Navigating the evolutionary routes of influenza viruses

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The objective of this study is to rigorously assess the repeatability and predictability of influenza virus evolution by experimentally evolving human seasonal influenza viruses in ex vivo human airway epithelium (HAE) cell cultures.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON48244

Source
ToetsingOnline

Brief title
NaviFlu

Condition

- Other condition

Synonym
flu, influenza

Health condition

influenza virus infections in the general population

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: European Research Council

Intervention

Keyword: airway epithelium, evolution, Influenza virus, prediction

Outcome measures

Primary outcome

The proposed experiments will allow us to quantify the predictability of influenza virus evolution and under what circumstances that evolution is predictable. If predictable, the protocols from this study will be used to inform the World Health Organization Influenza Vaccine Strain Selection process (the project leader was a member of the WHO committee that oversees this process from 2009-2015). If evolution is not meaningfully predictable the project results will be used to inform other vaccine design efforts.

Secondary outcome

does not apply

Study description

Background summary

Each year 5-15% of the world*s human population is infected with seasonal influenza viruses resulting in millions of hospitalizations and ~500,000 deaths. Vaccination is the primary strategy for reducing the public health burden of influenza virus infection. Nearly everyone will be infected with influenza viruses multiple times over the course of their lives. On average, children are re-infected every 2-5 years and adults every 5-10 years. These recurrent infections are possible because the virus*s antigenic phenotype evolves allowing it to escape immunity induced by prior infection and vaccination.

Influenza vaccine efficacy depends on the antigenic match between the viruses in the vaccine and those circulating in the human population. The composition of the seasonal influenza vaccines used worldwide is updated twice per year to keep pace with the evolution of the virus. This composition is determined by the World Health Organization (WHO), based on careful analysis of the viruses that circulated over the preceding 6-12 months. If a new virus variant appears in the months soon after the vaccine composition has been decided, manufactured and distributed, seasonal vaccine efficacy suffers and a valuable public health opportunity has been lost. Despite substantial effort by WHO and its Collaborating Centers, the seasonal influenza virus vaccine mostly plays catch up with the evolution of the virus. The ability to predict when and how seasonal influenza viruses will evolve would enable us to base the seasonal influenza vaccine composition decisions on the predicted evolutionary pathways of the virus.

Study objective

The objective of this study is to rigorously assess the repeatability and predictability of influenza virus evolution by experimentally evolving human seasonal influenza viruses in ex vivo human airway epithelium (HAE) cell cultures.

Study design

We will use human airway epithelial cultures to serially passage seasonal influenza viruses to mimic prolonged human infections. The study has three objectives-

1-Quantify the evolutionary dynamics of seasonal influenza viruses in the absence of antibody-mediated selection.
2-Determine how the antibody complexity of immune sera shape the evolutionary trajectories of virus antigenic evolution.
3-Quantify the impact of differences in selection pressures by site of infection and underlying host variation on virus evolution.

These experiments require the recruitment of human volunteers to obtain the starting material for the HAE cultures. Obtaining the material required to generate the HAE cultures involves taking direct nasal brushes from the middle meatus of the nose. In rare cases this might result in local bleeding at the biopsy site that would not require active intervention. These are routine procedures and pose very low risk to the volunteer. After the brushes have been performed, no further involvement of study participants is expected.

Seasonal influenza viruses will be serially passaged through the HAE cultures and the viruses from these studies will be genetically sequenced and phenotypically characterised to quantify the evolution of the viruses in each

experiment. Mathematical and statistical models will be applied to these data to assess the repeatability and predictability of virus evolution.

Study burden and risks

This project requires human airway epithelial cells for the production of cultures to simulate prolonged human infections. We will collect nasal epithelial samples from patients of ENT department the Academic Medical Center (AMC) in Amsterdam. Nasal brushes taken from the middle meatus of the nose, may in rare cases result in local bleeding at the biopsy site that would not require active intervention. These are routine procedures and pose very low risk to the volunteer. The ENT department has extensive expertise in collecting these airway mucosal samples in clinical and/or research settings.

Contacts

Public
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1105 AZ
NL
Scientific
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1105 AZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

participants with known allergic status

Exclusion criteria

immunological disorders
active viral or bacterial infections

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	05-03-2020
Enrollment:	30
Type:	Actual

Ethics review

Approved WMO

Date:	08-05-2019
Application type:	First submission
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL68838.018.19