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Display technologies: Application for the discovery of drug and gene delivery agents ☆

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Abstract

Recognition of molecular diversity of cell surface proteomes in disease is essential for the development of targeted therapies. Progress in targeted therapeutics requires establishing effective approaches for high-throughput identification of agents specific for clinically relevant cell surface markers. Over the past decade, a number of platform strategies have been developed to screen polypeptide libraries for ligands targeting receptors selectively expressed in the context of various cell surface proteomes. Streamlined procedures for identification of ligand-receptor pairs that could serve as targets in disease diagnosis, profiling, imaging and therapy have relied on the display technologies, in which polypeptides with desired binding profiles can be serially selected, in a process called biopanning, based on their physical linkage with the encoding nucleic acid. These technologies include virus/phage display, cell display, ribosomal display, mRNA display and covalent DNA display (CDT), with phage display being by far the most utilized. The scope of this review is the recent advancements in the display technologies with a particular emphasis on molecular mapping of cell surface proteomes with peptide phage display. Prospective applications of targeted compounds derived from display libraries in the discovery of targeted drugs and gene therapy vectors are discussed.

Keywords: Combinatorial peptide libraries; Vascular cell surface proteomics; Targetomics; Targeted therapies; Display scaffold; Phage display; Viral display; Bacterial display; Yeast display; Cell display; Ribosome display; mRNA display; Covalent DNA display

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1. Introduction

Strategies for identification of druggable disease markers and development of approaches for their ligand-directed targeting are required for drug design. In the first part of this review, we will discuss the development of the display technologies for high-throughput identification of agents targeting cell surface receptors. The second part includes a brief overview of libraries and display scaffolds used in ligand selection for clinically useful ligands, with a particular emphasis on phage peptide display. Finally, we will address current applications of individual display technologies to the emerging field, which we define as "targetomics".

2. Therapeutic needs and "targetomics"

Human disease is often caused and/or associated with alterations in protein expression [1–4]. The evidence for subject-specific heterogeneity in protein expression profile abnormalities illustrates the need for methodology to profile individual patients for disease markers toward personalized treatment [5–7]. Identification of reliable disease markers may enable the design of targeted therapies, as well as approaches to predict clinical behavior of affected tissues in a pathologically indistinguishable (but perhaps biologically diverse and heterogeneous) patient population. These issues are particularly important in considering malignant