Quantitative Screening Method for Peptide Identification and Optimization

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OTHER INFORMATION

KEYWORDS

Phage display, Peptide identification, Drug Discovery, indpharma

CATEGORIZED AS

- **Biotechnology**
  - Other
- **Medical**
  - Diagnostics
  - New Chemical Entities, Drug Leads
  - Research Tools
  - Screening
  - Therapeutics
- **Research Tools**
  - Screening Assays

RELATED CASES

2003-460-0, 2006-099-2, 2006-099-3, 2007-778-2

BRIEF DESCRIPTION

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.

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.

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.

APPLICATIONS

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

PATENT INFORMATION

UC Case No. 2003-460: “**Bacterial Polypeptide Display and Isolation Methodologies**” Expression vectors for displaying polypeptides on an outer surface of a biological entity within a carrier protein loop.. U.S. Patent No. 7,256,038, - *U.S. Patent Application Nos. 11/612,757 and 12/653,897*

UC Case No. 2006-099: "**Cell Surface Display Methodology for Determination of Enzyme Specificity and Activity**" Methods for screening a library of cells presenting the candidate peptides in peptide display scaffolds to identify a ligand for an enzyme. *U.S. Patent No. 7,666,817 - U.S. Patent Application No. 12/646,323*

UC Case No. 2007-778: "**Methods and Vectors for Enhancing Cell Display of Peptides and Proteins**" Methods of making and using bacterial display polypeptide libraries to enhance the display of proteins and peptides at the surface of bacteria *U.S. Patent Application No. 12/220,448*

This portfolio is available for licensing on a non-exclusive basis in the field of use of therapeutics, in vivo diagnostics, and prophylactics. The portfolio is available exclusively in all the other fields of use.

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

PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Issued Patent	11078479	08/03/2021	2003-460
United States Of America	Issued Patent	10,041,063	08/07/2018	2003-460
United States Of America	Issued Patent	8,361,933	01/29/2013	2003-460
United States Of America	Issued Patent	7,612,019	11/03/2009	2003-460
United States Of America	Issued Patent	7,256,038	08/14/2007	2003-460

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