A novel in-vitro model for COVID-19 virus propagation

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Abstract

Angiotensin-Converting Enzyme 2 (ACE2) is cell surface receptor responsible for SARS-CoV-2 entry highly expressed in maternal-fetal interface including placenta cells e.g. stromal cells, prevascular cells of deciduas, cytotrophoblast, syncytiotrophoblast. Several studies reported lack of transplacental transmission of SARS-CoV-2 from a COVID-19 positive mother to fetus suggests that the SARS-CoV-2 may not be transmitted from mother to her child due to some placenta barriers but may be replicating inside the placenta. Our earlier studies demonstrated that human placenta organ culture supports the replication of Japanese Encephalitis(JE) virus indicating their susceptibility and possibility to support propagation of other viruses. Based on our previous experience and present work, we propose that human Placental organ culture will be an ideal in vitro model for propagation of COVID-19 as it has the requisite receptors and tissue architecture needed for virus replication and vaccine development.

Letter to the Editor

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Key Words: Placenta, COVID-19, Vertical Transmission, Organ Culture, Virus Propagation, Vaccine Development, Culture Media, elution of virus

Research is an integral part in response to COVID-19 outbreak to indentify the loopholes in current available scientific knowledge. COVID-19 was reported as a pandemic threat to the global public health by World Health organization (WHO) because of its higher rate of community spread, level of severity and mortality [1]. In response to COVID-19 outbreak, there is an urgent need to speed up the development of vaccines and novel therapeutics [1]. Number of increased cases worldwide raised the anxiety about viral intrauterine transmission from mother to her fetus. It has been confirmed that the Angiotensin-Converting Enzyme 2 (ACE2) is cell surface receptor responsible for SARS-CoV-2 entry, increasing infections and transmission in humans; yet the capacity of vertical transmission of the virus is a mystery [2,3].

Findings by *Li et. al., 2020* suggested that ACE 2 receptor is highly expressed in maternal-fetal interface including placenta cells e.g. stromal cells, prevascular cells of deciduas, cytotrophoblast, syncytiotrophoblast [2]. Additionally, the findings reveals that the elevated levels of ACE-2 might increase the threat of vertical transmission of SARS-CoV-2 through placenta and increase the risk of fetal infections. However, there are no reports till date that COVID-19 infections in new born occur through nCoV infected mothers, yet the preeclampsia and fetal distress are predicted outcomes (Table 1).*Lu Q. and Shi Y. 2020* study is also reported the zero threat of transplacental transmission of SARS-CoV-2 from a COVID-19 positive mother to fetus; however the pneumonia infections is one of the leading cause of pregnancy deaths worldwide[4,5,6]. Current available knowledge suggests that the SARS-CoV-2 may not be transmitted from mother to her child due to some placenta barriers but may be replicating inside the placenta. Here, we hypothesize that

placenta could be carrier / reservoir for COVID-19. It will not transmit virus and may protect fetus. Hence placenta could be an ideal for propagation of virus for vaccine development.

Bhonde et.al. in 1985 shown that human placenta organ culture supports the replication of Japanese Encephalitis(JE) virus indicating their susceptibility and possibility to support propagation of other viruses [7]. An organ culture retains the most of the *in-vivo*histological features. An organ culture method is used to preserve tissue structure or functions; which allows the organ to still resemble and retain the characteristics they would have *in-vivo* [6,7]. Our team at Dr. D.Y.Patil Vidyapeeth has established in-vitro human placenta organ culture model, tested positive for pregnancy hormones HCG and prolactin indicating its fictional state (figure1). These findings may support our hypothesis. These human placenta organ cultures can present better results than traditional 2D cultures. We can use this human placenta organ culture as a virus reservoir and will see whether this in-vitro model system is supportive of the hypothesis. If the human placenta organ culture supports the viral propagation, this in-vitro system can be used further to scale up the viral replication for vaccine development in short term. Based on our previous experience and present data we propose that human Placental organ culture will be an ideal in vitro model for propagation of COVID-19 as it has the requisite receptors and tissue architecture needed for virus replication. It is also possible that virus will be eluted out into the culture medium making the antigen collection easier for vaccine development.

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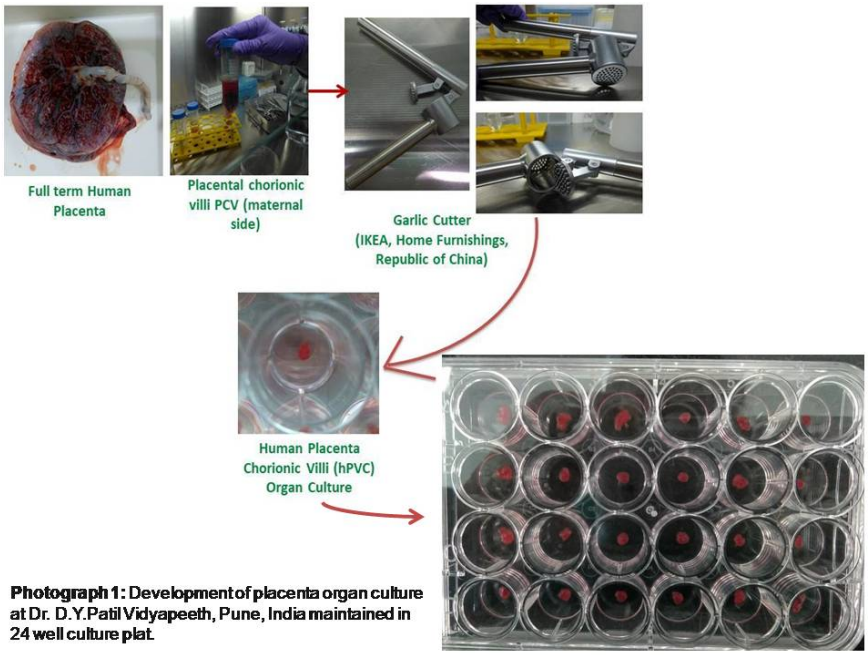
`Table 1.docx` available at https://authorea.com/users/318062/articles/448042-a-novel-in-vitro-model-for-covid-19-virus-propagation



Photograph 1: Development of placenta organ culture at Dr. D.Y.Patil Vidyapeeth, Pune, India maintained in 24 well culture plat.