# SELECTED OPPORTUNITIES IN BIOMATERIAL

Pharmacologically Active Microcarriers for efficient integration of transplanted cells in the host tissue

(BIO11360, GBM01306, GBM06412)

# PHARMACOLOGICALLY ACTIVE MICROCARRIERS FOR EFFICIENT INTEGRATION OF TRANSPLANTED CELLS IN THE HOST TISSUE (BIO11360, GBM01306, GBM06412)

## Product factsheet

*POC in vivo*

- **Technology:**
  - Pharmacologically Active Microcarriers (PAMs) for efficient integration of transplanted cells in the host tissue
- **Application:**
  - Cell therapy
- **POC & main Publications:**
  - Technology:
    - *Tatard et al., Biomaterials 2005*
    - *Giteau et al., European Journal of Pharmaceutics and Biopharmaceutics 2008*
    - *Tran et al., Eur J Pharm Sci 2012*
  - Cartilage repair:
    - *Bouffi et al., Biomaterials 2010*
    - *Morille et al., Journal of Controlled Release 2013*
  - Parkinson disease:
    - *Tatard et al., Cell Transplantation 2004 ;*
    - *Tatard. et al., Biomaterials 2007 ;*
    - *Tatard. et al., Bone 2007 ;*
    - *Delcroix et al., Biomaterials 2011;*
    - *Daviaud et al., Stem Cells TM 2015*
  - Ischaemic stroke:
    - *Garbayo et al., J. Neurochem 2011;*
    - *Quittet et al., Acta Biomateralia 2015*
  - Regeneration of post-ischemic tissues:
    - *Musilli et al., European Journal of Pharmaceutics and Biopharmaceutics 2012*
    - *Penna et al., J. Cell. Mol. Med. 2013*
- **Patents:**
  - PCT/ WO 03/092657 A1
  - PCT/EP2008/063147
  - PCT/EP2013/056813

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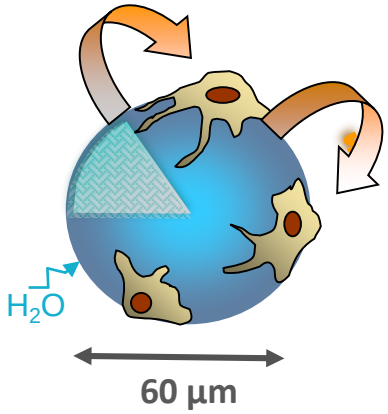
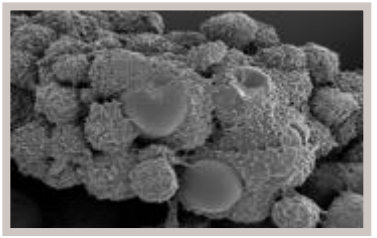
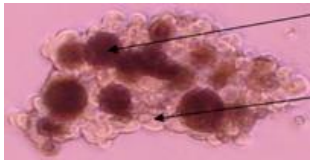
## Patented Technology

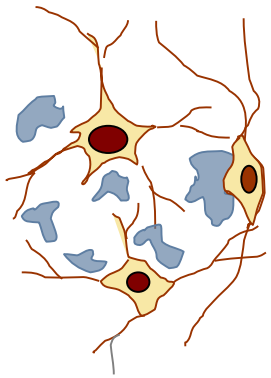
- **Pharmacologically Active Microcarriers (PAMs)**
  - Biocompatible and biodegradable microparticles
  - Coated with cell adhesion molecules
  - Conveying cells on their surface
  - Presenting a controlled delivery of growth factor
  - Survival/differentiation of transplanted cells
  - Modulation of the microenvironment
  - Integration of transplanted cells in the host tissue

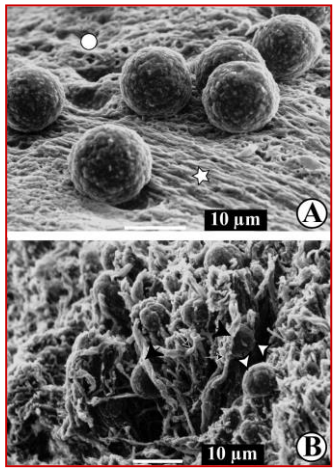
- **Publications:**
  - *Tatard V.M. et al., Biomaterials 2005 26(17) 3727-37*







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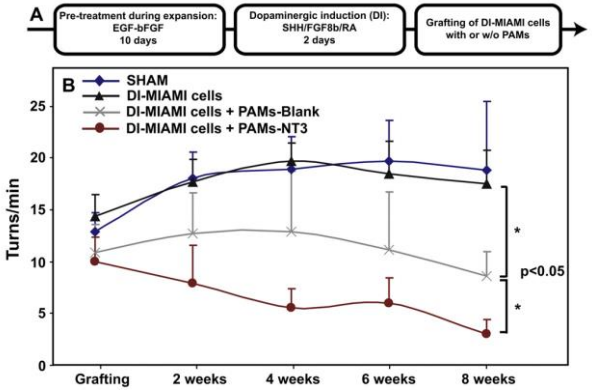
## Proof of concept

