Genetic Engineering of Elite Bioproduction Cell Lines

Create new tools for modifying the chemical structure of proteins that are produced by current biomanufacturing technologies to improve the therapeutic action of the manufactured protein.

Sponsor: Precision BioSciences, Inc.
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- Total project (est.): $5,453 K
- Requested TIP funds: $2,712 K

Precision BioSciences aims to develop a genomic engineering tool kit for reprogramming a key biological process that largely determines the yield, quality, safety and cost of monoclonal antibodies and other therapeutic proteins produced with Chinese hamster ovary (CHO) cells. The industry standard cell line, CHO cells are used to make about two-thirds of all glycosylated biopharmaceuticals, which in turn account for about a quarter of all new drugs approved for clinical use. The complex process—known as glycosylation—involves dozens of enzymes and other biomolecules. These enzymes are engaged in linking sugar molecules (saccharides) to various amino acids that make up a protein. The final arrangement of sugars affects the properties of the resultant glycoprotein, including its safety, effectiveness, availability and longevity in the body. Because of challenges in optimizing glycosylation, production of glycoproteins is time-consuming and costly. Achieving precise control of the process in CHO cells would make it far easier to optimize therapeutic proteins so that dosage requirements for some biopharmaceuticals now in the markets could be reduced by as much as 80 percent, according to Precision BioSciences.

Using its technology for cleaving strands of DNA at specific points and inserting new genetic instructions, the company will edit and reprogram multiple genes in a single CHO cell and modify reaction pathways involved in glycosylation to target specific sugars. The novelty and challenge of the project lie in its scope and in manipulating multiple genes in the same CHO cell line without negatively affecting its growth or capacity to produce biopharmaceuticals. Because it is difficult to manipulate the genomes of living mammalian cells, previous attempts to modify glycosylation have been limited to a single gene. In this TIP project, Precision BioSciences aims to optimize a large ensemble of genes and their products. Because CHO cells already are integral to a large segment of the biomanufacturing industry, implementation of process technologies resulting from the project would not require a major overhaul of the industry’s existing infrastructure. More efficient processes also would help to foster the emergence of a competitive generics market for biopharmaceuticals. Knowledge gained in this project is expected to advance the state-of-the-art in genomic engineering and synthetic biology.

For project information:
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