Cellular and molecular mechanisms of arrhythmias in cardiac fibrosis and beyond : from symptoms to substrates towards solutions

Askar, S.F.A.

Stellingen behorend bij het proefschrift

Cellular and Molecular Mechanisms of Arrhythmias in Cardiac Fibrosis and Beyond:

From Symptoms to Substrates towards Solutions

1. The myofibroblast is responsible for focal and reentrant arrhythmias *in vitro*. (This thesis)

2. Heterocellular fusion between cardiomyocytes and myocardial scar fibroblasts ameliorates fibroblast-induced arrhythmogeneity. (This thesis)

3. Anti-proliferative treatment may have anti-arrhythmic potential in cardiac fibrosis. (This thesis)

4. Phenotypically similar arrhythmicity may be caused by different pro-arrhythmic mechanisms and therefore may call for different anti-arrhythmic strategies. (This thesis)

5. Pro-arrhythmic effects of stem cell therapy *in vitro* warrant caution against increasing the engraftment rate *in vivo* for cardiac regeneration without appropriate counter-measures. (Based on Macia E, Boyden PA, Circulation 2009;119:1814-1823)

6. The expanding knowledge about the various pro-arrhythmic mechanisms of fibrosis urges us to develop future treatments against fibrosis-associated arrhythmias at the level of the common denominator instead of the individual mechanisms. (Based on Karagueuzian HS, Am J Cardiovasc Dis 2011;1:101-109)

7. Myofibroblasts may represent the main target of future anti-arrhythmic therapy in cardiac fibrosis, and genetic modification by adeno-associated virus vectors may be a very suitable dart.
   (Based on Rohr S, Circ Arrhythmia Electrophysiol 2012;5:442-452 and Pacak CA, Byrne BJ, Mol Ther 2011;19:1582-1590)

8. Modulating the vulnerable parameter remains relevant and important for the efficient treatment of arrhythmias in the setting of substrate-oriented therapy. (Based on Rosen MR, Janse MJ, J Cardiovasc Pharmacol:2010; 55:428-437)

9. Anti-arrhythmic drug therapy may antagonize a cardiologist's ego.

10. Een ritmestoornis in een kweekschaaltje is als een storm in een glas water.

11. Mild psychological dysfunction is not only a symptom of pursuing a PhD. Its etiological importance for this pursuit should also be recognized.

12. Het citeren van andermans stellingen voor een promotie is als plaatsnemen in de passagiersstoel tijdens een rijexamen.

S.F.A. Askar
11-12-13