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DNA vaccination against drug resistance in chronic viral infections, example of HIV-1

Maria Isaguliants[1,2,4], **Elizaveta Starodubova**[1,3], **Stefan Petkov**[1], **Athinakilpeläinen**[1], **Olga Krotova**[1,2], **Anastasia Latanova**[1,3], **Oleg Latyshev**[2] and **Britta Wahren**[1]
[1]Karolinska Institutet, Sweden
[2]DI Ivanovsky Institute of Virology, Russia
[3]WA Engelhardt Institute of Molecular Biology, Russia
[4]Riga Stradins University, Latvia

Strong immune response against viral antigens responsible for drug resistance can create a bottle-neck to viral evolution forbidding or hindering the development of drug resistance. In HIV-1, such response can serve as immunotherapy preceding and complementing highly active antiretroviral treatment (HAART). Main burden of drug resistance in HIV lies with viral enzymes: Reverse transcriptase/RT, protease/PR, and integrase/IN. Immune response against HIV enzymes can be induced by a cocktail of their genes shaped into DNA-vaccines. We pioneered the use of mutant and drug-resistant HIV enzyme genes as immunogens against drug-resistant HIV-1. Prototype DNA-vaccines based on drug-resistant RT, PR and IN of clades A and B with expression-optimized viral and consensus sequences have been designed and their immunogenicity was tested in mouse experiments. Mice were immunized by plasmid injections followed by electroporation, and immune response was screened by IFN-g/IL-2 Fluorospot, ELISA for perforin and granzymes, FACS with ICCS, antibody ELISA and also in live mice by assessing the extermination of cells co-expressing HIV-1 enzymes and luciferase reporter by in vivo imaging. All plasmids induced potent CTL and $CD4^+$ T-cell responses with lytic potential targeting multiple epitopes within HIV enzymes. Optimal multi-gene combinations and routes of plasmid administration were identified. Safety tests are on-going. The key issue of up-coming trials is to show that a pre-existing immune response against drug-resistant HIV enzymes can prevent or hamper the emergence and development of drug-resistance, and serve as a compliment of HAART.

Biography

Maria Isaguliants has done PhD in Chemistry in 1991 and Docentship in Immunology at Karolinska Institutet from 2007. She is a Project Leader at the Department of Microbiology, Tumor and Cell Biology, Karolinska Institutet, Stockholm, Sweden, and a Group Leader at the Ivanovsky Institute of Virology, Ministry of Health of the Russian Federation, Moscow, Russia. She is working on the design and preclinical testing of prototype vaccines against chronic viral infections including HIV-1 and HCV.

maria.issagouliantis@ki.se