Submitted Name: Mike Zhang
Submitted email: cmzhang@vt.edu

The influence of carrier proteins on the immunological efficacy of nanoparticle-based vaccines against nicotine addiction

Zongmin Zhao[1], Yun Hu[1], Theresa Harmon[2], Paul Pentel[2], Marion Ehrich[3], Chenming (Mike) Zhang[1]

[1]Department of Biological Systems Engineering, Virginia Tech; [2]Minneapolis Medical Research Foundation; [3]Department of Biomedical Sciences and Pathobiology, Virginia Tech

Tobacco smoking is the leading preventable cause of disease, disability, and death worldwide. It is responsible for more than 480,000 death per year in the United States. Current pharmacological medications for smoking cessation are only partially successful and associated with the risk of serious side effects. Nicotine vaccines, on the other hand, can elicit the production of nicotine-specific antibodies capable of sequestering nicotine in serum and reducing nicotine entering the brain and have shown to be a promising approach to treating nicotine addiction. Nanoparticle based vaccines have shown to be more immunogenic and are superior in sequestering nicotine in the blood than the first generation conjugate vaccines. The hypothesis of this work is that different carrier proteins may significantly impact the immunological efficacy of a vaccine. A series of nanoparticle-based nicotine nanovaccines were engineered with different carrier proteins (Keyhole limpet hemocyanin (KLH) multimer, KLH subunit, cross reactive material 197 (CRM_{197}), or tetanus toxoid (TT)). Vaccines with CRM_{197} or TT were processed by dendritic cells more efficiently than that with KLH multimer or subunit. Vaccines carrying $CRM1_{97}$ or TT exhibited a significantly higher immunogenicity against nicotine and a considerably lower immunogenicity against carrier proteins than NanoNicVac carrying KLH multimer or subunit in mice. The *in vivo* results revealed that vaccines with CRM_{197} or TT resulted in lower levels of nicotine in the brain of mice after nicotine challenge. All findings suggest that an enhanced immunological efficacy of a vaccine can be achieved by using CRM_{197} or TT as carrier proteins.