

DPA26BZ03-DV014
Real-Time Pathogen-Host Interactome Prediction
Frequently Asked Questions (FAQs)

1. Training data source: Is the use of *C. elegans* host-pathogen genetic screen data as the primary training dataset for a GNN predictor of pathogen-host protein-protein interactions consistent with the scope of Topic DPA26BZ03-DV014? The topic specifies prediction from pathogen protein sequence alone — our approach uses pathogen protein sequence as the sole input at inference time, but uses *C. elegans* experimentally characterized interactions as training supervision. Is this distinction acceptable?
A: The inference approach is compliant, but the model must be able to successfully predict interactions for human hosts, and not just for specific pathways.

2. Wet-lab validation requirement: Does the Phase I scope require experimental wet-lab validation (e.g., infection assays, co-immunoprecipitation, yeast two-hybrid) of the computational predictions, or is computational validation (cross-pathogen leave-one-out accuracy benchmarking; comparison to published interaction databases such as STRING, BioGRID, and IntAct) sufficient for the Phase I deliverable? We can include *C. elegans* infection lifespan assays as a validation arm if experimental validation is required, but wish to confirm whether this is necessary for Phase I.
A: This solicitation is a Direct to Phase 2 topic, while computational validation data is sufficient to show Phase 1 requirements, please see above for applicability to human hosts.

3. Scope of “host-pathogen interactions”: Does the topic scope encompass prediction of host immune pathway activation/suppression profiles (e.g., p38 MAPK activation, NF- κ B suppression) in addition to direct protein-protein binding interactions? Our platform predicts both: (a) direct pathogen protein – human host protein binding interactions, and (b) the downstream immune pathway consequences of those interactions. Is the second layer of prediction (pathway-level) within scope, or should the Phase I deliverable focus exclusively on direct protein-protein interaction prediction?
A: This solicitation is a Direct to Phase 2 topic, there are no Phase 1 deliverables, However, these predictions are in scope, but immune pathway interactions only are insufficient as an outcome of this model.