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Theranostic of atherosclerosis using human antibody-targeted multi-modal nanoparticles for *in situ* drug delivery

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Atherosclerosis is the leading cause of death in the world. This pathology is an inflammatory disease that results from an initial activation of the endothelial cells with further enhancement of oxidative stress, lipid and leucocyte recruitment. The lesions evolve to vulnerable plaques presenting large lipid cores covered by a thin fibrous cap at high risk of rupture and thrombi formation, thus precipitating the clinical conditions of stroke and myocardial infarction. Nowadays, there is an increasing interest in developing theranostic approaches combining molecular imaging and *in situ* drug delivery. Targeting the cellular and molecular components that underlie the risk of rupture is the stepping-stone for efficient imaging of vulnerable plaques and personalized therapy. Here, human antibodies (HuAbs) selected by *in vivo* phage-display in animal models are proposed as targeting ligands to functionalize nucleolipid-based nanoparticles loaded with iron oxide and drugs for Magnetic Resonance Imaging-guided therapy of atherosclerosis. HuAbs are mandatory for repeated use in humans in order to minimize immunogenic reactions. There is currently substantial interest to design HuAbs targeted nanoparticles with the aim of a direct translation into the clinic. Thanks to *in vivo* phage-display technology, the HuAb candidates have been selected for their targeting capabilities in the context of the pathology and have the potential to gain insight into the most relevant targets over-expressed in the disease by mass spectrometry analysis of immunoprecipitated antigens. In fine, efficient drug encapsulation may allow *in situ* drug delivery, which provides main advantages over systemic administration, avoiding for example potential deleterious side effects.

Biography

Gisele Clofent-Sanchez is currently a Director of Research in Bordeaux University (France). She is head of the "Molecular Targeting of Atheroma" group. She obtained her PhD in Immunology and Molecular Biology from the University of Montpellier in 1989. She became a permanent researcher in 1992 in the laboratory of Alan Nurden into the field of platelet immunology. She moved to translational approaches in atherosclerosis in 2003 and has acquired expertise in *in vivo* phage-display. Her team works on the selection of human antibodies recognizing molecules in the pathological context, for their transfer in potential diagnostic and/or therapeutic agents.

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