Genetically-Encoded Chemically-Modified Peptides as Tools for Ligand and Probe Discovery in Cancer Research

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Genetically-encoded (GE) libraries of proteins and peptides are one of the major mining tools for the discovery of biological drugs and the development of ligands. Selection of a single peptide or protein sequence from a GE-library of billion-scale diversity is a routine technique used in academia and industry for the discovery of biological drugs. However, this technique is often limited to structures made up of only the 20 natural amino acids. Our group uses organic synthesis to produce GE-libraries of peptide derivatives: such as glycopeptides\textsuperscript{1,2b} and macrocyclic peptides.\textsuperscript{2} Chemical modification of these libraries allowed us to develop a Genetically-Encoded Fragment-Based Discovery (GE-FBD) platform,\textsuperscript{3} which combines >10\textsuperscript{8} peptide fragments with variable, silently-encoded modifications.\textsuperscript{4} GE-FBD can be used to identify ligands for “undruggable targets” such as carbohydrate binding proteins,\textsuperscript{3} or cancer-specific proteins such as Nodal. Ongoing challenges also include the discovery of serological biomarkers and ligands that induce differentiation of Cancer Stem Cells (CSS) by binding to CSC-specific extracellular receptors.

To streamline the use of the GE-platform and attack cancer-related problems in molecular recognition, we established the screening service \url{www.48hourdiscovery.com}. Traditionally, molecular discovery is costly financially and time-wise. Complimentary to identifying a target via genomics mining tools; we have the ability to provide the identity of 50 ligands for the discovered target and thus can probe the “drug-ability” of the target. We offer this service to help academia and industry in molecular discovery in the areas of therapeutics, diagnostics and probe development. For some targets, we strive to provide discovery in as few as 48 hours for as little as "cost recovery".
References

Ratmir Derda received his undergraduate degree in Physics from Moscow Institute of Physics and Technology in 2001, Ph.D. in Chemistry from the University of Wisconsin-Madison in 2008, under the supervision of Laura L. Kiessling, and postdoctoral training at Harvard University under the supervision of George M. Whitesides and Donald E. Ingber. He joined University of Alberta in 2011 as an Assistant Professor in Chemistry. In 2012, he became a principal investigator at the Alberta Glycomics Centre. Derda lab develops genetically-encoded libraries to solve fundamental problems in chemical reactivity, molecular recognition and cell differentiation. Notable awards include Rising Star in Chemical Biology from the International Chemical Biology Society (2016); Young Investigator Award from the Boulder Peptide Society (2014); Canadian Rising Star in Global Health (2011).