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Intraplaque angiogenesis and therapeutic targeting of angiogenesis

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Stellingen behorend bij het proefschrift getiteld:

Intraplaque angiogenesis and therapeutic targeting of angiogenesis

Laura Parma, October 15th 2020

1. The two faces of angiogenesis: essential for physiological tissue repair but also a hallmark of pathological conditions (*this thesis*)
2. Pathological angiogenesis and inflammation are two intertwined processes that fuel each other leading to atherosclerotic plaque instability. (*this thesis and Herrmann J. et al. Angiogenesis in atherogenesis. Arterioscler Thromb Vasc Biol. 2006;26(9):1948-1957.*)
3. The accelerated atherosclerosis vein graft model not only highly resembles human advanced atherosclerotic plaques but also fulfils the need of a model for impatient researchers. (*this thesis*)
4. A successful therapy to stabilize advanced atherosclerotic lesions should decrease the number of neovessels as well as increase their structural maturation (*this thesis*)
5. Judicious application of antiangiogenic agents could prune and normalize immature intraplaque blood vessels, thereby preventing intraplaque haemorrhage. (*Sedding DG et al. Vasa Vasorum Angiogenesis: Key Player in the Initiation and Progression of Atherosclerosis and Potential Target for the Treatment of Cardiovascular Disease. Front Immunol. 2018;9:706*)
6. A sprouting blood vessel is like a car that requires an engine to drive. If the engine of the sprouting blood vessel, the EC metabolism, is jammed the angiogenic blood vessel will no longer be able to drive. (*Li, X. et al, Hallmarks of Endothelial Cell Metabolism in Health and Disease. Cell metabolism 2019, 30, 414-433*)
7. Combination therapy in advanced atherosclerotic plaques using two or more inhibitors with differing mechanisms of action is essential to achieve maximal therapeutic effect. (*Libby P, Everett BM. Novel Antiatherosclerotic Therapies. Arterioscler Thromb Vasc Biol. 2019;39(4):538-545*)
8. For local therapy to increase plaque stabilization it is essential to be able to identify rupture-prone lesions (*Kolodgie FD et al, Elimination of neoangiogenesis for plaque*

stabilization: is there a role for local drug therapy? J Am Coll Cardiol. 2007;49(21):2093-2101.)

9. The regulated A-to-I editing of MicroRNAs in neovascularization reveals that protein expression is regulated at yet another level and that the dogma DNA transcription and subsequent mRNA translation is too simplistic. (*van der Kwast RVCT... Parma L, et al. Adenosine-to-Inosine Editing of MicroRNA-487b Alters Target Gene Selection After Ischemia and Promotes Neovascularization. Circ. Res. 2018;122(3):444-456*)
10. In theory, there is no difference between theory and practice. But, in practice, there is. (*Unknown*)
11. Above all, don't fear difficult moments. The best comes from them. (*Referred to the ups and down of a PhD journey*) (*Rita Levi-Montalcini. "The Life and Work of Dr. Rita Levi-Montalcini." Hirsch, Elana, 2015.*)
12. I am among those who think that science has great beauty. A scientist in her laboratory is not only a technician: she is also a child placed before natural phenomena which impress her like a fairy tale. (Adapted from *Marie Curie. "Madame Curie : A Biography." Eve Curie Labouisse, 1937.*)