

COVID 19

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Miscellany 2

As befits Cambridge and Silicone Fen we have a weekly Newspaper... The Cambridge Independent. This paper has been rich with Science and Business articles recently.

27th May 2020 - Article 1. **Avacta's rapid Point of Care COVID 19 Antigen Test.** This Cambridge bio-therapeutic company has developed Affimer reagents that detect the SARS CoV-2 Virus spike protein. They do this using a designed, cloned protein one tenth the size of a natural antibody which mimics the molecular recognition of monoclonal antibodies in other applications (Wikipedia). Avacta is now supplying Cytiva, a multinational life science company, who will develop the reagents into a "**saliva based rapid antigen test strip**". Avacta's CEO Dr. Alistair Smith looks forward to achieving the capacity to meet the demand worldwide for 100's of millions of self administered (saliva) tests.

Affimer proteins were initially developed at the MRC Cancer Cell Unit in Cambridge and then across two Laboratories at the University of Leeds. They are produced in a recombinant system. A protein encoded by a gene-recombinant DNA (described as recombinant DNA) that has been cloned in a system that supports the expression of the gene and the translation of messenger(m)RNA, is termed a Recombinant Protein.

Article 2. **CCL able to run 500 COVID 19 tests a day for care homes.** Cambridge Clinical Laboratories (CCL) is part of a network of independent labs that has negotiated a deal with the Dept. Health & Social Care. CEO Dr.Tony Cook, has been frustrated by the centralised approach adopted by Public Health Bodies in the UK which left more than 100 private labs under-utilised. He believes that Matt Hancock's targets have been a device to force bureaucracy to get moving. He now looks to expand CCL using a £50,000 Government Innovation Loan and reports poor backing from the banks.

The lab will use the Gensig test from Prima Design in Southampton. The Gensig test uses a Polymerase Chain Reaction (PCR) to make multiple copies of a segment of DNA. This process, which is fundamental to much of genetic testing, as invented in 1984! PCR only works on DNA – so the detection of Covid 19 single strand RNA depends on it *first being converted to DNA*. This

conversion to DNA is called Reverse Transcription. RT- PCR originally relied on the use of radioisotopes for labelling. This labelling technique now uses fluorescent dyes - but a superficial search on line soon reveals an Educational video from the International Atomic Energy Agency. The nuclear industry is still maintaining a positive profile!!

Article 3. **Addenbrookes is taking part in a new national trial** and Professor David Menon, Professor of Anaesthesia - Head of my old Department, is one of the principal investigators. In this Trial, Convalescent Plasma will be given to people with COVID 19 who are struggling to develop an immune response.

Antibody rich plasma, known as “Convalescent plasma” is a product of blood donation from those who have fully recovered from COVID 19. The Plasma collected by NHS Blood & Transplant Service can be frozen for storage. The call has gone out for plasma donors, especially from those who have needed hospital treatment, are male or are over 35 years of age. People in these three groups are more likely to have high antibody levels.

The Cambridge Independent on 10th June reported that the three local Cambridgeshire NHS Trusts, Addenbrookes, Royal Papworth and Cambridge/ Peterborough Mental Health are participating in the CoV002 Trial, one of 8 UK centres taking part. This Trial will use the University of Oxford developed vaccine (ChAdOx1 nCov-19) now being produced at scale by Astra Zeneca on the Cambridge Biomedical Campus. The vaccine has been renamed AZD1222. The enrolment for the CoV002 Trials involves 5,000 in Phase 2 and in Phase 3 a further 5,000 adult volunteers in the UK, plus 30,000 in the USA and 2,000 in Brazil. Astra Zeneca has agreed to manufacture and distribute the vaccine. Search O.U. Covid 19 Trials) Astra Zeneca has signed agreements ‘to supply more than 2 billion doses globally with the first doses coming to the UK in September 2020, *if trials prove successful*. This commitment is made even more remarkable by that phrase. *Has an International Pharmaceutical Company ever before made such a step of faith in science?!!* Astra Zeneca have reached agreement with Europe’s Inclusive Vaccine Alliance (IVA), spearheaded by Germany, France, Italy and the Netherlands, to supply up to 400 million doses of the University of Oxford’s Covid 19 vaccine, with deliveries starting by the end of 2020. The CEO of Astra Zeneca has expressed his gratitude to those four governments for their commitment and swift

response. IVA aims to accelerate the supply of the vaccine and make it available to other European countries.

