

# Rosetta@Home fighting COVID-19

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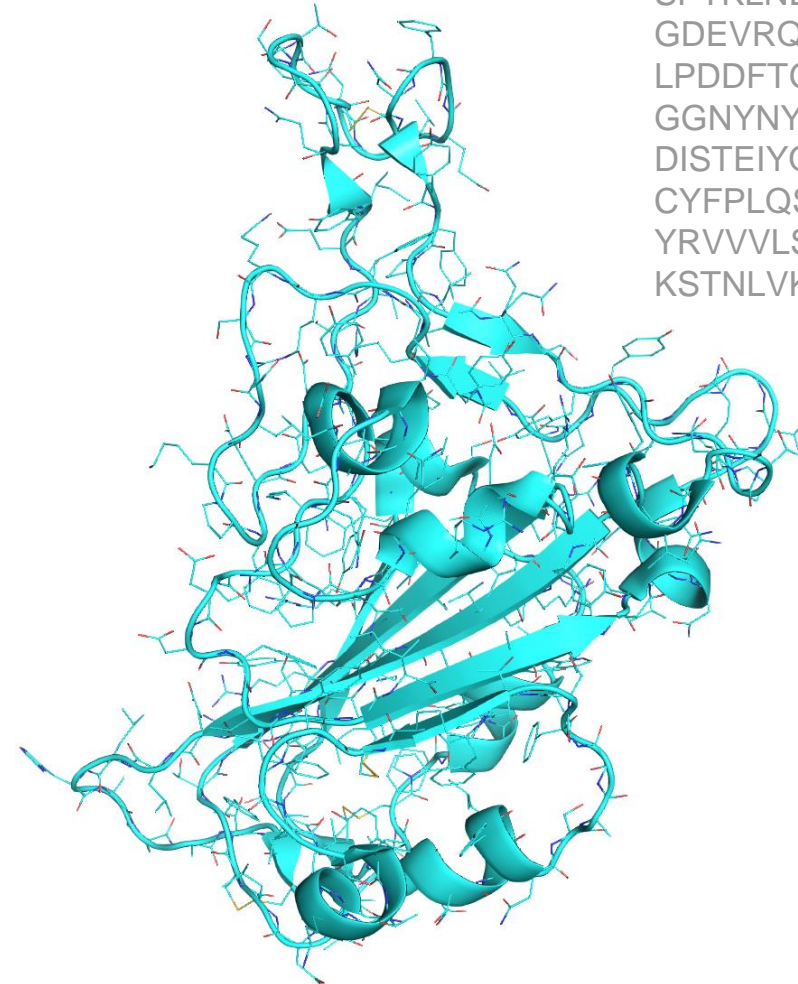
INSTITUTE FOR  
**Protein Design**

UNIVERSITY *of* WASHINGTON

# Protein Sequences Encode Their Structure

COVID-19 Spike Protein  
Receptor Binding Domain

```
RVQPTESIVRFPNITNLCPFGE  
VFNATRFASVYAWNRRKRISNC  
VADYSVLVNSASFSTFKCYGV  
SPTKLNDLCFTNVYADSFVIR  
GDEVQRQIAPGQTGKIADYNYK  
LPDDFTGCVIAWNSNNLDSKV  
GGNYNYLYRLFRKSNLKPFR  
DSTEIYQAGSTPCNGVEGFN  
CYFPLQSYGFQPTNGVGYQP  
YRVVVLSEFLLHAPATVCGPK  
KSTNLVKNKCVNF
```



