ARTICLE

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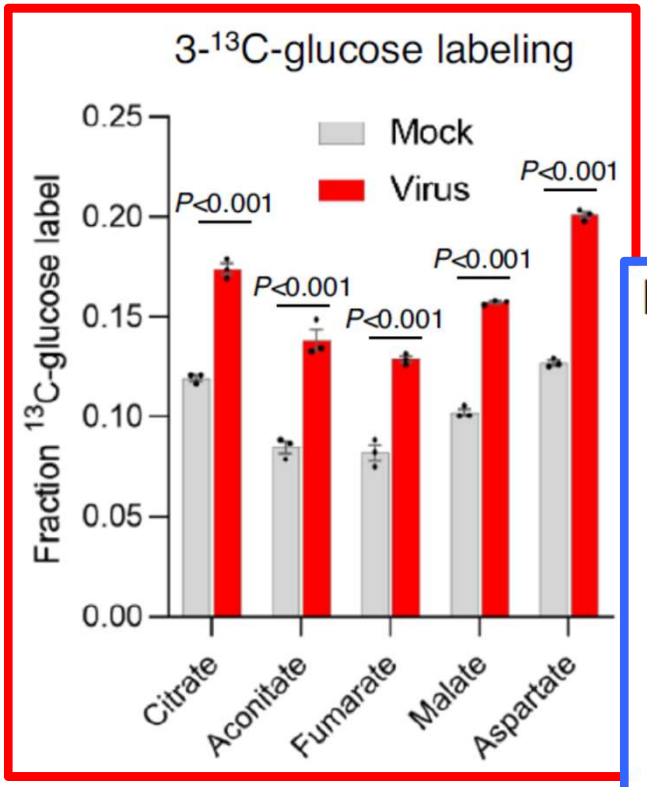
SARS-CoV-2 infection rewires host cell metabolism and is potentially susceptible to mTORC1 inhibition

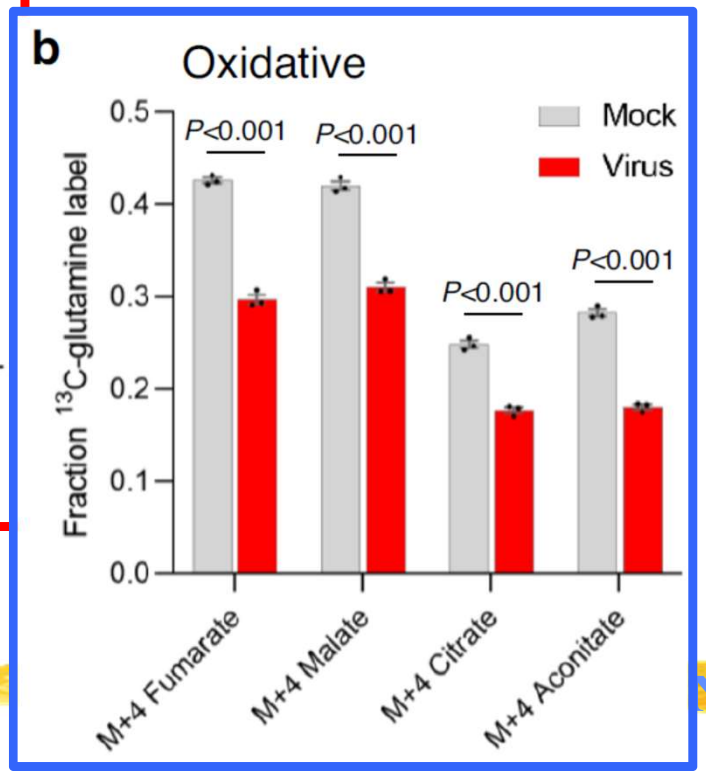
Peter J. Mullen[1], Gustavo Garcia Jr[2], Arunima Purkayastha[3], Nedas Matulionis[1], Ernst W. Schmid[1], Milica Momcilovic[4], Chandani Sen[3], Justin Langerman[1], Arunachalam Ramaiah[5], David B. Shackelford[4,6], Robert Damoiseaux[2,6,7,8,9], Samuel W. French[6,10], Kathrin Plath[1,4,6,9,11], Brigitte N. Gomperts[3,4,6,9,11], Vaithilingaraja Arumugaswami[2,6,12] & Heather R. Christofk[1,6,11,12]✉