In what Astra Zeneca describe as... *the next step in its commitment* to broad and equitable global access to Oxford's Covid 19 vaccine...*landmark agreements* have been signed for 750,000 million doses with CEPI and GAVI. CEPI is the Coalition for Epidemic Preparedness Innovations - created after the Ebola as *an agency of coordination working closely with WHO*, and GAVI is the Vaccine Alliance – a public-private global health partnership with the goal of increasing access to immunisation in poor countries. Astra Zeneca has committed to support the manufacturing, procurement and distribution of 300million doses with delivery starting by the end of 2020. Also, they have signed a licensing agreement with SII, the Serum Institute of India, to supply one billion doses for low and middle income countries with a commitment to provide 400 million doses in 2020.

On 21st May, Jane & I attended a **RSM Webinar on COVID19 & BAME**. From this more intimate Zoom Forum we heard learned opinions. Covid 19 is complex and subject vulnerability is multi-factorial. There is variation of the mechanism of infection across the world and it may be that certain chronic infections actually confer resistance. One contributor talked about the possibility of hidden mechanisms being active – “akin to postulating dark matter”! ACE Inhibitors (such as Irbesartan) are a standard medication for high blood pressure. Coronavirus enters cells via the Angiotensin-Renin Enzyme – ACE - system which is abundant in the lung epithelial cells. There is no clear evidence ACE Inhibitors are good or bad for Covid 19, so don't stop them. Remdesivir helps but there is no clear data that it reduces mortality. Low dose Heparin reduces platelet stickiness and small clot formation. Vitamin D is good for bone and the immune system. A French trial using supplements is underway. The question was posed whether PPE is regarded as automatic, a right or a privilege? PPE was *not* originally recommended in the care of mentally ill patients. We *now know* that properly donned PPE staff are *not* dying in disproportionate numbers. Were voices not heard? The final appeal was “We must get beyond BAME with good epidemiology”.

Finally, we attended a **Webinar from Exeter College, Oxford on 18th June**. Dr. Catherine Green leads the Clinical Bio-manufacturing Facility (CBF) for the

Nuffield Dept.of Medicine, collaborating with the Jenner Institute which, over the last 15 years, has developed many novel vaccines for clinical trials. These include malaria, TB, Ebola, MERS, Zika and rabies among others. Dr. Green declared that with this experience, CBF not only saw Covid 19 coming but also had a good idea how they would produce a vaccine. The trick, she explained, is always to find the funding! Her work is normally funded by government via the Engineering Research Council.

The genetic sequence for Covid 19 was released by the Chinese on the 10th January. After construct designing, CBF was in production by the 22nd January. CBF has extensive experience using a chimpanzee adenovirus. By genetic engineering, they first remove the virus's ability to replicate. Then a key antigen trigger - the Covid spike protein - is added. The result is a 'bag of membranes' which can enter human cells and provoke a strong and lasting immune response from host T and B cells.

From concept to Phase 1 (proving safety in humans) typically takes 5 years. For the Oxford Covid 19 Vaccine this has been condensed into as many months! Dr Green reflected that Astra Zeneca has really felt the white heat of academic vaccine research by collaborating with the CBF!

Currently, Phase 2 and 3 trials (2 x 5,000 volunteers) are underway across several areas in south and west UK. The regulators will soon be asked to unblind the results for the first 100 subjects.

If she were to be asked by the Prime Minister, Dr. Green would say **that Basic Science matters and the work on unloved exploratory territory is the vital foundation. It must be funded as well as the transformatory work.** Already further Government funding has also been awarded to Oxford Biomedica to convert the Old GPO Sorting Office in Oxford to hold four **clean rooms** for vaccine production!

David R Hughes

President IESF GB

30th June 2020