A method for predicting antiviral drug or vaccine targets

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A novel method to predict the most promising targets for antiviral drugs or vaccines is based on the conformational changes viral glycoproteins go through during the process of recognition and binding to the host cell. This prediction method, which targets backbone hydrogen bonds for motifs with the highest free energy, is published in *Journal of Computational Biology*.

Robert Penner, the René Thom Chair of Mathematical Biology at the Institut des Hautes Études Scientifiques (Bures-sur-Yvette, France) and University of California at Los Angeles, is the author of the article entitled "Backbone Free Energy Estimator Applied to Viral Glycoproteins."

During viral entry and absorption into a host cell, the virus typically undergoes dramatic reconformation to form fusion/penetration motifs. Penner presents a general method to predict the residues of high conformational activity from the three-dimensional structure of viral glycoproteins. The method involves analyzing the hydrogen bonds of a protein and computing the free energy differences of corresponding features to identify regions where conformational change is most likely. The methods presented in the paper are currently being implemented for the spike glycoprotein of SARS CoV-2, the virus that causes COVID-19.

"It is nothing short of miraculous for a mathematical idea to directly lead to a practical implication, but the pay-off can be enormous, as it happened to the Maxwell's theory of electromagnetic fields—this brought radio and television—and with Turing's and von Neumann's ideas on the theory of computation which opened the portal to our digital world," says Misha Gromov of Institut des Hautes Études Scientifiques (Bures-sur-Yvette, France) and New York University, renowned mathematician and Abel Prize winner (a.k.a. Nobel Prize for mathematics). "Such an idea may have a chance to work, only when its author, besides being a brilliant mathematician, has a broad scientific

vision, which is rare among even the best mathematicians of our time. Robert Penner is this kind of a rare mathematician, and his method of detection of patterns in the protein structures, a fruit of purely mathematical thinking, is different from everybody else's in the world. There is a positive chance this method will work and accelerate the development of antiviral drugs or vaccines. Only an experiment can tell if this is so."

More information: Robert C. Penner, Backbone Free Energy Estimator Applied to Viral Glycoproteins, *Journal of Computational Biology* (2020). DOI: 10.1089/cmb.2020.0120

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