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## Targeting glycolysis in endothelial cells to prevent intraplaque neovascularization and atherogenesis in mice

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## **Stellingen behorend bij het proefschrift getiteld: Targeting glycolysis in endothelial cells to prevent intraplaque neovascularization and atherogenesis in mice**

1. Without animal models it would be very difficult to gain detailed insight into the molecular mechanism of atherosclerotic plaque vulnerability and develop better therapeutic tools that improve plaque stability. (this thesis)
2. Modulation of EC metabolism offers a new strategy to treat atherosclerotic vessels wall in addition to the known lipid lowering therapies. (this thesis)
3. Partial inhibition of glycolysis impairs neovascularization in atherosclerotic plaques and favours an anti-inflammatory M2 macrophage subtype while suppressing the M1 pro-inflammatory phenotype in vitro. (this thesis)
4. PFKFB3 may represent a novel therapeutic target for preventing vein graft failure since PFKFB3 deletion in endothelial cells reduces intraplaque angiogenesis, lesion size and macrophage infiltration in a mouse model of venous bypass grafting. (this thesis)
5. Formation of intraplaque neovascularization is a crucial factor for plaque progression and destabilization. Therefore inhibition of intraplaque neovascularization is a promising novel approach to decrease the risk of acute cardiovascular events.<sup>1</sup>
6. Manipulation of endothelial cell metabolism represents a new therapeutic option for prevention or stimulation of vessel growth in multiple disorders.<sup>2</sup>
7. Single Cell RNA Sequencing is a powerful and novel approach for improving our understanding of the biological diversity of the cells that make up atherosclerotic plaques.<sup>3</sup>
8. Visualization of intraplaque neovessels network in whole intact tissue provides the anatomical basis for elucidating the role of angiogenesis in atherosclerosis plaques.<sup>4</sup>
9. In every scientist there is this child who always asks himself the reason for things and looks at the discoveries in awe and wonder.
10. There is knowledge and the presumption of knowledge. In Galileo Galilei's words, the former is born from 'sensible experiences and necessary demonstrations', the latter dies with them.
11. Progress is built on things not on words
12. The "Serendipity" relieves the scientist from the fatigue of a sought but missed discovery

Leiden , March 24, 2021.

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