Cardiovascular biomaterials and nanotools

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Cardiovascular biomaterials and tissue engineering

**Fucoidan**
from brown seaweeds
Poly(L Fucose) + sulfate groups

**Dextran**
Poly (α 1,6 glucose)

**Pullulan**
Poly (α 1,4 et α 1,6 glucose)

Polysaccharides + STMP (sodium trimetaphosphate) → 3D scaffold

Bone tissue engineering
Skin tissue engineering
3D cell culture

IMMATIS (IMplantable MAtrix and TISsue) Start-up

2 Patent applications (PCT 2009)
Adv Funct Mater (2008); Biomaterials (2010); Advanced Mater (2011)
Nanotools for imaging and treatment of atherothrombosis

Development of new ligands to image atherothrombosis

Fucoidan, a sulfated polysaccharide, interacts with P-selectin (Kd 0.3 nM)

Fucoidan coated USPIO allows MRI of aneurysmal thrombus

Fucoidan binds to $^{99m}$Tc to visualize heart ischemia, aneurysmal thrombus and endocarditis with SPECT

• Strategy

  Fucoidan with $^{99m}$Tc for GMP production in SPECT imaging and human clinical trial

Key refs

• Patent 2012: EP2416806
• J Nucl Med. 2011
• Chem Commun. 2011

Staff & Collab

• Algues & Mer; Guerbet
• IFR 02; Team 1 (platelets) Team 4 (imaging)
• P Saboural (Ph.D Student)

Funding

• FUI 11/OSEO/Medicen: 400 K€
• FP7 large scale 2012: 9 800 K€ (DL)
Nanotools for imaging and treatment of atherothrombosis

**Imaging**

**Nanotools**: polysaccharide or copolymer platforms for Ultrasonography

**In vivo**: elastase model of aneurysm on rat

**Treatment**

**Acute ischemic stroke**

**Drug**: tPA - fibrinolysis but bleeding risk

**Nanotools**: improve tPA furtiveness, targeting

**In vivo**: thrombi on mice

• **Strategy**
  - **Coated** systems with fucoidan for P-selectin targeting
  - **Loaded** targeted systems with PFOB for molecular imaging of aneurysmal thrombus

Collab with Team 1

In vivo intravital fluorescent microscopy

• **Strategy**
  - **Loaded** nanotools with tPA for thrombolytic activity without systemic bleeding risk

**Key refs**
- Patent 2012: WO2012028623
- Biomaterials 2010

**Staff & Collab**
- Bracco; nanoPET Pharma
- NanoAthero : 16 partners / 9 countries
- I. Baldi (ATER) & M. Derkaoui (Postdoc)
- T. Bonnard & B. Li (Ph.D Students)

**Funding**
- FP7 large scale 2012: 9 800 K€ (DL)
- ANR Emergence 2012: 200 K€ (CC)
Nanotoools: polysaccharide or copolymer platforms for Ultrasonography

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  - Loaded targeted systems with PFOB for molecular imaging of aneurysmal thrombus

Acute ischemic stroke
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Nanotoools: improve tPA furtiveness, targeting

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• Strategy
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Funding
Coordinators:
- FP7 large scale 2012: 9 800 K€ (DL)
- ANR Emergence 2012: 200 K€ (CC)
Magnetic nanoparticles interacting with living systems

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Cell microvesicles – multifunctional drug carriers inspired by nature

Encapsulation of drugs

- m-THPC
- TPCS2a
- Doxorubicine
- Tissue plasminogen activator (tPA)

Encapsulation of nanomaterials

- Iron oxide 9-nm nanoparticles
- Iron oxide 18-nm nanocubes
- Gold 5-nm nanoparticles
- Dimers gold / iron oxide 16-nm nanoparticles
- Quantum Dots
Cell microvesicles – multifunctional drug carriers inspired by nature

Encapsulation of drugs

- m-THPC
- µmagnet
- Doxorubicine

Encapsulation of nanomaterials

- Tissue plasminogen activator (tPA)

[Silva et al, Nanomedicine, 2012]

[Silva et al, Nanoscale, 2013]
Cell microvesicles – multifunctional drug carriers inspired by nature

Consortium setting with:

Seppo Vainio (University of Oulu, Finland)
Hadi Valadi (University of Gothenburg, Sweden)
Benedetta Bussolati (University of Torino, Italy)

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The life cycle of nanomagnets in the body

Optical birefringence signal induced by an external magnetic field

Interactions with proteins

Aggregation

Nanoparticle

Transformation, degradation, recycling and clairance

Cell internalisation

Mice tissues:
High-resolution TEM (imaging, diffraction, EDX chemical mapping) + Magnetization measurements

Lartigue et al, ACS Nano. 2013
Lévy et al, Biomaterials, 2011
Lévy et al, Nanoscale, 2011
Lévy et al, Contrast Media and Molecular Imaging, 2012

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Magnetic hyperthermia

Exposure to the alternating magnetic field (3x 30 min, 110 kHz, 24 kA/m)

Infrared camera monitoring

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