

Towards pan-pathogen therapy: Identifying converging pathways hijacked by multiple pathogens

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About Me

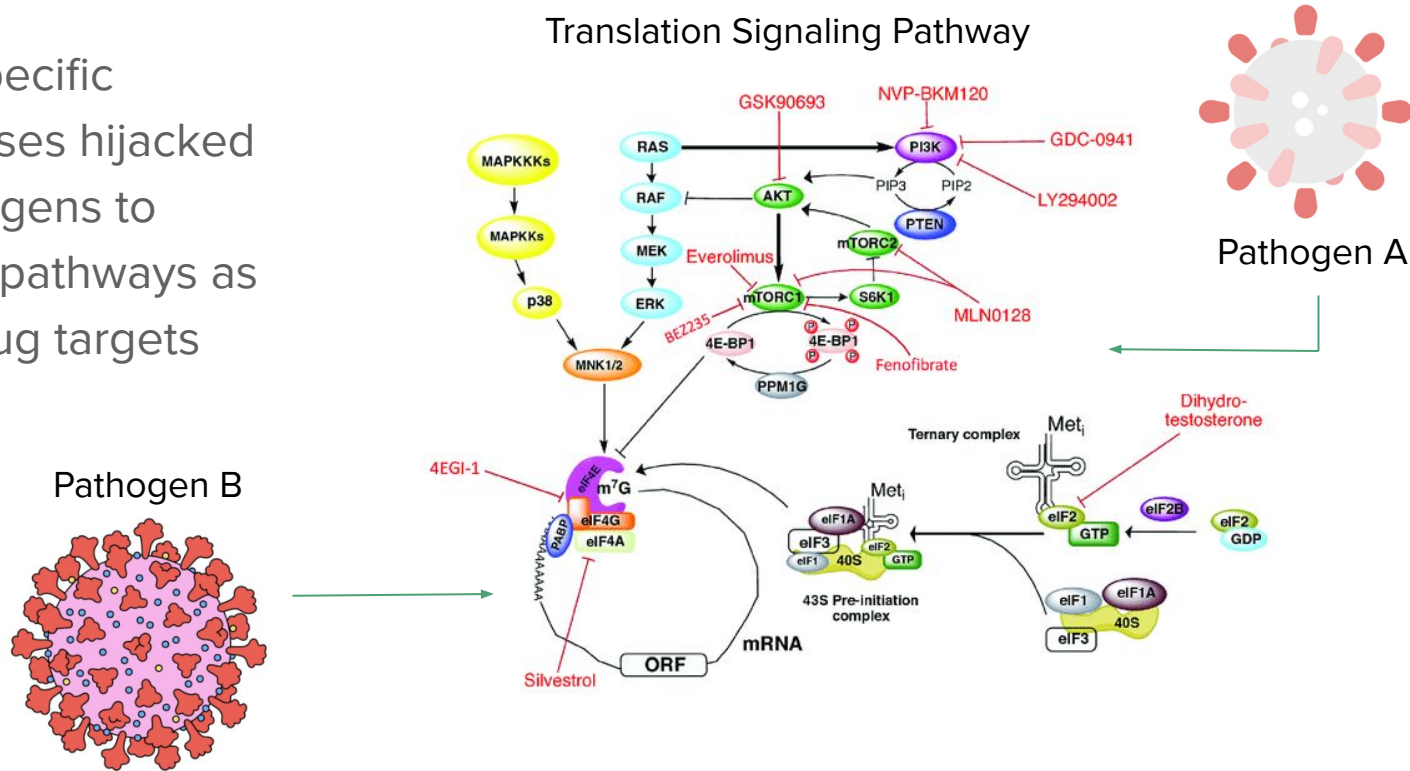
- Lucas Jang, summer intern (summer 2019 & 2020)
- Recently graduated Mills High School in Millbrae



- Will be attending Northeastern University in Boston this coming Fall as a Data Science and Biology major

