

# **HPC in Drug Discovery**

## Ashutosh Tripathi, Ph.D. Bankaitis Lab

Department of Molecular and Cellular Medicine

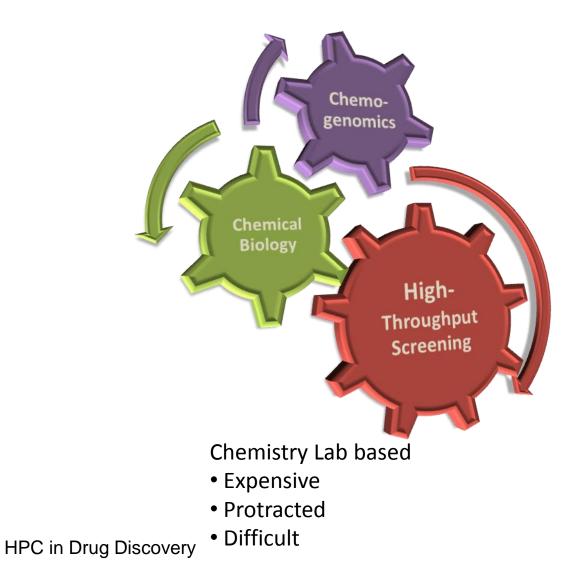
TAMHSC

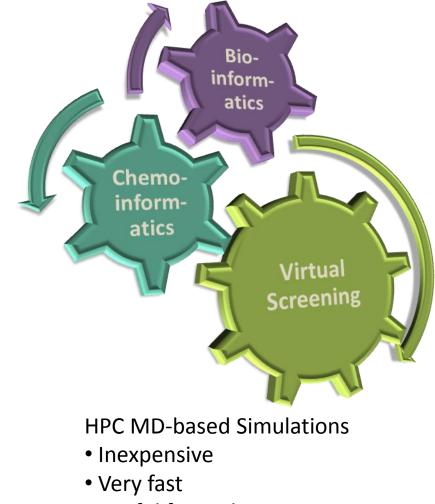


## **HPC in Drug Discovery**

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### **Technologies in Drug Discovery**



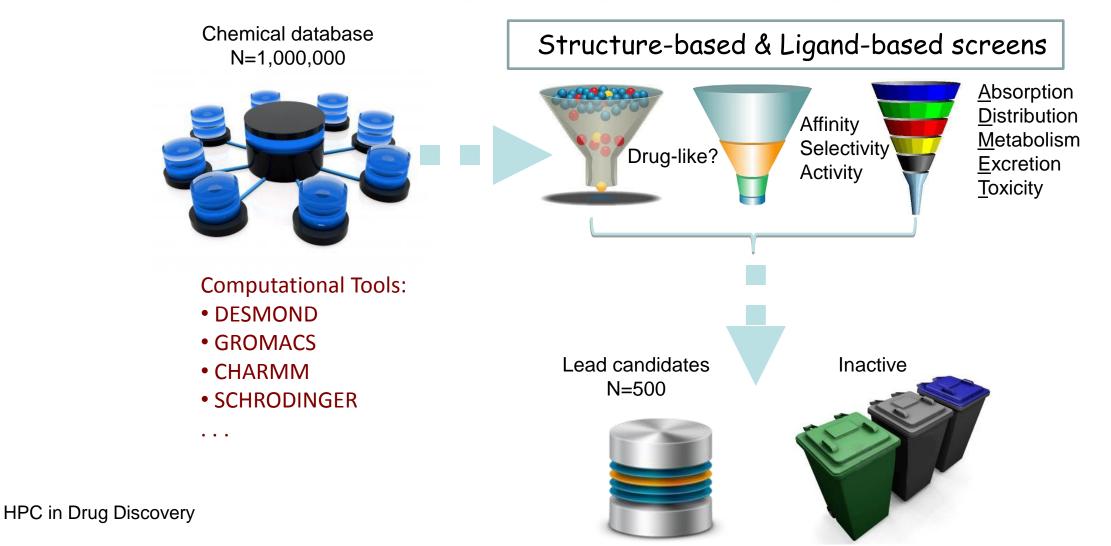


• Useful for early stages

## A HPC in Drug Discovery

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### In silico Screening Complements High-throughput Screening





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### **Drug Discovery: Driven by Computation and Experiments**

