

location of my laboratory

the National Emerging Infectious Diseases Laboratories (NEIDL)

**BOSTON
UNIVERSITY**



research focus of my laboratory



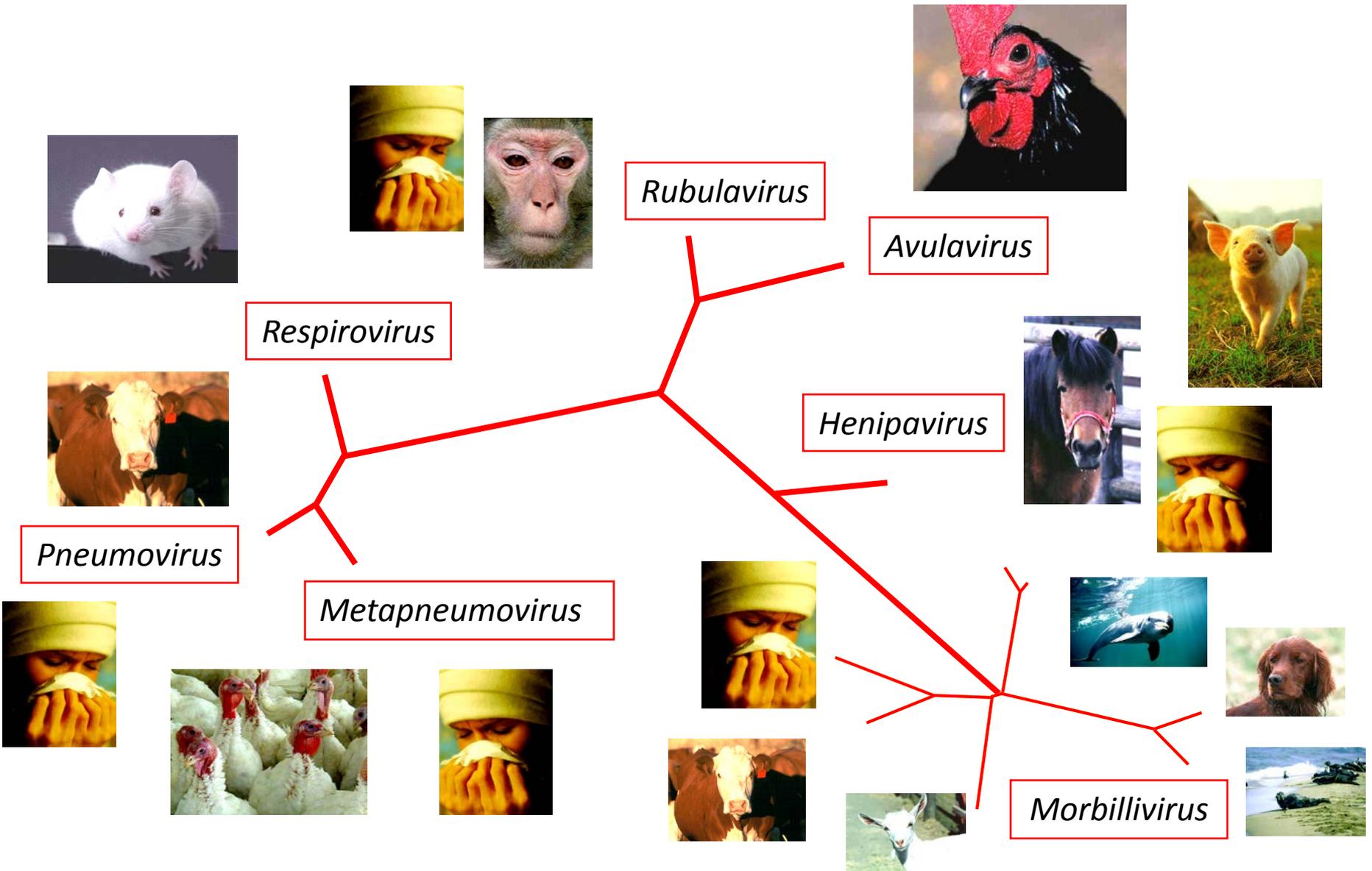
pathogenesis



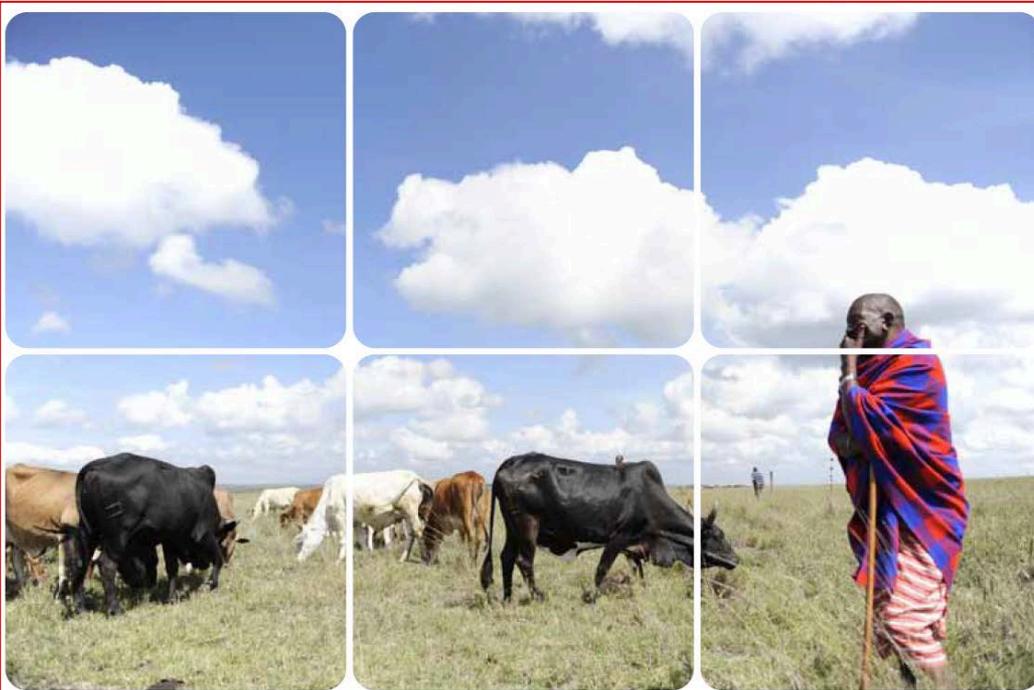
attenuation

BASIC UNDERSTANDING OF THE MOLECULAR BIOLOGY OF THE VIRUSES

a diverse family of human and animal viruses



global eradication of rinderpest in 2011



The Global Rinderpest Eradication Programme

Progress report on
rinderpest eradication:
Success stories and actions leading to
the June 2011 Global Declaration

PROGRESS TOWARDS RINDERPEST GLOBAL FREEDOM

	Last outbreak	2001
		2002
		2003
		2004
		2005
