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.

Recent Publications

1. Lucie Křížová, Milan Kuchař, Hana Petroková, Radim Osička, Marie Hlavničková, Ondřej Pelák, Jiří Černý, Tomáš Kalina, Petr Malý (2017). p19-targeted ABD-derived protein variants inhibit IL-23 binding and exert suppressive control over IL-23-stimulated expansion of primary human IL-17+ T-cells. Autoimmunity 2017 Mar 19;50(2):102-113.
2. Jan Maly, Ondrej Stanek, Jan Frolik, Marek Maly, Franka Ennen, Dietmar Appelhans, Alena Semeradtova, Dominika Wrobel, Marcel Stofik, Tereza Knapova, Milan Kuchar, Lucie Cervenkova Stastna, Jan Cermak, Peter Sebo, Petr Maly (2016). Biocompatible Size-Defined Dendrimer-Albumin Binding Protein Hybrid Materials as a Versatile Platform for Biomedical Applications. Macromol Biosci 2016 Apr 8;16(4):553-66
3. Lucie Marečková, Hana Petroková, Radim Osička, Milan Kuchař, Petr Malý (2015) Novel binders derived from an albumin-binding domain scaffold targeting human prostate secretory protein 94 (PSP94). Protein Cell 2015 Oct; 6(10):774-9.
4. Milan Kuchař, Lucie Vaňková, Hana Petroková, Jiří Cerný, Radim Osička, Ondřej Pelák, Hana Sípová, Bohdan Schneider, Jiří Homola, Peter Sebo, Tomáš Kalina, Petr Malý (2014). Human interleukin-23 receptor antagonists derived from an albumin-binding domain scaffold inhibit IL-23-dependent ex vivo expansion of IL-17-producing T-cells. Proteins 2014 Jun 23;82(6):975-89.

Biography

Petr Maly is head of Laboratory of Ligand 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 doctorate 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 to 2005 he was a research group leader at the IMG in Prague. As a visiting scientist he also worked at Department of Biochemistry and Molecular Biology, College of Medicine, University of Oklahoma, USA. He also was participating investigator of Consortium for Functional Glycomics (USA, 2001–2008) and Member of Editorial Board (2001-2005) and Editor (since 2003) of the Czech journal "Biologicke listy" (Biological Letters). Since 2008, he has been working on the development of combinatorial protein libraries derived from small protein scaffolds andconstruction of novel high-affinity protein binders with therapeutic and diagnostic potential.

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