Abstract: Viral-host protein-protein interactions (PPIs) enable viruses to manipulate the host’s cellular machinery. Identification of viral-host PPIs is crucial to understand molecular events mediating viral infection, yet our knowledge is exceedingly sparse. We implemented P-HIPSTer (Pathogen Host Interactome Prediction using STructure similarity; www.phipster.org), a computational tool that employs structural information to predict viral-host PPIs. We applied P-HIPSTer on 1,001 human viruses representing 28 viral families known to infect humans, obtaining an experimental validation rate of ~76%. Among our predictions we find i) Zika virus interacting human proteins that relate to clinical symptoms observed in recent outbreaks and; ii) viral-host PPIs associated with the oncogenic potential of human papillomaviruses. Moreover, our predicted pan viral-human PPIs enable the discovery of shared host machinery employed by human viruses. P-HIPSTer is the largest initiative to model the viral-human interactome, providing high-resolution interaction models for ~85,000 viral-human PPIs. In addition, atomic models of viral-host PPIs facilitate the evaluation of zoonotic risk of viruses such as Bombali ebolavirus (BOMV), a newly discovered virus found in bats. Modeling the BOMV-human PPI that mediates viral entry, along with experimental assays, showed that BOMV can indeed infect human cells. Altogether, our structure-based approach provides novel molecular insights into cellular processes underlying viral infection and enables the discovery of genotype-to-phenotype associations, such as clinical outcome or viral tropism.
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**Speakers**

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