	Vaccination stopped and provisional freedom from rinderpest	2006
		2007
		2008
	Targeted surveillance exercise	2009
	End of the field operations	2010
	Global declaration	2011

eradication of measles virus is also on the cards

it is the most infectious human pathogen on earth

rinderpest



measles



BUT ... refusal to vaccinate is leading to a resurgence of the virus in Europe and the US

the problem of wild, unsubstantiated speculation

our job as scientists is to *inform* and *educate* not to entertain or scare



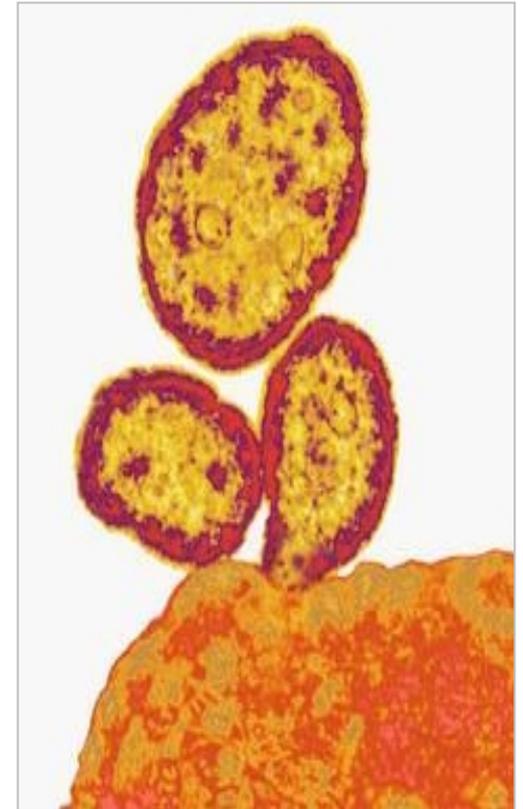
we are not living in a Hollywood movie ... we all have to be responsible

what are the barriers to cross-species infection?