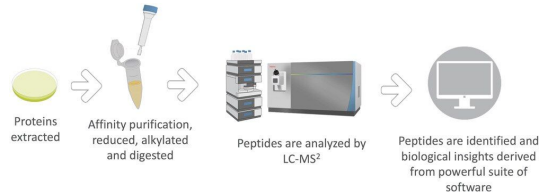
Motivation Behind My Project

Goal: Discover specific biological processes hijacked by multiple pathogens to identify potential pathways as pan-pathogen drug targets

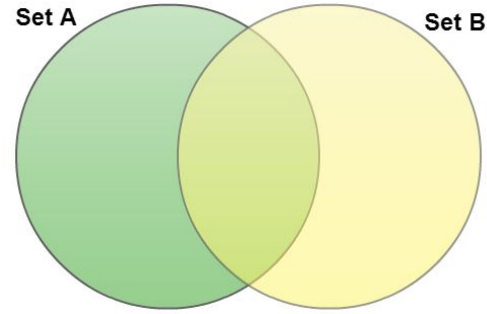


Pipeline

APMS Data from Multiple Pathogens

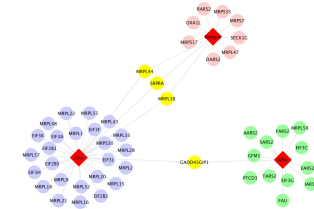


Enrichment of preys per pathogen



Gene Overlap for specific processes

Network Visualization of preys associated with a term