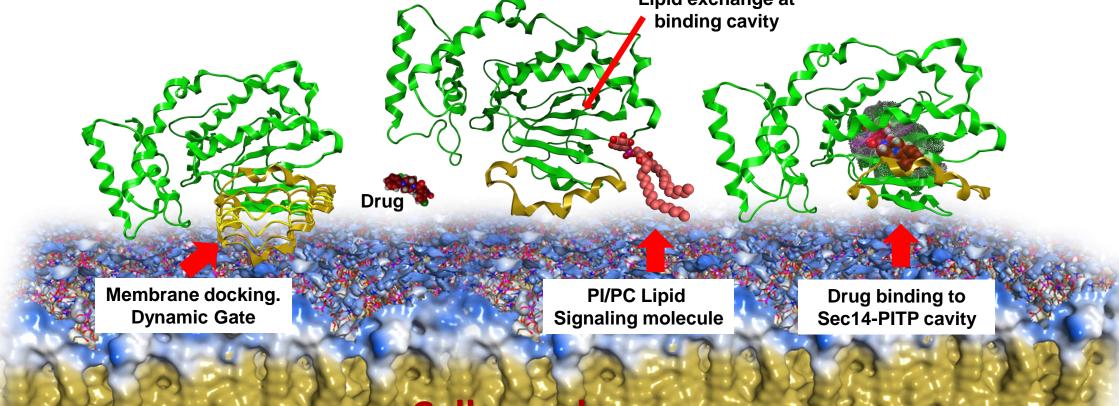


HPC in Drug Discovery



## Phosphatidylinositol Transfer Proteins (PITPs) Important in Cell Function

- Important in Lipid-mediated cell signaling and metabolism.
- Derangement in Signaling: Neurodegenerative diseases and many forms of cancers.



Cell membrane

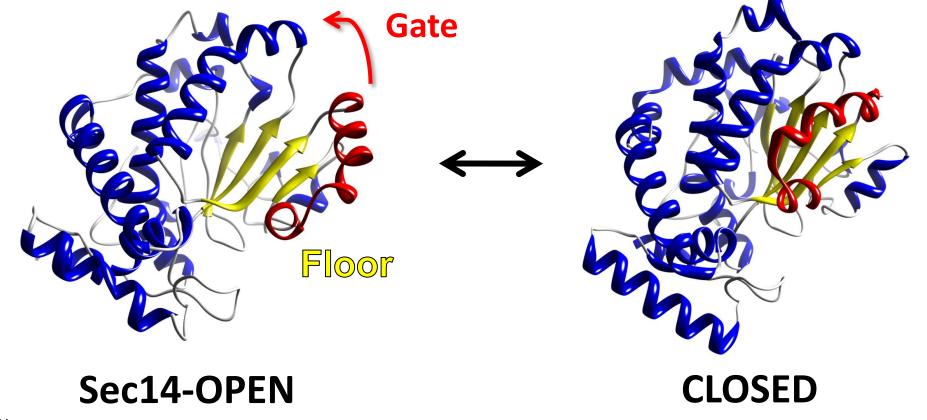


## Phosphatidylinositol Transfer Proteins (PITPs) Critical in Cell Function

• Important in Lipid-mediated cell signaling and metabolism.

'Transition state'?

- Derangement in Signaling: Neurodegenerative diseases and many forms of cancers.
- Undergoes Conformational Changes: Helical Gate Mediates Lipid Access/Exchange

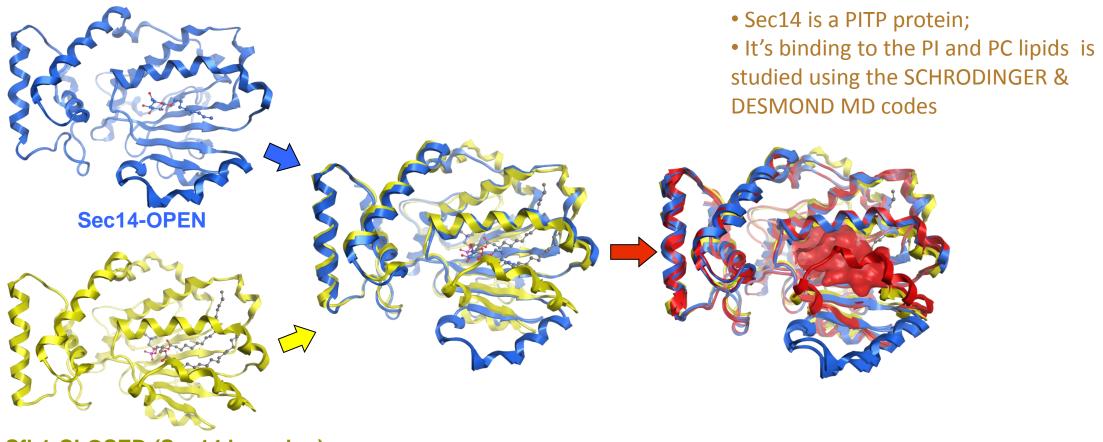


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## **AM** HPC in Drug Discovery

