Lab Animal Models Critical role against the COVID-19 pandemic intensifies- Part III.

There continues to be an abundance of articles on COVID-19 on animal models and treatments which are being captured on many different sites as examples:

AMP (Americans for Medical Progress)
https://www.amprogress.org/covid-19-resources/

CBRA (California Biomedical Research Association) https://ca-biomed.org/

FBR (Foundation for Biomedical Research)
 https://fbresearch.org/covid-19-resources-page/

EARA (European Animal Research Association) –
https://www.eara.eu/about-animal-research?mc_cid=91cdd59356&mc_eid=8f590880c0

NIH: COVID-19 Scientific Interest Group
https://oir.nih.gov/sigs/covid-19-scientific-interest-group#other

We continue our selection of recent important articles that emphasize the need of animal studies in allowing critical understanding of the pathogenesis and areas of intervention essential for the development of pharmaceutical products against COVID 19.   Having well-defined appropriate animal models allows the accelerated research responses.

Small animal models with the greatest availability and use to date have been the genetically engineered mice k18-hACE2 and variations of those by different labs. Others have been looking at hamsters, guinea pigs, ferrets and mink that have the angiotensin-converting enzyme 2 (ACE2) epithelial site receptor (the target of the SARS-CoV-2 virus of COVID-19) more closely aligned with the human ACE2 epithelial site receptor.   The

large animal focus has been Nonhumane primates with macaques (Rhesus and Cynos) as the primary focus but also African Greens, baboons and marmosets being studied as well.   As these models are being compared, we are getting a greater understanding of the basic science components of the pathogenesis and potential areas of therapeutic interventions.   The basic science is mostly focused on blocking the interaction of the spike protein of the SARS-CoV-2 virus with the ACE2 receptors present on the target respiratory epithelial cells using ACE2-Fc decoy proteins, as an example; COVIDTRAP™ (http://www.idahoreporter.com/2020/sorrento-therapeutics-stock-surges-after-covid-19-drug-breakthrough/).   Use of the animal models will validate the in-vitro cell studies to translate into the in-vivo testing that is needed for safety and efficacy of these concepts.   We have also seen reports of neutralizing antibody treatments for COVID-19 which has expanded the species spectrum for production of these with inclusion of Llamas, cows and pangolins with unique nanabodies from Llamas getting a fair amount of attention (https://www.inverse.com/science/animal-antibody-experiments-explained).   Again these in-vitro cells studies need to be translated into the in-vivo testing with the current animal models for safety and efficacy of these concepts.

Dozens of vaccines for the novel coronavirus and the disease it causes, COVID-19 are being studied by scientists. Virtually all of them have one thing in common — they're the product of animal research.   Medical progress is dependent on the animal research allowing critical understanding of the pathogenesis and areas of intervention essential for the development of pharmaceutical products against COVID-19 (SARS COV-2).

More than 60 candidate vaccines are now in development, worldwide, and several have entered early clinical trials in human volunteers, according to the World Health Organization. The best candidates have

started testing in animal models that will be most important for the safety and efficacy testing prior to wide dissemination and use in human populations. Some companies have moved timelines forward related to "strong animal data results" as mentioned by Johnson and Johnson Chief Scientfic officer Dr. Paul Stoffels during an interview with CNBC in regards to outcomes of NHP studies. Human clinical trails have been moved up to mid July from September time period (https://www.youtube.com/watch?v=dY1XMcPG9QA).   Moderna's leading mRNA vaccine has appeared to have cleared a safety hurdle due to some limited studies done in mice models, a paper is forthcoming and more studies are expected (https://www.reuters.com/article/us-health-coronavirus-moderna/moderna-covid-19-vaccine-appears-to-clear-safety-hurdle-in-mouse-study-idUSKBN23J2S4).

Dr Anthony Fauci the well-respected director of the National Institute of Allergy and Infectious Diseases earlier reminded all of us how important the animal research is for COVID-19 outcomes, especially with vaccine development. "There are diseases in which you vaccinate someone, they get infected with what you are trying to protect them with, and you actually enhance the infection. You can get a good feel for that in animal models," said during a White House briefing on March 26.

The real ground work for many of these COVID-19 outcomes have been building on earlier work done with MERS and SARS, outlining how important it is for this work to continue. The SARS COV-2 appears to be changing (some would say adapting and others mutating). The SARS COV-2 that is prominent in the US and Europe has 4-5 more protein spikes than the original variant from WuHan (https://cbs12.com/news/local/scripps-scientists-detect-covid-19-mutation).   "This has not made it more deadly or cause worse disease", it has allowed it to spread more quickly. There is also great debate if we have started the second wave now or if we are still in a prolonged first

wave. The good news is that the continued vaccine work appears to be effective with either variant currently. This is highlighting the critical need and development of the animal models and their importance in determining effective and safe solutions as we continue in this war on this virus.

On a different front of the war we shift our focus on how animal facility managers have had to realign their priorities and the staff to a full crisis management mode and still support the critically needed science. Their primary priorities of social distancing while providing adequate welfare and support to the animals, and having adequate PPE to protect the front line staff required multitasking abilities and skills for achievements that need recognition from the biomedical research community and the general public (https://www.nature.com/articles/s41684-020-0548-7). The front line staff also should be recognized for the difficult but needed work they continue to do to find the necessary preventions and treatments for this pandemic as well as other therapies and preventions needed through the use of animal models and animal research. Many institutions are putting FAQs on their web sites as to help guide the research and care staffs on operation protocols during the pandemic, a couple of examples are linked here: (https://research.uoregon.edu/covid-19-faq-researchers#animals); (https://www.urmc.rochester.edu/coronavirus/coronavirus-research/guidance-for-researchers/laboratory-and-animal-research.aspx); (https://www.research.psu.edu/covid_iacuc);(https://research.duke.edu/covid-19-animal-research).

The critical science and the science staffs that are directing and conducting the appropriate studies through use of the animal models need recognition for all that they have done and will continue to do to make these efforts as successful, rapid, and safe for the general public. As we adjust to our new normal, the biomedical research community

remains resilient, productive, effective, efficient and determined, all with and through the needed studies in animal models.   As has been stated many times, WE are all in this together…