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

Askar, S.F.A.

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**Author:** Askar, Saïd F.A.

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**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 kweekschachtje 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**