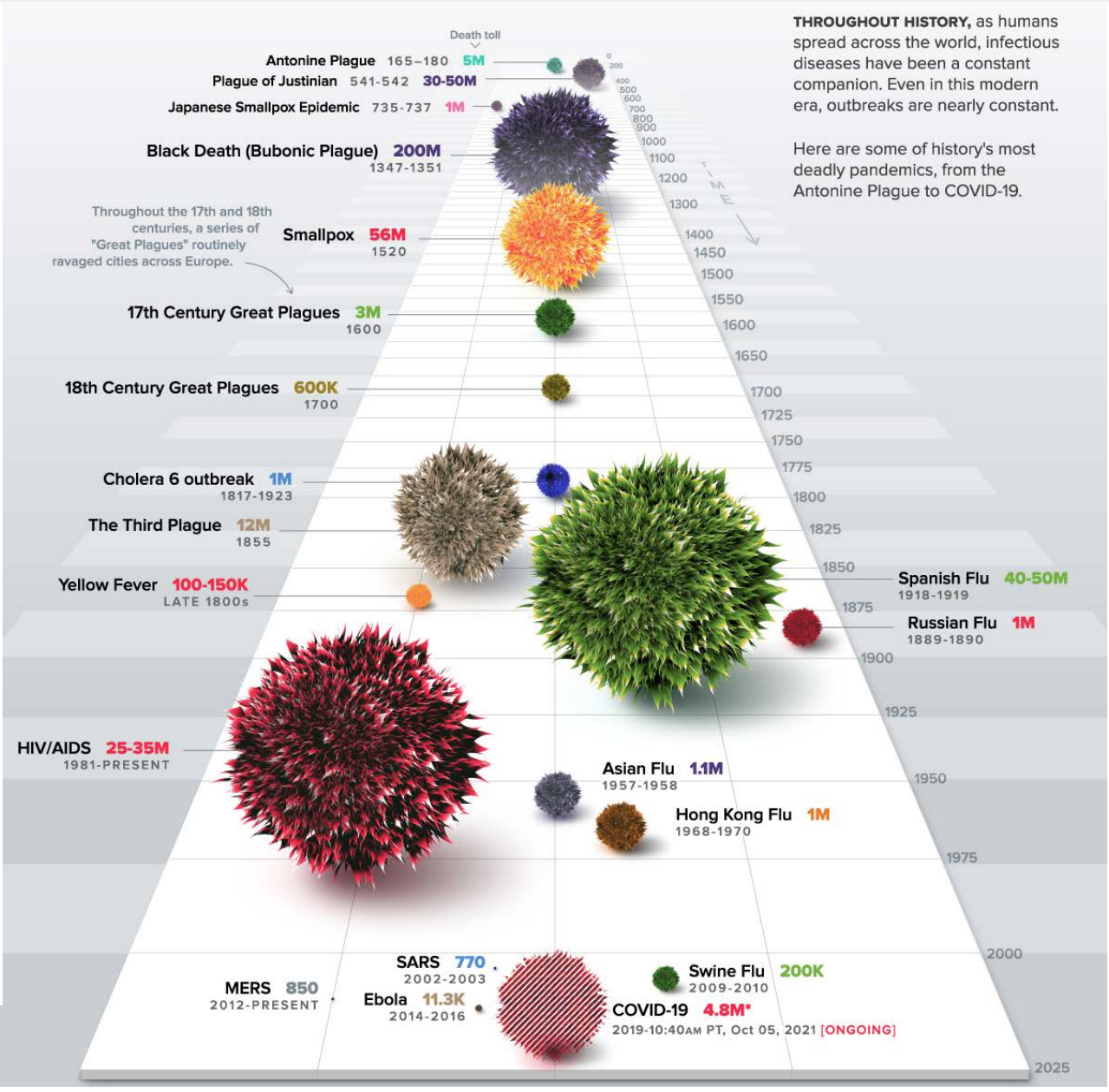
Developing SARS-CoV-2 assays and standards to enable studies of viral host range and vaccine development

