Cellular Depletion of Biomolecular Targets

Of the ~4,400 Escherichia coli (E. coli) open reading frames, roughly a third have not had their encoded protein functions experimentally verified. This collection of genes creates a significant black box in our understanding of fundamental cellular physiology, especially when considering those genes of unknown function that are essential for viability. Much of what is known about gene function has followed from studies in bacteria where there are suites of powerful tools available that have been refined in model systems such as E. coli. Despite astounding advances in DNA sequencing and synthesis technologies, there is a remaining fundamental question that has piqued the interest of hundreds of investigators: what are the minimal requirements for life? The predominant approaches to answering this question have been to either computationally compare genomes and identify conserved core genes, or to randomly disrupt the genomes using transposons and deduce which genes do not tolerate interruption. These combined strategies form the cornerstone of our understanding of what comprises an essential genome.

Technical Details
This invention focuses on a new method of testing the function and essentialness of certain proteins. By bonding certain peptide tags to pre-selected proteins, the processive protease within the cell targets and degrades the protein of interest. Degradation can be induced by activating the proteolytic activity, either by induction of the protease, induction of an adapter for the protease, or by addition of the protease to mixtures, allowing for the creation of novel cell physiologies. Cells lacking a putative drug target can be generated for comparative studies or for control experiments. Additionally, cell extracts or macromolecular assemblies can be generated that lack a specific component even if that component is necessary for the formation of the original complex.

Looking for Partners
Looking for partners to commercialize for research purposes and test/validate for preclinical use.

UCF Inventor
Sean Moore, Ph. D.

Benefits
• Tests multifunctional proteins more effectively
• Removes second site mutation complications

Applications
• Protein degradation
• Understanding diseases

Tech Fields
Cancer

Keywords
degradation, knockout, proteins

Patent Application Pub. No
US 2012/0214170 A1

ClpX (blue) engages proteins displaying certain peptide motifs (red) and uses the energy of ATP hydrolysis to unfold the protein and translocate it into the lumen of ClpP (green) where it becomes degraded into small peptides.