SPLIT CORE TECHNOLOGY ALLOWS EFFICIENT PRODUCTION OF VIRUS-LIKE PARTICLES PRESENTING A RECEPTOR-CONTACTING EPITOPE OF HUMAN IgE

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Introduction. Immunoglobulin E (IgE) plays a central role in type I hypersensitivity including allergy and asthma. Novel treatment strategy envisages development of a therapeutic vaccine designed to elicit autologous blocking antibodies against the IgE. We sought to develop an IgE-epitope antigen that induces antibodies against a receptor-contacting epitope on human IgE molecule.

Materials and methods. We produced genetically engineered constructs for bacterial expression of recombinant proteins which were thought to be capable of formation of virus-like particles (VLP). All constructs utilize hepatitis B virus core protein (HBcAg) as a carrier. The VLPs were engineered to present arrays of the receptor-contacting epitope of the human IgE on their surfaces. For this purpose the FG loop from domain Cs3 of human IgE molecule was cloned into a main immunodominant region (MIR) of the HBcAg.

Results and discussion. We produced three variants of the recombinant antigens. The first variant (HBcAg-IgE) has contiguous aminoacid sequence with the insert (FG loop) flanked with long glycine-rich linkers. The second variant (HBcAg-IgE/Cys) has contiguous sequence in which the insert is additionally flanked with adjacent Cys residues, introduced with intention to to impose the beta-hairpin conformation resembling the natural conformation of the FG loop. However, both variants of the IgE-epitope antigens with contiguous sequences did not produce VLPs, probably because of structural incompatibility between the carrier and the inserts. The third variant, namely the split core antigen HBcAg-IgE(SC) is an example of utilization of a novel approach for incorporation of foreign sequences into the hepadnavirus core protein which renders the resulting proteins capable of formation of VLPs. It relies on expression of two parts corresponding to the N- and C-termini of the HBcAg from different ORFs within the bicistronic mRNA. The ORFs are separated by an engineered internal ribosome binding site (iRBS). When applied as a carrier for presentation of the FG loop epitope, the split core HBcAg enabled production of the VLPs with an expected spherical shape and diameter. Immunization with the recombinantly expressed VLPs presenting the Cs3 FG loop epitope resulted in a generation of antibodies recognizing the human IgE.

Conclusions. Further development of this strategy is likely result in a long anticipated panallergy anti-IgE vaccine.

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