



Background: Atherosclerosis is the leading cause of cardiovascular diseases worldwide. One of the hallmarks of atherosclerosis is the accumulation of smooth muscle cells (SMCs) in the intima, while undergoing complex changes i.e. a switch from a contractile to a synthetic phenotype that refers to structural and functional changes. SMCs exhibit a remarkable plasticity depending on environmental cues/signals, even acquiring pro-inflammatory properties.

We have a longstanding experience in the implication of SMC heterogeneity in atherosclerosis and restenosis. We work with porcine coronary artery SMCs in culture and thanks to this experimental model, we identified the S100A4, a calcium-binding protein, as a marker of intimal SMCs, in both pig and human. We are currently investigating the role of S100A4 in the phenotypic modulation of intimal SMCs in vitro and in vivo.

Project: S100A4 exhibits intra- and extracellular functions. The role of S100A4 in SMC plasticity in atherosclerosis is still fairly unknown, as well as the mechanism by which it is secreted to medium. To address these questions, the project will consist in (1) in vitro, by using the CrispR-Cas9 approach, and recombinant specific antibodies, followed by biochemical and imaging analysis, and/or (2) in vivo, through the generation of a SMC-targeted mouse model, in which atherosclerosis will be developed.

Techniques: cell culture, transfection, immunofluorescence, fusion protein, confocal microscopy, western blotting, animal experimentation.

References:

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- ✓ Bochaton-Piallat ML, Bäck M. Novel concepts for the role of smooth muscle cells in vascular disease: towards a new smooth muscle cell classification. *Editorial. Cardiovasc. Res.* **2018**. 114:477-480.
- ✓ Allahverdian S, Chaabane C, Boukais K, Francis GA, Bochaton-Piallat ML. Smooth muscle cell fate and plasticity in atherosclerosis. *Cardiovasc. Res.* **2018**. 114:540-550.

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