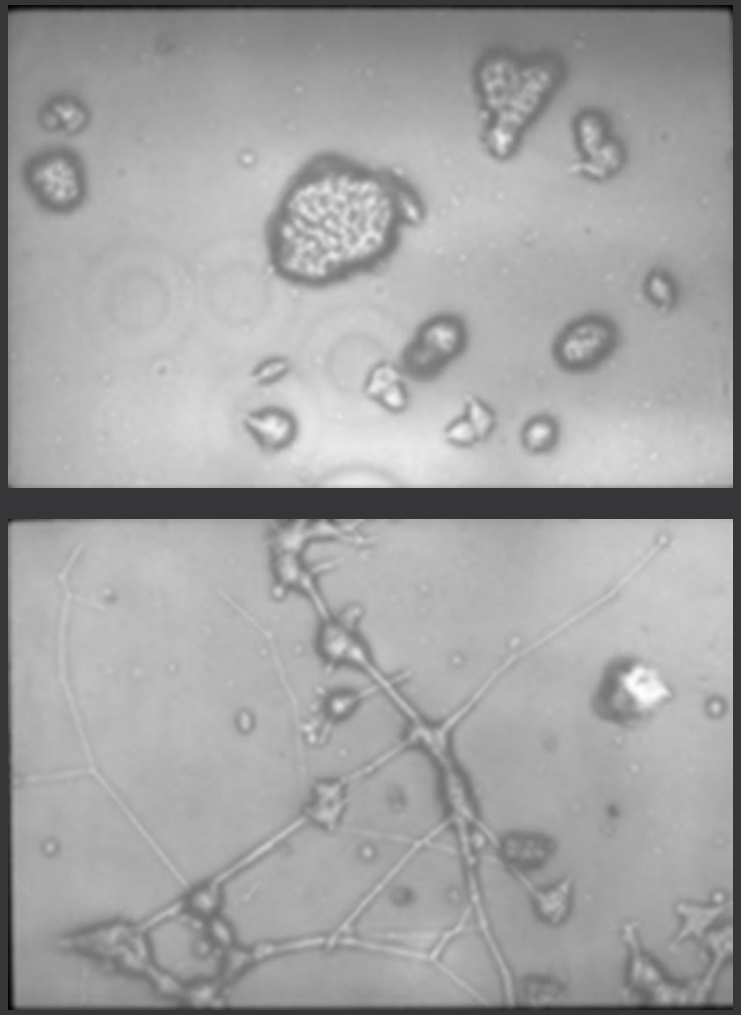

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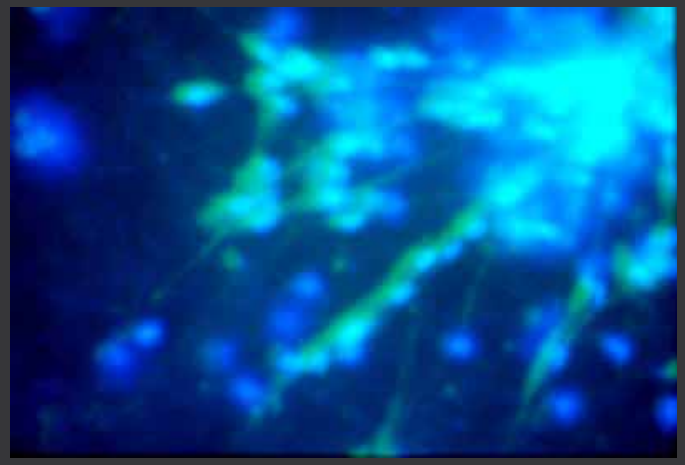
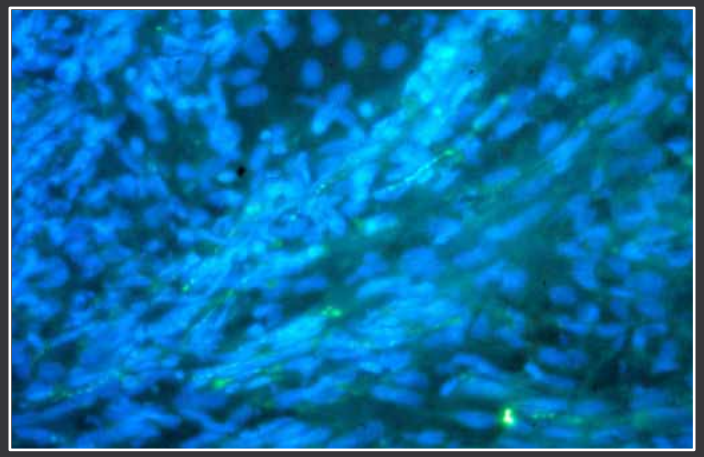




