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Targeting intraplaque angiogenesis : imaging and therapeutic interventions

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Targeting Intraplaque Angiogenesis: Imaging and Therapeutic Interventions

Fabiana Baganha Carreiras, May 28th of 2020

- 1.** For long, intraplaque angiogenesis and haemorrhage have not received attention in studies on atherosclerotic plaque destabilisation due to the lack of good animal model to study this phenomenon. (*this thesis*)
- 2.** Atorvastatin is more than a lipid lowering drug. (*this thesis*)
- 3.** By targeting the vicious cycle between intraplaque angiogenesis, intraplaque haemorrhage and inflammation in advanced atherosclerotic lesions, PCmAB is a promising candidate as a plaque stabilizing compound. (*this thesis*)
- 4.** Since clinical available imaging techniques to study plaque angiogenesis and intraplaque haemorrhage do not have sufficient spatial resolution, new high-resolution imaging techniques are required to visualize the detailed microvessels network in small size animal models. (*this thesis*)
- 5.** The fact that the number of vasa vasorum was increased 2-fold in vulnerable plaques and up to 4-fold in ruptured plaques compared with stable plaques with severe luminal narrowing, supports the important role for intraplaque angiogenesis in human atherosclerosis. (*Virmani et al Atherosclerotic plaque progression and vulnerability to rupture: angiogenesis as a source of intraplaque hemorrhage. Arterioscler Thromb Vasc Biol. 2005;25(10):2054-61*)
- 6.** A multitargeted approach involving selective antiangiogenic agents, along with improved imaging methods for visualizing plaque neovascularization to monitor treatment effects, will likely be required to prevent plaque progression and its clinical consequences. (*Kolodgi et*

al. Elimination of neoangiogenesis for plaque stabilization: is there a role for local drug therapy? J. Am. Coll. Cardiol. 2007;49(21):2093-101)

- 7.** CD163⁺ macrophages exert deleterious effects on atherogenesis, despite their anti-inflammatory profile. (*Pourcet et al. Alternative macrophages in atherosclerosis: not always protective! J Clin Invest. 2018;128(3):910-912.*)
- 8.** The combination of anti-angiogenic and anti-inflammatory therapies represent the future clinical regimens for long-term treatment of atherosclerosis, and prevention of plaque rupture. (*this thesis*)
- 9.** Future anti-angiogenic therapies in atherosclerosis should focus on restoring or maintaining microvessel integrity, and in that way, directly reducing intraplaque haemorrhage. (*this thesis*)
- 10.** With SARS-CoV-2 entering the pulmonary cells via ACE-2, cells may become depleted of ACE-2 at their surface, and consequently lacking ACE2 as a guardian to inactivate the ligands of bradykinin receptor type 1, the lung environment is prone for local vascular leakage leading to angioedema. (*van de Veerdonk F. et al. Kinins and Cytokines in COVID-19: A Comprehensive Pathophysiological Approach. Preprints 2020, 2020040023*)
- 11.** Imagination is more important than knowledge. For knowledge is limited, whereas imagination embraces the entire world stimulating progress, giving birth to evolution. It is, strictly speaking, a real factor in scientific research. (*Einstein A., Cosmic Religion: with other Opinions and Aphorisms, Covici-Friede, 1931*)
- 12.** An experiment is a question which science poses to Nature and a measurement is the recording of Nature's answer. (*Planck M., The Meaning and limits of Exact Science, Science 1949;110:2857:325.*)
- 13.** *Macacos me mordam.* (Typical Portuguese saying: "Monkeys are biting me.")