Enrichment Analysis Reveals Processes Shared by Multiple Pathogens

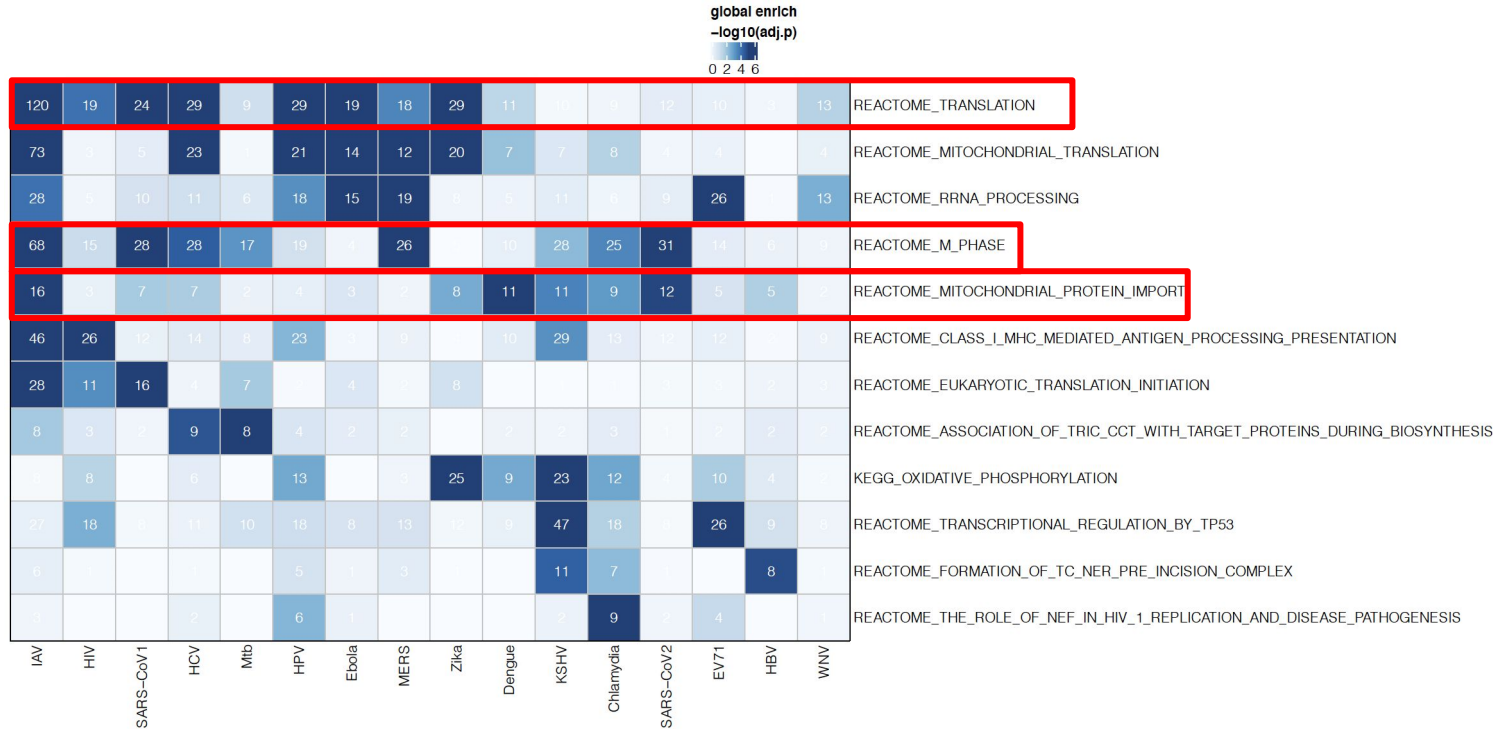
Pathogen
Interactome



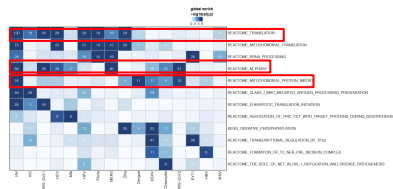
Enrichment
Analysis



Top Terms per
Pathogen

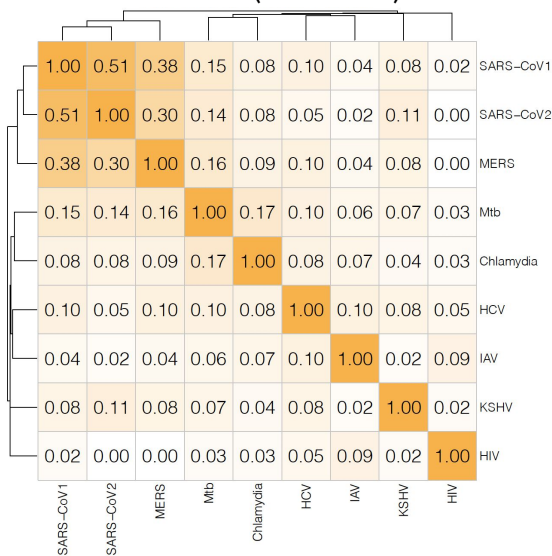


Low Jaccard Indices Indicate Low Gene Overlap



Top 3 Terms

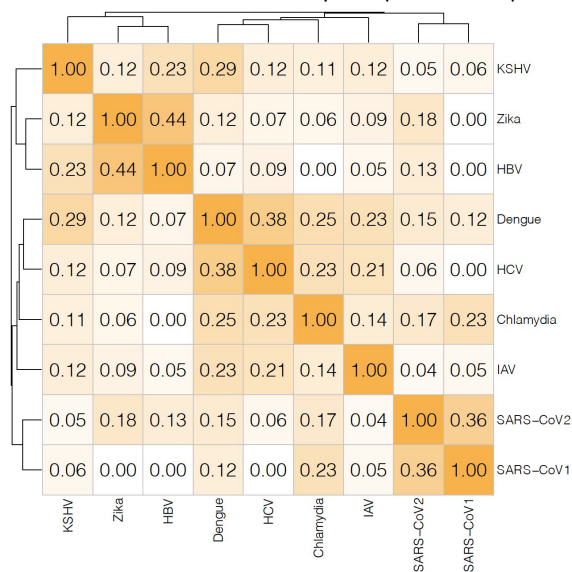
M Phase (reactome)



$pval < 0.05$

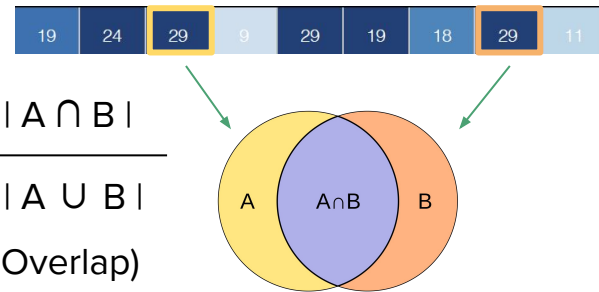
Terms with significant enrichment

Mitochondrial Protein Import (reactome)

