High-throughput strategies for the generation of RNA-based sensors and controllers

ABSTRACT: Next generation sequencing (NGS) techniques coupled with advances in synthetic biology are transforming the scale and complexity at which bioengineers can design and build new systems. I will describe recent examples in which NGS-based functional assays are being applied to transform our ability to generate tailored RNA-based gene control systems. Synthetic biology has provided many examples of functional RNA molecules that can act as sensors and controllers in living cells. However, scaling the design of new sensing-regulatory RNAs tailored to different systems has remained a challenge in the field. Methods that leverage next generation sequencing have recently been developed to address these scaling challenges. For example, FACS-Seq assays have been developed to measure the activities of hundreds of thousands of functional RNAs simultaneously, allowing for efficient activity optimization and new insight into sequence-structure-function relationships. More recently, we have developed a solution-based sensor selection pipeline that leverages Cleave-Seq assays and a robotics platform to automate and parallelize the process of generating new RNA-based biosensors to small molecule and protein ligands. These advances will be described, along with applications of these tunable sensor-controllers in biological systems.
**BIOGRAPHY:** Christina D. Smolke is Professor, Associate Chair of Education, and W.M. Keck Foundation Faculty Scholar in the Department of Bioengineering and, by courtesy, Chemical Engineering at Stanford University. Christina’s academic research program develops foundational tools that drive transformative advances in our ability to engineering biology. Christina is also Co-Founder and CEO of Antheia, a biotechnology company that leverages advances in synthetic biology, genomics, informatics, and fermentation to transform how we make and discover many of our most important medicines. Her impact in advancing the frontiers of biotechnology has been recognized with numerous awards, including Chan Zuckerberg Biohub Investigator, Nature’s 10, AIMBE College of Fellows, NIH Director’s Pioneer Award, WTN Award in Biotechnology, and TR35 Award.