ABSTRACT SYMPOSIUM NAME: Bridging the Gaps in Process Development

ABSTRACT SYMPOSIUM PROGRAM AREA NAME: BIOT

TITLE: Engineering in mammalian cells to streamline development of antibodies, antibody-like molecules and other proteins of therapeutic interest

AUTHORS: Jennifer Maynard, Annalee Nguyen, Ahlam Qerqez, Yutong Liu, Kevin Le

INSTITUTIONS: Chemical Engineering, University of Texas at Austin, Austin, TX, United States.

Engineering of antibodies and related receptors is most commonly performed using phage or yeast display, but mammalian cells are used for production. To streamline engineering of these and other membrane bound proteins, we developed a mammalian screening platform which allows for generation of large libraries and selection of variants with desirable characteristics in the manufacturing host. We initially demonstrated that this platform could be used to engineer antibody Fab domains and that it could anticipate issues associated with glycosylation that would be missed by other screening platforms. However, this system appears particularly well-suited to engineering of complex proteins that require mammalian components for folding or function: the mammalian membrane to support folding, post-translational modifications, or accessory proteins. Accordingly, we have used this platform to identify human T cell receptors with sub-nanomolar affinities and increased TCR stability, Fc variants with pH dependent binding to human Fc receptors and heavily glycosylated viral fusion proteins. Finally, we have used this platform to reduce tonic signaling issues in chimeric antigen receptors which may lead to increased persistence *in vivo*.