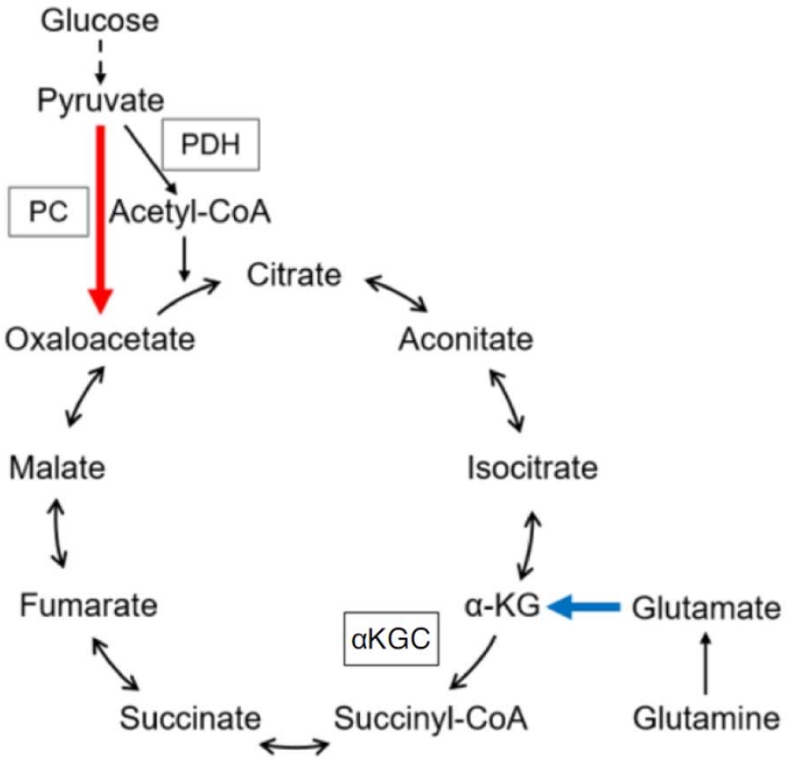
Viruses hijack host cell metabolism to acquire the building blocks required for replication. Understanding how SARS-CoV-2 alters host cell metabolism may lead to potential treatments for COVID-19. Here we profile metabolic changes conferred by SARS-CoV-2 infection in kidney epithelial cells and lung air-liquid interface (ALI) cultures, and show that SARS-CoV-2 infection increases glucose carbon entry into the TCA cycle via increased pyruvate carboxylase expression. SARS-CoV-2 also reduces oxidative glutamine metabolism while maintaining reductive carboxylation. Consistent with these changes, SARS-CoV-2 infection increases the activity of mTORC1 in cell lines and lung ALI cultures. Lastly, we show evidence of mTORC1 activation in COVID-19 patient lung tissue, and that mTORC1 inhibitors reduce viral replication in kidney epithelial cells and lung ALI cultures. Our results suggest that targeting mTORC1 may be a feasible treatment strategy for COVID-19 patients, although further studies are required to determine the mechanism of inhibition and potential efficacy in patients.

SARS-CoV-2 messes with the citric acid (TCA) cycle of infected kidney and lung cells

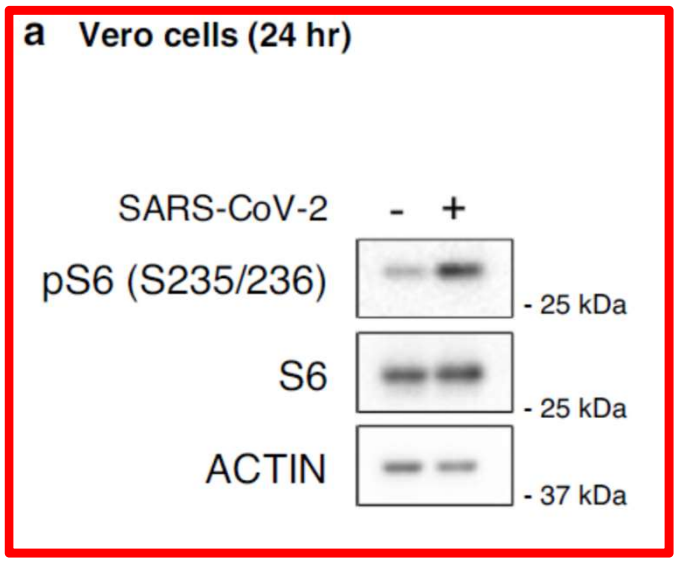
- **Pyruvate entry using pyruvate carboxylase is increased**
- **Oxidative use of glutamine is reduced upon infection**