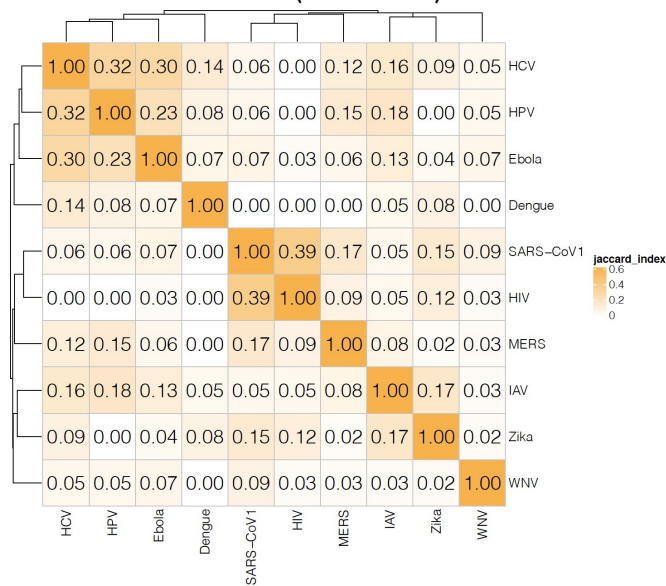


$$\text{Jaccard} = \frac{|A \cap B|}{|A \cup B|}$$

(Measure of Overlap)



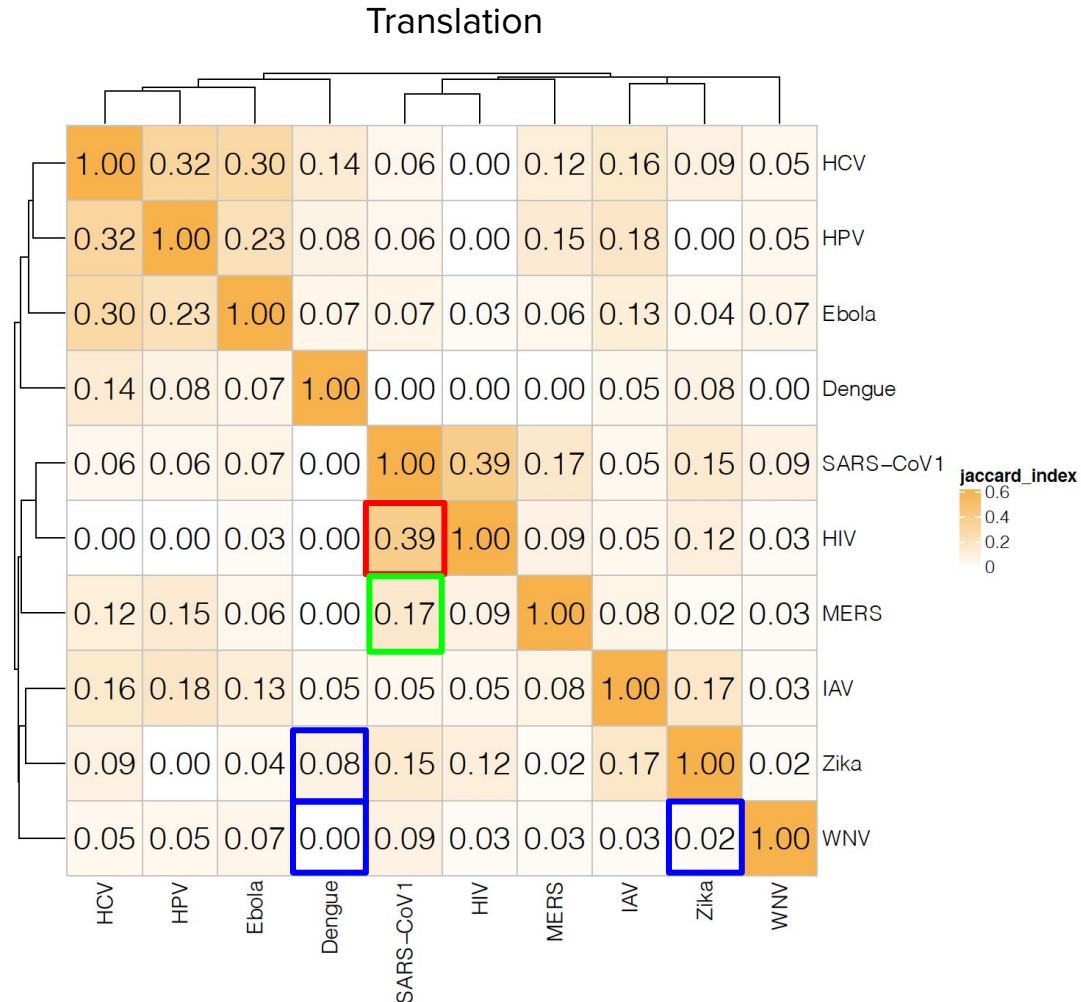
Translation (reactome)