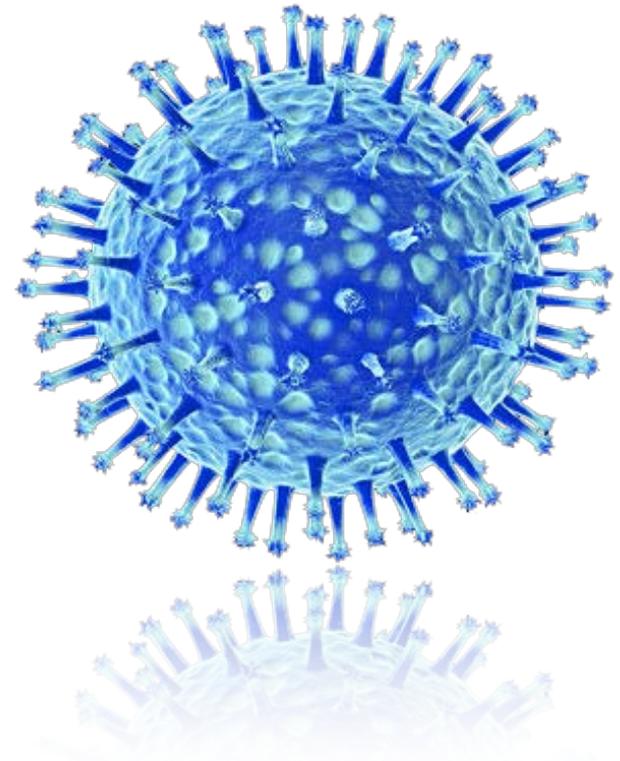
outline

- *... understanding cross-species infections*
 - questions virologists ask
 - approaches virologists use
- *... working with dangerous pathogens*
 - influenza ... but ...
 - it's not all about influenza
- *... engaging constructively and being transparent*
 - articulating the benefits
 - mitigating the risks



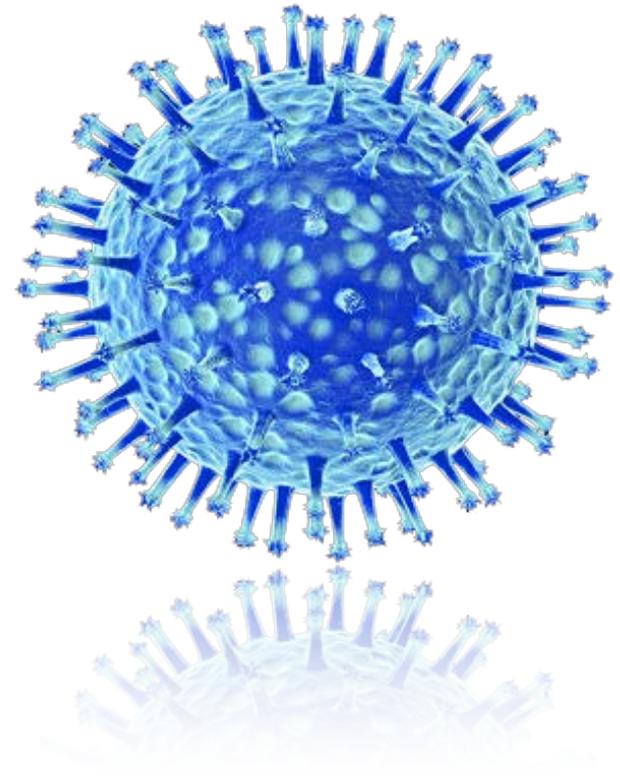
questions virologists ask

- *why* does the virus infect and kill mammals?
- *do* antiviral drugs work and *how* does the virus become resistant?
- *do* current or developmental vaccines provide protection and *can* the virus escape?
- *how* does the virus spread within animals and other humans?
- *how* does the virus spread from animals to humans and from humans to humans?
- *could* the virus cause a pandemic?
- *what* is the likelihood of (re)emergence or, worse, *de novo* synthesis of a virus for malintent?



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definitions are key



friend

(noun)

one of the
many strangers
on Facebook.

approaches virologists use

two basic strategies: loss and gain of function



many ways to destroy a phone but only a few ways to build one

reverse genetics

generating viruses using synthetic biology

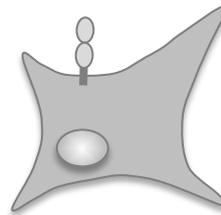
cDNA copy of genome



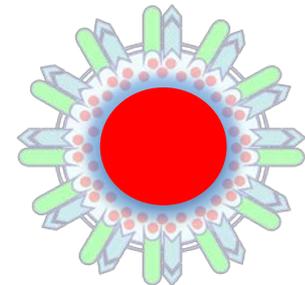
RNA



(+)



