Development of platform technology for vaccines for unmet medical needs using a novel cytoplasmic RNA viral vector and cataloguing of the recombinant vaccines

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We have developed a platform technology by which recombinant vaccines can be generated immediately after the emergence of any type of life-threatening new pathogens. We employed a non-propagative human parainfluenza virus type 2 (hPIV2) vector (hereinafter referred to as BC-PIV) in which vital *F* gene had been removed from the hPIV2 genome. The vector has a negative-strand RNA genome, and is able to display exogenous protein with retained native steric structure on its envelope. The parental hPIV2 shows little pathogenicity for people over the age of 5, of which genome does not enter cell nucleus, and infects respiratory tracts recurrently throughout a human lifetime, that make this virus ideal as a nasal vaccine vector. The recombinant BC-PIV vaccines can be produced at the maximum titer of $6x10^8$ PFUs/mL, by using a Vero/BC-F packaging cell line which expresses the hPIV2 F protein constitutively. We have already succeeded in creating the highly effective recombinant vaccines against Ebola virus and SARS-CoV-2, respectively. BC-PIV expressing prefusion-stabilized spike protein nearly completely protected lungs and nasal turbinates of the hamsters against SARS-CoV-2 challenge after nasal vaccination. Here we constructed a BC-PIV harboring prefusion-stabilized F protein of RSV in which DS-Cav1 mutations (S155C, S190F, V207L, and S290C) were introduced, and named it BC-PIV/DS-Cav1. Plaque forming assays using the RSV/EGFP revealed that the BC-PIV/DS-Cav1 showed efficient induction of neutralizing antibodies against RSV in sera of the hamsters after nasal vaccination. RSV challenge test revealed that one shot intranasal vaccination of BC-PIV/DS-Cav1 was sufficient to completely protect lungs of the hamsters. The recombinant BC-PIV vaccine was demonstrated to be stable for more than 6 months at 4℃, be able to be administered repeatedly through the nose to induce mucosal and systemic immunity, and no needle is required for vaccination. In our hands, a laboratory grade vaccine can be constructed within 3 weeks once the information of the antigen gene of the new pathogen becomes available. Thus BC-PIV platform technology is one of the most promising methods for producing new modality vaccines. The first in human study will be performed on the next stage after production under GMP control and the safety tests of the vectors. Development of non-propagative recombinant nasal vaccine against RSV may help eradicate RSV by inducing sterilizing immunity.