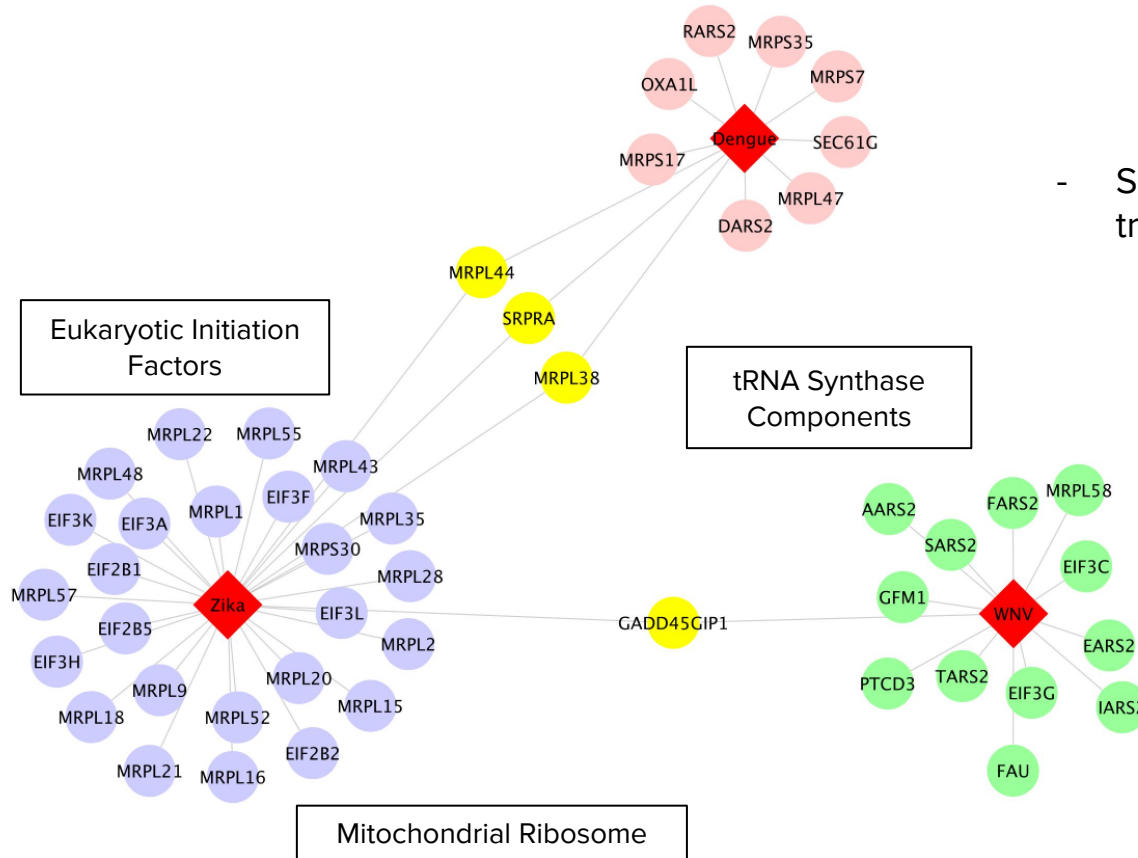
Closer Look at Translation

- Dengue, WNV, Zika
 - Same family yet little to no overlap in proteins used in translation

