DEVELOPMENT OF AN *IN SILICO* MOLECULE ASSESSMENT METHOD FOR PRODUCT EXPRESSION

Misha Lazebnik, Genentech
lazebnik.mihael@gene.com
Laura C. Simmons, Genentech

Key Words: computational method, developability, molecule assessment, antibody expression, QSPR

Protein products with expression-related manufacturability problems can present a significant barrier to the clinical and commercial feasibility of a project. Methods to identify and potentially eliminate poor-expressing therapeutic candidates early in the drug development process can simplify process development activities and facilitate platform fit, saving resources, costs and time. Existing experimental methods for screening expression level, such as transient transfection or stable pool yields, either lack the capability to accurately discriminate between candidates and/or they can be time-consuming, resource-intensive evaluations for multiple candidates. An *in silico* method was investigated with the goal of developing a more efficient and precise screening tool for determining expression level of therapeutic candidates. First, a series of homology models were generated for a training set of antibodies (i.e. – a set of representative antibodies that cover a wide range of stable cell line titers) using Molecular Operating Environment (MOE) software [1]. Subsequently, MOE was used to obtain a series of physicochemical properties for these antibodies. Selected properties were then combined into a multiparametric model using partial least squares regression. The resultant mathematical model demonstrated a robust predictive capability using a leave-one-out cross-validation (LOOCV) technique (Fig. 1). In addition, the model allowed for ascertaining the degrees of contribution of individual computed properties to the expression level. The development, evaluation and potential applications of the model will be further discussed.

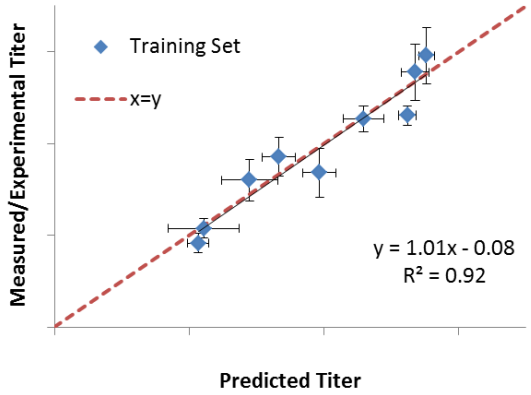

Figure 1 –Plot showing the predicted titers estimated using LOOCV versus the experimental titer values.

[1] *Molecular Operating Environment (MOE)*, 2013.08; Chemical Computing Group ULC, 1010 Sherbooke St. West, Suite #910, Montreal, QC, Canada, H3A 2R7, 2017.