R@H helps researchers predict  
protein structures

<https://rosetta.bakerlab.org>

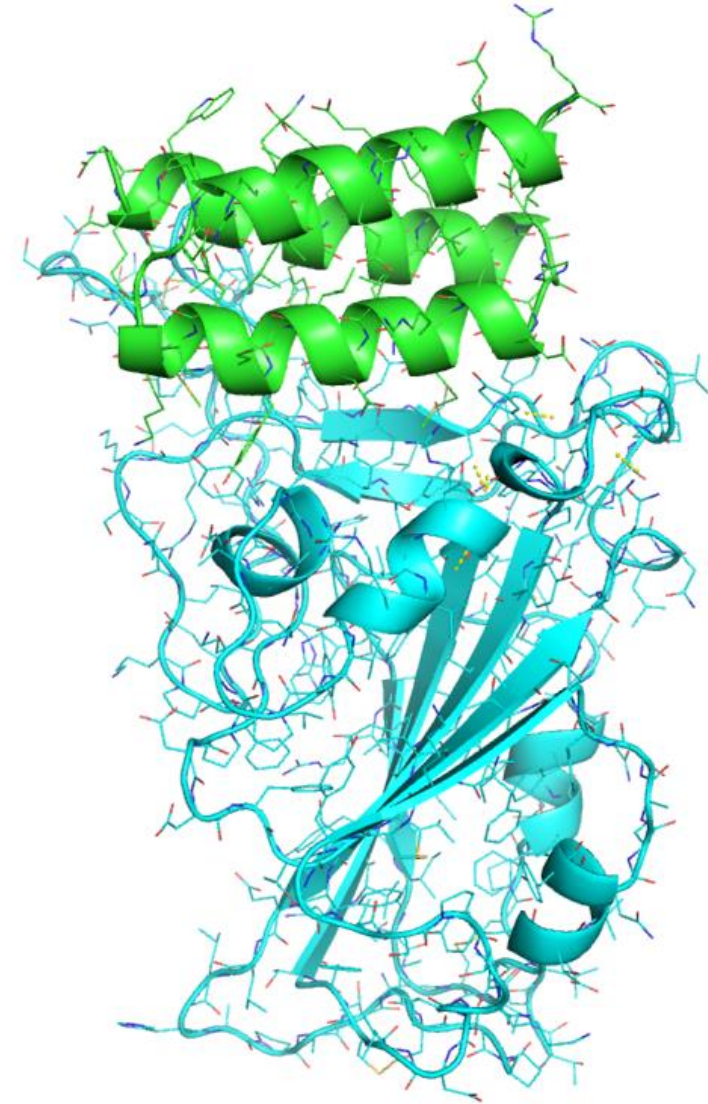
# The IPD designs proteins to fight COVID-19

Goal: Design a protein sequence that:

1. Folds into desired structure
2. Binds to target protein
3. Stops infection

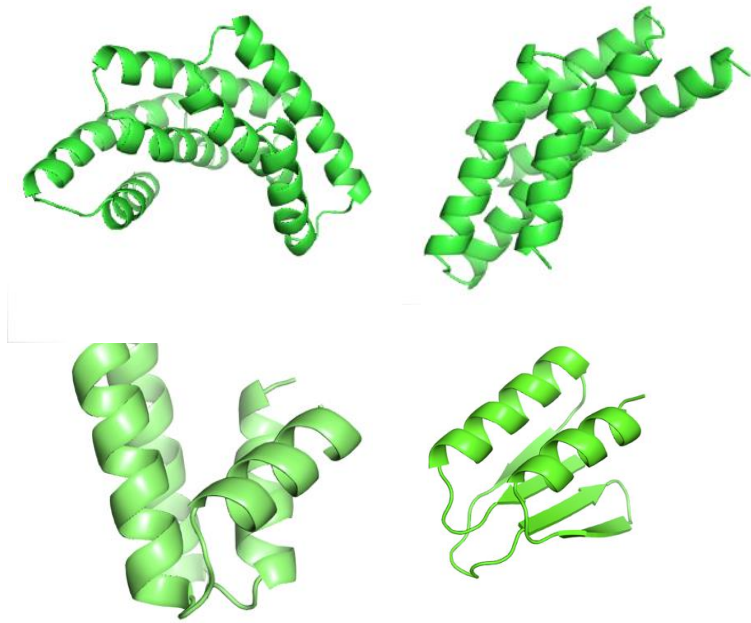
Current targets:

- a. COVID-19 itself
- b. Human biomarkers of ARDS

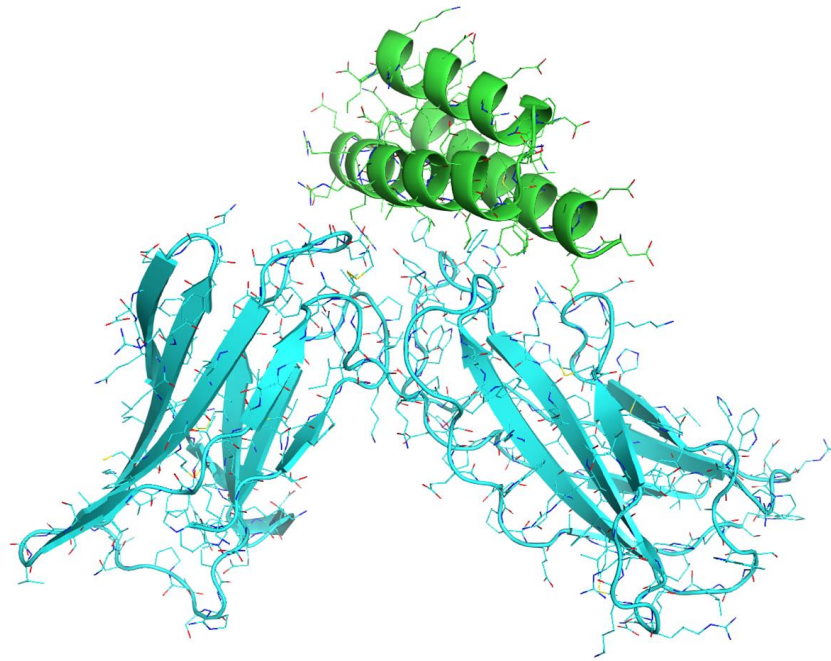


# R@H Gives the IPD the compute to do amazing things

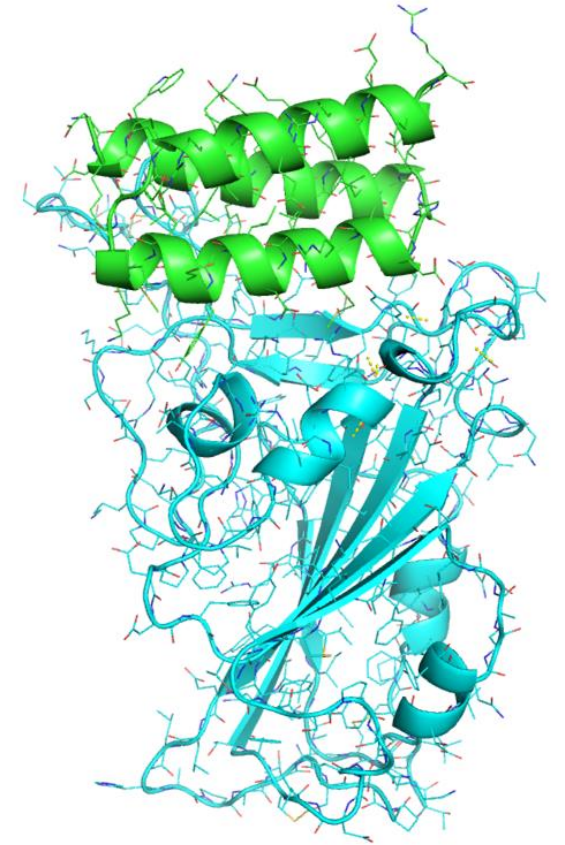
Numbers to date:



20,000,000  
Scaffold Proteins Designed



400,000,000  
Interfaces Designed



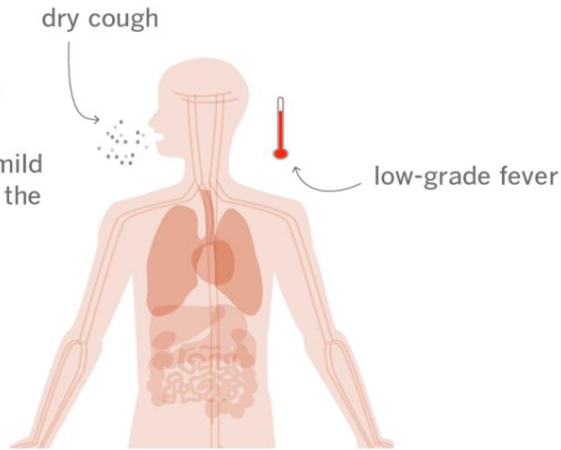
3,000  
Confirmed Binders

# Cytokine Storm in COVID-19 patients

## Acute respiratory distress syndrome (ARDS)

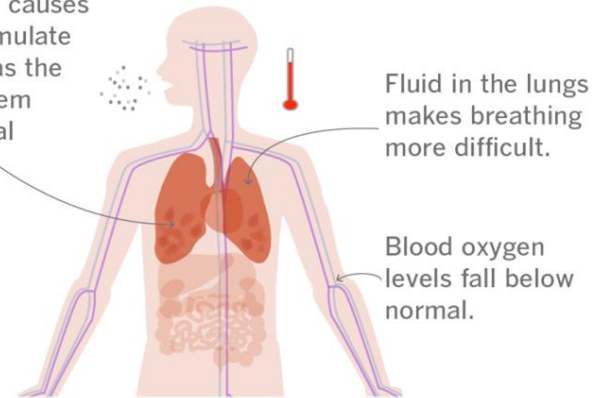
### Mild

Most cases of coronavirus infection are mild and resemble the flu.



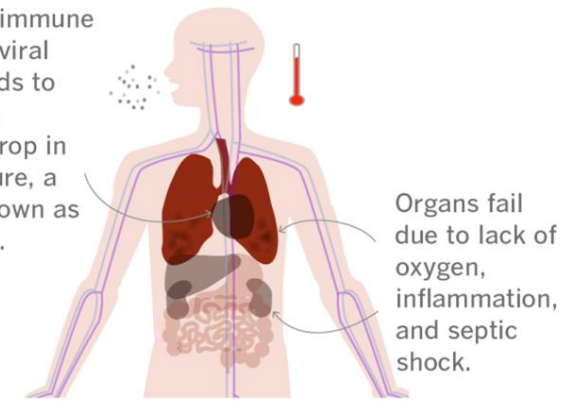
### Severe

Inflammation causes fluid to accumulate in the lungs as the immune system fights the viral infection.



### Critical

An outsized immune response to viral infection leads to sepsis and a dangerous drop in blood pressure, a condition known as septic shock.



## Cytokine Storm (CRS)

- Dead cycle of cytokine production and lymphocytes recruitment
- Causing damage to health cells
- Leading to acute lung damage