UNIVERSITY OF SUSSEX

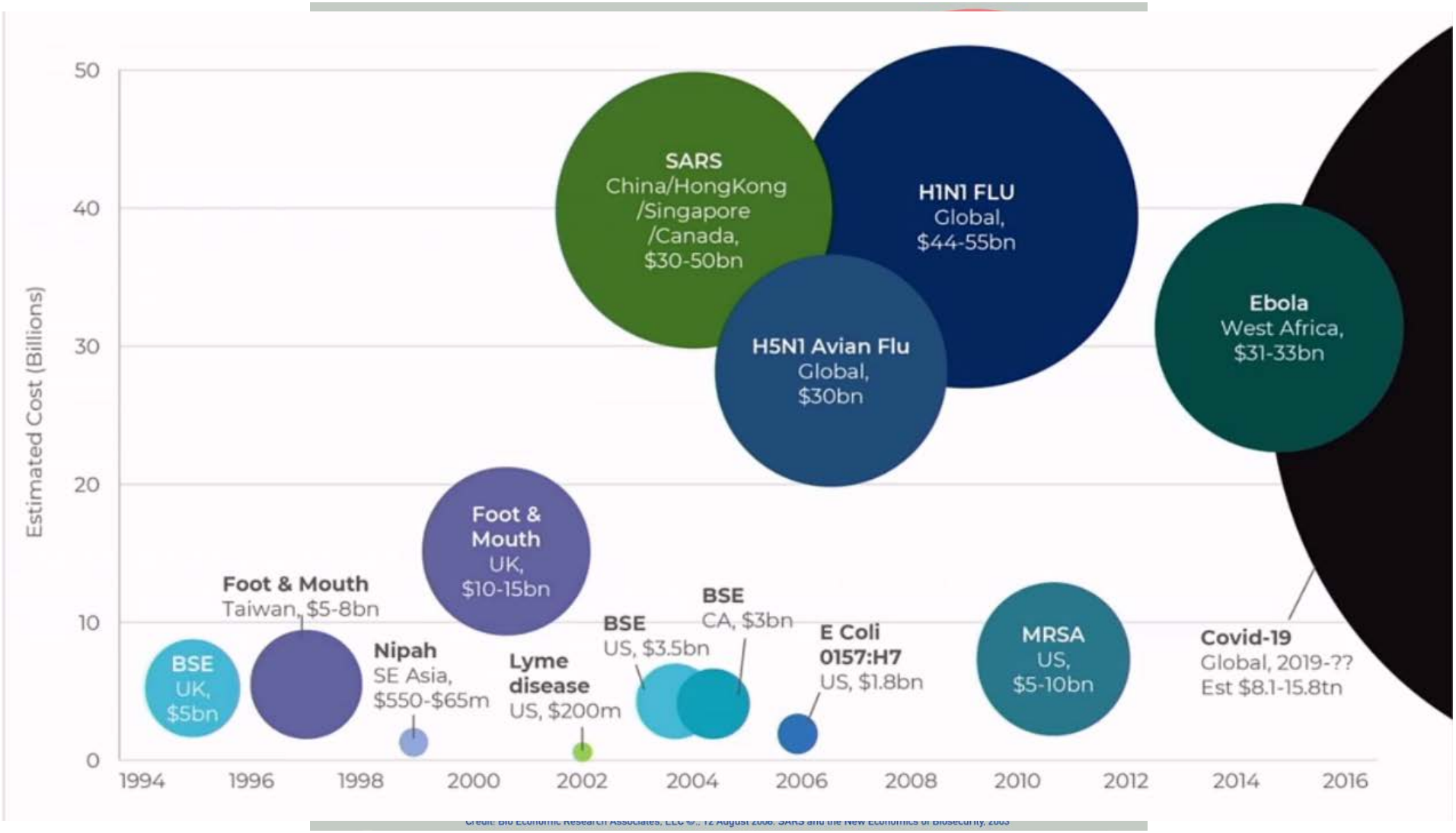
Infectious disease pandemics



VISUAL CAPITALIST

UNIVERSITY OF SUSSEX

Not just a public health impact



Health for Animals (2015)

UNIVERSITY OF SUSSEX

Research interests

- **Generation and characterisation of emerging virus pseudotypes to enable far reaching epidemiology studies, host-cell interactions and the development of vaccines and antivirals.**

