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MODERN STATE OF VACCINE DEVELOPMENT, DNA VACCINES

Conference theme: INTERNATIONAL RESEARCH CONFERENCE “KNOWLEDGE FOR USE IN PRACTICE”

Objectives: DNA is a rapidly developing vaccine platform for cancer, infectious and non-infectious diseases. The objective is to give overview of methods used in design of DNA immunogens, their delivery, and efficacy assessment.

Results: Plasmid immunogens encode proteins to be expressed in vaccinees. DNAs are mainly synthetic, ensuring enhanced expression. Their introduction induces antibody and cellular responses mimic those in viral infections. DNA vaccination strongly depends on the efficacy of DNA delivery. Plasmids are administered by intramuscular or intradermal injections, subsequent electroporation enhances delivery by 1000-fold. Other techniques are also used as noninvasive introduction by Biojectors, skin applications with plasters and microneedles/chips, sonication, magnetofection, and tattooing. In VACTRAIN project, we have accumulated vast experience in DNA electroporation into rodents, which we translated into non-human primates. An intense debate on pros and cons of different delivery routes is ongoing. According to some studies, delivery route determines the immunogenic performance, according to others, it can modulate the level of response, but not its specificity or polarity. Data obtained in VACTRAIN project supports the latter option. Immune response is further shaped by antigen processing, proteasomal or lysosomal, and presentation. This process can be manipulated. Routinely, antigen is processed by proteasome and presented by MHC I molecules. Processing can be re-routed to lysosome to be further presented in complex with MHC II. Same happen after antigen secretion. We have tested all approaches using retargeting signals. Signal of Lysosome Associated Membrane Protein I ensured lysosomal processing and induction of an optimally balanced Th1/Th2-type immune response.

Conclusions: Optimization of design, delivery, and immunogenic performance of DNA vaccines led to marked increase in their efficacy in large species and man. New DNA vaccines for treatment of infectious diseases, cancer, allergies and autoimmunity are forthcoming.

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