



## SYNTHETIC BIOLOGY AT THE AMERICAN CHEMICAL SOCIETY

*In the standing-room only seminar room at the recent ACS national meeting in San Diego, Dr. Jeremy Minshull of DNA 2.0 and Prof. Jay Keasling of UC Berkeley co-chaired a session that explored the emerging discipline of Synthetic Biology. Three application areas were discussed in the session: Cells as factories, Novel DNA-based chemistries and Biological engineering.*

### Cells as Factories

Dan Santi described how the increasing speed and decreasing costs of synthetic gene-length DNA sequences is contributing to small molecule drug discovery. Design and complete synthesis of ~30 kb polyketide synthase genes has enabled Kosan to create and express new polyketides in E coli. Exchanging specific segments of these huge genes changes the polyketide product in a semi-predictable way, moving the drug discovery effort towards a more hypothesis-driven mode. Jay Keasling showed how his group had used gene synthesis and metabolic pathway manipulation to achieve a million-fold increase in bacterial production of a precursor to the anti-malarial drug artemisinin.

### New DNA-Based Chemistries

Synthetic biology is having a qualitative as well as quantitative impact on biology. Ho Sun Cho described how Ambrx have expanded the genetic code to allow incorporation of non-natural amino acids into proteins, a technology that appears particularly promising in allowing site-specific protein modifications. Ed Driggers continued with this theme, showing how Ensemble Inc has used DNA templates to direct chemical reactions in a solution-based combinatorial chemistry.

### Biological Engineering

Synthetic biologists are also learning from engineers in other disciplines. Justin Gallivan (Emory University) and William Bentley (University of Maryland Biotechnology Institute) described the construction of artificial bacterial "circuits" to sense small molecules or improve the quality of expressed protein. Jeremy Minshull (DNA2.0) showed how traditional engineering analytical methods, coupled with efficient gene synthesis, can be used to effectively modify protein function

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The protease PCSK9 regulates the level of

without resorting to high-throughput screens.

Finally Chris Voigt (UC San Francisco) described his work to understand and manipulate the circuitry of bacterial signaling. By modeling the cell as a set of defined interacting components analogous to an electronic circuit board, Voigt has succeeded in conferring specific behaviors on his bacteria and appears to have made significant progress toward his goal of engineering therapeutic bacteria for treatment of tumors.

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cholesterol in the liver (Rashid *et al.*, Proc. Natl. Acad. Sci. 102:5374)

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