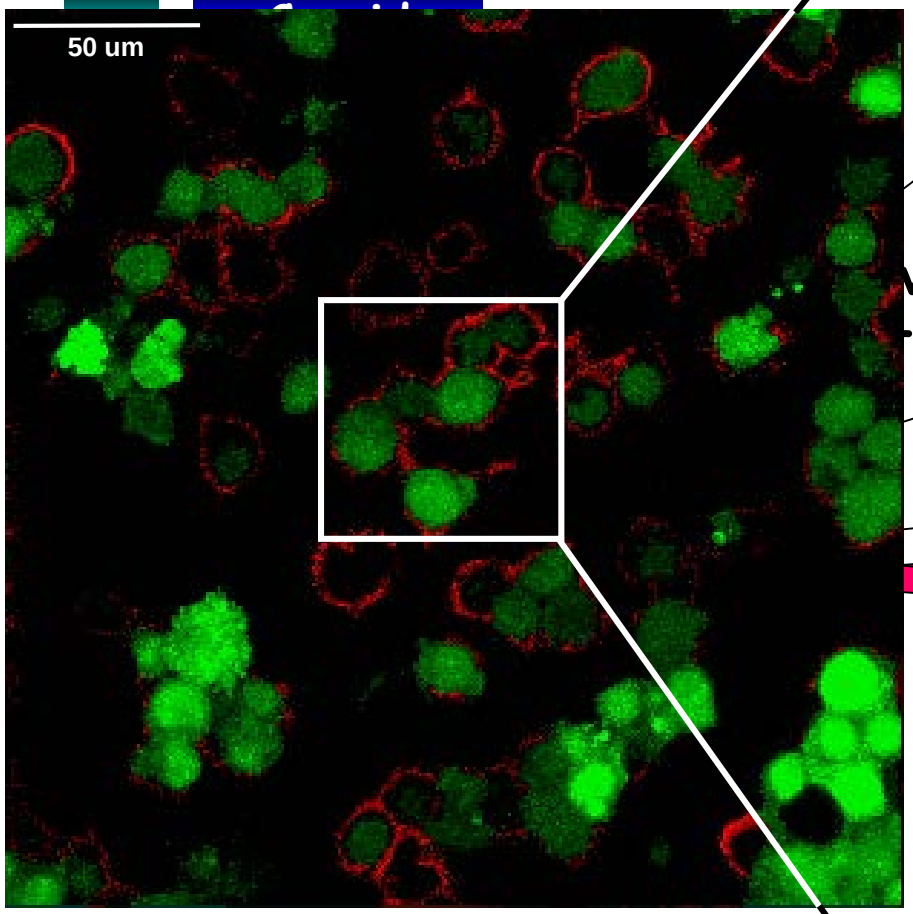
- **Sero-epidemiology of filoviruses and henipaviruses in African fruit bats to guide public health interventions.**

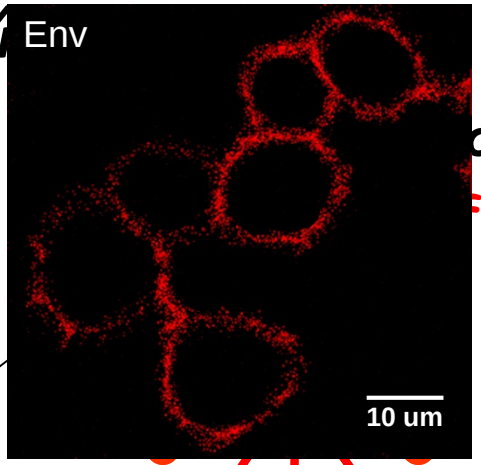
- **The study of the immunogenic hierarchy of viral envelope protein (VEP) epitopes to aid the construction of antigenically optimised isoforms.**

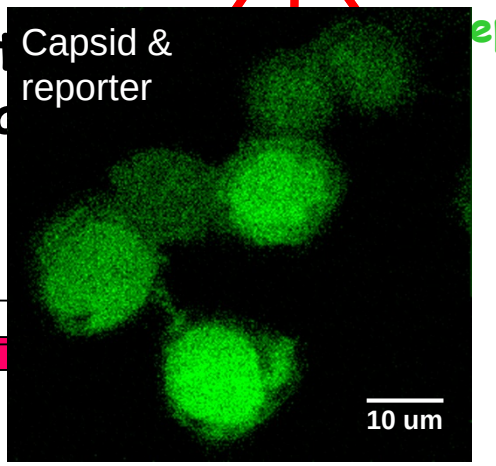
- **Bioinformatic analysis of VEP for the generation of antigens that stimulate a more potent neutralising response (DIOSynVax).**

