PROTEIN-PROTEIN INTERACTIONS
GENES TO FUNCTION TO THERAPEUTICS

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Protein-Protein Interactions

Central to all biological processes and structural scaffolds
The network is a medium for systems biology research
But 90% of protein-protein interactions are unknown today

~22,500 protein-coding genes

protein-pairs
~250 Million pairs

Human Interactome
~1 Million PPIs Estimated

Theme of Research in Madhavi’s Lab

Discovery of protein-protein interactions using Machine Learning methods over from large data sources

Results: 1000’s of Novel PPIs discovered Accurately
Every predicted PPI validated by experiment found to be true PPI!
TRANSLATIONAL RESULTS

**Revealed that cilia are intricately connected to Congenital Heart Diseases and Neuropsychiatric Diseases**

Nature 2015, Nature Genetics 2017

**Identified 5 drugs potentially repurposable for Schizophrenia (two in Clinical Trials)**

npj Schizophrenia 2016 & 2017, Scientific Reports 2019

**OASL-DDX58 interaction responsible for immunity in flue virus infection**

Immunity 2014

**Experimentally validated protein interactions. Every predicted PPI that was studied experimentally was found to be valid.**

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https://www.nature.com/articles/npjschz201612
https://www.nature.com/articles/nature14269
https://www.nature.com/articles/ng.3870
https://www.nature.com/articles/s41598-019-48307-w

Clinical Trials: https://clinicaltrials.gov/ct2/show/NCT03794076 (2nd with IRB review)

Computationally Predicted PPIs are making Translational Impact
**ONGOING WORK**

**COVID19 MOLECULAR PATHWAYS**

**INTERACTOME OF SPECIFIC TARGETS OF SARS-CoV-2**

- Host Protein
- Known Interactor
- Novel Interactor
- Viral Protein

**SARS-CoV2 nsp11**

- TAF9
- PAM
- TERCIP
- RAG1
- LHFPL2
- PHAX
- CNTN4
- EDL3
- AFF1
- HIC1
- TRXN1
- NUP210
- NUP153
- TIMM10B
- TIMM10
- TIMM9
- DNAJC11
- LINC03317
- TSE1N2
- EXOSC5
- PEX11G
- ZNF750
- ZNF591
- APOE
- MBD3L1
- TAF11
- ZNF659
- PPM1D
- APP
- USP15
- PRKACB
- MGC39
- PEX15
- SLC2A2
- SORCS3
- IGF1
- BRDT
- IGF2
- UCHL5
- NR3C1
- CREB3
- HAGHL
- NUP210
- CDK1
- LHCGR
- HDAC11
- TRIP5

**SYSTEMS BIOLOGY STUDIES**

- ELUCIDATE KEY PATHWAYS AND NETWORK MODULES

- Huntington's Disease Signaling
- Glucocorticoid Receptor Signaling
- Estrogen Receptor Signaling
- Neuregulin Signaling
- Opioid Signaling Pathway
- Senescence Pathway
- Cardiac Hypertrophy Signaling
- IL-8 Signaling

**SEEKING COLLABORATORS TO VALIDATE OUR PREDICTED INTERACTIONS**

**AND TO STUDY BIOLOGY OF POST-COVID19**

**NEUROLOGICAL AND CARDIOVASCULAR COMPLICATIONS**

*Human proteins targeted by virus identified by Gordon et al 2020
Interactome of those human proteins assembled and analyzed by us (Karunarakarn, Balakrishnan and Ganapathiraju, 2020, preprints)
https://www.researchsquare.com/article/rs-28592/v1*