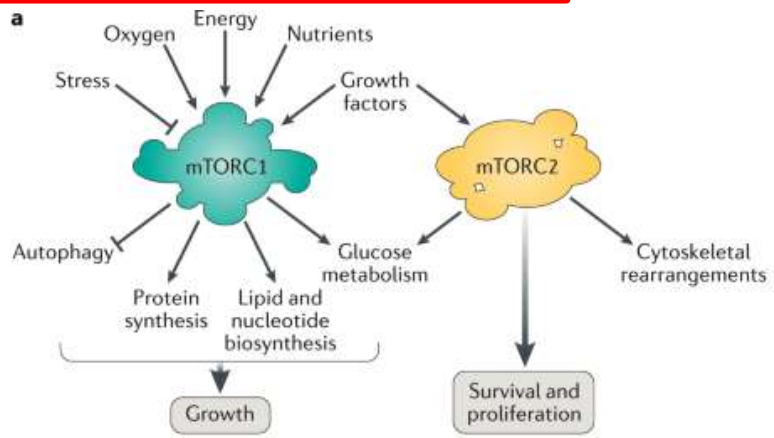


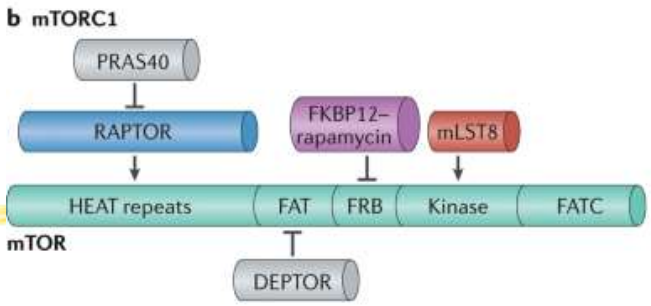


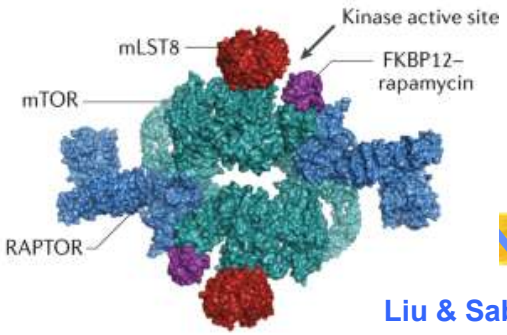


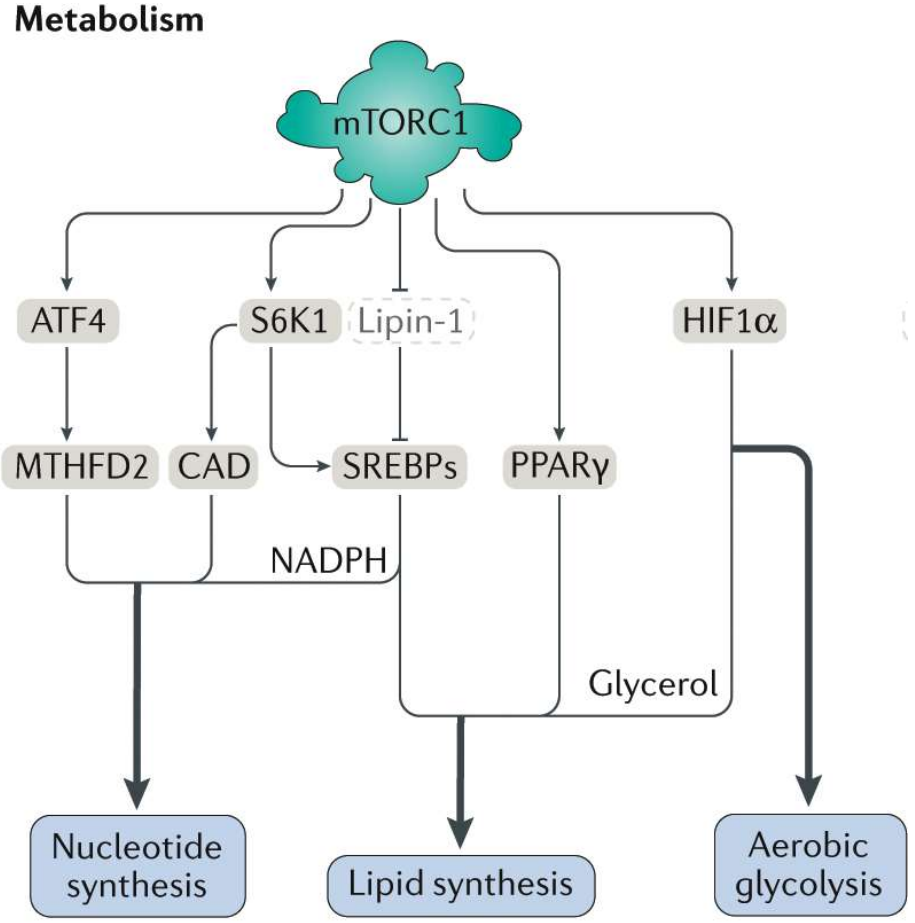
Master regulator mTORC1's activity is increased during SARS-CoV-2 infection