Tubes polymeriques pleins

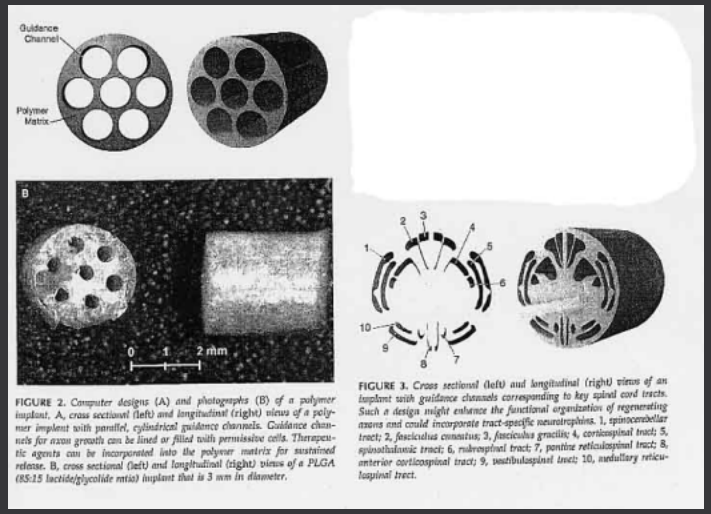
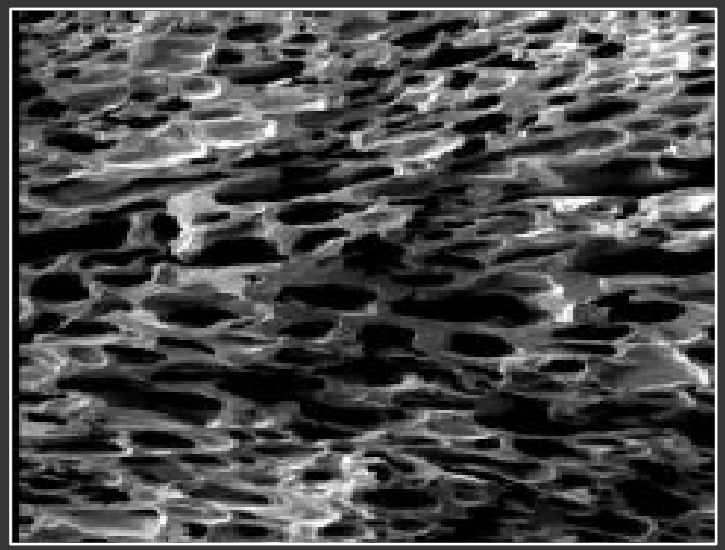
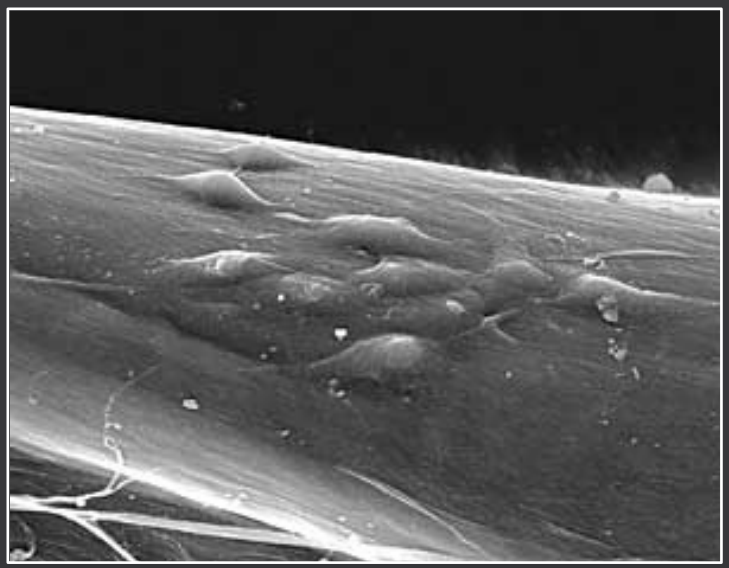
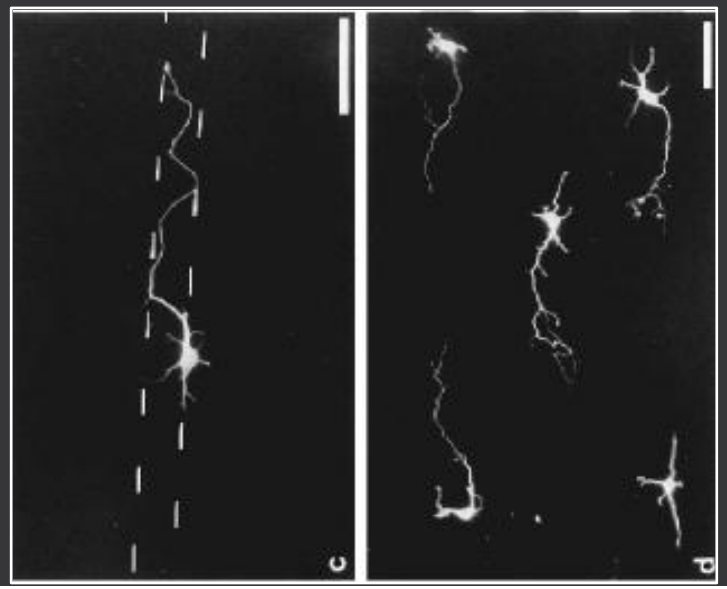


FIGURE 2. *Computer designs* (A) *and photographs* (B) *of a polymer implant.* A, *cross sectional* (left) *and longitudinal* (right) *views of a polymer implant with parallel, cylindrical guidance channels. Guidance channels for axon growth can be lined or filled with permissive cells. Therapeutic agents can be incorporated into the polymer matrix for sustained release.* B, *cross sectional* (left) *and longitudinal* (right) *views of a PLGA (85:15 lactide/glycolide ratio) implant that is 3 mm in diameter.*

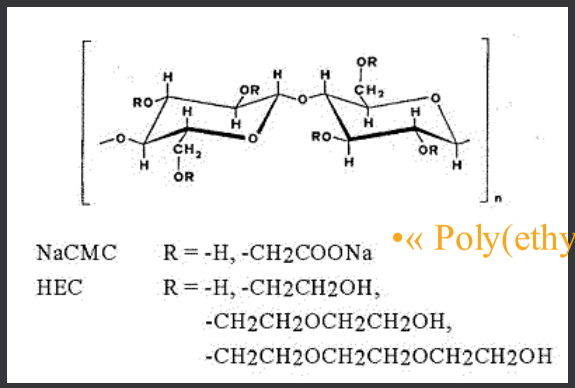
FIGURE 3. *Cross sectional* (left) *and longitudinal* (right) *views of an implant with guidance channels corresponding to key spinal cord tracts. Such a design might enhance the functional organization of regenerating axons and could incorporate tract-specific neurotrophins.* 1, *spinocerebellar tract;* 2, *fasciculus cuneatus;* 3, *fasciculus gracilis;* 4, *corticospinal tract;* 5, *spinothalamic tract;* 6, *rubrospinal tract;* 7, *pontine reticulospinal tract;* 8, *anterior corticospinal tract;* 9, *vestibulospinal tract;* 10, *medullary reticulospinal tract.*







