Claudine BOIZIAU, Ph.D
Researcher (CR1 – INSERM)

Research interests:

Host own repair mechanisms in the context of tissue engineering

After a first research experience in **artificial modulation of eucaryotic gene expression** (1988-1990 in INSERM U201, Paris; 1990-2003 in INSERM U386, Bordeaux), I was interested by the **role of inflammation regulation in multiple sclerosis**, a neurodegenerative disease (2004-2013, INSERM EA 29-66 and U1049, Bordeaux). I am presently working on the **impact of innate immunity on the biointegration of an implanted material**.

When a biomaterial is implanted in the blood circulation, many host reactions may be observed: i) in the first minutes, adsorption of blood proteins, complement activation, provisional matrix formation, ii) during the first days, innate immunity cell extravasation, granulocytes (24h) and monocytes (48h-72h and later), in response to chemoattractants. The role of this natural cascade of events is to prevent infections by pathogens and to initiate wound healing. In a later phase, chronic inflammation, whose duration depends on the biomaterial, is associated with the presence of macrophages and lymphocytes. Implantation of biocompatible materials allows rapid resolution of acute and chronic inflammatory responses. Material remodeling takes place in part orchestrated by matrix metalloproteinases (MMP) that have been implicated in healing after vascular injury. Increasing data demonstrate the central role of macrophages in implanted material biointegration, due to their homeostasis and wound healing properties.

Vascular substitution / vascular access

The need for vascular accesses is related to the worldwide increase of Chronic Kidney Disease (CKD) and End Stage Renal Disease (ESRD) prevalence. My topics of research in this field include i) the development of biodegradable vascular substitutes that will be able to promote biointegration using host self-repair mechanisms avoiding pre-cellularization prior to implantation (off-the-shelf strategy) and ii) the study of vessel remodeling after creation of an arteriovenous fistula.

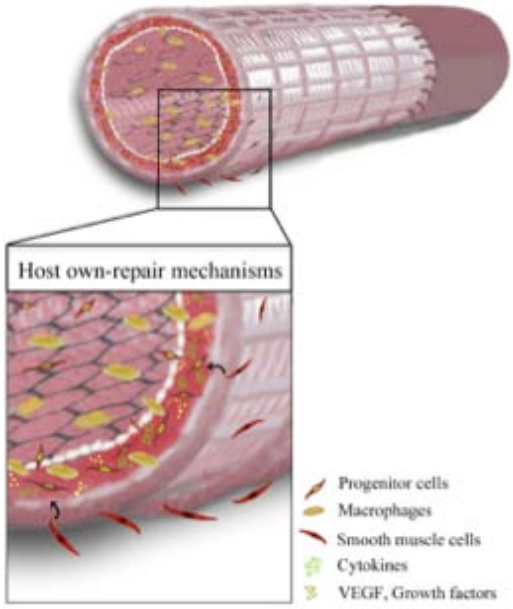

Schéma Patrick Guitton

The off-the-shelf strategy is based on the functionalization of a biodegradable scaffold that will favor the recruitment of progenitor cells, able to synthesize an extracellular matrix that will promote endothelialization. During the first days after implantation, the activation phenotype of macrophages is of major importance: indeed, after recruitment in the implantation site, the monocytes undergo maturation into macrophages. Depending on the microenvironmental cues, they can adopt a large spectrum of activation phenotypes, classified in two main subsets: i) classically activated macrophages, recruited by the chemokine CCL2 due to membrane CCR2 expression, enter tissues 48h-72h after injury, clear dead cells and cell debris and release reactive oxygen species and pro-inflammatory cytokines; ii) in contrast, alternatively activated macrophages produce anti-inflammatory cytokines, secrete growth factors, stimulate angiogenesis and tissue remodeling. There appears to be a delicate balance, where excessive macrophage infiltration can lead to neovessel occlusion, whereas complete macrophage inhibition impedes development of a well-formed layered vascular neotissue. Therefore, published results suggest that macrophages play a critical role in orchestrating tissue remodeling via a paracrine mechanism.

