Using synthetic biology to generate hyper-stable vaccines

Polypeptide vaccines effectively activate human T cells but suffer from poor biological stability, which confines both transport logistics and in vivo therapeutic activity. Synthetic biology has the potential to address these limitations through the generation of highly stable antigenic "mimics" using subunits that do not exist in the natural world. We developed a platform based on non-natural chemistry and used this platform to reverse engineer entirely artificial T cell agonists that immunogenicity more than 5-fold of their natural blueprints. This non-natural chemistry is highly stable in human serum and gastric acid. In vitro, these synthetic agonists expanded antigen-specific responses against multiple epitopes across multiple viruses. In vivo, synthetic vaccinated mice were protected from lethal challenge. Moreover, the synthetic agonists were immunogenic after oral administration. We have since expanded this technology to other human viruses, including SARS-CoV-2. These proof-of-concept studies highlight the power of synthetic biology to expand the horizons of vaccine design and therapeutic delivery.

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Biography

John Miles is Principal Research Fellow of Molecular Immunology at the Australian Institute of Tropical Health and Medicine, James Cook University, Australia. He is co-director for the Centre for Tropical Bioinformatics and Molecular Biology and theme leader for the Centre for Molecular Therapeutics at James Cook University. Professor Miles is an expert in human immune system monitoring and modulation, where he has published 117 papers (h-index 44 and 6,700 citations), I am in the 100th percentile in percentile by my worldwide Topic of Cluster Prominence in my field of T cell biology.

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