Hydrogels



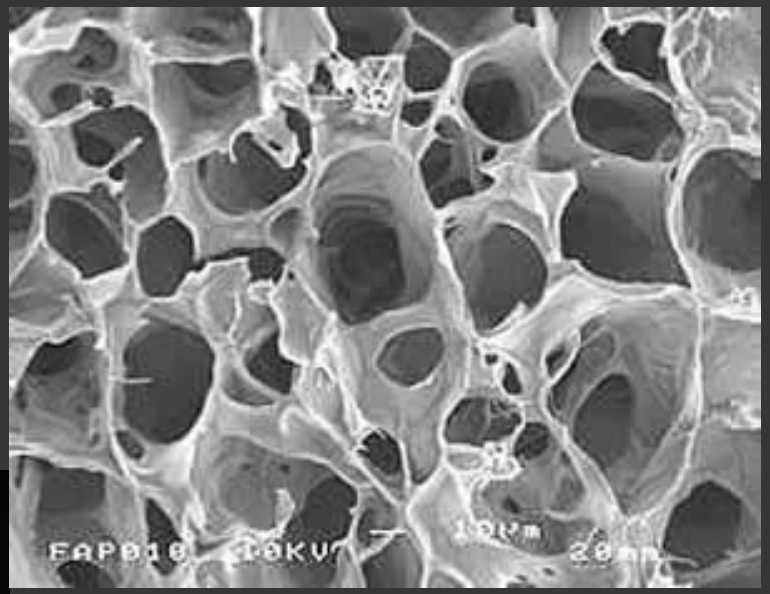
NaCMC R = -H, -CH_2COONa

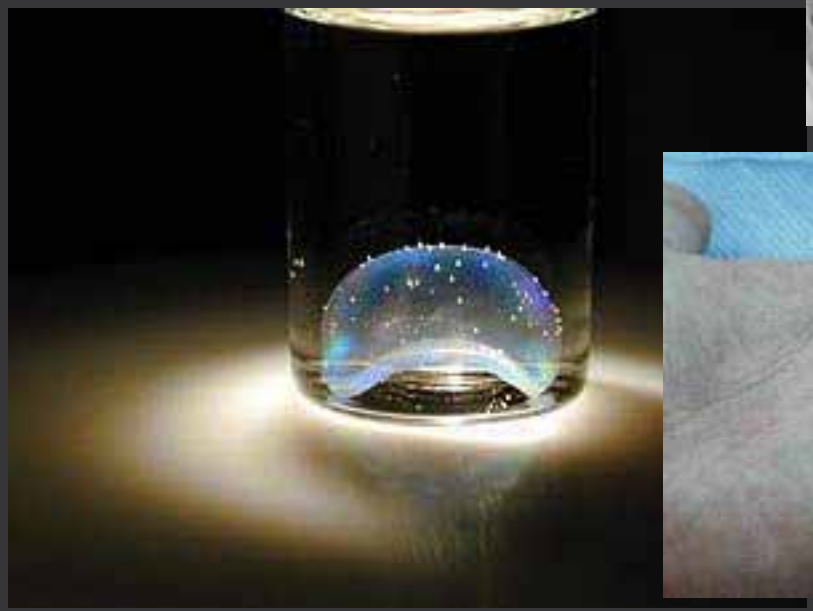
HEC R = -H, -CH_2CH_2OH, -$CH_2CH_2OCH_2CH_2OH$, -$CH_2CH_2OCH_2CH_2OCH_2CH_2OH$

