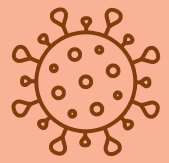
Dr. David Baker and His Contributions to the Fight Against SARS-CoV-2

We have been in the midst of a global pandemic for the last year and scientists have been hard at work trying to develop new technologies to combat coronavirus. Dr. David Baker and researchers at the Institute for Protein Design worked on designing picomolar SARS-CoV-2 miniprotein inhibitors. Dr. Baker works on understanding protein structure and function through computer programs he has designed. These programs were used in attempts to synthesize a drug to stop the spike proteins on the surface of coronavirus from infecting the human respiratory system.



Dr. Baker Lab's Process for Designing Miniproteins to Combat Coronavirus:

Goal: To design high-affinity protein minibinders to the coronavirus spike receptor binding domain [2].

Strategy 1: Incorporate an alpha helix from the human receptor into small proteins that would interact with the spike receptor binding domain to achieve higher affinity. A Rosetta blueprint builder was used to generate some miniproteins that incorporated the human alpha helix [2].

Strategy 2: Design a binder from scratch. This strategy was advantageous because it created a large range of possibilities. This approach utilized de novo (computer) design and rotamer interaction field docking [2].

The result of both strategies was a large quantity of possible minibinders. They were then tested to se how well they bind to the spike receptor binding domain. LCB1 and LCB3 were the miniproteins that showed the most neutralizing ability against coronavirus [1].

Movement of antivirals into clinical testing

Moving Towards the Future

Dr. Baker and his lab use computer algorithms to design synthetic proteins that may be beneficial in many different applications. During the COVID-19 pandemic, he used his resources to try and find a way to stop coronavirus from infecting people and reducing symptoms. This particular study shows that the developed computer programs and models developed can quickly respond to a viral threat [1]. Ultimately, Dr. Baker's ultimate goal is to be able to generate proteins with these computer programs within weeks of obtaining the genome of a virus, which would streamline the workflow of experiments. If Baker's online design platforms keep improving, this goal is well within reach.

Benefits for the General Public

In this study, Dr. Baker and his lab "produced the most potent antivirals, including LCB1, which is roughly six times more potent on a per mass basis than the most effective monoclonal antibodies reported thus far" [3]. The proteins that were designed also are much cheaper to commercially produce than antibodies, with great stability and few temperature concerns [1]. These are extremely valuable characteristics to mass vaccine production, seeing as many people could be quickly and safely protected from COVID-19.

Dr. Baker has a philosophy that the anyone has the ability to help accelerate science from their own homes, even people who are not scientists. His labs are extremely inclusive, and value the work that members of the community do in the public access computer programs he developed (such as Foldit and Rosetta@home) [4]. Seeing proteins designed by the public, can help Dr. Baker and his lab move forward in the development of solutions to issues in the energy, technology, and medicine sectors.

References

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[3] De novo minibinders target sars-cov-2 spike protein. (2020, September 09). Retrieved March 11, 2021, from https://www.bakerlab.org/index.php/2020/09/09/covid-minibinders/

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