**The therapeutic potential of human multipotent mesenchymal stromal cells combined with PAM transplanted in hemi-parkinsonian rats**

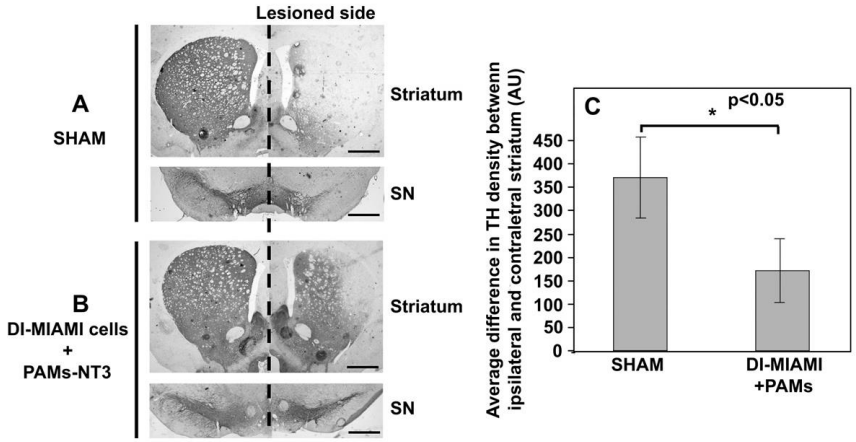
- hemi-parkinsonian Model
  - PAMs were coated with laminin and designed to release neurotrophin 3 (NT3)
  - Grafting of Marrow-Isolated Adult Multilineage Inducible Cells (MIAMI cells) on PAM-NT3
    - MIAMI cells : Homogeneous sub population of human Mesenchymal Stem Cells
    - Stimulate the neuronal-like differentiation of MIAMI cells and promote neuronal survival
  - Transplantation in hemi-parkinsonian rats (partially dopaminergic-deafferented striatum)




**Functional recovery during amphetamine-induced rotational behavior.**

Before transplantation, cells were pre-treated with EGF-bFGF and further induced toward a dopaminergic phenotype (DI-MIAMI cells) prior to their attachment to PAM biomimetic surface.

Rats transplanted with DI-MIAMI cells adhering to PAMs-NT3 resulted in a constant, and statistically significant, decrease of their rotational behavior until the end of the experiment.




**Neuroprotection/reparation of nigrostriatal pathway induced by PAMs/DI-MIAMI cell complexes**

Eight weeks after transplantation, Tyrosine Hydroxylase-positive fibres were observed in the striatum and the substantia nigra (SN).



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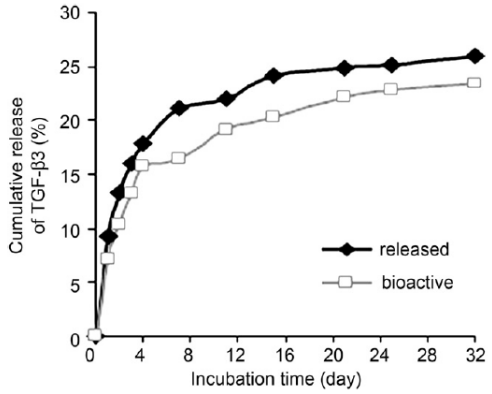
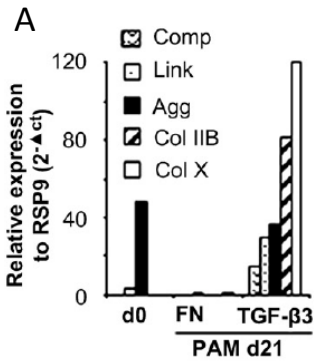
## Proof of concept

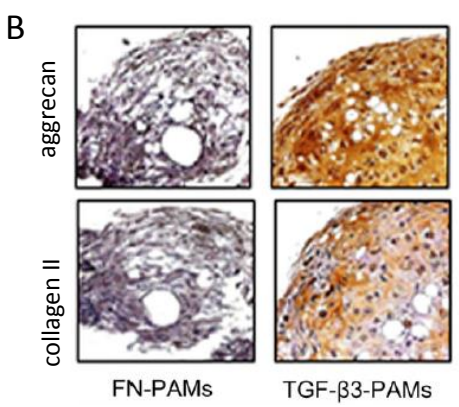
### PAM releasing TGF-b3 in cartilage formation *in vivo* by mesenchymal stem cells