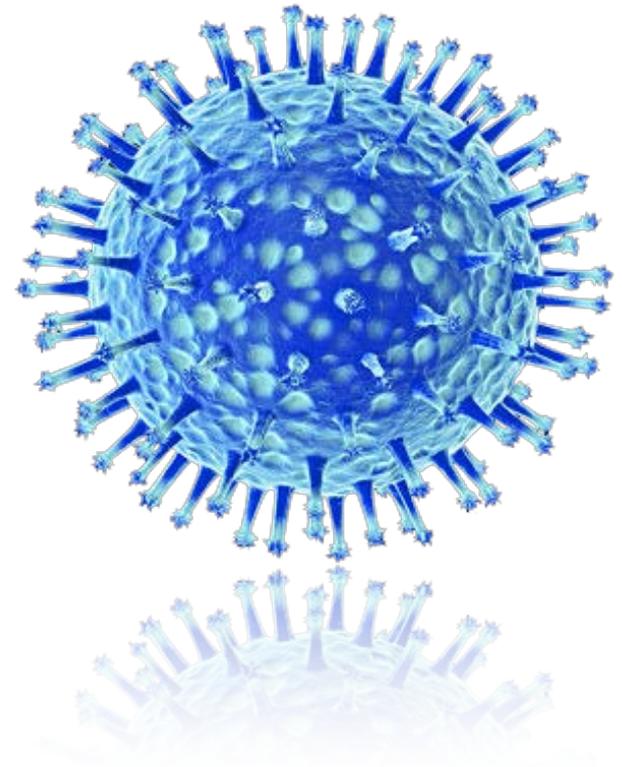
introduce into cells



recombinant
virus

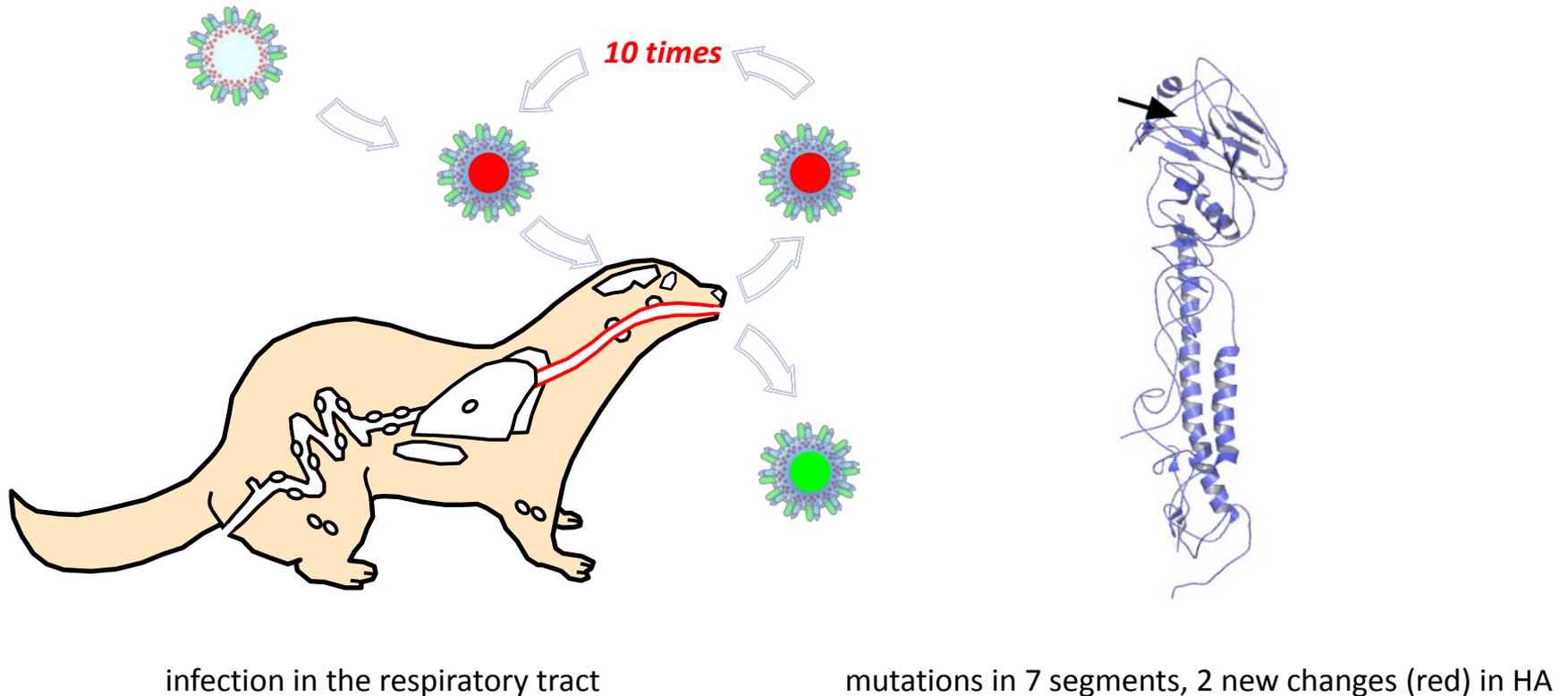
working with dangerous pathogens

the strange case of the tail wagging the dog



