Agnes Hajduczki, J Antivir Antiretrovir 2011, 3:4
doi: http://dx.doi.org/10.4172/1948-5964.S1.16

International Conference and Exhibition on
VIROLOGY
5-7 September 2011 Baltimore, USA

Engineering soluble membrane proteins and high-affinity ligands by phage display

Agnes Hajduczki
University of California, USA

Displaying proteins and peptides on the surface of viruses can allow protein engineering, such as affinity maturation of biomolecules. Hydrophobic and aggregation-prone, membrane proteins often prove too insoluble for conventional *in vitro* biochemical studies. To engineer soluble variants of human caveolin-1, a phage-displayed library of caveolin variants targeted the hydrophobic intra-membrane domain with substitutions to charged residues. Anti-selections for insolubility removed hydrophobic variants, and positive selections for binding to the known caveolin ligand HIV gp41 isolated functional, folded variants. Assays with several caveolin binding partners demonstrated the successful folding and functionality by a solubilized, full-length caveolin variant selected from the library. This caveolin variant allowed assay of the direct interaction between caveolin and cavin, an experiment requiring purified proteins. The approach provides a general method for solubilization and engineering of membrane-associated proteins by phage display. In addition, the interaction between caveolin and HIV gp41 served as the starting point for investigating derivatives of the HIV fusion inhibitor peptide T20 (Fuzeon) as potential caveolin ligands. Phage-displayed wild-type T20 provided the scaffold for homolog shotgun scanning libraries for affinity maturation of caveolin binders. The resulting variants have been shown to bind caveolin specifically and with high affinity in both *in vitro* and cellular experiments.

Biography

Agnes Hajduczki has completed her undergraduate studies at the University of California, Los Angeles. She is currently working on her Ph.D. at the University of California, Irvine, in the Department of Molecular Biology and Biochemistry.