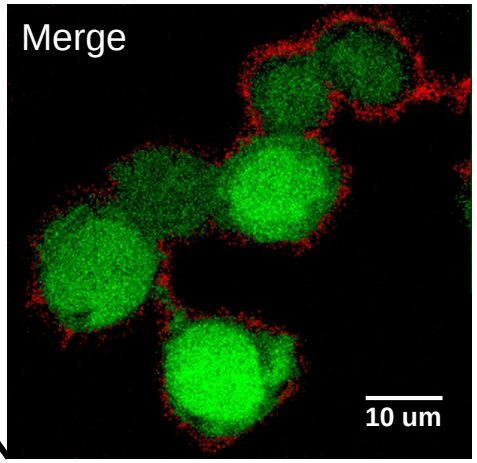
Pseudotype co

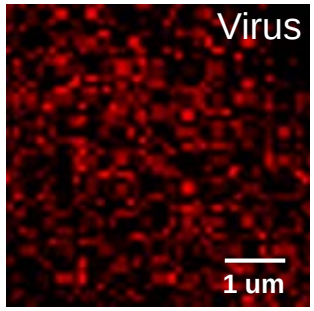
1 Plasmid transfection











article

Foreign envelope

Cell envelope

Capsid

eporter

vest

itro

Pseudotype construction

1 Plasmid transfection

Capsid

Env

Reporter

Mature particle

Foreign envelope

Cell envelope

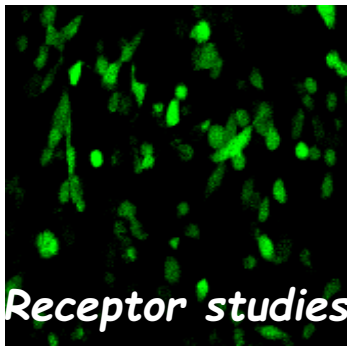
Capsid

Transfer gene

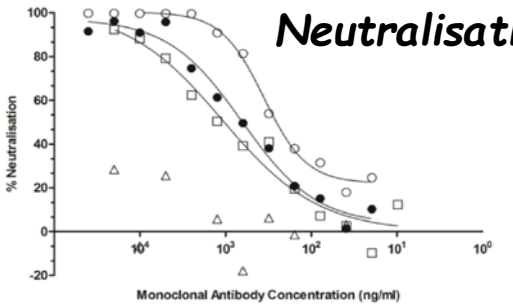
2 Harvest & titrate

3 Measure transduction

Stable integration



Neutralisation



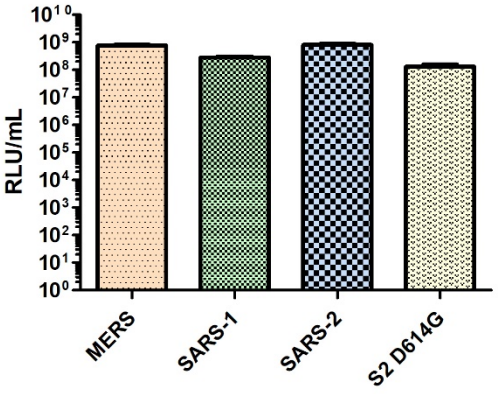
Application of SARS-CoV-2 PV

1. Developing assays and standards

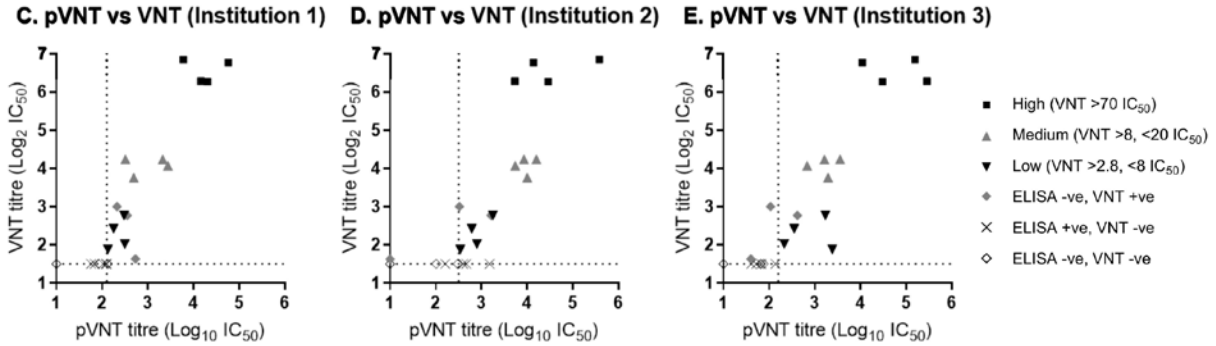
Murray *et al.* 2021 Journal of Infection
Di Genova *et al.* 2021 Bio-Protocols
James *et al.* 2021 Viruses

- Pseudotyped viruses [ELISA]

