

Nanomedicine and Nanotechnology in Health Care

July 25-27, 2016 Bangkok, Thailand

Targeted nanoparticles for multimodal molecular imaging in mouse model of atherosclerosis

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Cardiovascular diseases are the first cause of sudden deaths worldwide. The majority of them are due to a condition called atherosclerosis, an inflammatory disease of large and medium arteries, resulting in the build-up of atheroma plaques from circulating cholesterol. These plaques evolve under the combined influence of soluble (cytokines) and cellular (macrophages, platelets, etc.) factors. It is their rupture into the blood flow that causes the potentially lethal ischaemic accidents. The diagnosis of rupture-prone atheroma requires high resolution molecular imaging. Human antibodies (HuAbs) specific for the atheroma lesions have previously been selected by phage display biotechnology. TEG4 HuAb is a promising candidate due to its targeting of activated platelets (integrin $\alpha\text{IIb}\beta 3$), highly represented within the plaque. Single chain Fragment variable (scFv) fragments were processed from the selected phage-HuAbs and produced in *Pichia pastoris*. They were then used to functionalize original nanoparticles (NP), designed for multi-modal imaging, in a regio-selective way to preserve their activity. This was proven by immunohistochemistry (IHC) studies on murine, rabbit and human lesional tissue rich in platelets. Moreover, when multiple copies of scFv fragments were grafted to NPs, kinetics of binding as assessed by Surface Plasmon Resonance (SPR) analyses on integrin $\alpha\text{IIb}\beta 3$, showed a gradual increase in avidity. The same was true regarding the intensity of atheroma plaque recognition in IHC. Encouragingly, when injected into animal models of the pathology (ApoE^{-/-} mice), the multi-targeted objects bound to the lesions *in vivo*, allowing for near infrared fluorescence (NIRF) and magnetic resonance imaging (MRI) of the atheroma plaque.

Biography

Melusine Lariviere started her PhD in 2014 at the Bordeaux University, in collaboration with the Monash University (Australia), where she spent a year in the frame of the project. The topic she is investigating is the "targeting of atheroma plaque with human antibody fragments for molecular imaging in a mouse model of the pathology". She also received in 2014 the title of Doctor of Pharmacy (PharmD) from the Bordeaux University and a Master (MSc) in Biotechnologies from the Limoges University in 2013. Her current research interests include antibodies production and their engineering as targeting probe for translational *in vivo* imaging.

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