DEVELOPMENT OF A RECOMBINANT FOOT-AND-MOUTH DISEASE VACCINE

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Introduction. Foot-and-mouth disease (FMD) is important disease of cloven-foot animals including cows and swine. Although annual vaccination against the FMD is mandated in regions of South Kazakhstan, outbreaks of the disease are registered every year. These outbreaks result in huge economic losses because international rules require culling of all the diseased and contacted animals and all products from these animals must be destroyed. Currently available anti-FMD vaccines are all produced using the original technology of inactivation of virus (foot-and-mouth disease virus, FMDV) grown in cell cultures. Recombinant anti-FMD vaccine is a long anticipated development in the industry because the recombinant vaccine is safe and compatible with diagnostic tests for discrimination of diseased and vaccinated animals (DIVA).

Materials and methods. Recombinant polyepitope antigens (PA) of FMDV were produced. The PA are proteins composed from aminoacid sequences of the immunodominant antigenic determinants of virion proteins VP1, VP2 and VP3 of the FMDV. Recombinant FMDV antigens in the form of virus-like particles (VLP) presenting the FMDV antigenic determinants on their surfaces were produced using bacterial expression. The recombinant FMD antigens were tested for immunogenicity in laboratory animals (mice).

Results and discussion. Genes for the FMDV polyepitope antigens (PA) were constructed using the de novo synthesis. The PAs were constructed for FMDV serotypes O, A, Asia-1 which are epizootically important serotypes in Kazakhstan. Nucleotide sequences encoding the PAs were engineered into gene of carrier protein (HBcAg), insertion was done into a spike domain (main immunodominant region) of the HBcAg. Plasmids for bacterial expression pET22/HBcAg_EVRO (serotype O), pET22/HBcAg_EVRA (serotype A), and pET22/HBcAg_Asia1 (serotype Asia-1) were produced. The recombinant FMDV antigens in the form of VLPs presenting FMD epitopes on their surfaces were purified using gradient ultracentrifugation in sucrose gradients (20%-60%) and gel filtration on the Superose 6 10/300 GL column (GE Healthcare). The recombinant FMDV antigens were characterized by dynamic light scattering and transmission electron microscopy. Both methods revealed presence of particles with diameters 32-35 nm in preparations of the recombinant FMDV antigens. Mice we immunized with recombinant FMDV antigens (four injections, 25 mkg VLP antigen per injection). Immune sera were tested in ELISA against the purified recombinant VP1 protein, which carries the main neutralization determinant of FMDV. The VLP FMDV antigens produced in this project were capable of inducing anti-FMDV antibodies with titers 1:400 (serotype Asia-1) and 1:800 (serotype O).

Conclusions. Our results indicate possibility of producing the recombinant FMD vaccine based on presentation of antigenic determinants of the FMDV on particles formed from the FMDV-unrelated carrier.