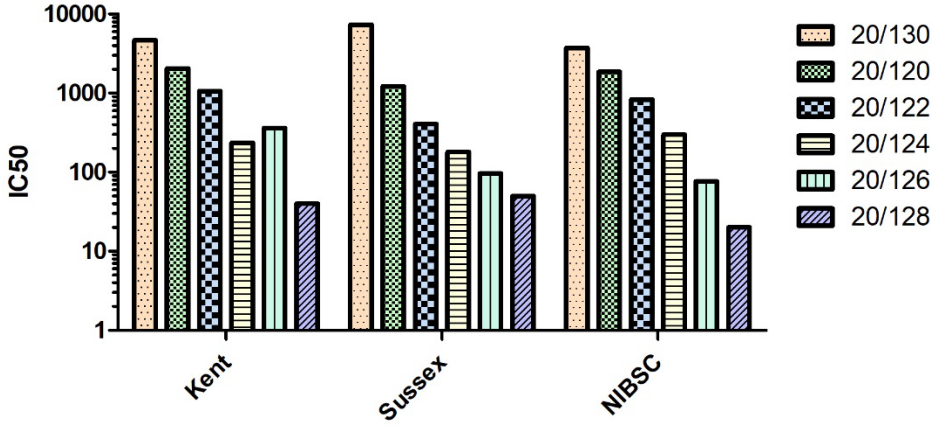
CoV titres



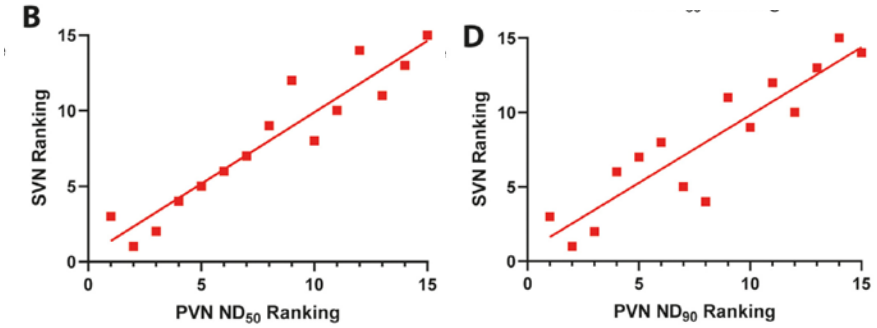
Correlation with authentic virus neutralisation



Neutralisation



Validation of commercial 'surrogate' neutralisation assay



Application of SARS-CoV-2 PV

1. Developing assays and standards

   - Pseudotyped viruses [ELISA]
   - Serological standard [NA]

World Health Organization

WHO/BS/2020.2403
ENGLISH ONLY

EXPERT COMMITTEE ON BIOLOGICAL STANDARDIZATION
Geneva, 9 - 10 December 2020

Establishment of the WHO International Standard and Reference Panel for anti-SARS-CoV-2 antibody

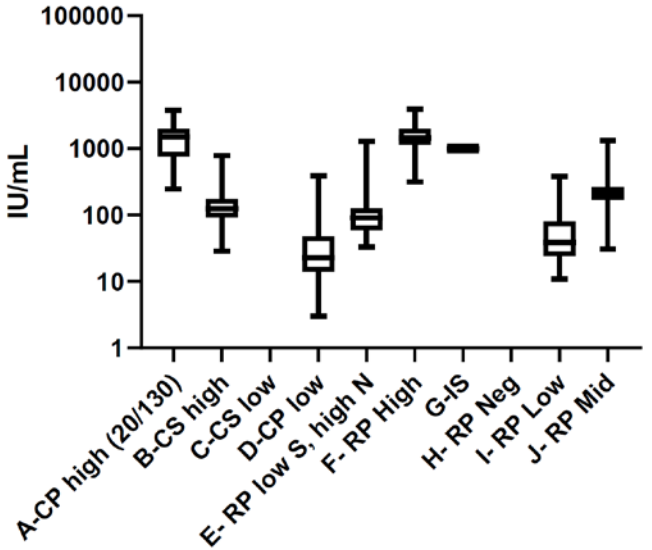
Table 1. Collaborative study samples

Samples were shipped under NIBSC dispatch reference CS678

Sample	Description	formulation/vol (mL)
A-CP high (20/130)	20/130, Convalescent plasma from one patient, positive	liquid 0.1
B-CS high	Convalescent sera pool, positive	liquid 0.2
C-CS low	Convalescent sera pool, very weak positive	liquid 0.2
D-CP low	Convalescent plasma from one donor, weak positive	liquid 0.2
E-RP low S, high N	20/144, Reference Panel member, weak S, high N	f/d 0.25
F-RP high	20/150, Reference Panel member, high	f/d 0.25
G-IS	20/136, Candidate WHO IS	f/d 0.25
H-RP neg	20/142, Reference Panel member, negative	f/d 0.25
I-RP low	20/140, Reference Panel member, low	f/d 0.25
J-RP Mid	20/148, Reference Panel member, mid	f/d 0.25

CP: convalescent plasma, CS: convalescent serum; RP: reference panel; IS: International Standard; f/d: freeze-dried

