A NOVEL STRATEGY FOR GENERATION OF EFFECTIVE AND SAFE ALZHEIMER'S DISEASE VACCINE BASED ON CONVENTIONAL INFLUENZA VIRUS VACCINE MODIFIED TO EXPRESS Aß₁₁₀

H. Davtyan¹, A. Ghochikyan¹, N. Movsesyan², I. Petrushina², R. Cadagan³, D. Zamarin³, L. Martinez-Sobrido⁴, R.A. Albrecht³, A. García-Sastre³, M.G. Agadjanyan¹

¹Institute for Molecular Medicine, Huntington Beach, ²Institute for Memory Impairments and Neurological Disorders, University of California, Irvine, Irvine, CA, ³Mount Sinai School of Medicine, New York, ⁴Department of Microbiology and Immunology, University of Rochester School of Medicine and Dentistry, Rochester, NY, USA

Introduction: Antibodies to the beta-amyloid peptide endows therapeutic protection against AD. This approach is currently hampered by elicitation of pathological autoreactivity. We have developed several strategies to limit generation of autoreactive Th cells. We previously developed a vaccine comprising Aß₄₂ B cell epitope fused with a foreign Th cell epitope, PADRE, which induced high titers of anti-Aß antibodies without generation of autoreactive T cells.

Aims: To reach our goal we expanded our studies with a more clinically applicable system based on a safe and effective dual use influenza virus vaccine that could simultaneously protect pre-symptomatic elderly people from flu infection and development of AD pathology.

Methods: A plasmid-based reverse genetics system was used to rescue a recombinant influenza virus containing the immunodominant B cell epitopes of Aß₄₂ (Aß₁₋₁₀) inserted into the influenza virus hemagglutinin protein.

Results: We demonstrated that this dual vaccine activates only anti-influenza Th cells and induces robust anti-Aß and anti-influenza antibodies in wild-type mice. Currently, we are investigating the role of anti-viral immunity by pre-existing Th memory cells in rapid and efficient generation of anti-Aß antibody responses in mice. These experiments could simulate the immune responses of people with pre-clinical stage AD repeatedly vaccinated/infected with flu virus and boosted with the dual use vaccine.

Conclusions: If successful, this dual use vaccine could be used in elderly people with early-onset AD that could be diagnosed by measuring tau/Aß and ptau/Aß ratio in CSF and/or by screening for accumulation of Aß in the brains using PIB-PET scan.