di Bernardo

Engineering Synthetic Gene Circuits for Gene Therapy

Synthetic gene circuits offer considerable potential for engineering human cells to perform complex functions for innovative biotechnological and therapeutic applications. However, current approaches are limited by the lack of versatile, scalable and modular molecular components. This project aims to overcome these barriers by engineering a novel class of regulators: i.e. Modular Artificial Dimerizing transcription factors (MADTFs) whose activity is dynamically regulated through interaction with competitive inhibitory proteins (ΔTFs). These DTFs competitively heterodimerize with MAD-TFs preventing their homo-dimerization and thus their function. This dual strategy enables dynamic and reversible regulation of gene expression, establishing a novel technological platform to build synthetic circuits and program cell behaviour. The compact and modular design of MADTFs and ΔTFs not only facilitates their integration into a variety of biotechnological applications but also enhances their potential for clinical translation. Computational modelling and machine learning techniques will be employed to explore the design space of synthetic circuits based on these components, ensuring they meet desired regulatory functions. This framework will guide the experimental implementation of synthetic circuits in human cell lines with applications to gene therapy.

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