reverse and forward genetics: virus evolution/adaptation

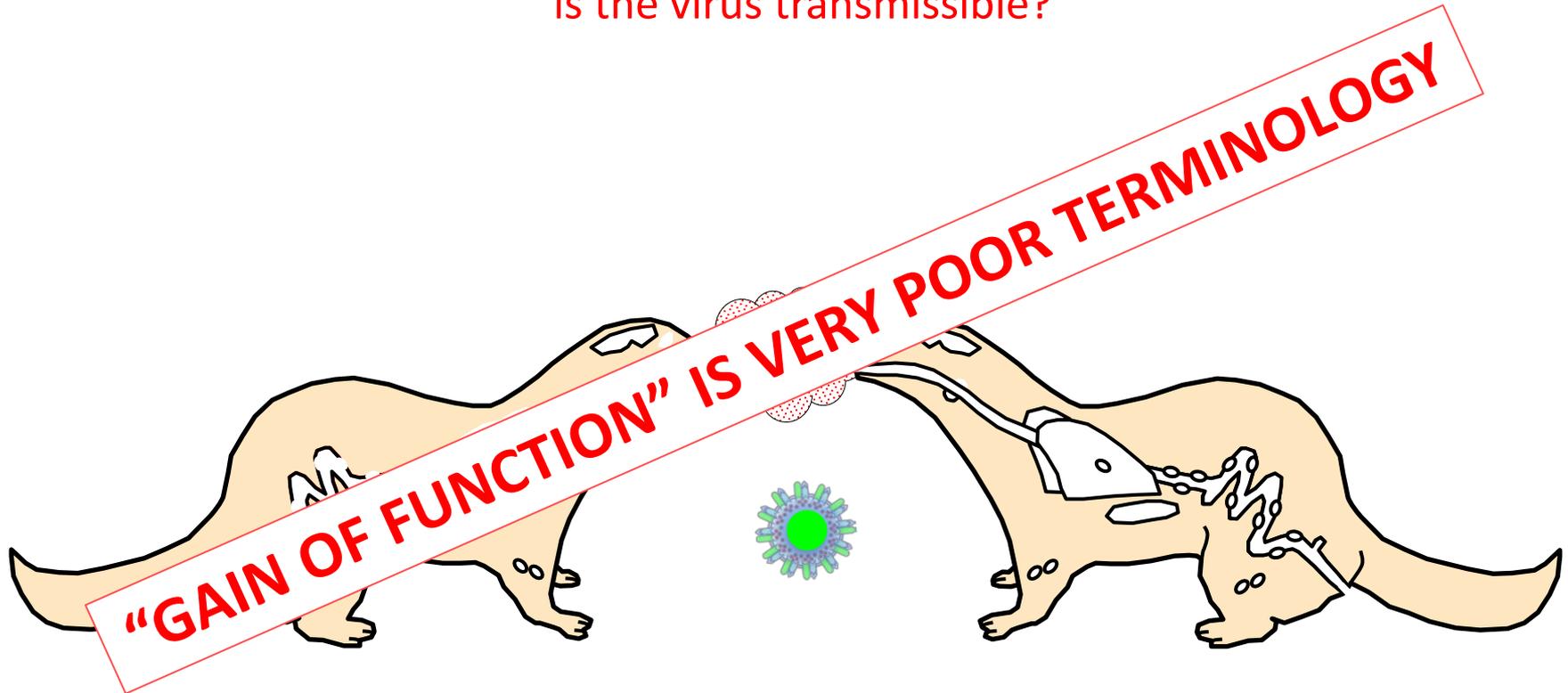
Indonesian H5N1 strain: Ron Fouchier (2012)



is the virus transmissible?

reverse and forward genetics: virus evolution/adaption

is the virus transmissible?