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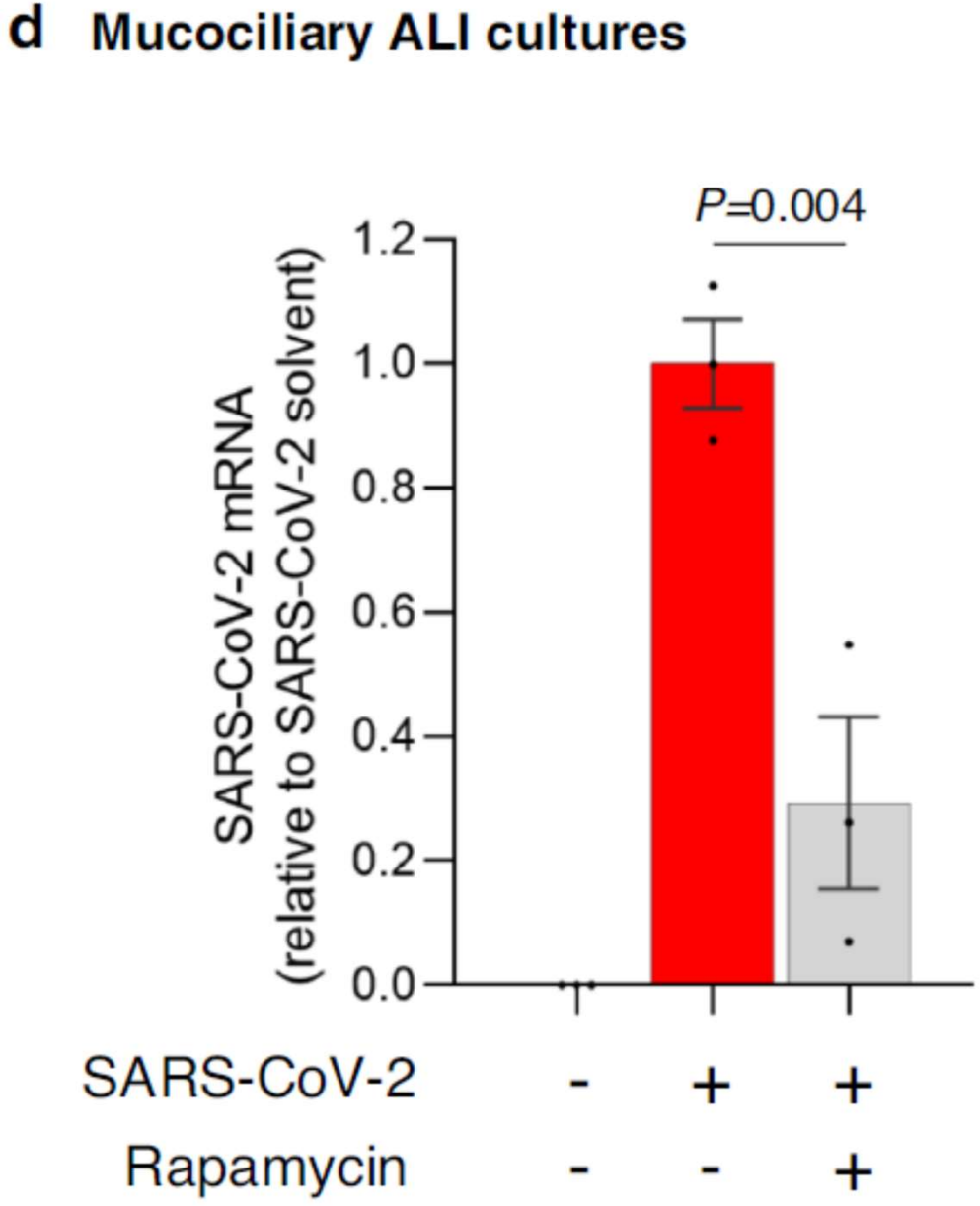
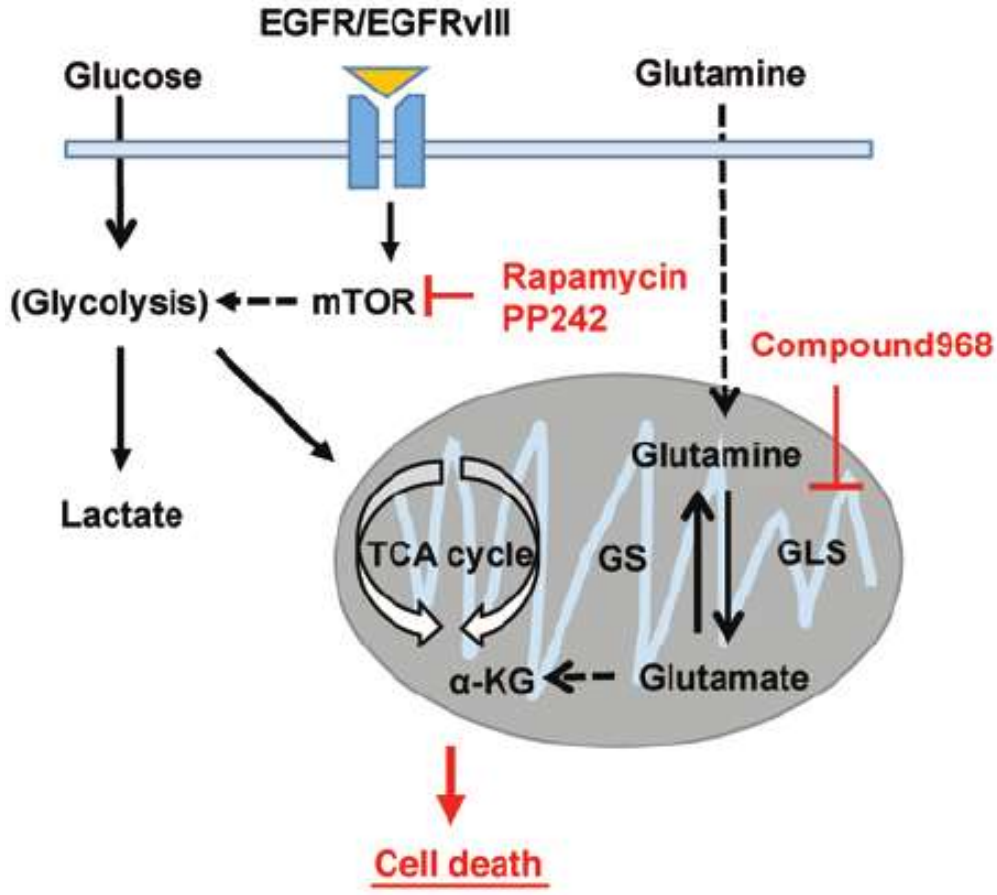
mTORC1 inhibitors reduce SARS-CoV-2 infection in air-liquid interface (ALI) cells





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