B

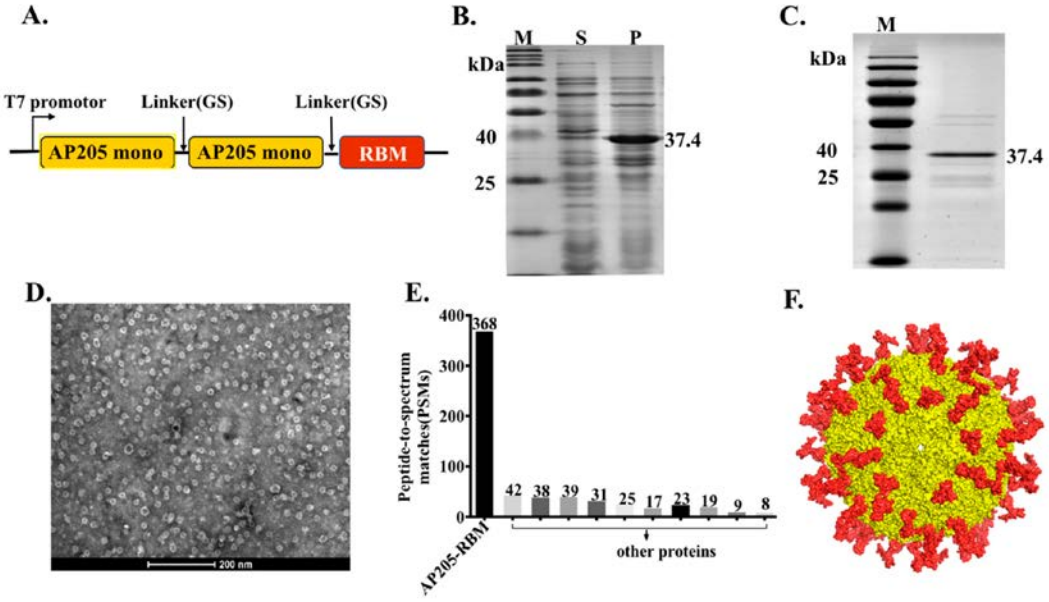


Application of SARS-CoV-2 PV (2)

