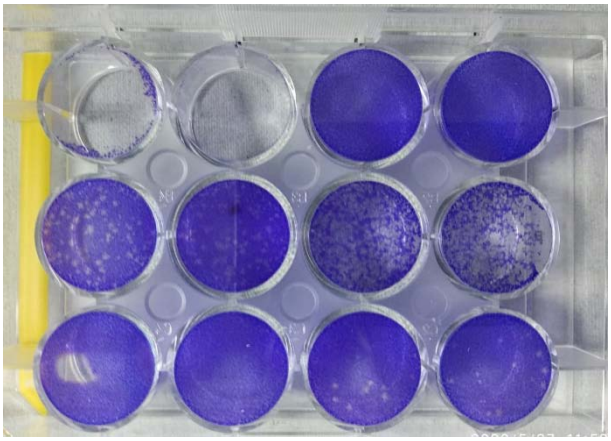
Coronavirus cell culture to make vaccines and test drugs at CCMB

Over the last month and a half, CSIR-Centre for Cellular and Molecular Biology (CCMB) has establishedstable cultures of COVID-19 causing coronavirus, SARS-CoV-2 from patients' samples.A team of researchers led by the Virologist in CCMB, Dr. Krishnan H Harshan have isolated infectious viruses from several isolates. The ability to culture the virus in lab enables CCMB to work towards vaccine development and testing potential drugsto fight COVID-19. It also makes them a potential donor of the culture to other authorized centres that can continue growing the virus for their own use.

PhD students in Krishnan lab working with the viral culture

This virus is known to infect epithelial cells in human respiratory tract. The viruses infect these cells by interacting with receptor proteins called the ACE-2 following which the virus is internalized by a process namely endocytosis. Virus RNA is later released into the cytoplasm of the cells where it makes viral proteins first and then starts to replicate the genomic RNA. Thus, the virus uses resources from these cells to make more copies of itself. Therefore the virus needs a set of host factors that allow it to replicate. "Currently, primary epithelial cellsgenerated from human origins do not growfor many generationsin labs, which is keyto culturing viruses continuously. And hence, CCMB and other labs who are growing the virus need an 'immortal' cell line", says Dr Krishnan. They use Vero cells – kidney epithelial cell lines from green African monkey, which express ACE-2 proteins and carry a mutation that allows them to proliferate indefinitely.



Viruses growing as white translucent plaques among blue live Vero cells

Potential uses of cultured SARS-CoV-2

1. Vaccine: Vaccines are those specific agents generated from a particular pathogen that trigger immune response in the host organism that can be used as a protection from infection by the respective pathogens. Usually, proteins specific to pathogens are good candidates as vaccines. Such proteins with antigenic properties trigger antibody response in the host. Depending on the nature of the antigens, the antibody response could be long-term or short-term. Historically, attenuated or killed viruses are used as vaccines in several cases such as in the case of polio. Though the inactivated virus can not initiate infection, their structural proteins trigger antibody production in the cells. The efficacy of inactivated SARS-CoV-2 as vaccine candidate is currently being investigated by several groups.
2. Antibodies or anti-dotes: Inactivated viruses can trigger antibody response in other mammalian hosts in addition to humans. Various such hosts are currently under test for their efficiency of antibody response. They can vary from small rodents such as mice to large mammals such as horses and camels. Such antibodies generated in these non-human hosts can be purified and processed for injecting into humans. Such antibodies can trigger antiviral response upon injection into humans and have the potential of limiting the infection. These antibodies are not vaccines, but can be considered as anti-dotes against the virus.
3. Testing of antibodies: A class of antibodies referred to as neutralizing antibodies have the ability to bind to viruses thereby preventing them from infecting cells. Such neutralizing antibodies can be generated in other mammals as explained above. During the characterization of such antibodies, their neutralizing capacity is studied by incubating with infectious virus to check the prevention of infection. Effective antibodies are those that block the infection successfully. Virus cultures are very important components in identifying such antibodies.
4. Drug-screening: The phase I of antiviral drug trial is based on the effect of a potential drug on limiting the replication of virus. Here, cells are infected with SARS-CoV-2 in the presence or absence of a potential drug. Subsequently, the effect on viral replication is studied. A good drug would have a profound effect on virus replication in culture. However, a quick way to identify a good drug is to repurpose those that are already being used in humans for various other conditions. Such drugs have undergone clinical trials including toxicology studies. If found having anti- with SARS-CoV-2 effects, they can be quickly tested in humans for limiting Covid-19.
5. Testing of various disinfectants: Currently there is a huge need for surface disinfectants that can kill with SARS-CoV-2 on various surfaces including PPE kits and clothes. Virus culture is a key component in studies that can test the efficacy of several proposed disinfectants. Here, the ability of the key ingredients of the disinfectant will be tested for their ability to kill the virus.

6. Testing of Instruments: Ultraviolet rays (UV) are well known agents that can effectively kill virus particles and prevent infection. There is a huge demand both for domestic and industrial activities to eliminate with SARS-CoV-2 from various materials including packaging materials. Such instruments need to be tested for their efficiency in killing SARS-CoV-2 after exposing virus cultures to the UV rays. Here again, with SARS-CoV-2 cultures are the key component in such tests.

“Using the Vero cell lines to grow the coronavirus, CCMB is now in a position to isolate and maintain viral strains from different regions. We are working towards producing viruses in huge quantities that can be inactivated, and used in vaccine development and antibody production for therapeutic purposes. We have also started testing potential drugs with other partners such as DRDO using this viral culture. We hope that such systems are replicated at multiple research institutes and private companies to become a useful resource in the fight against this pandemic as well as for future preparedness”, says CCMB Director, Dr Rakesh Mishra.