Stellingen behorend bij het proefschrift / Propositions as part of this thesis

Cellular models and viral vectors for skeletal and cardiac muscle research

1. Since postnatal cardiomyocytes (CMCs) display very limited proliferation any significant loss of these cells causes alterations in myocardial structure and composition that may lead to cardiac arrhythmias. (This thesis)

2. Specific inhibition of Kir3.1/Kir3.4 and Kir3.4 channel activity is a promising anti-arrhythmic strategy for atrial fibrillation without ventricular pro-arrhythmic risk. (This thesis)

3. Induction of pathological hypertrophy in cultured CMCs results in the prolongation of action potential duration mostly in the phases at which early afterdepolarizations occur. Therefore, *in vitro* models of pathological cardiac hypertrophy can provide novel insights into the mechanisms underlying these type of arrhythmias and help to develop new therapies. (This thesis)

4. In cell-to-cell fusion assays that are based on fusion-dependent gene activation proper design of the reporter gene is crucial. (This thesis)

5. Numerous lines of evidence suggest that nonmyocytes support the growth of myocytes in culture and are important for generating engineered constructs. (Hirt MN, *et al*. *Circ Res*. 2014;114(2):354-367)

6. Genetic modification with viral vectors in general and stable integration of the therapeutic gene into the host cell genome bear concerns with respect to different levels of personal or environmental safety. Among them, insertional mutagenesis by enhancer-mediated dysregulation of neighboring genes or aberrant splicing is still the biggest concern. (Rothe M, *et al*. *Curr Gene Ther*. 2013;13(6):453-468)

7. Because fibroblasts in normal myocardia are literally buried within densely packed cardiomyocytes, a direct investigation of their function in situ is extremely difficult if not impossible to achieve. (Rohr S. *J Cardiovasc Pharmacol*. 2011;57(4):389-399)

8. For tissue engineering, an appreciation of the chemical and mechanical properties of a tissue construct, its interaction with host tissue in the body, the mass transport

requirements for the tissue, and the requirements for manufacturing a construct in an economical way are all important. (Webber MJ, *et al. Ann Biomed Eng.* 2014;[Epub ahead of print])

9. Three important issues in science are: creativity, dedication and open eyes.

10. In experimental science, the absence of an effect does not mean the absence of the effector.

11. *In vitro* is not the brother of *in vivo*, but the stepbrother.

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