

Influenza vaccine innovations and the need for a European influenza research and outbreak response network

Florian Krammer

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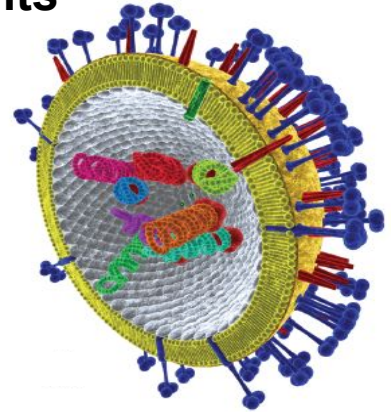
Next generation influenza vaccines

- Provide an incremental improvement over traditional influenza vaccines
- Almost all based on mRNA platforms
- Include hemagglutinin and hemagglutinin + neuraminidase-based vaccines
- mCombrax (influenza + COVID-19) now licensed in the European Union
- Lots of development with pandemic influenza vaccines (clade 2.3.4.4b)
- mRNA vaccine development now supported by CEPI
- The US has dropped support for mRNA-based vaccines, the EU is now leading this field (at least from a regulatory and funding perspective)



Broadly protective and universal influenza vaccines

- **Broadly protective:** Meaning against all strains within a subtype (including drift variants), with limited need to update vaccines
- **Universal:** Protection against all subtypes and drift variants
- **Targets:** Hemagglutinin stalk domain, neuraminidase, conserved internal proteins
- **Little development in the last few years**
- **Two T-cell based approaches failed in phase III trials**
- **Stalk-based approaches showed promise in early clinical trials but have not progressed much**



adapted from Krammer
and Grabherr, Trends
Mol Med 2010

Changes in access

Home administration of FluMist/FluEnz in the US

FluMist Home is as easy as 1, 2, 3...4



Patients order for their household online



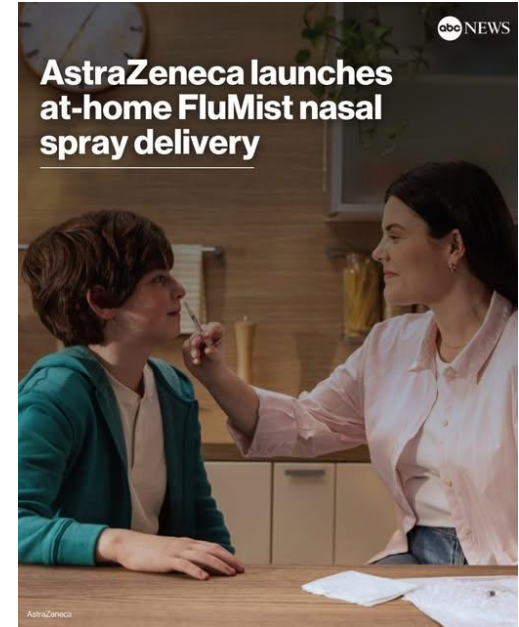
A healthcare professional reviews and approves order^{3†}



FLUMIST gets delivered to the patient's door[‡]



Patients and caregivers administer FLUMIST at home¹



<https://www.flumisthcp.com/at-home-administration>

New vaccine/drug hybrids

- CD388
- Antibody Fc with neuraminidase inhibitor (zanamivir)
- Fc is modified for a long half life
- Is given once before the influenza season
- Phase II efficacy over one season:
 - 450mg 76%
 - 300mg 61%
 - 150mg 58%
- Endpoints: laboratory and clinically confirmed influenza over 24 weeks

Drug–Fc conjugate CD388 targets influenza virus neuraminidase and is broadly protective in mice

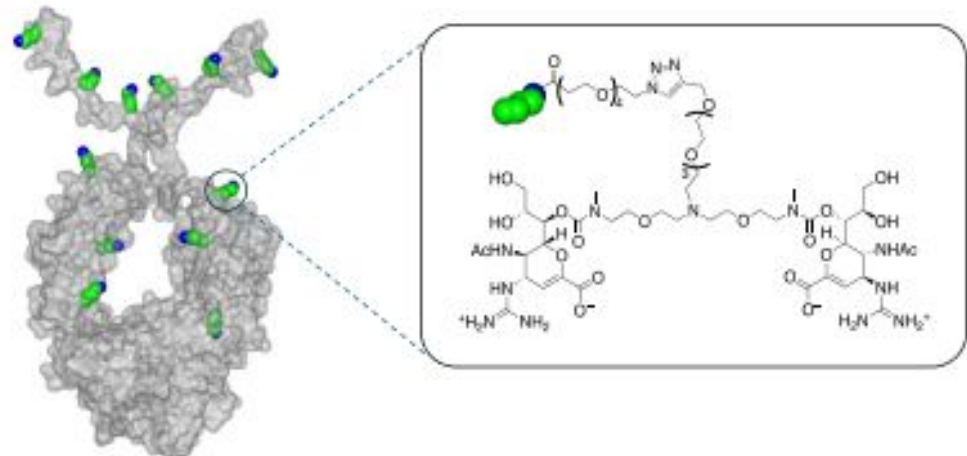
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 Check for updates

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The need for a European Influenza Research and Outbreak response Network (IRON)

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Europe needs a sustainably funded influenza research and response network

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Panel: The role of the US Centers of Excellence for Influenza Research and Response

The Centers of Excellence for Influenza Research and Response (CEIRR; formerly known as Centers of Excellence for Influenza Research and Surveillance; CEIRS) is funded by the National Institute of Allergy and Infectious Diseases (NIAID) at the US National Institutes of Health (NIH) and was established for two key tasks: first, to perform influenza virus research and surveillance in peace time; and second, to rapidly respond to emerging issues, such as the 2009 H1N1 pandemic, the 2013 H7N9 outbreak, and the ongoing cattle H5N1 outbreak. The CEIRR network currently consists of six scientific centres and a data processing centre, which are each generously funded (approximately up to US\$109 million/year across the centres, divided into core funding and optional funding) for 7 years. CEIRR investigators are in constant communication with NIAID, have published a sizeable percentage of the global influenza literature, and have generated a large proportion of data that directly influence influenza policy. CEIRR has also provided data to support decision making by the US Food and Drug Administration and the Centers for Disease Control and Prevention during the current H5N1 outbreak. The programme has a strong One Health focus and is exceptional in training young investigators. CEIRR has also played a crucial role in responding to the COVID-19 pandemic with many of the investigators in NIH's SARS-CoV-2 Assessment of Viral Evolution programme also being CEIRR investigators. The highly successful CEIRR network is now in its third 7-year iteration. A sister programme focused on vaccine development, the Collaborative Influenza Vaccine Innovation Centers, was launched in 2019.