Structure-based network analysis of viral proteins reveals potential epitopes for vaccine targeting in SARS-CoV-2

Lizzy Rossin MD PhD Massachusetts Eye and Ear Retina Society 2020







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• None

Summary

Network Analysis

- We use network analysis to summarize the structural and interactive nature of folded proteins
- Application to prior biological problems
 - RPE65, HIV vaccine design
- Learning about COVID protein structure with network analysis
 - And the potential for a T-cell based vaccine

How can we better understand a folded protein?



- Which amino acids are important?
- What should we include in a vaccine?
- Which parts, if mutated, would cause disease?

Structure-based Network Analysis

Traditional structural analysis is not easy to interpret!



A protein is a network



Proteins NODE = Amino Acid EDGE = Intermolecular Interaction

Network analysis tells us about local and global importance



Structure-based Network Construction and Analysis

Crystal Structure



Network score predicts damaging mutations in model proteins



Gaiha & Rossin et al. *Science* 2019

Network analysis predicts damaging mutations in RPE65





Blue = known disease-causing mutations Red = known benign mutations



Network score correlates with natural control of HIV

Blue = controllers; Red = progressors





Gaiha & Rossin et al. Science 2019

Application to SARS-CoV-2 for a T-cell based vaccine

https://www.gatan.com/gatan-salutes-all-scientists-cutting-edge-coronavirus-research

Rationale

- Viral mutations can evade the immune system
- Targeting sequence conserved sites has fallen short
- Patients whose T cells target structurally constrained sites in HIV do not need treatment

 \rightarrow Can we identify targets in the COVID proteome that would be good for a T-cell based vaccine?

Rationale



Can we make it universal to Betacoronaviruses?



Wu et al. Genome Composition and Divergence of the Novel Coronavirus (2019nCoV) Originating in China. *Cell Host Microbe*. 2020

Find highly networked spots within CoV-2 proteins





Highly networked sites are conserved in betacoronaviruses



Highly networked sites are conserved in SARS and MERS



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Conserved and structurally important amino acids

Translate to a vaccine: identify a set of T-cell epitopes with high network scores



Translate to a vaccine: identify a set of T-cell epitopes with high network scores

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## Identify high scoring epitopes





## Identify high scoring epitopes



### Structurally important epitopes are recognized by population HLA → good vaccine candidates













### Conclusions



- Proteins can be represented as networks
- Network analysis allows insight into critical sites
- This has potential importance for COVID (and other viral) T-cell based vaccine design

## Thank you!

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