

Pre-clinical efficacy of a universal influenza vaccine candidate inducing complementary humoral and cellular immunity

Inhalt

Current influenza vaccines primarily induce strain-specific antibodies against the variable hemagglutinin (HA) head while eliciting limited T cell immunity, resulting in suboptimal protection against drifted and emerging zoonotic influenza viruses. We developed an Orf virus-based influenza vaccine (ORFV-Flu) combining chimeric HAs with conserved influenza T cell epitopes to induce coordinated broadly reactive humoral and cellular immunity. The ORFV platform has already demonstrated clinical safety in humans, supporting rapid clinical translation.

Following systemic prime and respiratory boost immunization ("prime-and-pull") of HLA-A*02-transgenic mice, ORFV-Flu provided complete protection against lethal heterologous influenza challenge and reduced pulmonary viral loads by up to 99%, clearly outperforming seasonal vaccination. Remarkably, ORFV-Flu exclusively induced pulmonary tissue-resident memory T cells, together with broad HA stalk-specific IgG, mucosal IgA, and robust helper and cytotoxic T cell responses targeting the HA stalk and conserved influenza virus antigens. Collectively, these findings identify ORFV-Flu as a clinically translatable universal influenza vaccine candidate with the potential to protect against seasonal, drifted, and emerging zoonotic threats, including H5N1.

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Yes, I am a junior scientist.

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