RNA-based Logic Circuits with RNA Binding Proteins, Aptamers and Small Molecules
Technology #16631

Applications

This invention is an RNA-based genetic circuit which can produce antigens or numerous proteins including: therapeutic, cell death, fluorescent, and selection proteins. This technology may be used for a number of applications including, but not limited to, selective stem cell reprogramming or vaccination.

Problem Addressed

Synthetic biology, which has the potential to provide genetic circuits with greatly improved output control over traditional pharmaceuticals, has remained DNA-centered, and genetic circuit design always relies exclusively or partially on transcriptional regulation. However, messenger RNA (mRNA), as a platform for gene transfer, has numerous advantages over plasmid DNA, including the lack of requirement for crossing the nuclear envelope and has negligible risk of genomic integration, making it a significantly safer alternative. However, no control mechanisms have been developed to regulate replicon-based expression. Efforts to engineer post-transcriptional devices based on microRNA, aptamers, or aptazymes have been characterized to have a very low dynamic range and have resulted in devices not suitable for construction of scalable circuits. This technology is the successful construction of synthetic circuits using RNA and RNA binding proteins (RBPs).

Technology

Devices based on RBPs can be easily wired together to create synthetic circuits of various complexities or to interconnect cellular and synthetic signaling pathways. The design to control protein expression includes two translational repressors, L7Ae, which blocks ribosome scanning if placed in the 3' ultrasound region (3'UTR), and a fusion protein MS2-CNOT7. MS2 is another RNA binding coat protein from bacteriophage, MS2, and CNOT7 is a human deadenylase that can efficiently repress translation of mRNA. This platform provides a plug-and-play post-transcriptional regulation framework through an engineered set of diverse regulatory circuits including a multi-input cell type classifier, a cascade, and a two state switch. For instance, the Inventors have designed a circuit that recognizes a microRNA profile that is specific for Hela cells and it only triggers a response if the profile is matched, which if the response includes a pro-apoptotic gene, can selectively induce apoptosis in Hela cells. Tunable expression of RNA agents can also be achieved using aptamers or a cascade and a switch between two different therapeutic agents.

Advantages

- Minimal risk of harmful genomic integration
- Tunable/controllable circuit behavior
Categories For This Invention:
Life Sciences
Research Tools
Other (Research Tools)
RNA
Synthetic Biology
Therapeutic (Synthetic Biology)
Therapeutics
Vaccine

Intellectual Property:
GIC circuits with RNA binding proteins, aptamers and small molecules
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