

Accepted Manuscript

Universal influenza virus vaccines and therapeutic antibodies

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PII: S1198-743X(17)30097-6

DOI: [10.1016/j.cmi.2017.02.009](https://doi.org/10.1016/j.cmi.2017.02.009)

Reference: CMI 857

To appear in: *Clinical Microbiology and Infection*

Received Date: 9 January 2017

Revised Date: 5 February 2017

Accepted Date: 6 February 2017

Please cite this article as: Nachbagauer R, Krammer F, Universal influenza virus vaccines and therapeutic antibodies, *Clinical Microbiology and Infection* (2017), doi: 10.1016/j.cmi.2017.02.009.

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10 11 12 Abstract

13 **Background:** Current influenza virus vaccines are effective when well matched to the circulating
14 strains. Unfortunately, antigenic drift and the high diversity of potential emerging zoonotic and
15 pandemic viruses make it difficult to select the right strains for vaccine production. This
16 problem causes vaccine mismatches which lead to sharp drops in vaccine effectiveness and
17 long response times in case of novel pandemic viruses.

18 **Aims:** To provide an overview of universal influenza virus vaccines and therapeutic antibodies in
19 pre-clinical and clinical development.

20 **Sources:** PubMed and clinicaltrials.gov were used as sources for this review.

21 **Content:** Universal influenza virus vaccines that target conserved regions of the influenza virus
22 including the hemagglutinin stalk domain, the ectodomain of the M2 ion channel or the internal
23 matrix and nucleoproteins are in late pre-clinical and clinical development. These vaccines
24 could confer broad protection against all influenza A and B viruses including drift variants and
25 thereby abolish the need for annual re-formulation and re-administration of influenza virus
26 vaccines. In addition, these novel vaccines would enhance our preparedness against emerging
27 influenza virus pandemics. Finally, novel therapeutic antibodies against the same conserved
28 targets are in clinical development and could become valuable tools in the fight against
29 influenza virus infection.

30 **Implications:** Both universal influenza virus vaccines and therapeutic antibodies are potential
31 future options for the control of human influenza infections.

32 33 Introduction

34 Human influenza virus infections cause a significant public health and economic burden
35 worldwide. According to a World Health Organization (WHO) estimate annual epidemics cause
36 2-5 million severe cases and 250,000 to 500,000 deaths [1]. The European Center for Disease
37 Control (ECDC) estimates that seasonal influenza virus infections cause 38,500 annual excess
38 deaths in Europe [2]. In the United States seasonal influenza virus infections are responsible for
39 24,000 deaths per year on average (3,000-49,000 per season for seasons between 1976-2007)

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