

## **Prosthetic Gene Networks for Biomedical Applications**

Since Paracelsus' (1493-1541) definition that the dosing makes the drug the basic treatment strategies have largely remained unchanged. We continue to use a precise prescribed dose of a small-molecule drug, a protein therapeutic or a therapeutic transgene to modulate or complement the activity of a disease-relevant target. However, this treatment concept does neither consider the metabolic dynamics nor the interdependence of the most important pathophysiologies of the 21<sup>st</sup> century such as obesity, diabetes and cardiovascular disorders. Synthetic biology-inspired prosthetic networks may act as metabolic prostheses that provide the dynamic interventions, the immediate pre-disease action and the multi-target capacity required to meet with the treatment challenges of the future. Prosthetic networks consist of synthetic sensor-effector gene circuits that (i) seamlessly operate in implanted designer cells, (ii) constantly sense, monitor and score metabolic disturbances in peripheral circulation, (iii) process OFF-level concentrations of pathologic metabolites, and (iv) coordinate an adjusted therapeutic response in an (v) automatic and self-sufficient manner. We will present our latest generation of synthetic mammalian gene circuits and provide a few examples of prosthetic networks operating in animal models of prominent human diseases to highlight the challenges and impact of synthetic biology on future biomedical applications.

contact: Prof. Dr. Martin Fussenegger

ETH Zurich, Department of Biosystems Science and Engineering, Basel, Switzerland

Tel: +41 61 387 31 60, E-Mail: [martin.fussenegger@bsse.ethz.ch](mailto:martin.fussenegger@bsse.ethz.ch)