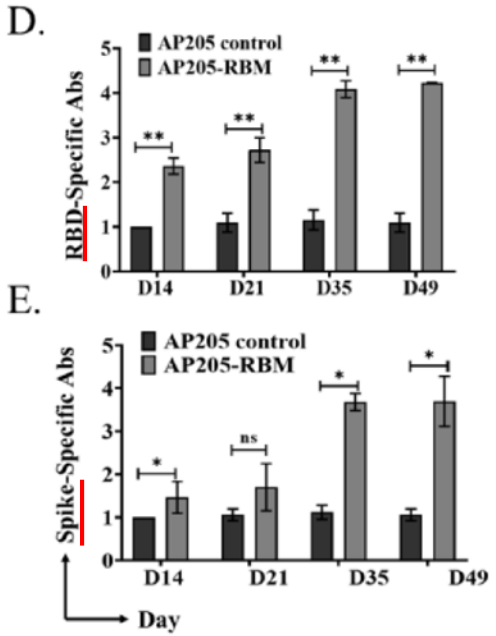
2. Vaccine development

Liu *et al.* 2021 Vaccines

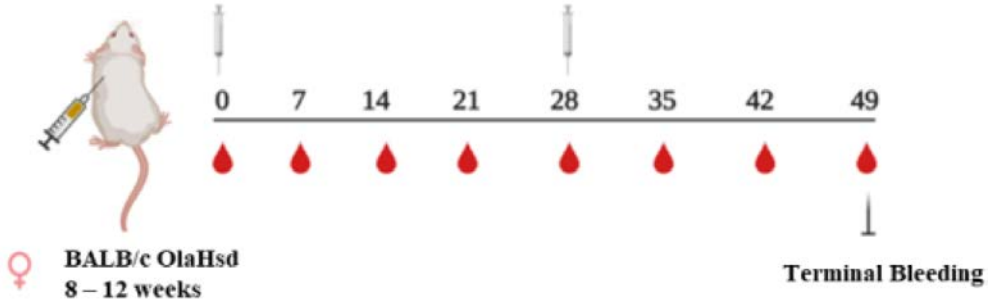
AP205-RBM VLP-based vaccine



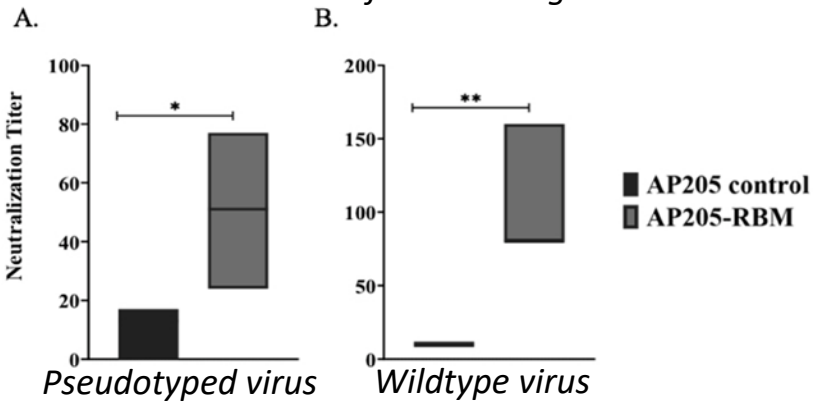
Stimulation of binding Abs



Vaccination and bleeding schedule



Stimulation of neutralising Abs



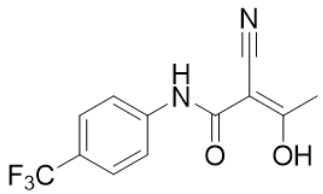
Application of SARS-CoV-2 PV (3)