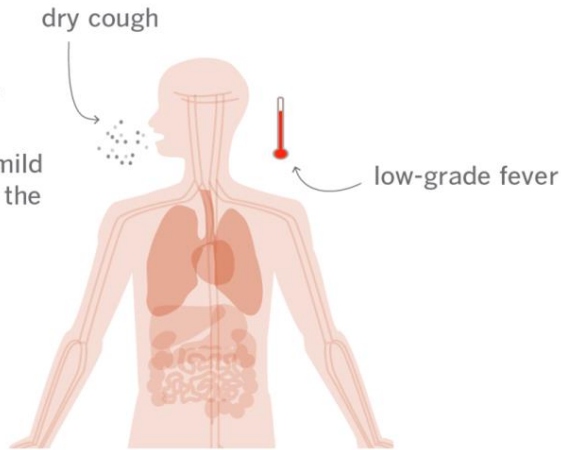


# Cytokine Storm in COVID-19 patients

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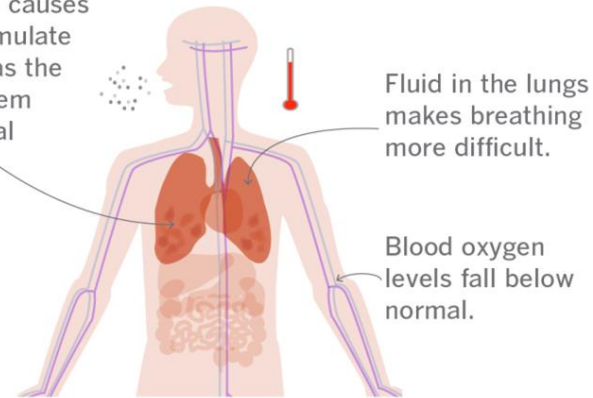
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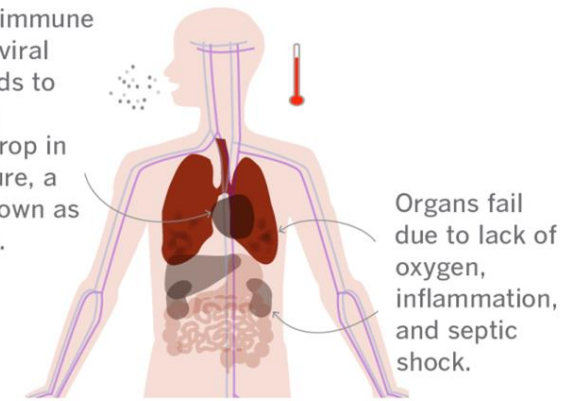
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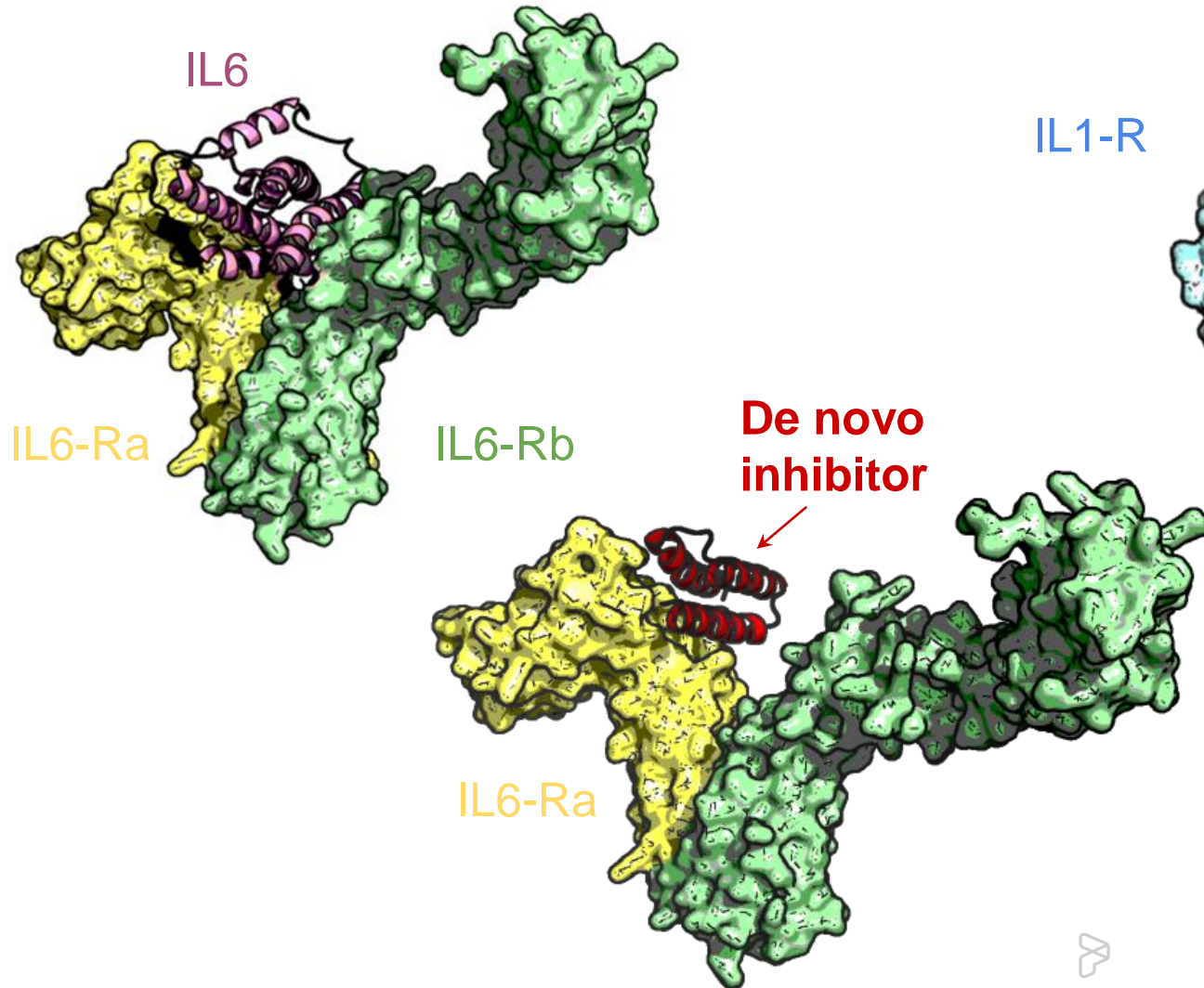
## Key players in Cytokine Storm

- Interleukin 6 (IL6)
- Interleukin 1 (IL1)
- Both lead to strong inflammation causing severe/critical ARDS