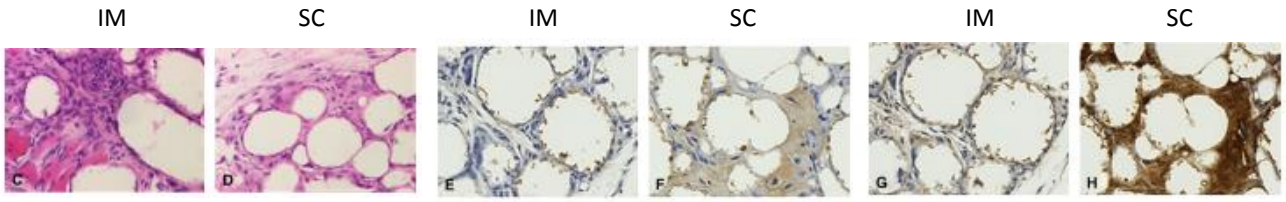
***In vitro* release of TGF-b3 from PAM** by ELISA (released) or by using a specific bioassay (bioactive)




***In vitro* differenciation of MSC/TGF-b3-PAM complexes**. **(A)** Chondrogenic markers expression profiles by RT-qPCR at day 0 and 21 after culture of MSCs. **(B)** Aggrecan and colagen II immunostaining of MSC/PAM complexes at day 21.




***In vivo* differenciation of MSC/TGF-b3-PAM complexes** 2 weeks after intra-muscular (IM) or sub-cutaneous (SC) implantation in SCID mice.



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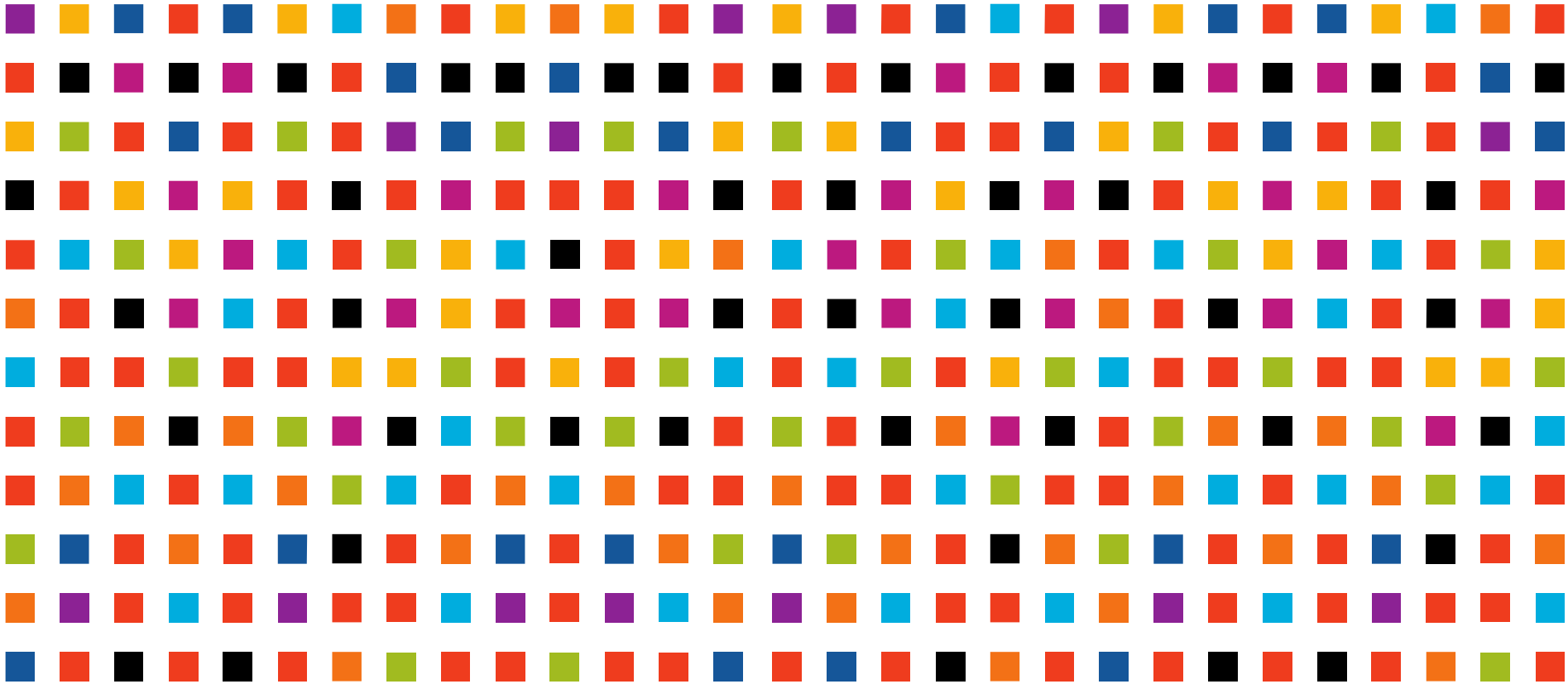

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