

Investigating the Neuroinvasive Potential of SARS-CoV2 using Human Brain Organoid Cultures and Human iPSC-induced Microglia

The current outbreak of a coronavirus (CoV)-associated acute respiratory disease called coronavirus disease 19 (COVID-19) represents the third documented spread of an animal CoV to humans in less than 20 years with the original severe acute respiratory disease-associated CoV (SARS-CoV) and middle eastern respiratory-associated CoV (MERS-CoV) representing the first two outbreaks. SARS-CoV2 is the third CoV that has emerged and is the cause of COVID-19. Hallmark clinical features of all three CoV's following infection include fever, cough, and respiratory distress that can, in certain cases, lead to pneumonia. However, there is now emerging evidence that SARS-CoV2 may be able to infect the central nervous system (CNS) as some infected individuals exhibit signs including headache, loss of taste/smell, and altered mental state. Physicians have also reported COVID-19 patients exhibiting signs of stroke, seizures as well as encephalitis (inflammation of the brain). Collectively, the evidence certainly supports the possibility that SARS-CoV2 is able to enter the CNS and this raises some interesting and important questions. If SARS-CoV2 is able to enter the CNS it will be imperative to design effective anti-viral drugs that are capable of entering the CNS to dampen viral replication and spread throughout the brain. How CoV infects the CNS and causes disease is an area of expertise of several laboratories at UCI and how SARS-CoV2. Our recently funded award from UCI's CRAFT-COVID committee will explore the anti-viral activity of a novel drug following infection of both human brain organoids as well as human neurons and microglia with the goal of inhibiting SARS-CoV2 replication as well as possibly enhancing anti-viral immune responses.