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### Homology Modeling of Sec14 (Closed Conformation)



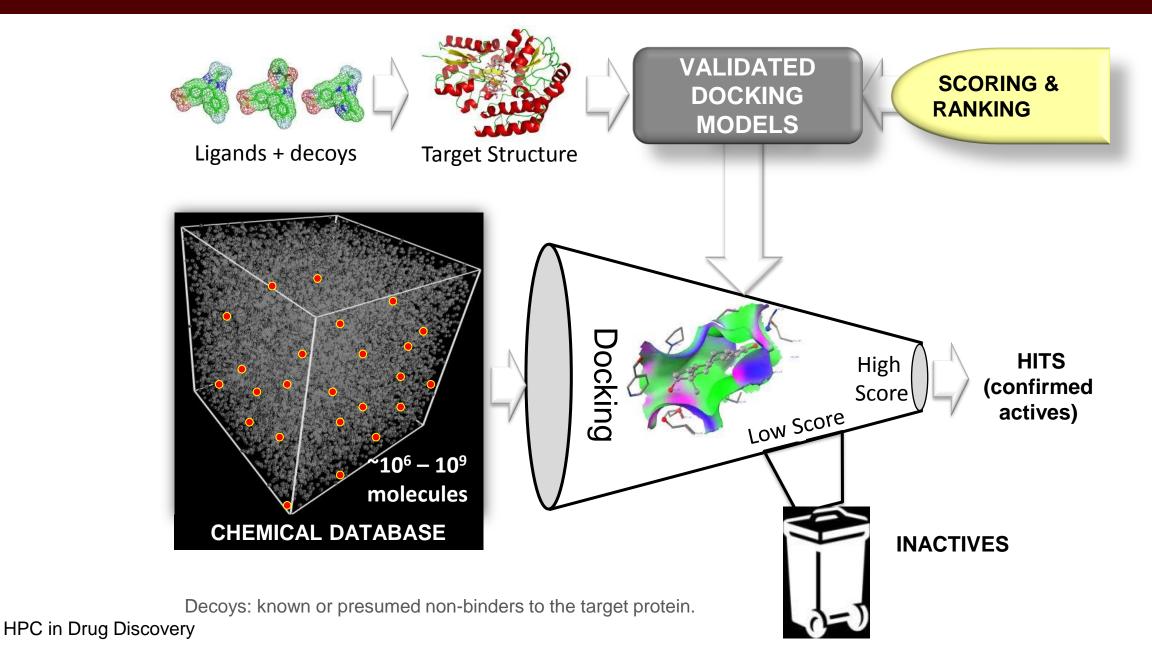
Sfh1-CLOSED (Sec14 homolog)

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Identity: 62 % Similarity: 78 % Homology: 77 % Yellow: Sfh1 Blue: Sec14-OPEN Red: Sec14 Homology Model-CLOSED



