APPLYING SYNTHETIC BIOLOGY AND COMPUTATIONAL BIOLOGY TO ADVANCE BIOLOGICS EXPRESSION PLATFORMS

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After the first approval of a recombinant biopharmaceutical in 1986, Chinese hamster ovary (CHO) cells have been the mainstream workhorse of biologics expression systems . Since then, significant advances have been made in various aspects of CHO cell line development including improvements in transfection, selection, vector design, single cell cloning, and screening. However, vector design traditionally relies upon a fixed plasmid containing a small set of genetic components, many of which are non-optimal for a given molecule or exhibit performance issues, such as epigenetic silencing.

Here we present a biologics expression platform that integrates an extensively characterized CRISPR-engineered CHO host, a library of well characterized genetic parts to control various aspects of the cell, and computational tools for design and analysis of producer cells. Collectively, these genetic and software tools enable fine tuning of heavy chain/light chain expression and exogenous glutamine synthetase expression for selection, machine learning-based codon optimization for increased translational efficiency, and transposase-enabled integration of expression vectors at high copy with long-term stability. In conclusion, we demonstrate the potential of integrating synthetic biology and computational biology to advance biologics expression in CHO cells.