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Live-attenuated influenza vaccines based on premature termination codon (PTC) - Harboring Viruses

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Abstract

The conversion of life-threatening viruses into live but avirulent vaccines represents a revolution in vaccinology. In a proof-of-principle study, we expanded the genetic code of the genome of influenza A virus via a transgenic cell line containing orthogonal translation machinery. This generated premature termination codon (PTC)–harboring viruses that exerted full infectivity but were replication-incompetent in conventional cells. Genome-wide optimization of the sites for incorporation of multiple PTCs resulted in highly reproductive and genetically stable progeny viruses in transgenic cells. In mouse, ferret, and guinea pig models, vaccination with PTC viruses elicited robust humoral, mucosal, and T cell–mediated immunity against antigenically distinct influenza viruses and even neutralized existing infecting strains. The methods presented here may become a general approach for generating live virus vaccines that can be adapted to almost any virus.

Biography:

Huan Xu has her expertise in discovery of new biotechnology drugs including recombinant long-lasting protein, bispecific antibody and vaccines. She received her bachelor and doctoral degree both from Peking University. After graduation, she joined the North China Pharmaceutical Company as a senior scientist. The methods presented here utilize expansion of the genetic code (Lei Wang 2001) of influenza a virus. It may become a general approach for generating live virus vaccines.

Speaker Publications:

1. Longlong S, Huan X, (co-first author) (2016) Generation of Influenza A Viruses as Live but Replication-Incompetent Virus Vaccines. Science, 354(6316):1170-1173.

2. Huan X, (2016) Re-exploration of the codon context effect on amber codon-guided incorporation of non-canonical amino acids in E. coli by the blue–white screening assay. ChemBioChem., 17(13):1250-1256.

3. Bo Z, Huan X, (2015) Development of next generation of therapeutic IFN-alpha2b via genetic code expansion. Acta Biomater.,19:100-111.

4. Ziwei Z, Huan X, (2017) Construction of an inducible stable cell line for efficient incorporation of unnatural amino acids in mammalian cells. BBRC, 489(4):490-496.

5. Yongxiang Z, Fei Y, Yiming W, Longlong S, Huan X,(2015) Broaden the versatility of lentiviral vector as a tool in nucleic acid research via genetic code expansion. Nucleic Acids Res., 43(11):e73

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