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Research Interests:

Biomaterial as a template for an endothelialized vascular arterial prosthesis

While finishing my master in cell biology and physiology, I worked as a technician in the emergency department of the Blood Transfusion Center in Bordeaux. My daily contact with blood transfusion problems and with banking organs for transplantation, motivated me to prepare a PhD on vascular prostheses while working. My Ph D work was focused on the development of a vascular prosthesis made of polyester coated with an intra-luminal surface of vascular endothelial cells. This work, inspired by Peter ZILLA and co-workers in Deutschland, was focused on endothelial cells and their unavoidable part in the success of such a prosthesis[1, 2]. My Ph D work led me to join in with a preclinical trial of the laboratory INSERM U577 (where I completed my PhD) with the group of Peter ZILLA.

The auto-assembly concept for arterial vascular prosthesis production

Encouraged by the results in my Ph D work, I went to Quebec to continue researching on vascular prosthesis - this time without the assistance of a biomaterial. At LOEX (Laboratoire d'Organogénèse EXpérimentale), I was completely excited by the concept of cells auto-assembly for generation of organ substitute[3]. My work was focused not only on the quality of the endothelium lining the Tissue-Engineered Vascular Blood Vessel (TEBV) produced in the laboratory[4] , but also on the mechanical forces generated by the cells into the construct (i.e. Vascular Smooth Muscle Cells and Fibroblasts)[5,8] to produce a prosthesis with properties similar to its native counterpart. It was also during this period that I familiarized myself with stem cells harvested from the human umbilical cord.

Back to material scaffolds for engineered organs

After I came back to France in 2003, I had the opportunity to compare academic research, when I got hired as Associated Assistant to my Ph D mentor (Pr Laurence BORDENAVE, INSERM U577, Bordeaux University), to the industry where I was later on recruited as an Engineer (Laboratoire d'Evaluation des Matériaux Implantables, Martillac). During this period, I was in charge of scientific project elaboration and Biomaterials teaching (Bordeaux University), and at the same time was managing the progress of European Scientific projects on vascularized bone scaffolds for LEMI company[18]. In 2006, I applied to and was selected for an Engineer position at Bordeaux University.

The potential use of stem cells and the mechanical forces in combination with biomaterials for organ engineering

As an engineer (2006) my first work was to isolate endothelial progenitor cells as potential constituent of vascular prosthesis in place of mature endothelial cells. At the time, according to the available literature, human endothelial cells (EC) could be harvested from bone marrow (BM), peripheral blood (PB) and blood from umbilical cord (UCB). I was in charge of testing these sources and of finding a reproducible procedure to routinely isolate EC: I succeeded with UCB, while the success was only 50 % for PB and 0% for BM. These new EC from UCB were produced, and characterized in comparison with mature EC. As they presented comparable properties, they were used for experiments in place of mature EC[9, 10, 12].

Because of my previous expertise in mechanical properties applied to cells in Quebec, I contributed to the development of devices to apply heamodynamic strength (i.e. shear stress (SS)) to endothelial cells in benches for 2D (i.e. planar materials) and 3D (i.e. tubular conduits) coated with EC[7]. The devices were used to demonstrate that CE seeded onto vascular materials are able to sustain arterial shear stress and to respond in an appropriate behavior. The devices are nowadays used for co-culture experiments.

Then, I worked on the interface between materials and cells: I quantified adhesive contacts to select appropriate peptides able to be grafted on materials[11], I studied spreading and migration [15], modification of cytoskeleton under SS [16] and I analyzed the geometry of the support to guide tubulogenesis[17].

Because of my expertise, I was included in many projects[6, 21] not only in main research work at the laboratory but also in international collaborations with: LOEX (Laboratoire d'Organogénèse EXpérimentale – Québèc – Canada), the Unit for Biotechnology and Bioingeneering at CHUQ (Québèc – Canada), the Institute "Matière Condensée et Nanosciences", at Louvain University (Begium)[19], the Institute of Physiology (Academy of Sciences – Prague – Czechoslovakia)[23] and the Biomedical Imaging center of the Institute of Technology (New Delhi – India)[20].

At the same time, I expanded my expertise with stem cells from apical papilla in models of bone reconstruction[24].

The use of new technology for organ morphogenesis: laser assisted bioprinting

For the last few years, BIOTIS has been developing a new method for organ engineering: laser assisted bioprinting. My expertise in cell culture and organ regeneration has therefore been focused on helping with this method : we have tested cells (vascular EC, mesenchymal stem cells, adipose tissue stem cells…) to be printed, as well as biomaterials such as printed hydrogels (alginate, collagen, fibrin glue) and finally molecules (genipin, riboflavin)[13, 14, 22]. From 2014, my work has been focused on morphogenesis of capillary networks for bone application.

