# IMAGINE BioSecurity: Integrative Modeling and Genome-Scale Engineering for Biosystems Security

Katie L. Arnolds[1], Lukas R. Dahlin[1], Jeffrey G. Linger[1], Chao Wu[1], Jianping Yu[1], Wei Xiong[1], Lin Ding[2], Yo Suzuki[2], Cristal Zuniga[3], Karsten Zengler[3], and **Michael T. Guarnieri**[1*] (**Michael.Guarnieri@nrel.gov**)

[1]National Renewable Energy Laboratory, Golden, CO; [2]J. Craig Venter Institute, La Jolla, CA, [3]University of California, San Diego, La Jolla, CA

http://www.nrel.gov/bioenergy/imagine-biosecurity.html

**Project Goal:** The IMAGINE SFA team proposes to establish a design knowledgebase and achieve predictive control in phylogenetically-diverse, DOE-relevant microbes to enable secure biosystems designs while maintaining optimal performance in controlled environments.

**Abstract:** Genetically modified organisms (GMOs) have emerged as an integral component of a sustainable bioeconomy, with an array of applications in agriculture and bioenergy. However, the rapid development of GMOs and associated synthetic biology approaches raises a number of biosecurity concerns related to environmental escape of GMOs, detection thereof, and impact upon native ecosystems. In order to establish a secure bioeconomy, novel biocontainment strategies — informed by a fundamental understanding of systems level governing mechanisms — are needed. We have established the Integrative Modeling and Genome-scale Engineering for Biosystems Security SFA Team (**IMAGINE BioSecurity**) to achieve predictive control of engineered systems to enable secure biosystems design. Our team integrates core capabilities in synthetic and applied systems biology to develop a high-throughput platform for the design, generation, and analysis of biocontainment strategies in industrially-relevant and next-generation biocatalysts. IMAGINE will leverage NREL's metabolic engineering and multi-scale omics capabilities in industrial microbial hosts and unique pilot-scale deployment capacity to expand DOE's knowledgebase into deployment-relevant systems. These capabilities are complemented by expertise in synthetic genomics and genome-scale and community metabolic modeling to enable predictive design strategies for next-generation microbial production platforms. The IMAGINE SFA is establishing an extensive library of biocontainment modules and strains, testing platform, and systems knowledgebase. These outputs will lay the foundation for predictive computational design of biocontainment strategies with enhanced stability and resilience in diverse bacterial and yeast hosts, while maintaining maximal fitness and bioproductivity. Combined, these efforts will reduce the risk associated with deployment of engineered biosystems, ultimately enabling a secure bioeconomy.
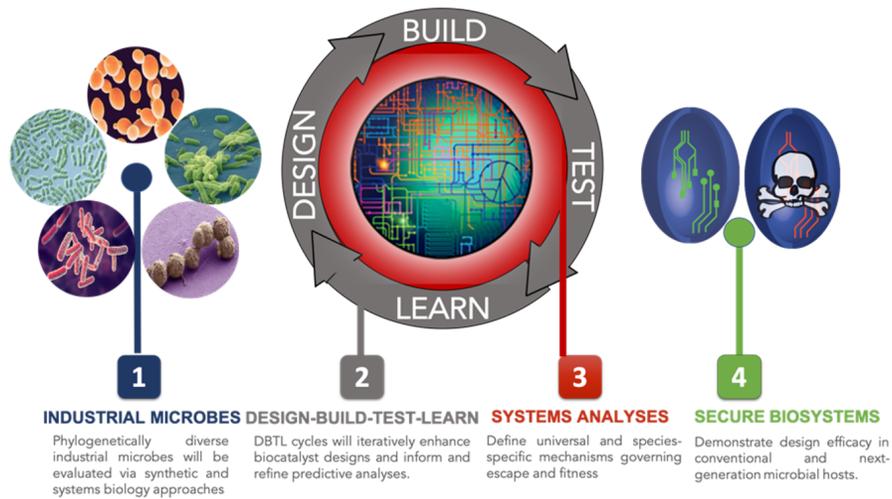
**Figure 1. SFA Overview.** We will evaluate combinatorial biocontainment strategies in diverse microbial hosts (1). Design-Build-Test-Learn cycles (2) and Systems Level Analyses (3) will be iteratively integrated to enable predictive design and generation of biocontainment modules that reduce microbial escape frequency while minimizing metabolic burden. Successful design will be demonstrated in a series of industrial microbes and next-gen biocatalysts (4).