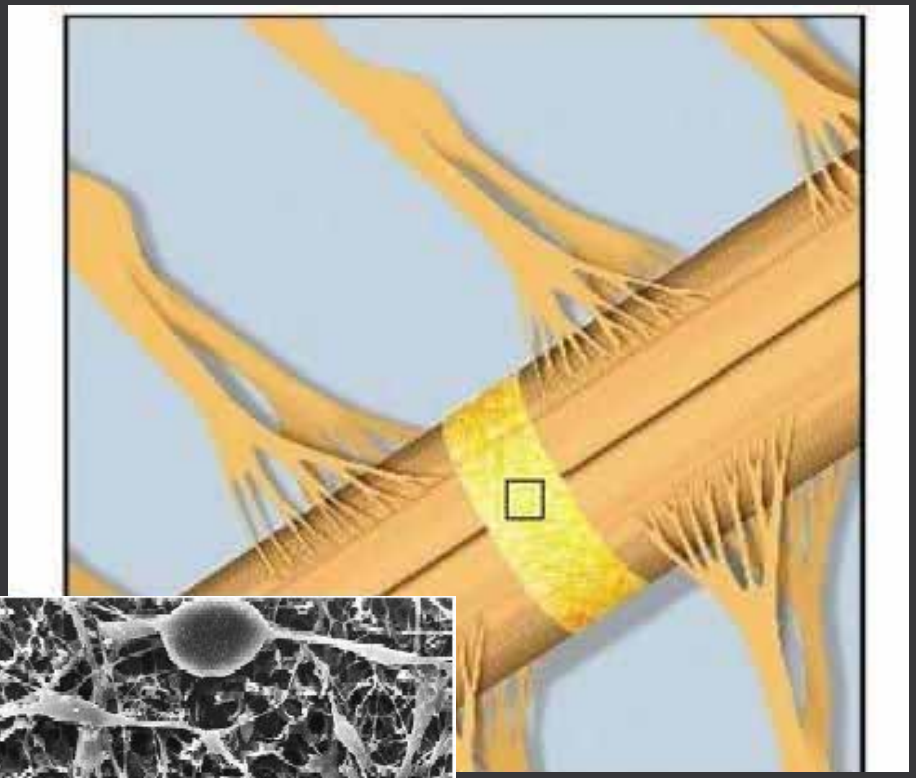
- « Poly(ethylène oxides) » PEO

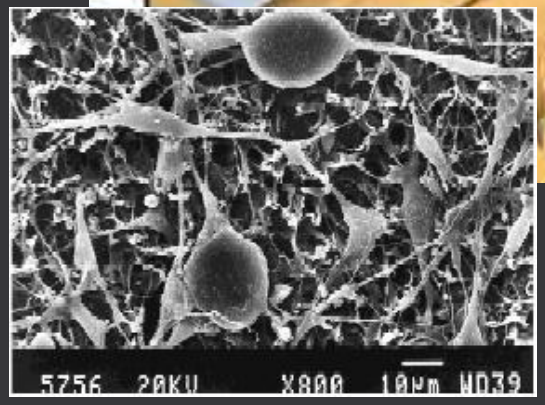
Hydratation facile

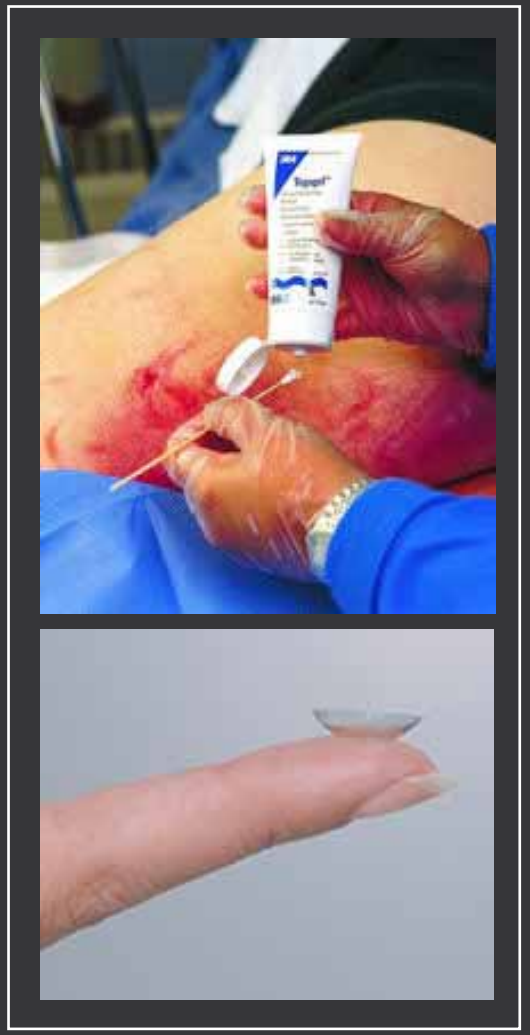
Non biodégradables





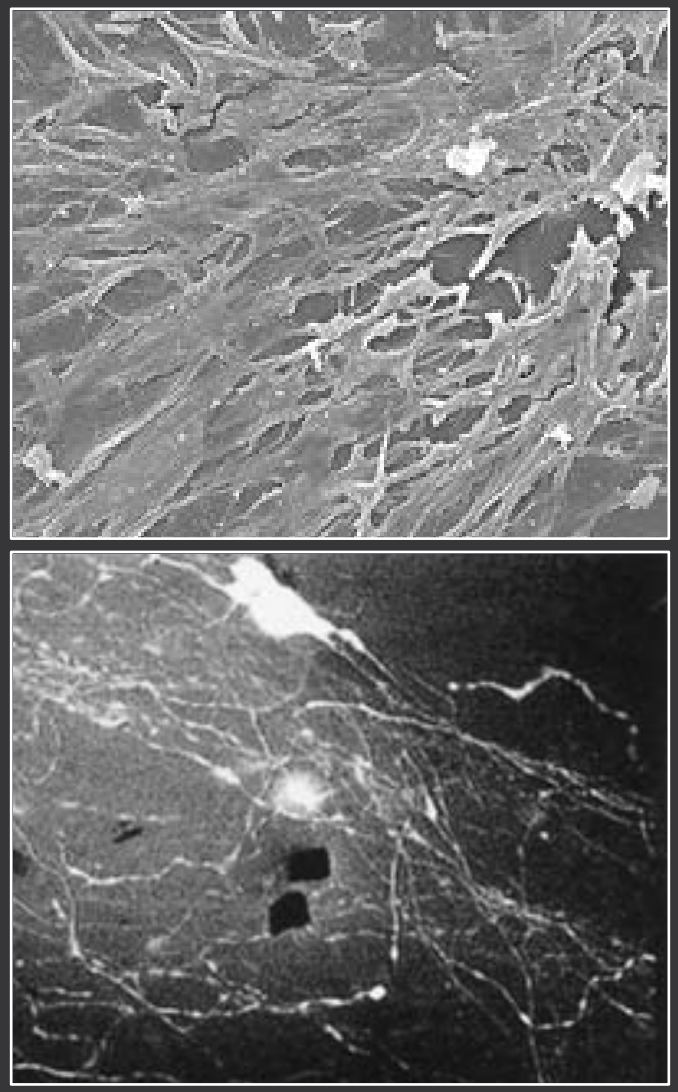



5756 20KV X800 10µm WD39

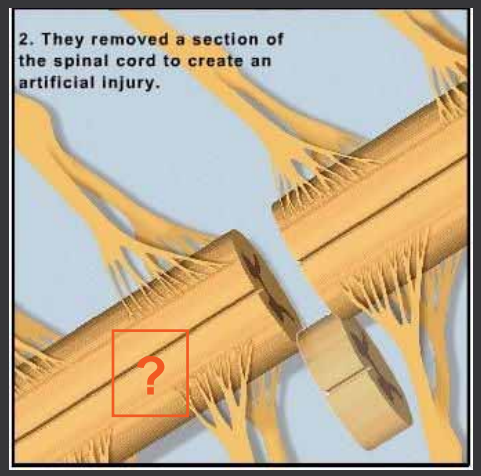


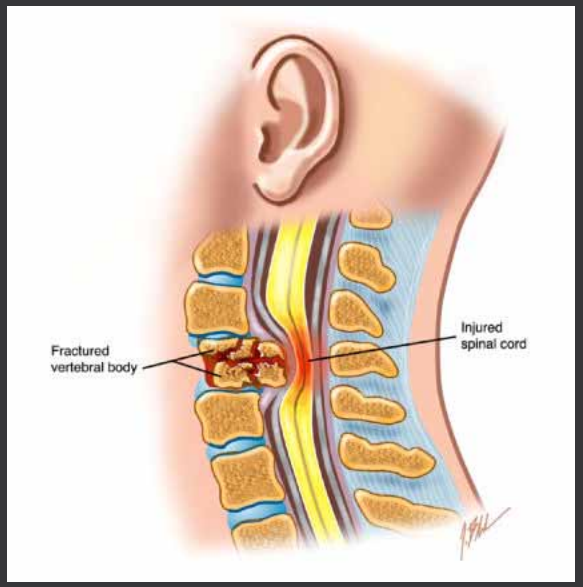
Hydrogels « améliorés »

- Hydrogel pré-habité par cellules
- Hydrogel contenant ds molécules de la matrice extracellulaire ou des facteurs neurotrophiques

