Quantitative Screening Method for Peptide Identification and Optimization

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Technology description

Researchers at UCSB have developed a novel system and methods that provides efficient display and screening of peptide libraries at the cell surface, and enables rapid and quantitative characterization of the candidate peptides. This system has been demonstrated to especially effective for peptide and microprotein ligand isolation and affinity maturation. Furthermore, this system has been applied extensively to developed optimized peptide substrates for proteases that can serve as activity probes, in vivo imaging agents, and prodrug activation substrates. The method enables rapid construction and screening of very large libraries with high precision and efficiency, providing an effective system to streamline the identification and optimization of binding ligands and substrates.

This new screening system has already been used commercially to develop lead compounds expected to enter clinical trials in 2011.

A novel system and methods that provides efficient display and screening of peptide libraries at the cell surface, and enables rapid and quantitative characterization of the candidate peptides.

Additional Information

Other Information

"Protease specificity determination by using cellular libraries of peptide substrates (CLiPS)" - Kevin T. Boulware and Patrick S. Daugherty -PNAS, May 2006

"Protein engineering with bacterial display" - Patrick Daugherty -ScienceDirect, August 2007

"Bacterial display enables efficient and quantitative peptide affinity maturation" - Sophia Kenrick and Patrick Daugherty -Protein Engineering, Design & Selection, November 2009

Background

Combinatorial library screening and selection methods are common tools for identifying binding ligands, and enzyme substrates or inhibitors. The most widespread technique is phage display, where the target protein is expressed as a polypeptide fusion to a bacteriophage coat and is subsequently screened by binding to immobilized or soluble ligands. Phage display has been successfully applied to antibodies, DNA binding proteins, protease inhibitors, short peptides and enzymes. Nevertheless, phage display possesses shortcomings. For example the nature of phage display precludes quantitative

and direct discrimination of ligand binding parameters, such as quantitative characterization of protease specificity and substrate cleavage kinetics. Additionally, the phage display library selection process involve many laborious and time consuming experimental steps, that can reduce the diversity of ligands and substrates identified during selection.

Application area

Drug discovery (new proteins and peptide-based therapeutics)
Diagnostic (proteins, peptides, antibody biomarkers in human fluids)

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