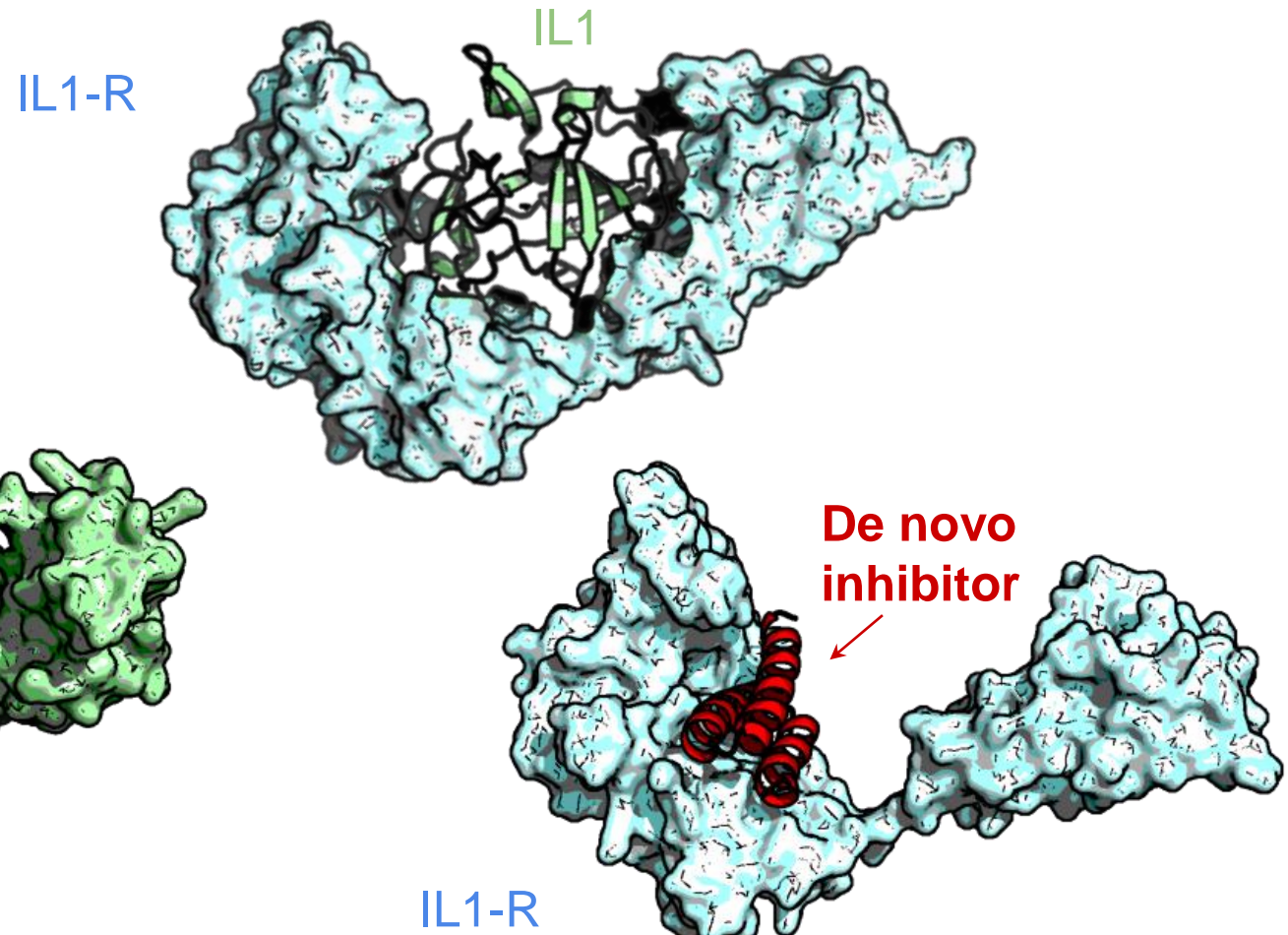


# Inhibitor design to calm down Cytokine Storm

## Blocking Interleukin 6 (IL6)

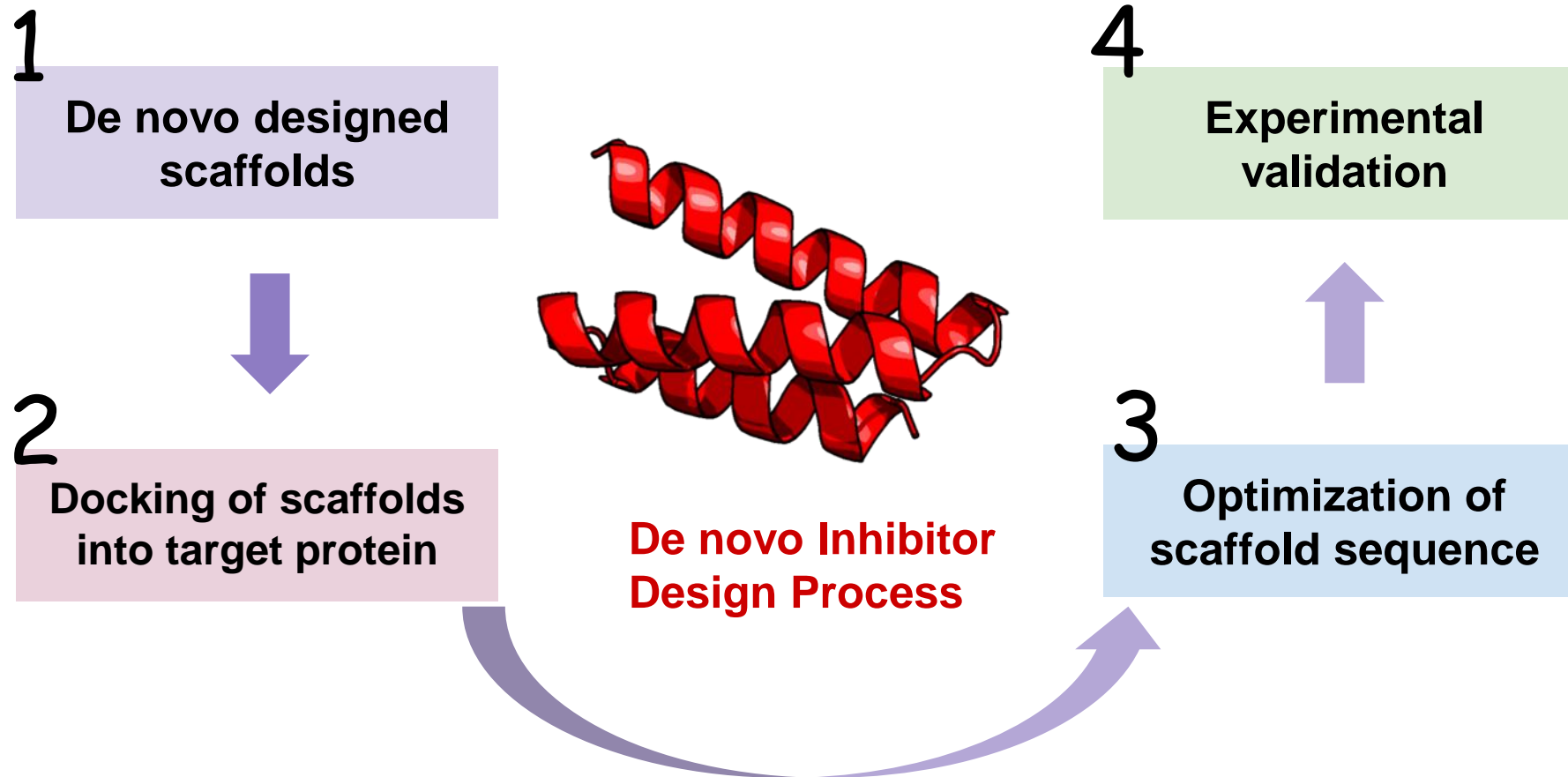


## Blocking Interleukin 1 (IL1)



# Inhibitor design to calm down Cytokine Storm

With the a massive number of CPU hours provided by BOINC, the interface design procedure can efficiently generate high-quality inhibitor candidates



## Without BOINC

- 5000 scaffolds
- 200,000 designs
- Less than 10 successful designs

## With BOINC

- 30,000 scaffolds
- 10,000,000 designs
- 200~1000 successful designs



# Acknowledgements

Institute for Protein Design Members

**R@H Users**