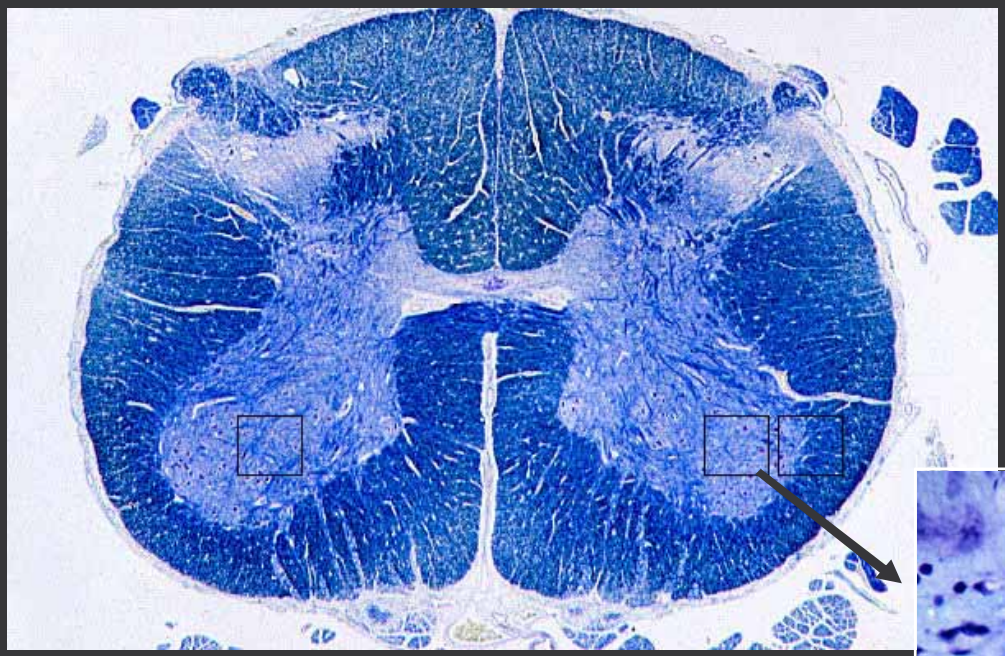


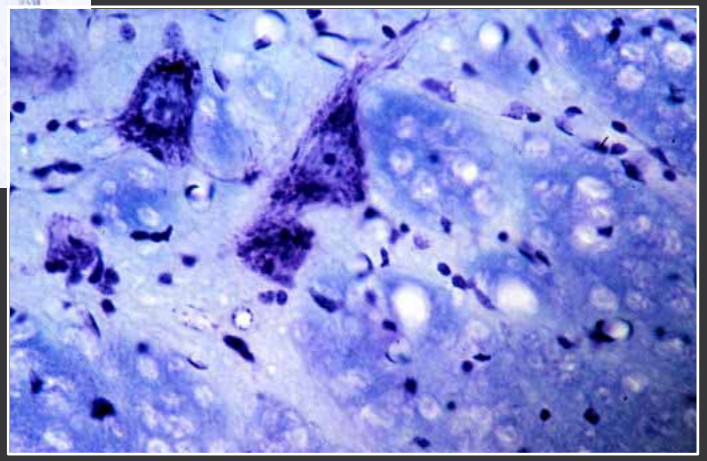
Mais la réalité est tout autre





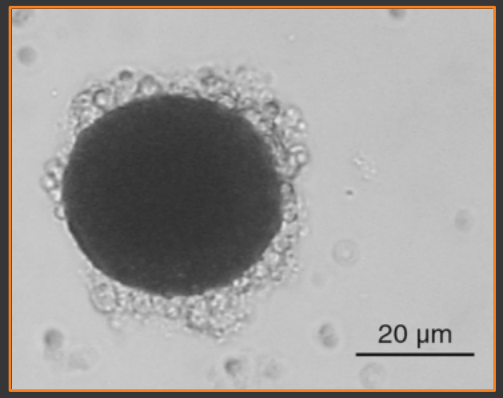
Et la moelle n'est pas faite que de fibres





Il faut reconstruire les connexions, remplacer les cellules et sans détruire le tissu restant!

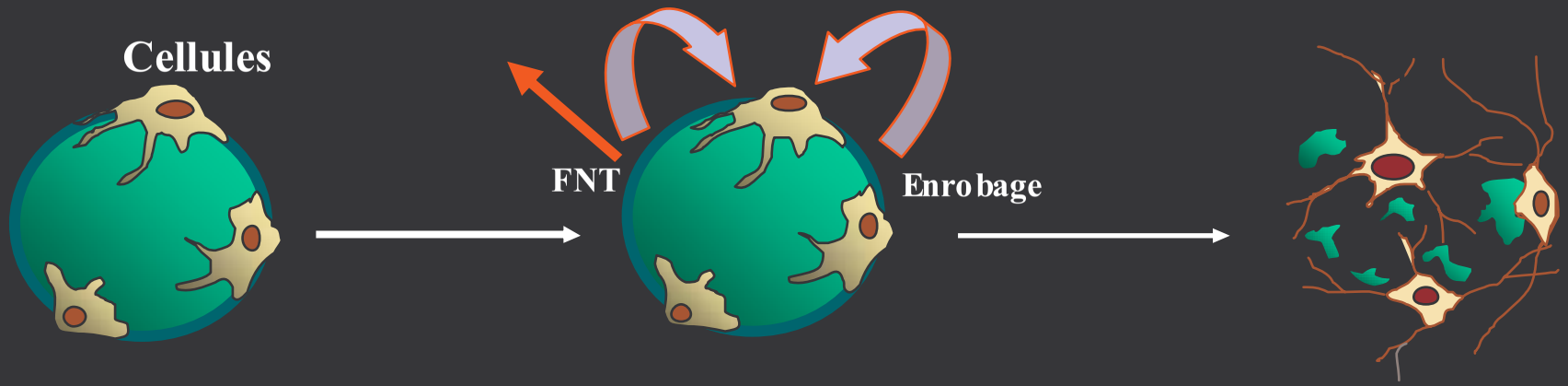
L'ingéniérie tissulaire doit passer à l'échelle micrométrique… en attendant l'échelle nanométrique …



Principe des Microcarriers Pharmacologiquement Actifs

Cellules différenciées

Cellules

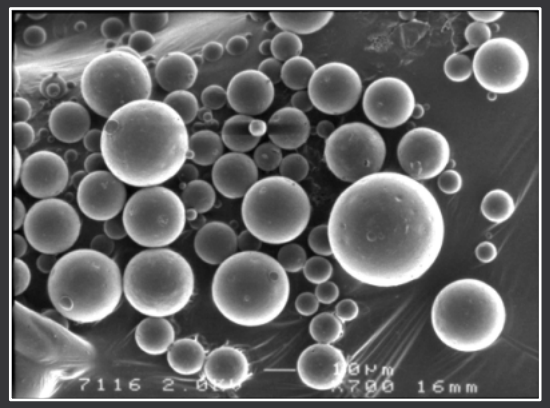


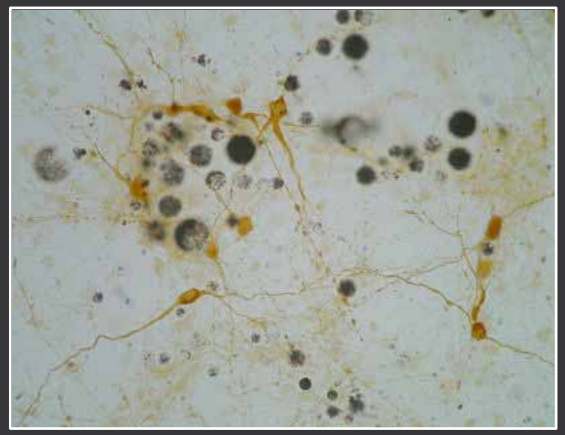
MPA : Support pour la culture cellulaire et les transplantations (aggrégats- 3D)

