

BIOENGINEERING

PRESENTS

Synthetic Approaches for Understanding Sequence-Function Relationships



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2101 ENGINEERING V

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ABSTRACT:

A decade removed from the Human Genome Project, much of how the genome directs expression still remains a mystery. Consortia like ENCODE seek to identify functional DNA elements in humans and other model organisms by correlating functional outputs with sequence using genome-wide data sets. Combinations of DNA elements act as codes controlling particular functions like transcription, splicing, localization, and silencing. Deciphering these codes is difficult, as the limited set of natural variants is typically insufficient to control for variables such as sequence composition or element combinations. Proving that particular sequences have causative effects on gene expression requires carefully controlled reverse genetic studies. Conducting such experiments on genome-wide scales is difficult because of our inability to (1) rapidly alter the sequence and context of individual genetic elements and (2) quantify the consequences of thousands of such changes.

Our central vision is to decipher cis-regulatory codes controlling gene expression by scaling reverse genetics experiments to genomic scales using multiplexed measurements of defined synthetic DNA libraries. We will build upon our work developing (1) next-generation gene synthesis technologies and (2) multiplexed reporter assays to (3) systematically determine how sequences governing mammalian gene expression act in concert by doing thousands of controlled experimental tests simultaneously.

BIOGRAPHY:

Dr. Sri Kosuri received his B.S. in Bioengineering at UC Berkeley working with Prof. Adam Arkin on bacterial systems biology in 2001. He received his Sc.D. in Biological Engineering at MIT with Prof. Drew Endy working on systems and synthetic biology of bacteriophage T7 development in 2007. He was the first employee of Joule Unlimited from 2007-2009, and returned to academia as a member of the Advanced Technology team at the Wyss Institute working with Prof. George Church. There he developed large-scale gene synthesis technologies combined with multiplexed measurements based on next-generation sequencing to better understand sequence determinants of gene expression. In 2014, he became an Assistant Professor of Chemistry and Biochemistry at UCLA. Dr. Kosuri was awarded the NIH Director's New Innovator Award in 2014, and was named a Searle Scholar in 2015.