University of Bristol COVID19 Emergency Research Group (UNCOVER)[1] – Written evidence (COV0040)

This submission focuses on virology and research needs, and is led by Dr David Matthews, Reader in Virology[2], and Dr Andrew Davidson, Reader in Systems Virology[3],at the University of Bristol's COVID19 Emergency Research Group (UNCOVER)

The University of Bristol's expertise in coronavirus research includes MERS-CoV, SARS-CoV and related animal coronaviruses. It had the only UK facility actively working with live MERS-CoV prior to the outbreak, and was working with live SARS-CoV-2 by March.

Key points

- Fundamental research on SARS-CoV-2 was not immediately supported by UKRI. Many UK-based virologists were sent home from their laboratories instead of being supported to repurpose their research into the virus.
- The University of Bristol characterised the virus and published the UK's first SARS-CoV-2 live virus research output at the end of March.
- These findings about virus adaptation had significant consequences for vaccine testing efforts, and resulted in urgent global guidance from WHO to teams testing SARS-CoV-2 vaccines.
- This expertise in handling dangerous respiratory pathogens has been crucial to help establish safe virus inactivation protocols for teams elsewhere, including some of those leading the testing and genome sequencing efforts.

From our perspective, virology research was neglected by UKRI whose agenda appears to have been rapidly dominated by teams focussed on progressing research that could be done in the absence of active live coronavirus research or facilities to handle the virus.

By contrast, at Bristol we had expertise in both MERS-CoV and SARS-CoV coronavirus research, and related animal coronaviruses, working at Containment Level 3. We had established this facility with help and advice from colleagues at PHE Porton Down. Thus, at the beginning of the outbreak we had the only CL3 facility in a UK university actively working with MERS-CoV.

In 2013/14, we had worked on the Ebola virus outbreak in W. Africa, with PHE Porton Down, Liverpool University and the US Food and Drug Administration. Because of this we were able to work with our UK collaborators again and secure immediate further funding from the FDA for SARS-CoV-2 research.

Thanks to this funding, just 5 weeks after receiving a live sample, we characterised the virus and published the UK's first SARS-CoV-2 live virus research output, a pre-print, at the end of March[4].

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[1] https://www.bristol.ac.uk/research/impact/coronavirus/research-priorities/

[2] https://research-information.bris.ac.uk/en/persons/andrew-d-davidson

[3] https://research-information.bris.ac.uk/en/persons/david-a-matthews

[4] Characterisation of the transcriptome and proteome of SARS-CoV-2 using direct RNA sequencing and tandem mass spectrometry reveals evidence for a cell passage induced in-frame deletion in the spike glycoprotein that removes the furin-like cleavage site

In this work we found that the virus rapidly changed and adapted when grown in the laboratory using the one cell line being used globally for viral growth. This adaptation had and has significant real-world consequences for global efforts to test a vaccine. Our findings were sufficiently serious to have been immediately discussed at the WHO steering committee on COVID-19 and resulted in urgent global guidance to teams testing SARS-CoV-2 vaccines.

Subsequently, with colleagues at Bristol we identified Neuropilin-1 as a highly significant host cellular co-factor for virus infection[5]. In addition, we have helped numerous teams (including those leading the testing and genome sequencing efforts) to establish safe virus inactivation protocols for their work – absolutely critical to these efforts and something that can only be undertaken by teams with expertise in the handling of these dangerous respiratory pathogens. We have also been instrumental in helping develop qRT-PCR and serological tests for SARS-CoV-2, with others in the UNCOVER team.

Our experience of the UK response has been that it was focussed on a narrow agenda that suited institutions which had no access, expertise or facilities capable of working with the virus. We have been left with the impression that this is linked to a mindset within UKRI that fundamental research should not be prioritised – setting a tone (deliberately or inadvertently) that benefited institutions with limited or no direct expertise or experience with coronaviruses.

At the outset, Bristol was the only UK university with an active coronavirus research programme with in-house expertise, facilities to work with live human coronavirus and previous experience of outbreak research. Despite all this, we were heavily reliant on US funding to stay open, conduct valuable research and help other teams in the UK with their efforts. Only at the end of June – more than six months after the start of the outbreak - have we finally secured funding from UKRI.

Finally, from our perspective, the concept that fundamental research on SARS-CoV-2 should not be immediately supported is a serious and inexplicable error of judgement. Outside of Bristol, this led to many talented UK virologists being sent home from their laboratories instead of repurposing their experience and talents into gaining insights into this dangerous virus. Such research could have uncovered important findings that could have significantly contributed to the global effort against this virus.

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bioRxiv 2020.03.22.002204; doi: https://doi.org/10.1101/2020.03.22.002204

[5] Neuropilin-1 is a host factor for SARS-CoV-2 infection
James L. Daly, Boris Simonetti, Carlos Antón-Plágaro, Maia Kavanagh Williamson, Deborah K. Shoemark, Lorena Simón-Gracia, Katja Klein, Michael Bauer, Reka Hollandi, Urs F. Greber, Peter Horvath, Richard B. Sessions, Ari Helenius, Julian A. Hiscox, Tambet Teesalu, David A. Matthews, Andrew D. Davidson, Peter J. Cullen, Yohei Yamauchi
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