**Bioremediation of the future: Tissue-engineered pseudo-organism with toxin-induced enzyme scavenger activation by micro RNA switches**

*Nina M. Pollak\*A,B,C, Nick R. GlassB,D, Aswathi GopalakrishnanB,D, Justin J. Cooper-WhiteB,D,E, and Joanne MacdonaldA,F*

AGenecology Research Centre, School of Science and Engineering, University of the Sunshine Coast, Sippy Downs, QLD, Australia; BAustralian Institute for Bioengineering and Nanotechnology, The University of Queensland, Brisbane, QLD, Australia; CCSIRO Synthetic Biology Future Science Platform. DUQ Centre for Stem Cell Ageing and Regenerative Engineering, The University of Queensland, Brisbane, QLD, Australia; ESchool of Chemical Engineering, The University of Queensland, Brisbane, QLD, Australia; FDivision of Experimental Therapeutics, Department of Medicine, Columbia University, New York, NY, USA.

**Introduction**

The development of new systems to target environmental pollution is critically important for improved bioremediation. Our group is exploring the production of novel multicellular structures, which can move and sense their environment in an organism-like fashion. These multicellular structures, also called “pseudo-organisms”, are constructed from biological and synthetic hybrid components using a 3D bioprinting approach.

**Methods**

Heart tissue derived from stem cells is used to provide a mechanical pump via synchronized cell contractions that enables movement. In addition, we are engineering the pseudo-organisms to break down toxins in water by ligand-induced activation of an enzyme scavenger. Specifically, RNA interference (RNAi)-mediated gene silencing is being implemented to dynamically control the expression of an enzyme, cytochrome P450 1A2 (CYP1A2).

**Results**

The control of an enzyme with turnover proved difficult, as it requires a more stringent switch than the traditional fluorescent markers. Using established protocols, we showed small but significant fold-changes in CYP1A2 expression of up to 1.8-fold. However, following a new design approach, which took advantage of naturally occurring micro RNAs, we induced fold-changes ranging from 2.9 to 3.3, markedly improving extrinsic user-defined control over the intracellular molecular activation of CYP1A2 enzyme activity.

**Discussion/Conclusions**

Our data is highly significant for improved synthetic control of enzyme production in mammalian systems. We are implementing the system to enable activation of detoxification enzymes in our synthetic tissue engineered multicellular structures. Our approach has potential to develop a modular aquatic detoxification system for industry by offering a mobile scavenging system that is highly specific, yet without harmful side products. Importantly, these pseudo-organisms cannot reproduce and disintegrate in water, representing a unique solution to ethical and social impact deliberations compared to the use of GMOs, which creates new possibilities in water management.

\*Corresponding author: npollak@usc.edu.au