Researchers unveil landscape of human-pathogen protein interactions

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Researchers at the Virginia Bioinformatics Institute and the Department of Computer Science at Virginia Tech have provided the first global analysis of human proteins interacting with viral proteins and proteins in other pathogens.

The scientists examined publicly available experimental data for 190 different pathogens that comprise 10,477 interactions between human and pathogen proteins. This approach provides a highly detailed network map of human proteins interfacing with proteins in different pathogens. The network of interactions was published recently in the journal *PLoS Pathogens* and reveals possible key intervention points for the future development of therapeutics against infectious diseases.

Matt Dyer, of Martinez, Calif., a bioinformatician at the institute and a graduate student in Virginia Tech's genetics, bioinformatics, and computational biology program, remarked: "Infectious diseases result in millions of deaths each year. Although much effort has been directed towards the study of how infection by a pathogen causes disease in humans, only recently have large data sets for protein interactions become publicly available. We have leveraged this opportunity to compare protein interactions between human and pathogen proteins from 190 different pathogens to provide important insights into the strategies used by pathogens to infect human cells."

The researchers paid particular attention to two networks of human proteins – proteins that interact with at least two viral pathogens and

proteins that interact with at least two bacterial pathogens. Gene ontology terms computed for both sets of proteins provided key information on the functions of the different proteins. Some of the striking findings of the study included a clear demonstration that pathogens preferentially interact with two classes of human proteins referred to as hubs and bottlenecks. Hubs are popular proteins that interact with many other proteins in the human protein interaction network. Bottlenecks are proteins that lie on many of the shortest paths in the network.

Pathogens appear to maximize their likelihood of success by targeting these high-impact, influential proteins during infection. In many cases, human proteins that mediate pathogen effects are proteins that are known to be involved in cancer pathways, for example, the transcription factor STAT1 or the tumor suppressor protein TP53. This finding suggests interesting parallels between pathogen infection and cancer and opens up future areas for research.

T. M. Murali, an assistant professor in the Department of Computer Science at Virginia Tech, added: “Previous studies have suggested that protein interaction networks have topologies that are resilient to attacks on random nodes but are susceptible to targeted attacks, for example on hubs. Our results provide a striking example of how pathogens may have evolved the ability to exploit the structure of interactions between human proteins in order to promote infection. This global study also suggests that many viruses share similar strategies to control the human cell cycle, regulate programmed cell death, and transport viral genetic material across the nuclear membrane in the human cell.”

Bruno Sobral, executive and scientific director of the Virginia Bioinformatics Institute, commented: “Infectious diseases are placing a huge burden on public health systems around the globe. At the same time, the pharmaceutical and biotechnology industries are facing the

daunting challenge of increasing innovation and productivity in their drug and vaccine discovery and development pipelines. This groundbreaking study provides an exciting strategic tool for anyone in the scientific community interested in prioritizing anti-viral and anti-bacterial targets."

Source: Virginia Polytechnic Institute and State University