Establishing an Automated High-throughput Screening Platform

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Project Goals:

Automation of molecular biology workflows is accelerating strain development cycles in model organisms; however, such processes have yet to be fully integrated in non-model organisms such as gas-fermenting clostridia. Implementation of automation technology to these organisms has been impeded by the biological limitations in transforming, modifying and screening the organism in presence of anaerobic conditions and toxic flammable gases. As a part of establishing a new interdisciplinary venture, the clostridia Foundry for Biosystems Design (cBioFAB) that combines advancements in cell-free and *Clostridium* engineering metabolic engineering we are developing a fully automated system for strain generation and screening of *Clostridium autoethanogenum*.

Rising levels of greenhouse gases in atmosphere, and resulting instability in climate, pose significant economic and social challenges at a global scale. Technologies that enable capture and conversion of waste gases, such as carbon dioxide and carbon monoxide, into useful product streams can help mitigate negative effects of climate change while enabling a new carbon (neutral) economy. LanzaTech was founded with this mission in mind, and in its fifteen years of existence, it has demonstrated successful conversion of waste gaseous streams into fuels and chemicals (such as ethanol, acetone, isopropanol) at scale and commercialization of gas-to-ethanol production with over 11 million gallons of ethanol produced to date. LanzaTech has, over the past two years, developed a custom built, fully automated strain engineering and screening platform in context of anaerobic conditions and toxic and flammable gases.

Currently, the system is capable of performing fully integrated and automated workflows including transformation, picking colonies, liquid handling operations. This enables us to do automated strain engineering, knock-outs/ins, plasmid introduction and performing high-throughput growth experiments and make and review freezer stock of the resulting strains. The system has a current capacity of screening thousands of strains at a time.

We have validated the capabilities of the system through growth experiments in several different multiwall plate formats, and through testing thousands of strains for various combinatorial libraries for the production of target molecules such as acetone, butanol, 3-hydroxybutyrate (3-HB), 1,3-butanediol (1,3-BDO) or monoethylene glycol (MEG).

The large amount of generated data is automatically captured in a custom-built LIMS system and feeding into genome scale model and machine learning tools.

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