Discovery of mechanics of drug targets for COVID-19

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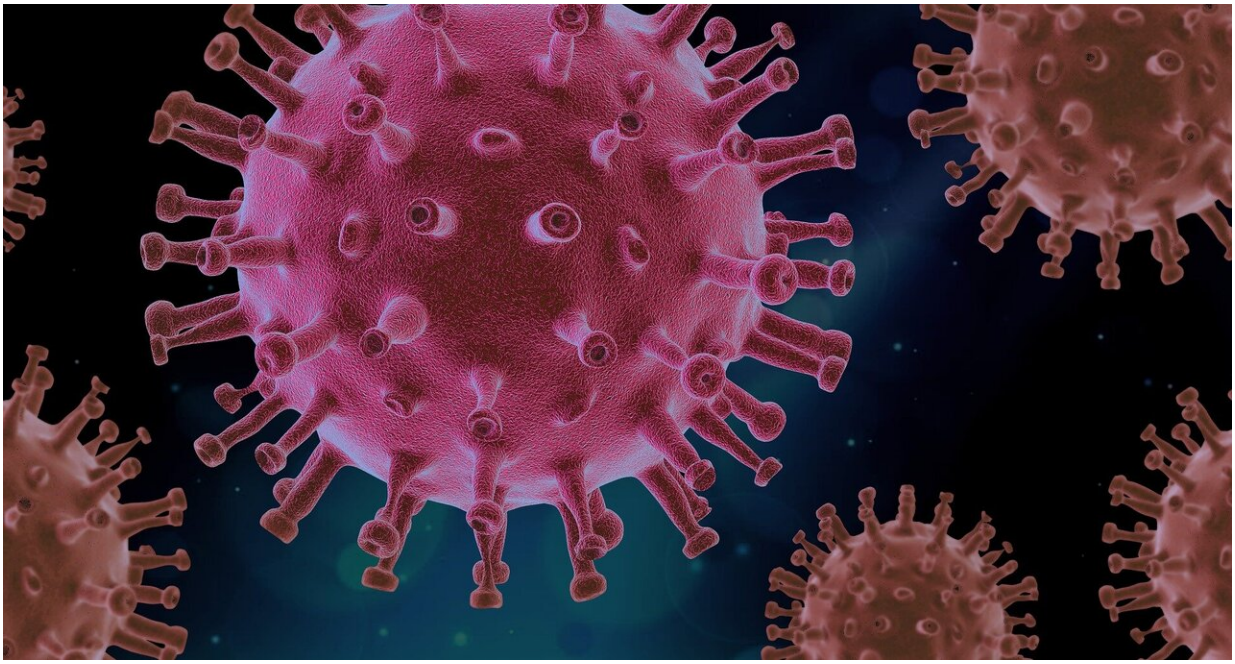

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A team of international researchers, including McGill Professor Stéphane Laporte, have discovered the working mechanism of potential drug targets for various diseases such as cancer, rheumatoid arthritis, and even COVID-19. The findings published in *Molecular Cell* uncover the inner workings of cell receptors that are involved in cancer progression and inflammatory diseases.

"The complement system is an integral part of our body's defense mechanism against pathogenic attacks including viruses. When bacteria or viruses enter our body, the complement system is activated including two different membrane receptors called C5aR1 and C5aR2," says Arun Shukla, the Joy Gill Chair Professor at IIT Kanpur who spearheaded the study. "While activation of the complement system is essential to combat harmful pathogens, excessive and sustained activation leads to inflammation, even life-threatening conditions like the ones responsible for severe complications in COVID-19."

Using cutting-edge technologies such as CRISPR and cryogenic electron microscopy, the researchers unraveled the inner workings of C5aR2, providing an additional opportunity for therapeutic targeting for COVID-19. "To treat COVID-19, some scientists are already trying to block the activation of the C5aR1 receptor and clinical trials are already underway for Avdoralimab in patients with COVID-19 induced sever pneumonia. Our study opens up the possibility of targeting C5aR2 by designing new drug molecules that can bind to this receptor and block its activation and inflammation response," says Stéphane Laporte, a Professor in the Faculty of Medicine and Health Sciences.

Cells in the human body are surrounded by receptors that are important drug targets where medicines produce their beneficial effects. These receptors work as messengers because they receive and transmit signals that allow the cells to trigger physiological processes in our body, the researchers explain.

"We are very excited to decipher the finer details of these receptors using cutting-edge technologies. Such information should enhance our fundamental knowledge about cellular signaling and allow us to translate our findings into novel drug discovery," concludes Arun Shukla.

More information: ShubhiPandey et al, Intrinsic bias at non-

canonical, β-arrestin-coupled seven transmembrane receptors *Molecular Cell* (2021). DOI: 10.1016/j.molcel.2021.09.007