STRUCTURAL BIOLOGY

Human-virus interactome atlas

In silico modeling and mapping of cross-species protein–protein interactions.

Much is known about the human protein interactome, but our understanding of how human proteins interact with those from pathogens is less developed. The P-HIPSTER (pathogen–host interactome prediction using structure similarity) database is a comprehensive catalog of virus–human protein–protein interactions (PPIs) predicted based on structural information from the PDB, and on homology modeling of more than 12,000 proteins from 1,001 fully sequenced human-infecting viruses and more than 20,000 human proteins. P-HIPSTER uses a Bayesian framework that calculates the likelihood of two proteins interacting with each other, and the database contains ~282,000 PPIs available as an interactive webserver (<http://phipster.org>). Barry Honig and Sagi Shapira, from Columbia University Medical Center, have recently published this resource along

with several notable analyses that highlight its ability to capture known biology and to uncover new biological insights previously undiscovered using other tools.

Among these is the identification and validation of the estrogen receptor, ESR1, as a regulator of Zika virus replication; overexpression of ESR1 led to ~2,000-fold reduction in viral replication. Sharipa explains how this fits with previously known clinical data, “Women during the first trimester are particularly at risk [for Zika infections], and that’s when the estrogen is at the lowest.” Another important finding was determination of PPIs in HPV that can discriminate between strains with low and high oncogenic potential. These results would enable researchers to focus on previously underappreciated interactions as drug targets. They also explore the convergent and divergent evolutionary

relationship among various human-infecting viruses, as well as the evolutionary pressures imposed by viruses on primate lineage.

When asked which results he felt the most excited about, Shapira said “In each one of the vignettes there is a message that, I think, is quite important, and the observations could not have been made without having this large of a database, without having the tool”. This tool is available for others to use for their own research as well as to extend such analyses to other pathogens.

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Research paper
 Lasso, G. et al. A structure-informed atlas of human–virus interactions. *Cell* **178**, 1526–1541 (2019).

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