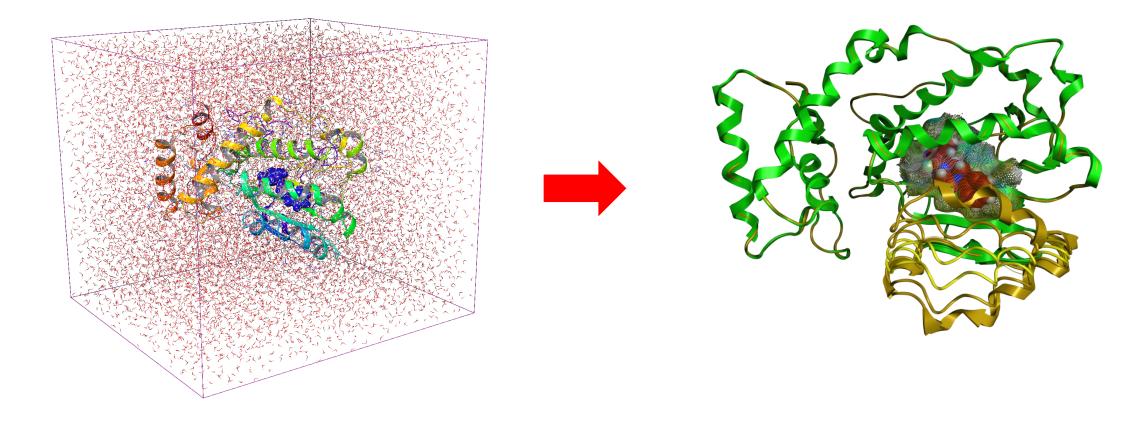
## **Docking-Based Virtual Screening**





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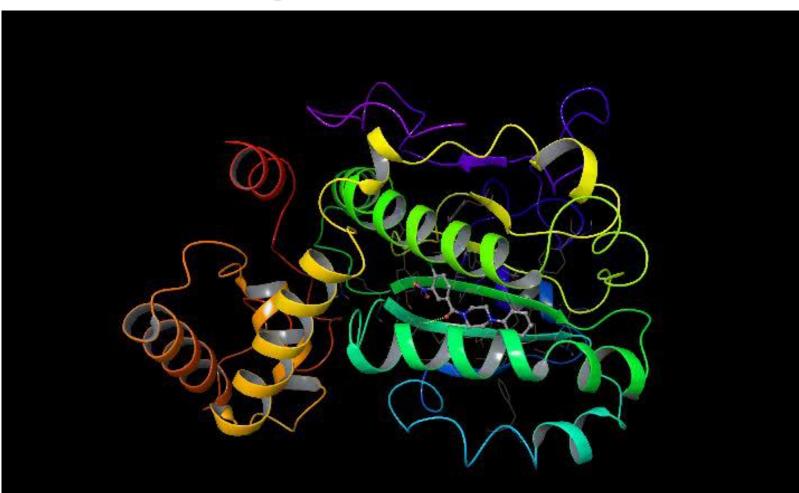
### Sec14 Homology Model: All-Atom MD Simulation



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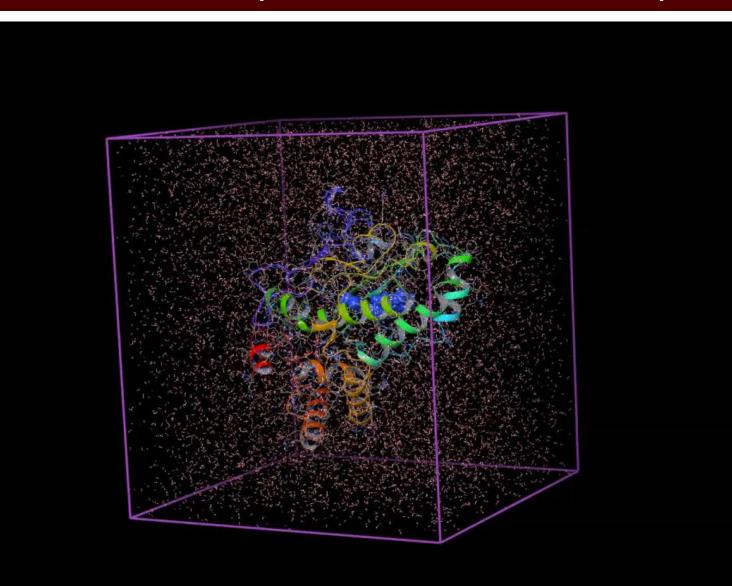
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### Simulation of Drug Binding to Protein Using DESMOND MD Code





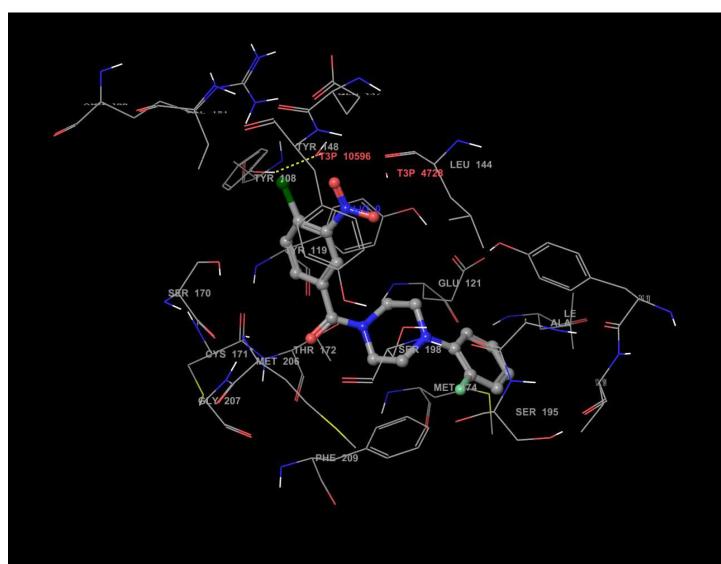
### All-Atom Simulation of Sec14 in Explicit Water Molecules (used DESMOND MD Code)



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#### Small molecule (drug) vibrating in Sec14 binding pocket (Used DESMOND MD Code)



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## AM HPC in Drug Discovery

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#### Ashutosh Tripathi, Ph.D.

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#### **Research Interest**

- Computer-aided drug design.
- Algorithm and software development for designing new drugs.
- Cancer therapeutics.
- Clinical informatics.
- ADME/Tox QSAR modeling.