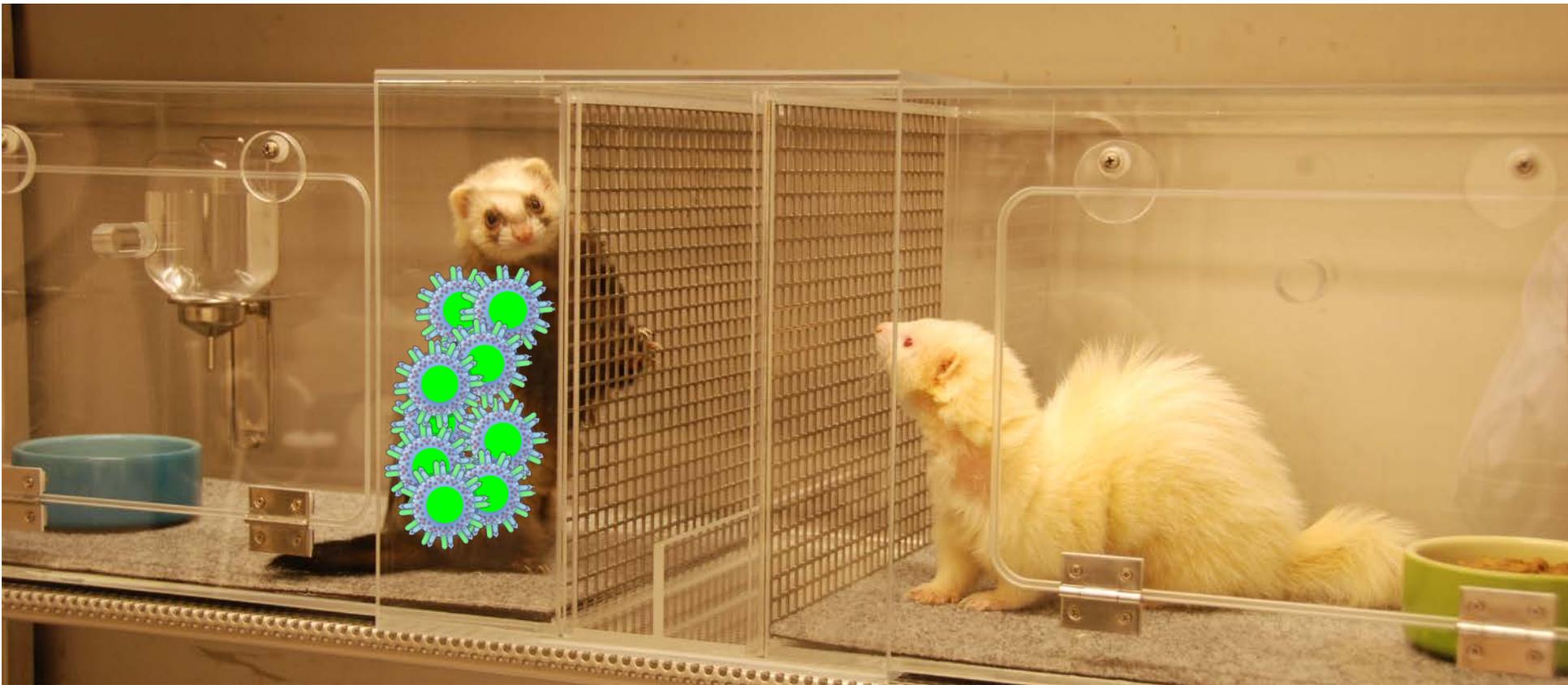


infection in the respiratory tract

the virus transmissible: THIS IS A "GAIN OF FUNCTION" EXPERIMENT

these studies must have a controlled *in vivo* dimension

prove mechanistically what is needed to make an avian influenza transmit



the animals did not die from the infection

uncontrolled transmission “experiments”

