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Immunological effects of HIV-1 p24 fusion to murine HSP70 - cellular response-eliciting strategy

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Mammalian and some microbial heat shock proteins (HSP's) have been confirmed as adjuvants appropriate for induction of cell- and antibody-mediated immune responses specific to HSP-complexed or HSP-fused recombinant protein- or peptide-based antigens. The adjuvant effect is associated with HSP ability to activate naive dendritic cells and to support cross-presentation of HSP-associated antigen. Stimulatory potential of HSP is frequently attributed to endotoxin contamination arising either from bacterial expression systems used for preparation of vaccination constructs or from purification procedures. Here we analyzed the immunological effects of depyrogenated recombinant HSP70 and HIV-1 p24 fusion proteins. HIV-1 p24 cDNA was cloned at the 5' or 3' end of murine hsp70 cDNA into prokaryote expression plasmid and recombinant proteins were produced, purified and depyrogenated until each preparation contained less than 2.5 endotoxin unit (EU) per mg of antigen. Final preparations were administered to experimental BALB/c mice. p24 specific cellular and humoral immune responses were measured. In parallel, bone marrow-derived dendritic cells were *in vitro* exposed to hsp70-p24 fusion proteins and hsp70 endocytosis and parameters of activation were determined. The fusion of p24 to hsp70 enhanced endocytosis of p24and activation of dendritic cells *in vitro*. After intradermal immunization of experimental mice with either p24, p24-hsp70, hsp70-p24 or hsp70, hsp70-p24 fusion protein induced strongest p24-specific serum antibody response with substantial proportion of IgG2a and IgG2b isotypes (corresponding to Th1 type) and production of IFN-γ by CD4+ and $CD8^+$ T cells in splenocytes preparations. In contrast, p24-hsp70 or p24 itself induced weaker humoral and cell-mediated immune responses.

Biography

Raska M has completed his PhD from Palacky University, Olomouc, Czech Republic. He spent his Postdoctoral fellowship at the University of Alabama at Birmingham, USA at the laboratories of Dr. Mestecky and Dr. Novak. He is currently an Associate Professor of Immunology at Faculty of Medicine and Dentistry, Palacky University, Czech Republic. He has published more than 40 papers in peer-reviewed journals. His research is focused on novel approaches in design of recombinant protein-based and DNA vaccines and on liposome-based delivery systems.

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