As in the case of vascular substitution, vessel remodeling is an essentiel step after the creation of an arteriovenous fistula (AVF). Indeed, between 20 and 40 % of AVF fail to mature due to a wrong remodeling and therefore cannot provide vascular access for dialysis, often leading to the use of sub-optimal access solutions. The mechanisms that control the vein maturation towards success or failure remain only partially understood. It is therefore of great interest to understand the mechanisms of vascular remodeling and the physiopathological pathways that determine AVF maturation success or failure.

Bone regeneration

A developing area in tissue engineering is the use of human Amnion Membrane (hAM), as this tissue is described to have anti-inflammatory and anti-fibrotic properties, with no graft rejection. Therefore, hAM emerges as a possible scaffold for bone regeneration in critical bone defects. It is supposed that, during the wound healing process, hAM could modulate mechanisms involved in innate immunity control by acting on the kinetics, the cell recruitment efficiency and the cell phenotypes in the bone defect. Indeed, hAM has been used in promoting efficient wound healing in medical contexts such as ophtalmology (dermal burns, non-healing ulcers) and dermatology (corneal disorders). Trophic factors secreted by hAM cells could exert angiogenic, growth promoting, anti-inflammatory and anti-fibrotic effects following transplantation.

Keywords/expertise:

- Tissue-engineering
- Regenerative Medicine
- Inflammation
- Vascular graft
- Bone regeneration
- Neuroinflammation
- Macrophages
- Arteriovenous fistula
- Pre-clinical studies
- In vivo imaging
- Histology
- Immunofluorescence
- Molecular biology
- Technology transfer
- Safety and Hygiene
- CHSCT

Selected publications:

- Oliveira H, Catros S, Boiziau C, Siadous R, Marti-Munoz J, Bareille R, Rey S, Castano O, Planell J, Amédée J & Engel E. The proangiogenic potential of a novel calcium releasing biomaterial: Impact on cell recruitment. Acta Biomater (2015), 29:435-45.

- Mikita J, Dubourdieu-Cassagno N, Deloire M.S.A., Vekris A, Biran M, Raffard G, Brochet B, Canron M-H, Franconi J-M, Boiziau C & Petry K.G. Altered M1/M2 activation patterns of monocytes in severe relapsing experimental rat model of Multiple Sclerosis. Amelioration of clinical status by M2 activated monocyte administration. Mult Scler (2011), 17:2-15.

- Tourdias T, Mori N, Dragonu I, Cassagno N, Boiziau C, Aussudre J, Brochet B, Moonen C, Petry KG & Dousset V. Differential aquaporin 4 expression during edema build-up and resolution phases of brain inflammation. J Neuroinflammation (2011), 8:143 (16 pages).

- Petry KG, Brochet B, Dousset V, Vignes J-R & Boiziau C. Inflammation induced neurological handicap processes in Multiple Sclerosis: New insights from preclinical studies. Review. J Neural Transm (2010), 117:907-17.

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- Brochet B, Dousset V, Deloire M, Boiziau C & Petry KG. MRI to predict severe tissue damage in inflammatory lesions in animal models of multiple sclerosis. Brain (2008), 131:e92.

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- Boiziau C, Dausse E, Yurchenko L & Toulmé J-J. DNA aptamers selected against the HIV-1 TAR RNA element form RNA/DNA kissing complexes. J Biol Chem (1999), 274:12730-12737.

- Boiziau C, Thuong NT & Toulmé J-J. Mechanisms of the inhibition of reverse transcription by antisense oligonucleotides. Proc Natl Acad Sci USA (1992), 89:768-772.

Patents:

- Boiziau C, Vekris A & Petry KG (2011). Procédé d'hybridation soustractive entre deux populations d'acides nucléiques. Patent FR 2952071-A1.

Memberships:

Société Française d'Immunologie**.**

Education:

2000	Hab. à Diriger des Recherches	Université de Bordeaux, France INSERM U386, Bordeaux
1988-91	Ph.D. in Mol & Cell Pharmacology	Université Paris 6, France Muséum National d'Histoire Naturelle, Paris INSERM U201, Paris CJF 90-13, Bordeaux
1985-88	Engineer school	ENSTA ParisTech, France

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