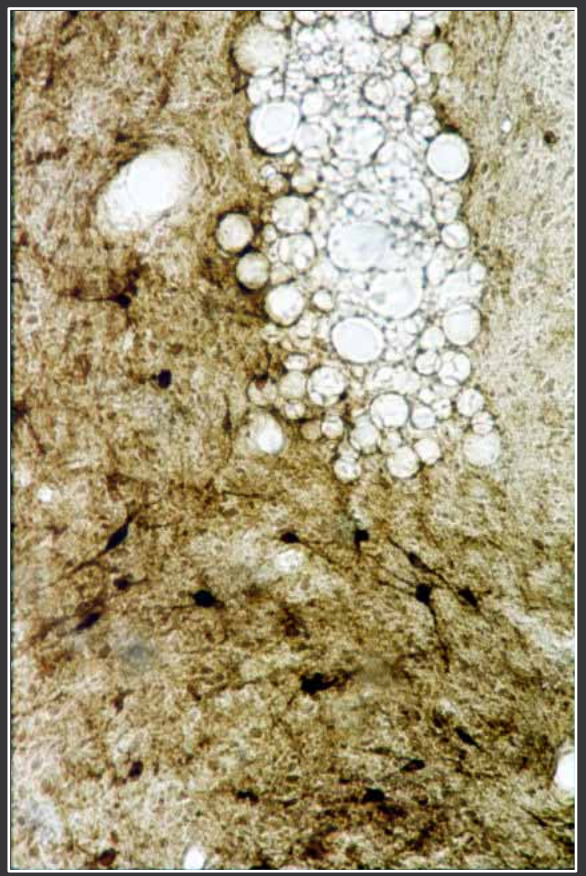
Augmentation de la survie et de la différenciation des cellules greffées et modification de l'environnement

Après dégradation complète des MPA, les cellules peuvent intégrer le parenchyme

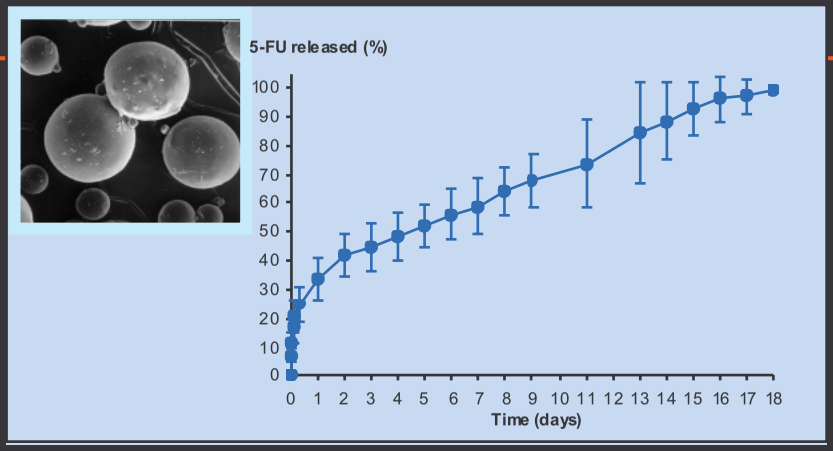
Microsphères biodégradables libérant des facteurs neurotrophiques (NGF, GDNF)







Microsphères biodégradables libérant du 5-FU



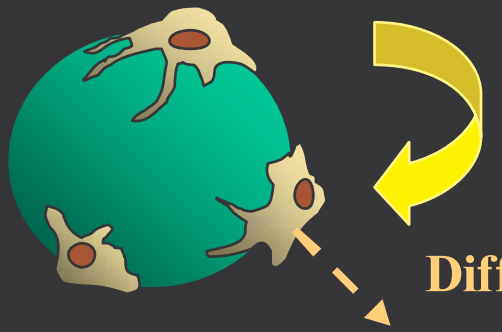
Phase I: Menei et al. *Cancer* 1999

Phase IIb: randomisée multicentrique Menei et al. *Neurosurgery* 2004

Phase I: Menei et al. *Cancer* 2003

Développement de MPA (modèle PC12 et NGF))

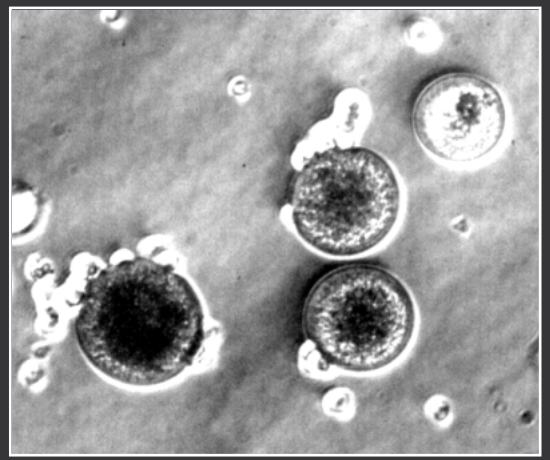
PC12

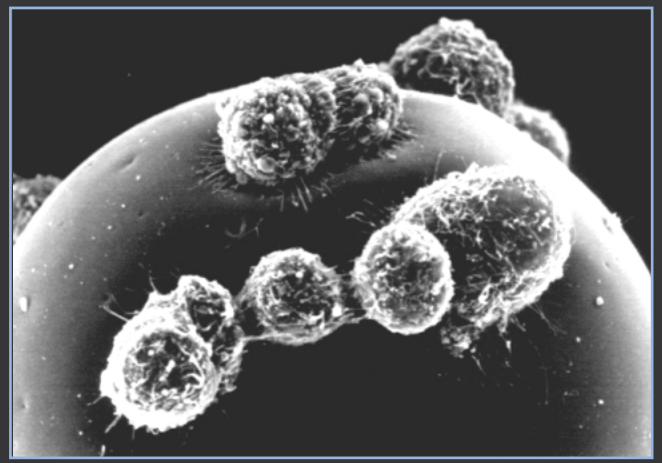


NGF

Différenciation en « neurone sympathique»

