Optogenetic investigation of cardiac arrhythmia mechanisms

Feola, I.

Stellingen behorend bij het proefschrift:

OPTOGENETIC INVESTIGATION OF CARDIAC ARRHYTHMIA MECHANISMS

1. Prolonged activation of light-gated cation channels produces a depolarizing current of sufficient strength and duration to allow inhibition of excitation. (this thesis)
2. The mechanism involved in the interruption of the anatomical reentry, as described in our study, is based on the temporary inhibition of excitability in only a specific part of the reentrant pathway via optogenetic modification and patterned illumination technology. (this thesis)
3. Interactions between the rotor core and the region of conduction block has important consequences for the dynamical behaviour of the rotors and may result in their stabilization through conversion into anatomical reentry. (this thesis)
4. Localized targeting of rotors in atrial monolayers, by means of optogenetic induction of a conduction block at the site of the rotor core region, only leads to termination if the line of block reaches from the core region to at least one unexcitable boundary. (this thesis)
5. By delivering optical control at the speed (millisecond-scale) and with the precision (cell type–specific) required for biological processing, optogenetic approaches have opened new landscapes for the study of biology, both in health and disease. (Deisseroth K, *Nature Methods* 2011, 8:26–29)
6. Optogenetics allows both excitatory and inhibitory stimuli, as Bacteriorhodopsins and Halorhodopsins induce hyperpolarization (thereby potentially suppressing excitability), while conventional Channelrhodopsins, induce depolarization and therefore can augment excitability. (Gruber A, Edri O and Gepstein L. *Europace* 2018)
7. Spiral waves underlie many natural phenomena, such as vortices in bodies of water, tropical storms like hurricanes, chemical reactions in solutions, and the movement of spiral galaxies. In cardiac tissue, a spiral wave is initiated when a wavefront encounters an inexcitable (for example, refractory) barrier and circulates around it. (Nattel S, Xiong F and Aguilar M, *Nat Rev Cardiology* 2017, 14:509-520)
8. The availability of a disease-specific gene therapy to 'cure' and 'revert' the genetically-determined arrhythmogenic substrate would be a very appealing and innovative approach. (R Bongianino and SG Priori; *Nat Rev Cardiology* 2015, 12: 531–546)
9. Common goals, good communication and trust are the essential ingredients of successful teamwork.
10. You can be anything you want to be, and no one should tell you differently.
11. "I didn't fail 1.000 times. The light bulb was an invention with 1.000 steps." (Thomas Edison, 1879). If we fail and we are able to understand why then we are on the way toward success.

Iolanda Feola,

Leiden, 11 december 2018