An Engineered influenza virus to deliver antigens for lung cancer vaccination

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The development of cancer neo-antigen vaccines that prime the antitumor immune responses has been hindered in part by challenges in delivery of neo-antigens to the tumor. Here, using the metastatic pulmonary melanoma tumor expressing the model antigen ovalbumin (OVA), we demonstrate a chimeric antigenic peptide influenza virus (CAP-Flu) system for delivery of antigenic peptides bound to influenza A virus (IAV) to the lung. We first covalently displayed OVA on an attenuated IAV using click chemistry and then anchored IAV-CPG with the innate immunostimulatory agent CpG. Vaccination with this construct not only yielded robust antigen uptake by dendritic cells but also various responses from immune cells and even a significant increase in tumor-infiltrating lymphocytes compared to peptides alone. Lastly, we engineered the IAV to express anti-PD1-L1 autocrine nanobodies that led to further regression of lung metastases and prolonged mouse survival after re-challenge. Such an engineered IAV can be equipped with any neo-antigenic peptides against lung metastasis tumors, like colorectal cancer or breast cancer, to generate therapeutic lung cancer vaccines.

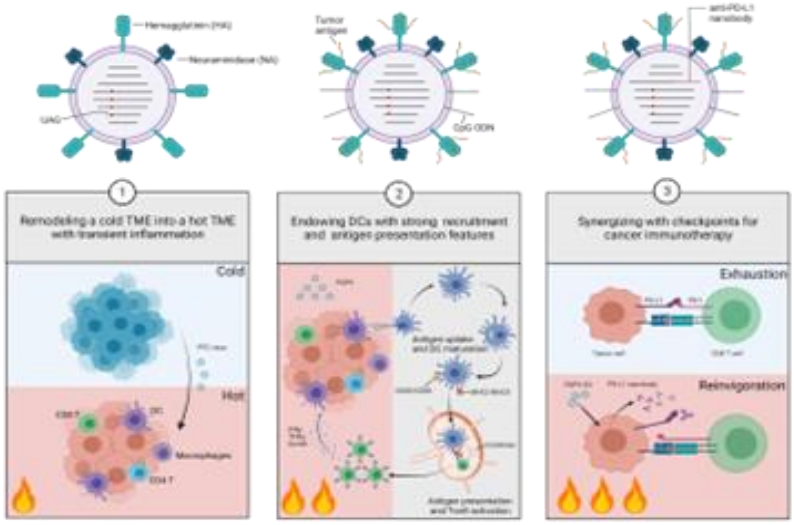

Figure 1. Design of APVI platform for personalized cancer immunotherapy. PTC virus bearing NAEK on HA was conjugated with DBCO modified Ag peptide (DBCO-Ag) via click chemistry, and subsequent incubation with cholesterol-modified CpG (Cho-CpG) leads to formation of PTC virus co-loaded with Ag