SEMS: RESEARCH PROJECT DESCRIPTION

1. Project Background and Description

High Throughput multiplexed CRISPR platform to facilitate drug studies

We have developed a highly accurate, scalable, high throughput CRISPR platform, which has been used for large scale CRISPR knock out and development of CRISPR knock in studies. This unique platform seeds CAS9 stable mammalian cell lines on micro-spots containing multiple sgRNA per spot. An innovative electroporator has been developed to transfect difficult cell lines, with > 70% transfection rate for endothelial cells and fibroblasts. Our automated single cell analysis system enables to analyse individual cells in each spot (of ~100 cells) with great speed and accuracy.
Complex disease's – like Atherosclerosis, Tumours, Auto-immune disease - are treated by a combination of drugs and drug interactions is an emerging field of research. Multiplexed CRISPR- based gene networks can play an essential role in this process, as digital AND ports have been developed enabling to monitor the synergy of (small) molecules on a genome-wide scale. We aim to design a synthetic AND circuit where activation of two digital ports leads to fluorescence. Our platform is - to the best of our knowledge - the only one capable of perfusing (combination of) compounds serially for monitoring addition/negation/synergy genome-wide. Furthermore, this capacity can be used in any mammalian cell of interest.

Aims:
1: Creating the worlds-first high throughput multiplexed CRISPR-based platform
2: Applying this platform to a genome-wide combinatorial screen for drug synergy.

2. Project Scope

Objectives

1. To develop gRNA arrays using plasmids
2. To create dCAS9/dCAS12a stable cell lines using viral methods
3. To apply to an existing HT CRISPR platform for drug studies

3. Desired Skills from the Student

Key skills

1. Cell culturing
2. Working/designing plasmids
3. Creating stable cell lines with lentiviral vectors
4. Affinity to work with microscopes
5. Affinity to work with dispensing robotics.

4. Supervisory Team

Primary: Professor Rob Krams, School of Engineering and Materials Science

Secondary: Professor Pedro Catillas, Medicine and Dentistry