what is needed to make an avian influenza transmit



does not provide mechanistic data

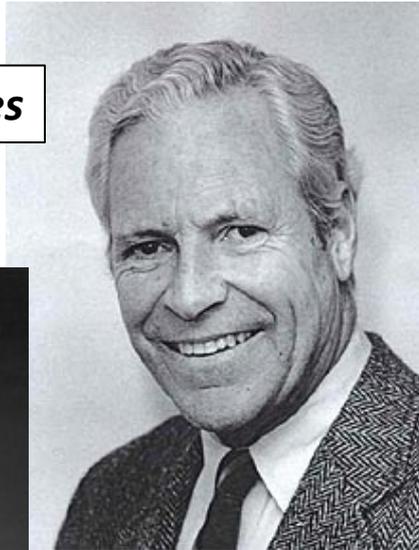
it's not all about influenza



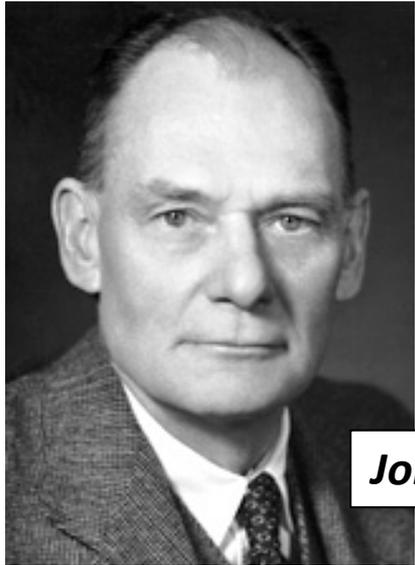
working with dangerous pathogens

8 million people were dying of measles per annum

Thomas Peebles



John Enders



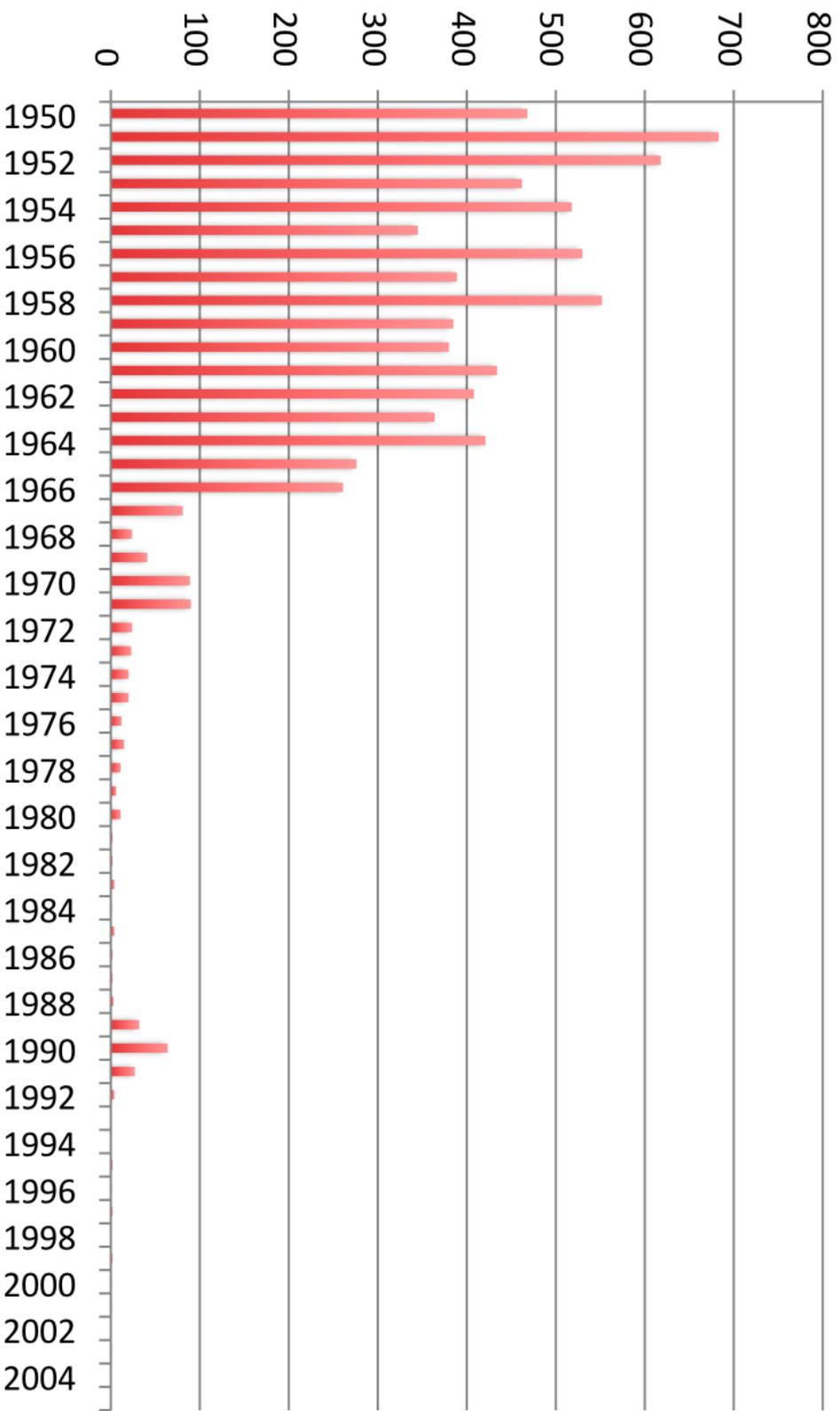
measles



so they decided to try and isolate and culture it

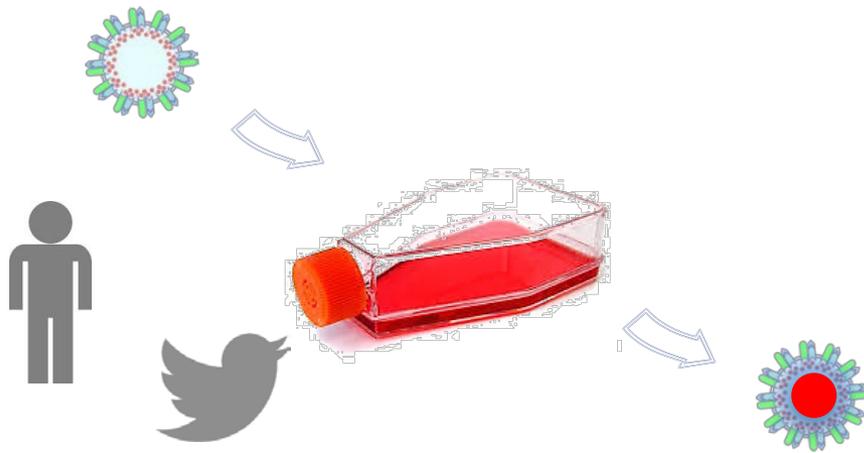
how virologists study dangerous pathogens