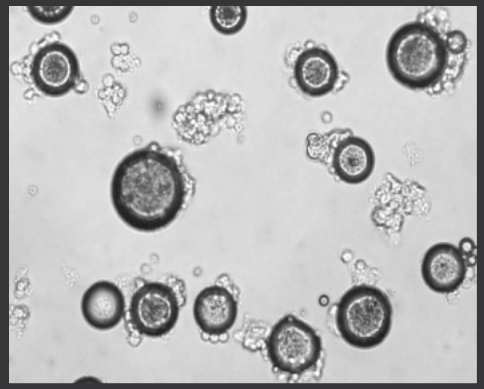
Libération dopamine

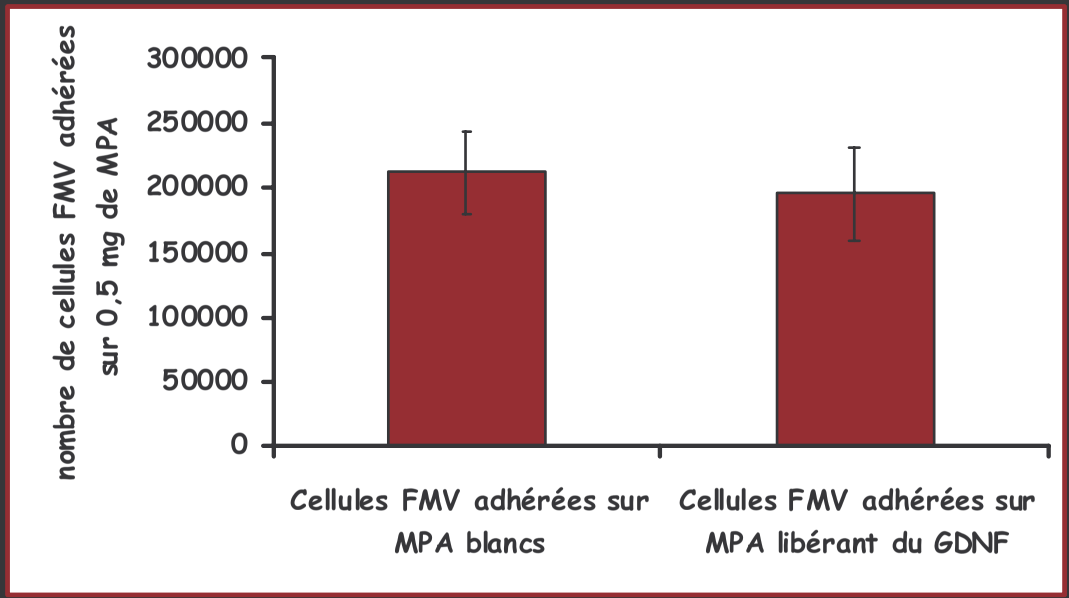




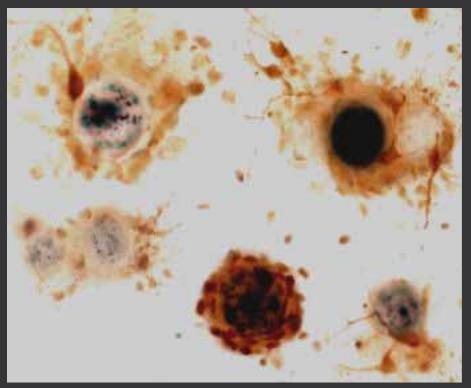
Développement MPA: modèle neurones dopaminergiques fœtaux et GDNF

