

**TITLE OF RESEARCH TOPIC: Regulation of proteins for therapy of mammalian cells based on synthetic biology****Summary:**

Synthetic biology aims to introduce new properties into biological systems. This is particularly interesting for engineering mammalian (human) cells that can be used for cell therapy, such as for cancer immunotherapy. This project will develop new tools that will enable external control of mammalian cells to regulate cellular processes that could be used for therapy. The advantage of regulation of cellular processes based on proteins is a substantially faster response in comparison to transcriptional regulation. This project will take advantage of the expertise of the host lab in coiled-coil-based regulation of biological assemblies and recent spectacular advances in machine learning for protein design that can be harvested for more effective therapeutics.

**Research techniques used:**

Research techniques will include a broad range of techniques in molecular biology, cell biology, biochemistry, molecular modeling, and structural biology. The host lab has excellent equipment that covers the range from atoms to animals, including confocal fluorescence microscopy, high-content microscopy, flow cytometry, biophysical techniques, monitoring cell activation based on luminescence and fluorescence, cryoelectron microscopy. The candidate will have the opportunity to learn a broad range of techniques from experienced researchers that will be excellent for her/his professional development and interdisciplinarity.

**The reason why the topic is innovative:**

The host lab has a good reputation in the field of synthetic biology with an excellent track record in innovative technologies and this project will represent a new advance. The combination of protein design and mammalian cell synthetic biology is innovative since it opens the possibility to achieve a faster and stronger response of cells. Results could be combined with recent innovations in the host lab, such as the use of fully humanized regulators (Rihtar et al., Nat.Chem.Biol. 2023), fast-regulated secretion or membrane presentation of proteins from mammalian cells (Praznik et al., Nat.Comm. 2022), orthogonal coiled-coil regulators in mammalian cells (Lebar et al., Nat.Chem.Biol. 2020) and fast responsive systems based on split proteases and coiled-coils (Fink et al., Nat.Chem.Biol. 2019). This project will have the opportunity to develop a technology that could be translated into therapy in connection with the newly established Centre for Technologies of Gene and cell therapy.

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