SCIENCE AT THE ADVANCED PHOTON SOURCE

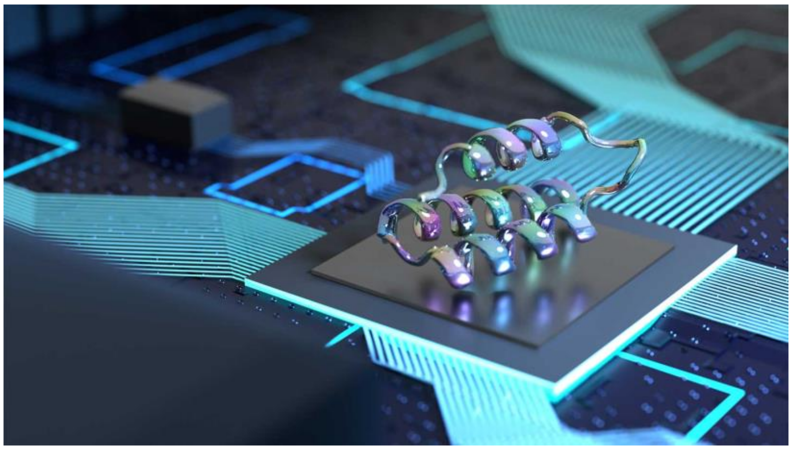
NEWLY CREATED MOLECULES BLOCK CYTOKINE STORM

Cytokine storms are potentially life-threatening overreactions of the immune system. Two key players are cytokines interleukin-6 (IL-6) and interleukin-1 (IL-1). Currently available inhibitors of IL-6 and IL-1 relieve the cytokine storm associated with rheumatoid arthritis, but not with COVID-19.

Scientists from the University of Washington have computationally designed protein inhibitors that may prevent the COVID-19-related cytokine storm. X-ray macromolecular crystallography revealed a near-perfect match between the computational designs and their real-life counterparts, which blocked the cytokine storm in a human heart organoid. This suggests that computational design has the power to create entirely new proteins that function as viable therapeutics against the cytokine storm associated with COVID-19.

Both IL-6 and IL-1 rely on a third protein—GP130 in the case of IL-6, and an accessory protein in the case of IL-1—to send a signal when they bind with their receptors. The scientists used Rosetta, a proprietary protein design program, to create inhibitors that would occupy (a) binding sites on the IL-6 receptor, (b) the site on GP130 where IL-6 and its receptor would bind, and (c) the site on IL-1 where it would bind to both its receptor and the accessory protein.

For the scientists to assess the accuracy of their design methodology, they used the resources of the Advanced Photon Source (APS) to collect data from crystals of the GP130 inhibitor bound to GP130, as well as the structures of the IL-1 and IL-6 inhibitors. The experimentally determined protein structures were nearly identical to their corresponding computational models.

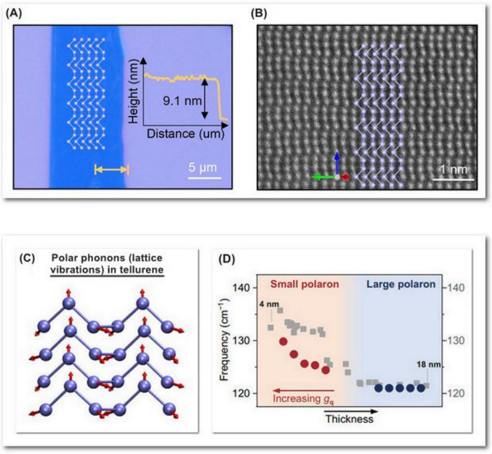


B. Huang, et. Al., "De novo design of miniprotein antangonists of cytokine storm inducers," *Nat Commun* **15** 7064 (2024)

Advances in computational design tools now enable functional proteins to be created from scratch. *Image courtesy University of Washington.*

The effectiveness of these computer-generated proteins, as well as the close match with their intended structures, underscores the potential of creating potent therapeutic inhibitors through *de novo* computational design.

MANIPULATING POLARONS IN THIN-FILM TELLURENE SHOWS PROMISE FOR ADVANCED ELECTRONICS



K. Zhang, et. Al. "Thickness-dependent polaron crossover in tellurene," *Sci Advances,* **11** 2 (2025)

Optical image (A) of a tellurene flake. A scanning transmission electron microscopy (STEM) image of tellurene (B). Red arrows in panel (C) indicate lattice vibrations of individual tellurium atoms, shown as purple spheres. Plot of polaron size versus flake thickness in (D) shows that smaller polarons (with higher vibration frequency) arise in thinner flakes. *Image courtesy Rice University.*

Polarons are quantum entities that arise in crystalline solids due to interactions between electrons and quantized lattice vibrations (phonons). Characterizing polaron behavior is important to scientists because they can play an important role in solid-state phenomena such as thermoelectricity, ferroelectricity, magnetoresistance and high-temperature superconductivity.

Scientists probed flakes of tellurene with thicknesses of less than 20 nanometers, using a technique called extended X-ray absorption fine structure (EXAFS) spectroscopy. The EXAFS measurements characterized the structural changes in tellurene as flake thickness decreased, suggesting a transition from large-to-small polarons at a thickness of 10 nanometers.

These new findings will aid in developing the significant potential of tellurene for various technological applications, such as use in advanced transistors and sensing devices, and as a superconducting material. More broadly, these findings will also contribute to a deeper understanding of polaron behavior in other thin-film materials.

Read more about the upgraded APS at aps.anl.gov

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