Keywords/expertise:

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- Tissue-engineering
- Biocompatibility
- Vascular grafts
- Vascular biology
- Human cell culture
- Stem cells
- Laser assisted biotechnology
- Immunofluorescent technics
- Cell mechanical stress

Selected publications:

1. Beware of commercial human thrombins used to stimulate cultured endothelial cells. **Rémy M**, Bordenave L, Bareille R, Lauroa C, Lefebvre F, Guerin V, Baquey C. Biomaterials, 1995 Feb, 16(3): 193-9.
2. *In vitro* and *in situ* intercellular adhesion molecule-1 (ICAM-1) expression by endothelial cells lining a polyester fabric. **Rémy M**, Valli N, Brethes D, Labrugère C, Porté-Durrieu MC, Dobrova NB, Novikova SP, Gorodkov AJ, Bordenave L. Biomaterials, 1999 Feb, 20(3) : 241-51. Erratum in: Biomaterials 1999 Jun, 20(12): 1151.
3. Tissue engineering of the vascular system: from capillaries to larger blood vessels. L. Germain, **M. Rémy-Zolghadri**, F.A. Auger. Medical and Biological Engineering and Computing, 2000, 38: 232-240. Review.
4. Endothelium properties of a tissue-engineered blood vessel for small-diameter vascular reconstruction. **Rémy-Zolghadri M**, Laganière J, Oligny JF, Germain L, Auger FA. Journal of Vascular Surgery, 2004 Mar, 39(3): 613-20.
5. Tissue reorganization in response to mechanical load increases functionality. Grenier G, **Rémy-Zolghadri M**, Larouche D, Gauvin R, Baker K, Bergeron F, Dupuis D, Langelier E, Rancourt D, Auger FA, Germain L. Tissue Engineering, 2005 Jan-Feb, 11(1-2): 90-100.
6. Investigation of the cytotoxicity of CCVD carbon nanotubes towards human umbilical vein endothelial cells. E. Flahaut, M.C. Durrieu, **M. Rémy-Zolghadri**, R. Bareille, Ch. Baquey. Carbon, May 2006, 44(6): 093–1099.
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8. Mechanical loading modulates the differentiation state of vascular smooth muscle cells. Grenier G, **Rémy-Zolghadri M**, Bergeron F, Guignard R, Baker K, Labbé R, Auger FA, Germain L. Tissue Engineering, 2006 Nov, 12(11): 3159-70.
9. Signal transduction and procoagulant state of human cord blood-progenitor-derived endothelial cells after interleukin-1alpha stimulation. Daculsi R, **Rémy-Zolghadri M**, Grellier M, Conrad V, Fernandez P, Bareille R, Bordenave L. Endothelium, 2007 May-Jun, 14(3): 163-71.
10. Capability of human umbilical cord blood progenitor-derived endothelial cells to form an efficient lining on a polyester vascular graft *in vitro*. Bérard X, **Rémy-Zolghadri M**, Bourget C, Turner N, Bareille R, Daculsi R, Bordenave L. Acta Biomaterialia, 2009 May, 5(4): 1147-57.

11. The effect of RGD density on osteoblast and endothelial cell behavior on RGD-grafted polyethylene terephthalate surfaces. Chollet C, Chanseau C, **Rémy M**, Guignandon A, Bareille R, Labrugère C, Bordenave L, Durrieu MC. Biomaterials, 2009 Feb, 30(5): 711-20.

12. Human progenitor-derived endothelial cells vs. venous endothelial cells for vascular tissue engineering: an *in vitro* study. Thebaud NB, Bareille R, **Rémy M**, Bourget C, Daculsi R, Bordenave L. Journal of Tissue Engineering and Regenerative Medicine, 2010 Aug, 4(6): 473-84.

13. Laser assisted bioprinting of engineered tissue with high cell density and microscale organization. Guillotin B, Souquet A, Catros S, Duocastella M, Pippenger B, Bellance S, Bareille R, **Rémy M**, Bordenave L, Amédée J, Guillemot F. Biomaterials, 2010 Oct, 31(28): 7250-6.

14. Laser-assisted bioprinting for creating on-demand patterns of human osteoprogenitor cells and nano-hydroxyapatite. Catros S, Fricain JC, Guillotin B, Pippenger B, Bareille R, **Rémy M**, Lebraud E, Desbat B, Amédée J, Guillemot F. Biofabrication, 2011 Jun, 3(2): 025001.

