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Proteomics of SARS-CoV-2-infected host cells reveals therapy targets.

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Abstract

A novel coronavirus was recently discovered and termed SARS-CoV-2. Human infection can cause coronavirus disease 2019 (COVID-19), which has been rapidly spreading around the globe[1,2]. SARS-CoV-2 shows some similarities to other coronaviruses. However, treatment options and a cellular understanding of SARS-CoV-2 infection are lacking. Here we identify the host cell pathways modulated by SARS-CoV-2 infection and show that inhibition of these pathways prevent viral replication in human cells. We established a human cell culture model for infection with SARS-CoV-2 clinical isolate. Employing this system, we determined the SARS-CoV-2 infection profile by translatome[3] and proteome proteomics at different times after infection. These analyses revealed that SARS-CoV-2 reshapes central cellular pathways, such as translation, splicing, carbon metabolism and nucleic acid metabolism. Small molecule inhibitors targeting these pathways prevented viral replication in cells. Our results reveal the cellular infection profile of SARS-CoV-2 and led to the identification of drugs inhibiting viral replication. We anticipate our results to guide efforts to understand the molecular mechanisms underlying host cell modulation upon SARS-CoV-2 infection. Furthermore, our findings provide insight for the development of therapy options for COVID-19.

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