measles deaths in the US



evolution and adaption of a virus to non-human cells

a common approach in virology

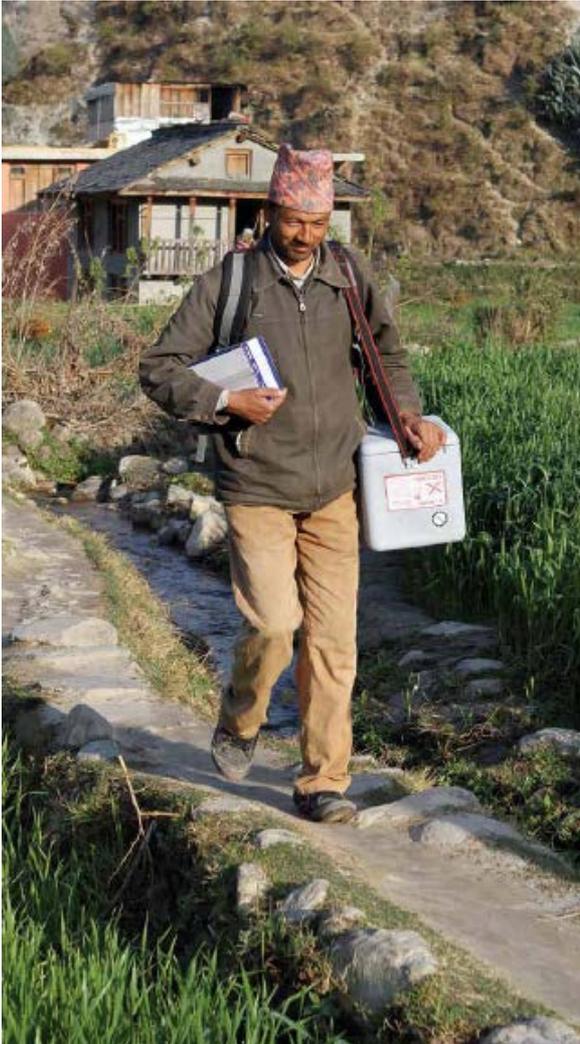


infects immune, epithelial and neural cells (tri-tropic)

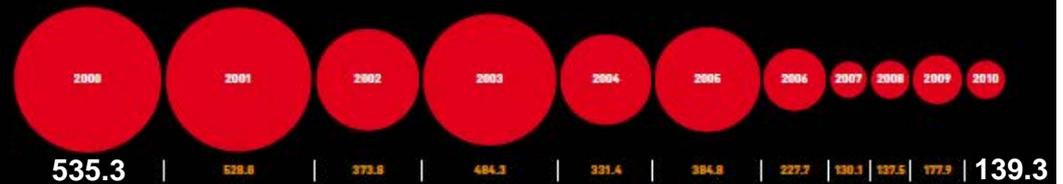
infects every human cell type due to a major alteration of receptor usage (pantropic)

tropism was expanded: THIS IS A "GAIN OF FUNCTION" EXPERIMENT

towards measles eradication



number of estimated measles deaths (in thousands) globally 2000-2010



unforeseen risks

forward genetics + gain of function = vaccine

rinderpest



measles



should vaccination be discontinued in a measles-free world when zoonosis occurs?

unforeseen benefits

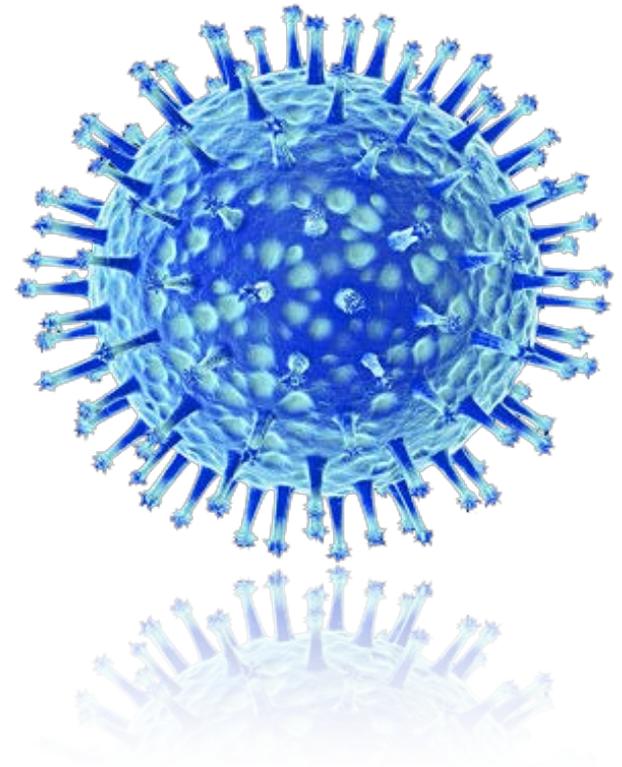
reverse genetics + gain of function = oncolytic virotherapy



it is unlikely Enders would have predicted such a use for the vaccine

biosafety is bigger than influenza

the strange case of the tail wagging the dog



what they tell us, their utility and what we should realize

specifically based on influenza virus “gain of function” studies

- transmissible virus is more stable at lower pH and higher temperatures than poultry adapted viruses
- avian viruses are transmissible from mammal to mammal
- experiments can be performed safely at BSL3+
- biopharmaceutical industry is taking notice
- public health policy makers are being informed
- the end of the world has not arrived
- we need to continue to think globally

mechanism

transmission

biosafety

vaccinology

surveillance

apocalyptic

international

virologists are responsible scientists

we understand and mitigate risk for ourselves, our staff and our communities



*"With great power comes
great responsibility"
~Voltaire*

good communication and transparency is critical



Scientists for Science

Scientists for Science are confident that biomedical *research on potentially dangerous pathogens can be performed safely and is essential* for a comprehensive understanding of microbial disease pathogenesis, prevention and treatment.

The *results of such research are often unanticipated* and accrue over time; therefore, risk-benefit analyses are difficult to assess accurately.

...only by engaging in open constructive debate can we learn from one another's experience. Most importantly, we are united as experts committed to ensuring public health is not compromised and the reputation of science in general, and microbiology in particular, is defended.

“gain of function” studies are only one element of this wider debate

“gain-of-function” studies ...

... their history, their utility and what they can tell us ...

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Paul Duprex

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