Stellingen behorende bij het proefschrift

'Molecular pathogenesis of Fibulin-4 associated aortic aneurysms'

1. *In vivo* non-invasive molecular imaging of matrix metalloproteinase activity using protease-activatable fluorescent sensors can identify the risk of developing an aortic aneurysm while the aortic dilation itself has not yet appeared. ~ *this thesis*

2. A generalized susceptibility to extracellular matrix defects and secondary inflammation can underlie the co-occurrence of aortic aneurysms and COPD. ~ *this thesis*

3. A subtle genetic defect in the extracellular matrix, in combination with specific lifestyle factors, can predispose to late-onset vascular, pulmonary and atherosclerotic diseases. ~ *this thesis*

4. Increased secretion of TGF-β2 by Fibulin-4 deficient aortic smooth muscle cells plays an important role in thoracic aortic aneurysms and might prove relevant as a therapeutic target or biomarker. ~ *this thesis*

5. Fibulin-4 expression levels can determine the severity of cardiovascular diseases and therefore milder mutations affecting the expression level of the protein should also be considered as potentially pathogenic. ~ *this thesis*

6. "There is no disease more conducive to clinical humility than aneurysm of the aorta" ~ Sir William Osler, Founding professor Johns Hopkins Hospital, 1900

7. "Longevity is a vascular question, which has been well expressed in the axiom that man is only as old as his arteries. The onset of what may be called physiological arterio-sclerosis depends, in the first place, on the quality of arterial tissue which the individual has inherited, and secondarily on the amount of wear and tear to which he has subjected it" ~ Sir William Osler, 1891

8. One of the key things that can be changed to reduce the risk for cardiovascular disease is diet; a diet low in animal products and processed foods, but with plenty of fresh fruits and vegetables, nuts, seeds, whole grains and soy is beneficial. ~ World Heart Federation, Cardiovascular disease risk factors

9. Since modern science is increasingly interdisciplinary, complex and costly, collaborative research activities are required for efficient scientific productivity. ~ *The Impact of Research Collaboration on Scientific Productivity*, Barry Bozeman, Sooho Lee, 2003

10. "The way we communicate with others and with ourselves ultimately determines the quality of our lives" ~ *Unlimited Power: The new science of personal achievement*, Anthony Robbins, 1986

11. "Take up an idea, devote yourself to it, struggle on in patience, and the sun will rise for you" ~ Swami Vivekanand

Natasja W.M. Ramnath, 2014