UC San Diego
UC San Diego News Center

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CHO Systems Biology Center Pioneers Efforts to Improve Cell Production of High-Value Pharmaceuticals

With new genomic data, genome editing technologies and systems biology models, researchers work to rationally engineer CHO cells to optimize production of protein-based drugs

Living systems serve as “factories” that manufacture more than $140 billion in protein-based drugs, called biologics, annually. Optimizing these systems, specifically CHO (Chinese hamster ovary) cell lines, to accelerate biologic drug development is a goal of the CHO Systems Biology Center at the University of California San Diego Jacobs School of Engineering. Center researchers are developing new technologies and training the next generation of cell line engineers and systems biology specialists to advance CHO cell engineering research.

CHO cells are the most commonly used cells to produce protein-based drugs for treating cancers, autoimmune diseases and much more. CHO cells are used to make more than half of the top-selling therapeutic proteins on the market today, including Humira, Avastin and Rituxan, to name a few.

Despite their wide use, many researchers still do not have an in-depth understanding of how to control CHO cells to optimize production of high-value pharmaceuticals. For example, the protein yields from CHO cells are sometimes low — a factor that contributes to the high costs of biologic drugs.

The CHO Systems Biology Center is pioneering efforts to address these challenges. The Center brings together an interdisciplinary team of engineers and systems biologists from UC San Diego and Sanford Burnham Prebys Medical Discovery Institute to develop and refine the tools to engineer and optimize CHO cell lines. These efforts will enable Center researchers to control a wide range of properties of biologic drugs — properties that can increase yield and quality and drive down production costs.

“In the hands of innovative cell engineers trained in big data analytics and systems biology, these tools will enable the design of the next generation of CHO cells,” said Bernhard Palsson, director of the Center and Galetti Endowed Chair Professor in the Department of Bioengineering at UC San Diego.

“An aim of this Center is to provide a richer view of the CHO cell, which in the past has been a black box,” said Nathan Lewis, a professor in the Department of Pediatrics at UC San Diego and the Center’s co-director. “We are developing novel techniques and approaches to understand all the processes, reaction steps and molecular players in the cell well enough to rationally engineer the system to optimize production of the desired protein-based drugs.”

State-of-the-art CHO cell engineering toolkit

The Center is home to a plethora of unparalleled cell engineering and systems biology resources that researchers can employ to rationally engineer CHO cells for biopharmaceutical development. These resources include new genome sequencing efforts, which have resulted in the highest quality genome sequences of the CHO cell line, and next-generation genome editing technologies that will facilitate discovery of genes that produce desirable traits in CHO cells.

The Center houses data on a growing library of engineered CHO cell lines to aid cell line engineering efforts. Center researchers are also developing maps of “safe harbor” integration sites — sites in the CHO genome where human genes can be safely inserted to improve protein expression — and sophisticated methods for analyzing and interpreting omic data. They are also working to “clean” up CHO cell lines of contaminants to drive cell production exclusively to the desired proteins.

In addition, the Center is leading international efforts to develop genome-scale metabolic models that will enable researchers to map the biochemical pathways in CHO cells more accurately, completely and in finer detail. “These models are the ‘wiring diagrams’ that can help us understand how all the parts in the cell are put together. Add these models to the other tools we have at the Center and we have a comprehensive toolkit for rationally engineering CHO cells to optimize cell productivity,” Lewis said.

Training the next generation of experts for pharmaceutical industries

The Center provides specialized training for the next generation of biopharmaceutical researchers and leaders. “Here at UC San Diego we are uniquely positioned to train scientists in CHO cell design and expand the CHO cell engineering toolbox. Our research teams at UC San Diego are helping to open an era of rational CHO cell engineering,” Palsson said.

“We are providing a rich environment where students and postdocs can become experts in using these transformative tools, and acquire a novel skill set to address the challenges and needs of pharmaceutical industries,” Lewis said.

The Center is engaging with industrial partners to identify these challenges in order to translate innovations into new solutions for drug development and protein production. The Center offers industrial partners access to state-of-the-art genomics technologies and expertise that enable and accelerate cutting edge pharmaceutical research and development.

Center faculty

Director: Professor Bernhard Palsson, Galetti Endowed Chair, Department of Bioengineering
Palsson is a pioneer in systems biotechnology research and education. He is the Principal Investigator of the Systems Biology Research Group at UC San Diego, where his research focuses on developing methods to analyze metabolic dynamics and constructing models of the human red blood cell, *E. coli*, CHO cells and several human pathogens.

Co-director: Professor Nathan Lewis, Department of Pediatrics
Lewis’s research focuses on building genome-scale models of metabolic pathways to probe the mechanisms of drug development in CHO cells. Lewis serves as the center’s expert in systems biology and genome editing technologies, and is helping lead public CHO genome sequencing efforts.

Professor Prashant Mali, Department of Bioengineering
Mali’s expertise is in the fields of genome engineering and regenerative medicine. He has helped pioneer the development of CRISPR/Cas9, a powerful genome engineering tool with wide applications in both basic biology and human therapeutics.

Professor Christian Metallo, Department of Bioengineering
Metallo specializes in understanding how metabolism contributes to disease. His experience in cancer metabolomics research provides insights into CHO cell metabolism and how it affects the quality of the drug produced.

Professor Vineet Bafna, Department of Computer Science and Engineering
Bafna is a leader in proteogenomics, which involves the use of mass spectrometry data for the annotation of genomes. His research includes developing new tools to analyze complex regions in the genome. Bafna's role in the center involves refining the CHO cell genome and improving the quality of its annotation.

Professor Jeffrey Esko, Department of Cellular and Molecular Medicine
Esko's research focuses on understanding the structure and function of glycans, which are polysaccharide chains that cover the surfaces of cells and play a role in various cell interactions. His expertise is in studying a particular group of glycans, called proteoglycans and glycosaminoglycans. Esko is leading efforts in glycan engineering and research in CHO cell genetics.

Dr. Randal Kaufman, Sanford Burnham Prebys Medical Discovery Institute
Kaufman is a leader in the cell biology of protein folding and secretion and CHO cell engineering. His research into the fundamental processes that regulate protein synthesis and folding provides key insights for understanding genetic diseases that result from protein folding defects. Kaufman is the Principal Investigator and Director of the Degenerative Diseases Program at Sanford Burnham Prebys Medical Discovery Institute.

The CHO Systems Biology Center is one of a series of "agile" research centers launched by teams of faculty at the Jacobs School of Engineering. These centers were established as an initiative by Jacobs School Dean Albert P. Pisano to bring together interdisciplinary groups of researchers and industry partners to address big challenges facing society. Each agile center is built around a coordinated research area such as wearable sensors, extreme events research, visual computing, and sustainable power and energy.

Learn more about the CHO Systems Biology Center at www.jacobsschool.ucsd.edu/cho.

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