Cellular models for fundamental and applied biomedical research

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Stellingen behorend bij het proefschrift

Cellular models for fundamental and applied biomedical research

1. HP1α is the critical link between prelaminA accumulation and the delayed DNA damage response and premature aging phenotype of *Zmpste24*$^{-/-}$ cells. *(this thesis)*

2. iAM-1 is a line of conditionally immortalized atrial myocytes allowing their massive amplification and synchronous differentiation into fully functional cells resembling primary atrial myocytes. *(this thesis)*

3. Conditionally immortalized mouse brown preadipocytes display long-term proliferation capacity and can differentiate into adipocytes with multilocular lipid droplets, high uncoupling protein 1 expression and the response to adrenergic stimulation. *(this thesis)*

4. Allosteric modulation of the K_v11.1 channel efficiently suppresses the proarrhythmic risk of unintended K_v11.1 blockers, raising the possibility to resume the use of medicines previously recalled from the market because of their K_v11.1-related cardiotoxicity and to approve new compounds with fortuitous I_{Kr} blockade effects. *(this thesis)*

5. Cultures of cardiomyocytes can mimic physiological or pathological conditions, making them well-suited for proof-of-concept studies and for developing novel therapeutic interventions for specific cardiac diseases. *[Parameswaran S. et al. Can J Physiol Pharmacol. 2013;91:985-998]*

6. Currently, generating cardiomyocytes by inducing proliferation of existing cardiomyocytes or by reprogramming of non-myocytes in the heart is vastly inefficient. Thus, to enhance cardiac regeneration, it will be important to develop procedures that increase the yield and efficiency of generating new cardiomyocytes. *[Xin M. et al. Nat Rev Mol Cell Biol. 2013;14:529-541]*

7. Doxycycline-induced immortalization (Tet-on system) works as a kind of 'yin and yang' switch, enabling cells to engage in opposite processes: proliferation and differentiation.

8. The development of fully controllable transgenes has enabled the creation of conditionally immortalized cells that can be expanded to clinical quantities in a stable and consistent fashion, yet can be returned to a normal, non-dividing state for therapeutic delivery to the patient. *[Wall IB. et al. Cell & Gene Therapy Insights 2016;2: 391-396]*

9. Thinking is a compulsory course for every PhD candidate to become an expert.

10. Stay Hungry. Stay Foolish. *[Steve Jobs (1955-2011)]* (Never be satisfied by what you have achieved in the past. Be ready to step out of your comfort zone and try new things.)