3. Treatment/Entry inhibitor development

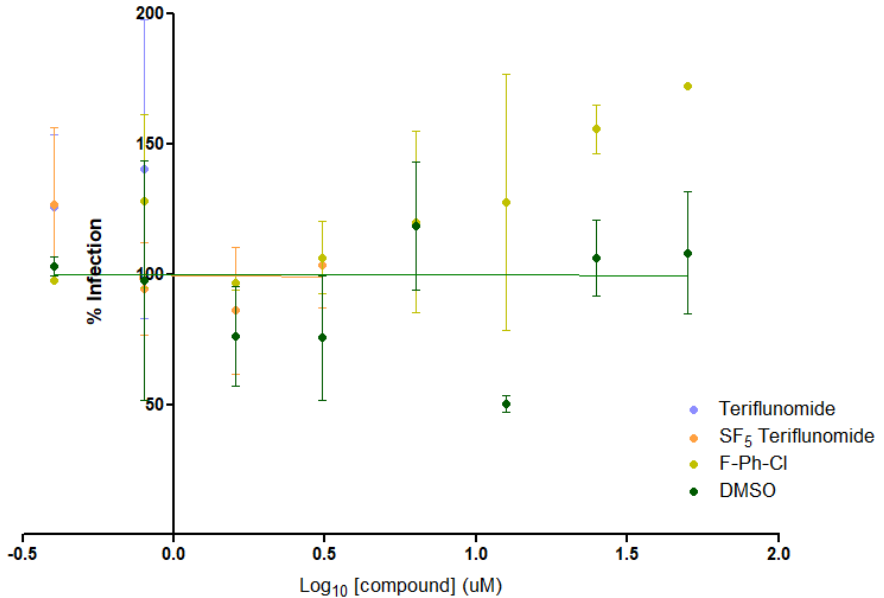
Jose *et al.* 2021 Submitted

- Small molecule inhibitors

Protease inhibitors

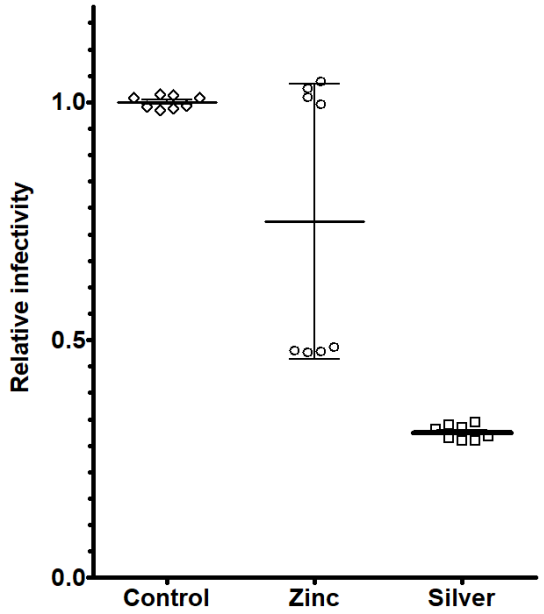


teriflunomide



Metal nano-particle polymer membranes

Control *Zinc* *Silver*



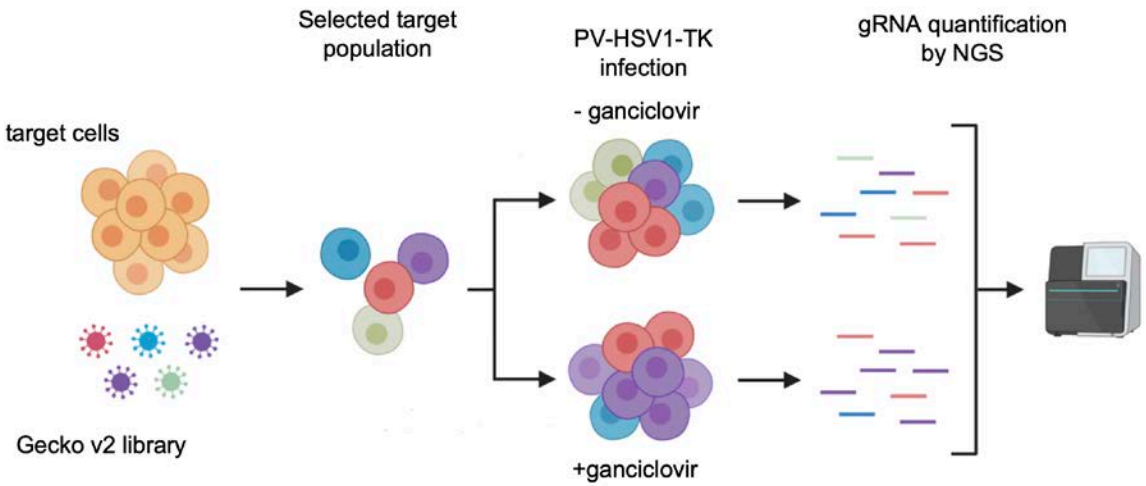
Application of SARS-CoV-2 PV (3)

3. Treatment/Entry inhibitor development

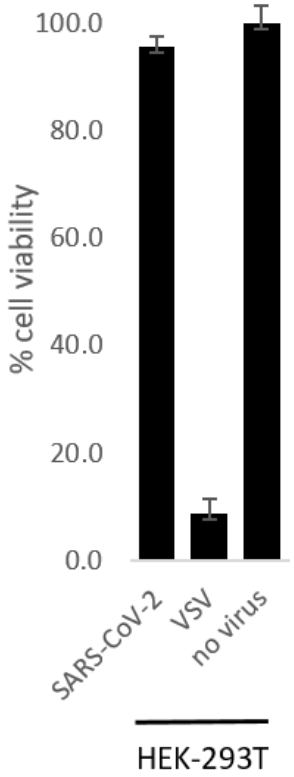
Jose *et al.* 2021 Submitted

- Small molecule inhibitors
- CRISPR/CAS-9 genomic screen for entry inhibitors

Negative selection CRISPR/PV screen



SARS-CoV-2 TK PV induced cell death



Application of SARS-CoV-2 PV (4)

Thakur *et al.* 2021 In preparation

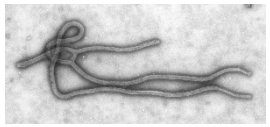
4. Animal hosts and tissue tropism

   - VoC reverse zoonosis threat (Dalan Bailey - Pirbright Institute)
   - Infection of blood vessel cells (Catherine Hall, Luca Biasetti - Psychology UoS)

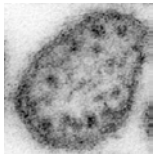
UNIVERSITY OF SUSSEX

Pseudotyped virus panel

Lyssavirus - At least one isolate from each species

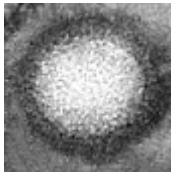


Filovirus - At least one isolate from each species

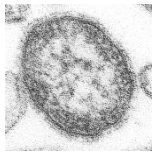


Lassa virus - At least one isolate from each lineage

Henipavirus - Malaysian, Bangladeshi, Ghanaian

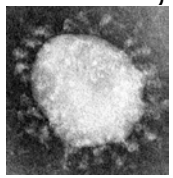


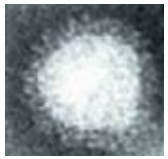
Bunyavirus - Rift Valley fever virus



Morbilivirus - Measles virus

Coronavirus - SARS1, MERS, SARS2, $\alpha/\beta/\gamma/\delta$ VOC, bat CoV





Togavirus - Chikungunya and Mayro species

…plus many chimeric, antigenically altered VEP

Acknowledgements

UNIVERSITY OF SUSSEX
Mariliza Derveni
Beth Auld

Leandro Castellano
Tom Stiff

Luca Biasetti
Catherine Hall

Arathy Jose
John Spencer

Rachel Lam
Barny Greenland

Adam Watson
Tony Oliver
Helfrid Hochegger
Tony Carr
Michelle West

ANIMAL AND PLANT HEALTH AGENCY
Ash Banyard

NIBSC
Emma Bentley
Mark Page
Giada Mattiuzzo

Saiba

Life Sciences

Ewart Bequest

PIRBRIGHT INSTITUTE
Nazia Thakur
Toby Tuthill
Dalan Bailey

UKRI Medical Research Council

UNIVERSITY OF KENT
Nigel Temperton
Simon Scott

UNIVERSITY OF CAMBRIDGE
Rebecca Kingsley
George Carnell
Jonathan Heeney

UNIVERSITY OF BERN
Mona Mohsen
Martin Bachmann