Protein binders mimicking surface glycoprotein epitopes recognized by broadly neutralizing antibodies as a new platform for identification of peptide-prints as tools for development of more protective vaccines

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Carbohydrates-based immunogens are generally less effective in generation of long-lasting antibody responses and neutralizing epitopes of surface glycoproteins are poorly immunogenic. Therefore, proteins mimicking glycan epitopes represent a promising alternative for development of more protective vaccines. Highly complex combinatorial libraries derived from scaffolds of small and robust protein domains represent an excellent tool for the identification of protein binders mimicking surface glycopeptide epitopes of viruses or bacteria that are recognized by broadly neutralizing antibodies. We use our established concept of a highly complex combinatorial library derived from scaffold of 46 amino acid albumin-binding domain (ABD) and, in combination with ribosome display, we target broadly neutralizing (bn) IgG to identify unique binding candidates recognizing antigen-binding-domain of the tested bn IgG. In our proof-of-concept study we target glycan epitopes carried by gp120/gp41 protein complex of the HIV-1 Env.ABD variants as potential (glyco)peptide mimetics are currently being characterized for the stimulation of HIV-1 gp120-specific neutralizing antibody response. Thus, ABD-derived recombinant mimotopes could serve as a useful molecular clue for generation of more efficient HIV-1 vaccine and provide a platform for development of other viral or bacterial disease-preventing vaccines. The project was supported by Czech Ministry of Health grant AZV MZ 15-32198A and Czech Ministry of Education, Youth, and Sport grant CEREBIT CZ.02.1.01/0.0/0.0/16_025/0007397.

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Biography
Petr Malý is head of Laboratory of Lipid Engineering at the Institute of Biotechnology, Czech Academy of Sciences in Vestec, Czech Republic. He studied at Department of Biochemistry, Faculty of Science, Charles University in Prague, Czech Republic (1980-1985) and completed doctoral at the Institute of Molecular Genetics ASCR (IMG) in Prague. He spent postdoctoral fellowship (1992-1995) at Department of Pathology and Howard Hughes Medical Institute, The University of Michigan Medical School, Ann Arbor, USA, in the laboratory of Prof. John B. Lowe where he published several substantial papers related to in vivo role of mammalian glycosyltransferases. Since 1998 he was working on development of combinatorial protein libraries derived from small protein scaffolds and construction of novel high-affinity protein binders with therapeutic and diagnostic potential.