- HIV, SARS-CoV1
 - High overlap
 - Higher than MERS, SARS-CoV1



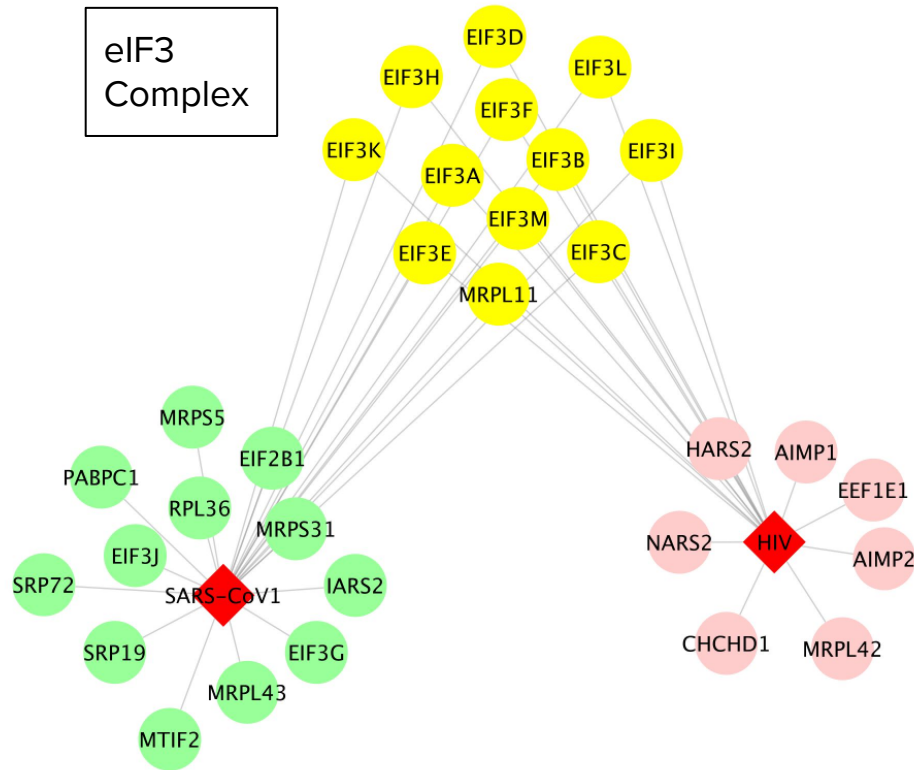
Translation-Associated Networks of Pathogen-Host Interactions



- Small overlap between proteins used in translation among Flaviviruses

	Dengue	WNV	Zika
Eukaryotic Initiation Factors	No	Yes	Yes
tRNA Synthase Components	Yes	Yes	No
Mitochondrial Ribosome	Yes	Yes	Yes

Translation-Associated Networks of Pathogen-Host Interactions



- SARS-CoV1 and HIV both exploit the eIF3 protein complex
- Knockdown of eIF3D, eIF3E, eIF3F enhances HIV infectivity by a factor of 3 to 5 (Jager et al., 2011)

Conclusion

By systematically comparing biological processes exploited by distinct pathogens, we can identify candidate pathways for pan-pathogen therapies.

Future Directions

Test inhibitors of shared processes across different viruses

- Translation Inhibitors
 - Perform eIF3 knockdowns to assess SARS-CoV1 infectivity
- Cell Cycle Inhibitors (CDK inhibitors)

Testing for changes in cellular proliferation upon infection

- M Phase

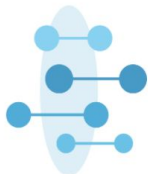
Perform more fine grain mechanistic studies looking into why pathogens exploit certain biological processes

- Why pathogens are hijacking similar processes

Acknowledgement



CC
MI



Cancer Cell
Map Initiative

HP
MI



Host Pathogen
Map Initiative



Quantitative
Biosciences
Institute

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