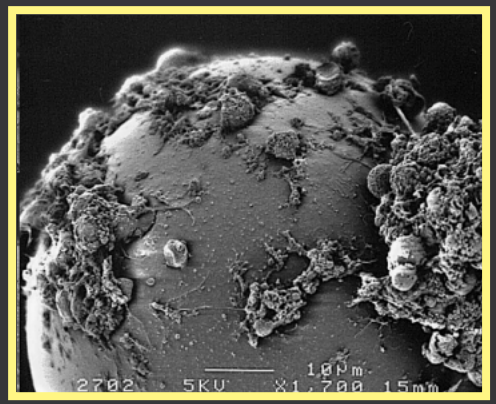
Adhérence sur les MPA

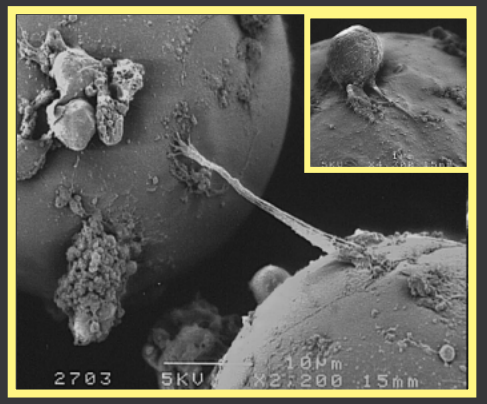




Marquage de la TH après 11J de culture



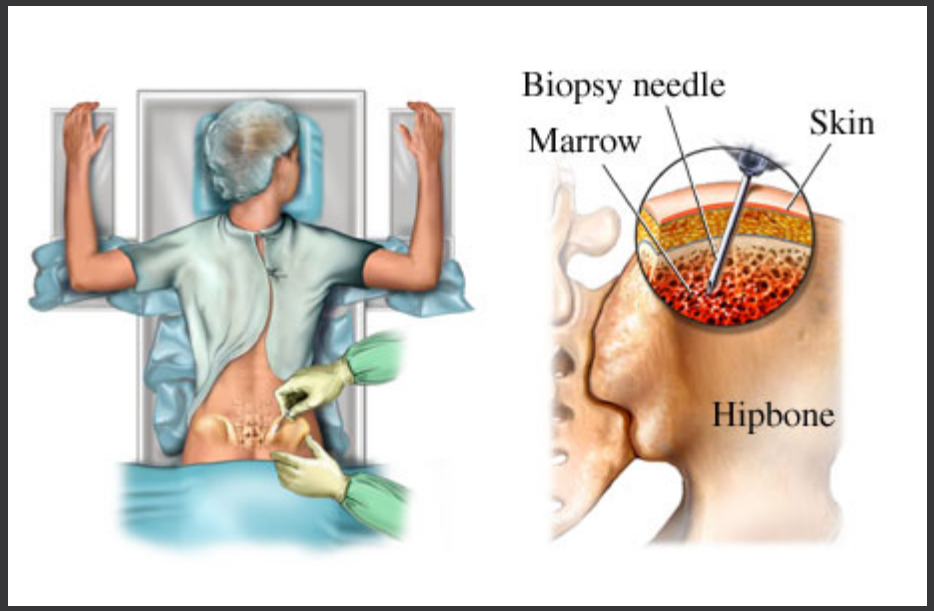


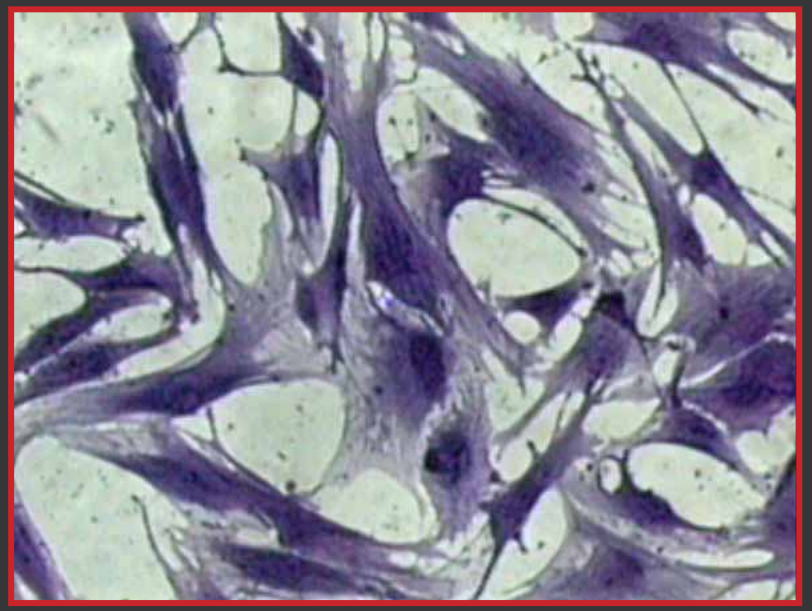


Images de MEB

Développement MPA et cellules souches mésenchymateuses

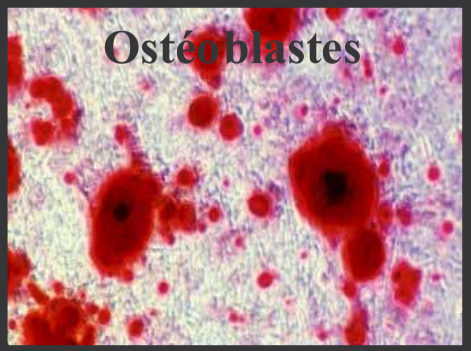
Cellules MIAMI : « Marrow Isolated Adult Multilineage Inducible »

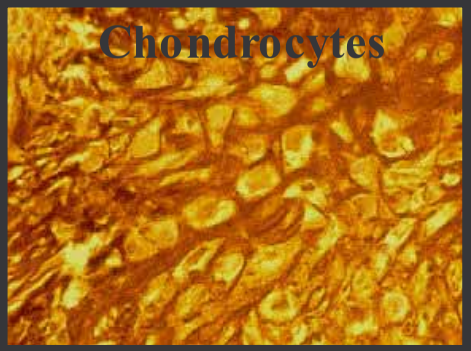


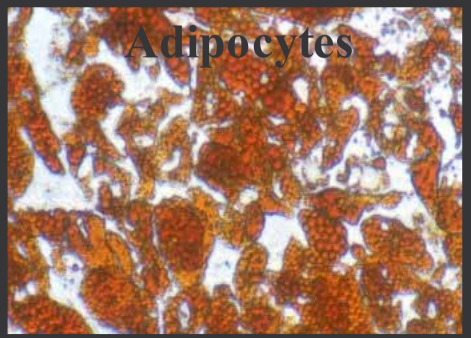


Pluripotentialité des cellules MIAMI

Mésoderme

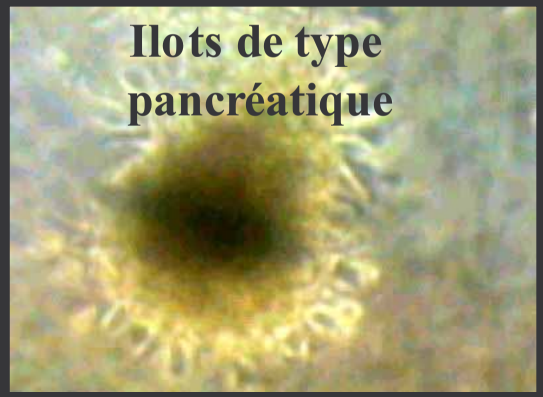


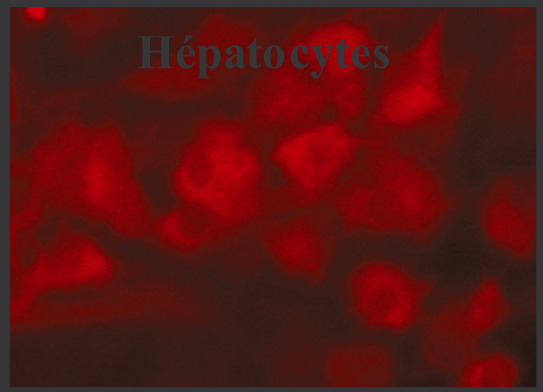




Cellules MIAMI

Endoderme



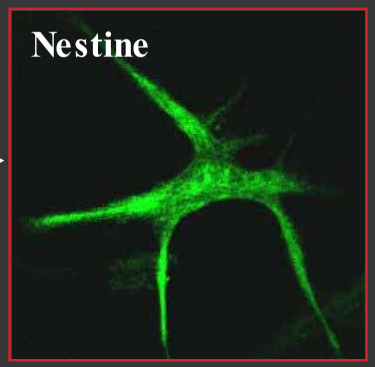


Différenciation des cellules MIAMI en cellules neuronales

Cellules MIAMI

Etape 1
spécification

bFGF, 24 H

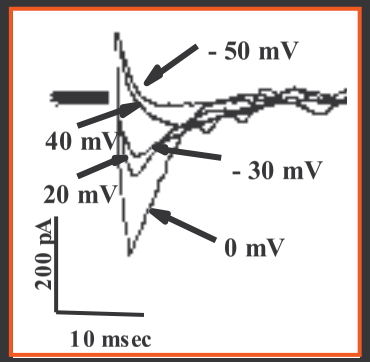


Précurseurs de type neural

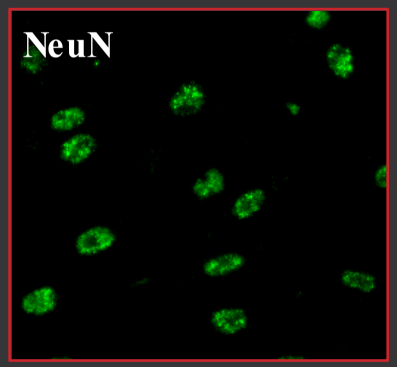
Etape 2
« commitment »

NT-3, 48 H

Précurseurs neuronaux



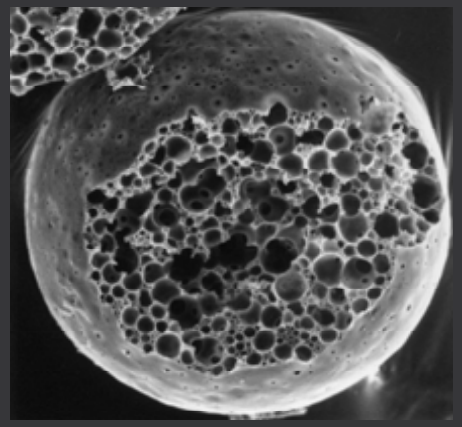
Propriétés électrophysiologiques



Neurones
Neurofilament M (NFM) +

Etape 3
différenciation

NT-3, BDNF, NGF
3 Jours



Travail collaboratif:

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Remerciements à l’IRME