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Mucosal influenza vaccine comprising of M2e-HSP70 formulated with TMC nanoparticles induced strong M2e specific immune responses

Mehran Dabaghian[1,2], Seyyed Mahmoud Ebrahimi[1], Gholamreza Nikbakht Brujeni[2], Majid Tebianian[1], Ali Rezaei Mokarram[1], Mahdi Fasihi Ramandi[1] and Hamid Najminejad[1]

[1]Correspondence to Mehran Dabaghian, Department of Biotechnology, Razi vaccine and serum research Institute, P.O.Box 31975/148, Karaj, Tehran, Iran,
[2]Faculty of Veterinary Medicine Department of Microbiology and Immunology University of Tehran, Tehran-Iran

Influenza outbreaks have become a great life-threatening disease in the world. The first step in the viral entry is the binding of the hemagglutinin-neuraminidase (HN) to its receptor on respiratory epithelial cells. Nasal vaccines can induce systemic IgG and mucosal IgA antibody responses, which establish two layers of immune defense against infectious pathogens like influenza. Mucosal vaccines have to overcome several limitations, including mucociliary clearance and the inefficient uptake of soluble antigens. Therefore, nasal vaccines require potent adjuvants and delivery systems to enhance their immunogenicity and to protect their antigens. In this study, ectodomain of the conserved influenza matrix protein 2 (M2e) which has been found to induce heterosubtypic immunity was fused to C-terminus of Mycobacterium tuberculosis (MBT) HSP70 and a derivative of chitosan, three methyl chitosan (TMC), was used as a carrier for this fusion protein. Chitosan is a biodegradable, nontoxic and mucoadhesive natural polymer that has immune adjuant effect and capable of opening the tight junctions between epithelial cells. Ionically crosslinked nanoparticles were formulated with M2e-HSP70 protein using the ionic gelation technique with pentasodium tripolyphospate (TPP) as a crosslinking agent. Nanoparticles showed high loading efficacy and physical properties of nanoparticles was investigated using Zetasizer Nano particle analyzer (Malvern) and Transmission electron microscopy (TEM). Nanoparticles had a size in the range of 200-300nm and positive surface charge. TEM images revealed a spherical shape of nanoparticles. Intranasal immunization with M2e-HSP70/TMC in BALB/c mice induced significantly higher M2e specific antibody, IgA in nasal secretions and IgG in serum, than those induced in control groups (M2e-HSP70, TMC and HSP70). The anti-M2e IgG subtype induced was mainly IgG2a. Cellular immune response was evaluated by cytokine production assay of splenocytes after in vitro stimulation. M2e-HSP70/TMC-immunized mice were fully protected against lethal challenge (MLD90) of influenza A infection (PR/8) compared to control groups of mice with survival rates of 20% to 30%. This data confirmed that M2e-HSP70 fusion protein formulated with TMC nanoparticles could be an effective construct to induce strong immunogenicity and obtain full protection as a promising candidate mucosal influenza vaccine.

Biography

Dr. Mehran Dabaghian has completed his DVM degree at university of Tehran and now he is the student of immunology (Ph.D.) at university of Tehran, Iran. He is now conducting immunological parts of project on M2e-based influenza A recombinant vaccine in Razi vaccine and serum research institute. His success is owed to his respected supervisors Dr. Seyyed Mahmoud Ebrahimi, Dr. Majid Tebianian, Dr.Gholamreza Nikbakht Brujeni and his coworker Dr. Mohammad Hossein Zabeh Jazi.