15. Peptide immobilization on polyethylene terephthalate surfaces to study specific endothelial cell adhesion, spreading and migration. Lei Y, **Rémy M**, Labrugère C, Durrieu MC. Journal of Material Science: Material in Medicine, 2012 Nov, 23(11): 2761-72.

16. Impact of peptide micropatterning on endothelial cell actin remodeling for cell alignment under shear stress. Chollet C, Bareille R, **Rémy M**, Guignandon A, Bordenave L, Laroche G, Durrieu MC. Macromolecular Bioscience, 2012 Dec, 12(12): 1648-59.

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19. Polyethylene terephthalate membrane grafted with peptidomimetics: endothelial cell compatibility and retention under shear stress. **Rémy M**, Bareille R, Rerat V, Bourget C, Marchand-Brynaert J, Bordenave L. Journal of Biomaterials Science, Polymer Edition, 2013, 24(3) : 269-86.

20. A novel route to polycaprolactone scaffold for vascular tissue engineering. Patra S., **Rémy M**, Ray AR, Brouillaud B, Amedee J, Gupta B, Bordenave L. Journal of Biomaterial and Tissue Engineering, 1013, (sous presse).

21. Interspecies differences with in vitro and in vivo models of vascular tissue engineering. **Rémy M**, Durand M, Menu P, Voegel JC, Ponsot JF, Bérard X, Harmand MF, Bordenave L. Biomaterials. 2013 Dec;34(38):9842-52

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23. The gene expression of human endothelial cells is modulated by subendothelial extracellular matrix proteins: short-term response to laminar shear stress.Chlupac J, Filova E, Havlikova J, Matejka R, Riedel T, Houska M, Brynda E, Pamula E, **Rémy M**, Bareille R, Fernandez P, Daculsi R, Bourget C, Bacakova L, Bordenave L. Tissue Eng Part A. 2014 Aug;20(15-16):2253-64.

24. In vitro assessment of a collagen/alginate composite scaffold for regenerative endodontics. Devillard R, **Rémy M**, Kalisky J, Bourget JM, Kérourédan O, Siadous R, Bareille R, Amédée-Vilamitjana J, Chassande O, Fricain JC. Int Endod J. 2015 Dec 9.

Patents:

Brevet provisoire aux Etats-Unis (2003): *"Method for isolating umbilical cells"* **Rémy-Zolghadri M.**, Hayward C.J., Auger F.A., Germain L.

Brevet déposé aux Etats-Unis: *"Method for Improving Functionality of Tissue Construct"* **Rémy-Zolghadri M.**, Grenier G., Larouche D., Germain L., Auger F.A.

Brevet français FR1054404 du 4 Juin 2010. « *Nouveaux substituts vasculaires biodégradables* **».** Bordenave L, David L, Montembault A, **Rémy M.**

Book Chapters:

Mesenchymal Cell Culture : Blood vessels Germain L., **Rémy-Zolghadri M.**, Auger F.A. In Methods of Tissue Engineering, edited by Anthony Atala and Robert Lanza, Academic Press, 2002, Chapter 28: 359-370.

A Truly New Approach for Tissue Engineering : The LOEX Self-Assembly Technique Auger F.A., **Rémy-Zolghadri M.**, Grenier G., Germain L. In Stem cell Transplantation and Tissue Engineering, Ernst Schering Research Foundation, Workshop 35, edited by A. Haverich and H. Graf, Springer Verlag. 2002, 73-88.

Teaching Activities:

2006-2015	Coordinator in the Master "Biomatériaux et Dispositif Médicaux" (BiDiM) - Mention Biologie-Santé – Master in Sciences et Technologies.
2011-2015	Responsible de 3 Unités d'Enseignements du master BiDim
2009-2011	Organisatrice for the laboratory des Ateliers pour la Fête de la Science.

Education:

1993-99	Ph D Biologie-Santé	Université Bordeaux 2, France INSERM Unité 577 – Biomatériaux et réparation Tissulaire
1990	DEA Biologie-Santé	Université Bordeaux 1, France. Loboratoire CNRS - Immunologie des Invertébrés
1987-89	Maîtrise Biologie cellulaire	Université Bordeaux 1/2, France
1986	DEUG Sciences de la vie	Université Bordeaux 1, France
1985	BTS Sc. Biologiques-biochimiques	Université d'Angers, France