

A One Health approach to COVID-19 research in the UK

Eleanor Riley

Institute of Immunology and Infection Research



THE UNIVERSITY *of* EDINBURGH

Learning from animal coronaviruses: 1

Virus emergence and evolution

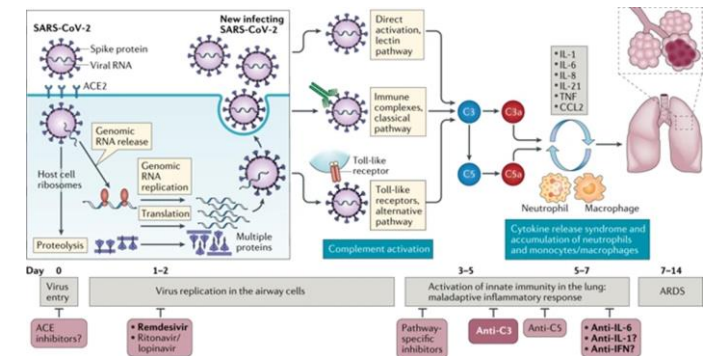


- **Coronaviruses have regularly and repeatedly emerged** in new host species, often via virus recombination within an intermediate host, e.g.
 - cattle for HCoV OC43 (1890s)
 - camels for HuCoV 229E and MERS (2010s)
 - civet for SARS (2000s)
- **East Asia is a hotspot for emergence of coronaviruses**, in pigs as well as humans. E.g. in pigs: porcine epidemic diarrhoea virus (PEDV), transmissible gastroenteritis virus (TGEV), porcine deltacoronavirus (PDCoV), and severe acute diarrhoea syndrome (SADS-CoV; 2017)
- **Human CoVs have been historically poorly studied** as they “just” cause common cold. E.g we don’t know how HCoV OC43 has evolved in the last 100 years – if we did it might help us predict what will happen to SARS-CoV-2.
- **Evidence for cross-protection between CoV species**, e.g. porcine respiratory coronavirus (PRCV) cross protects vs TGEV, as both viruses endemic world wide TGEV has become less of a clinical problem

Learning from animal coronaviruses: 2

Pathophysiology: variation in disease presentation/severity

- canine respiratory betacoronavirus:
 - asymptomatic, or kennel cough, or severe bronchopneumonia;
- bovine CoV:
 - dysentery, respiratory symptoms, pneumonia, fever
- porcine respiratory coronavirus:
 - clinically mild respiratory infection or pneumonia
- feline alphacoronavirus:
 - mild disease; virus accumulates in-host mutations to cause feline infectious peritonitis, similar pathophysiology to pediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 (PIMS-TS)



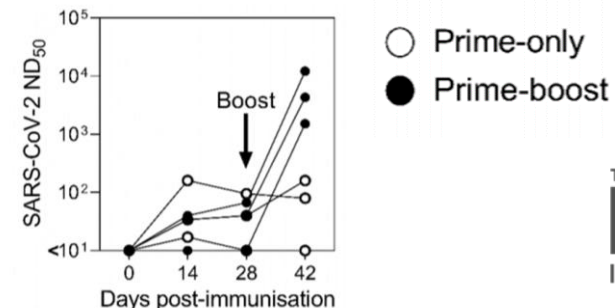
Learning from animal coronaviruses: 3

Vaccines

- effective vaccines exist to protect against CoVs in cats, dogs and livestock
- vaccines remain effective for decades, indicating slow evolution and lack of viral escape
- live attenuated (e.g. porcine TGEV) and inactivated (e.g. porcine SADS and bovine CoV) whole virus vaccines can work
- antibodies and cellular immunity both important.
- passive immunity conferred by neutralising Ab in milk.
- **but:** avian infectious bronchitis virus (IBV) - virus attenuation provides poor cross protection, reversion to virulence, and varying efficacy; full length spike vectored vaccine is more protective than subunit vaccines but still limited cross protection.

Animal models

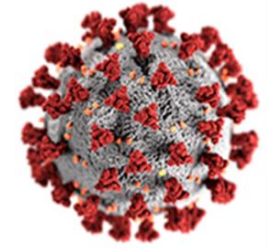
- Conserved biology of CoVs – using animal viruses to screen antivirals
- Vaccine immunogenicity testing in pigs: ChAdOx1 nCoV-19 (AZD1222) vaccine two doses better than one



Planning ahead: UK Vaccines R&D Network

- Established in 2016 – post Ebola, co-incident with Zika
- Members from medical *and* veterinary vaccines research and manufacturing communities
- Agreed a prioritised list of pathogens with epidemic potential for which we lack vaccines, included MERS and “disease X”
- Developed a decision tree to determine relevance of emergency vaccine development in any particular outbreak scenario
- Developed a tool to identify bottlenecks for vaccine development and manufacture
- Conducted a review of vaccine manufacturing capacity in UK
- Provided £110M funding for
 - Research on One Health approaches to vaccine development; vaccine epidemiology; vaccine development for priority diseases; novel vaccine platforms (including ChAdOx and RNA vaccines); post vaccination Guillain-Barre syndrome; manufacturing
 - Future Vaccine Manufacturing Research Hub
 - Vaccines Manufacturing Innovation Centre

Funding and Policy



UK Research and Innovation (UKRI) COVID-19 Taskforce:

- bringing together researchers across all disciplines (including social sciences, humanities, economics, physical sciences as well as biological, biomedical and clinical) with government agencies and SAGE

Direct funding from government:

- Epidemiology; clinical studies; clinical trials; vaccine, diagnostics and drug development

Rapid Response funding:

- £50M via UKRI for research with public health impact within 12 months
- £20M joint funding UKRI and Department of Health and Social Care
- new tranche of funds expected this month

Coordination:

- portfolio review, gap identification, commissioning research to fill gaps

Current gap:

- human-animal interface, potential for reverse zoonosis, establishment of new animal reservoirs of infection

One Health approach in Edinburgh:

Moredun Research Institute and Scotland's Rural College (SRUC)

- Providing capacity for SARS-CoV-2 virus diagnostics

Roslin Institute conducting research on

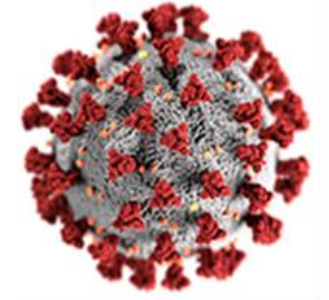
- Virus dissemination in waste water (with Scottish Water)
- Functional genomics of SARS-CoV-2
- Construction of pseudoviruses for drug screening
- Expression of SARS-CoV-2 spike proteins in influenza A and rotavirus vaccine mimics
- Tracking virus transmission via virus phylogeny
- Generating a hACE2 gene edited pig as a large animal model of Covid-19
- Adapting EPIC livestock disease simulation models to inform disease control policy and assess the unique risks to Scotland's demography
- Developing an epidemiological decision support toolbox to inform policy and decision making in Uganda and Kenya

Global Academy of Agriculture and Food Security

- Assessing the socio-economic impact of COVID-19 and the lockdown on food security, e.g. on broiler and fish value chains in India and Bangladesh



Can we do better?



The international research community has “played a blinder”

In 6 months, we have

- identified and sequenced the virus (thousands of times) and mapped its spread
- initiated > 200 vaccine development programmes with at least 5 in human trials
- significantly improved case management

But, we still don't know

- why some people are severely ill whilst others are very mildly affected
- is there protective immunity and how long does it last?
- will any of the vaccines work and if so, why?
- is the virus evolving or just drifting?
- where did the virus come from?



*A One Health approach can help (or is essential)
to answer all of these questions*