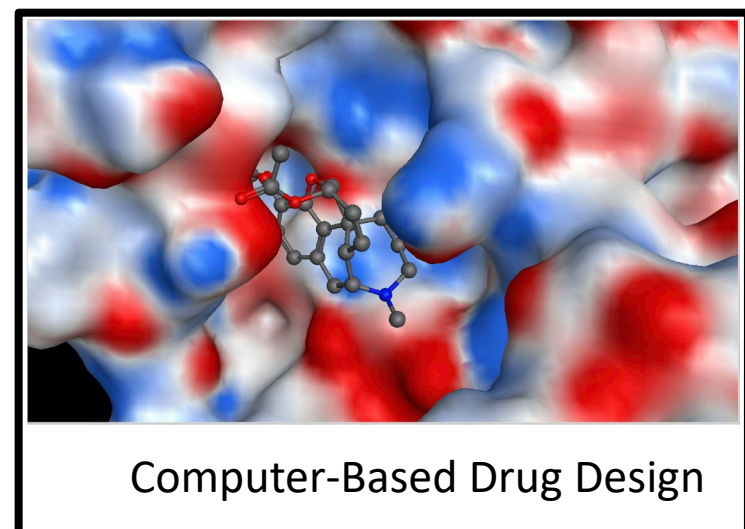
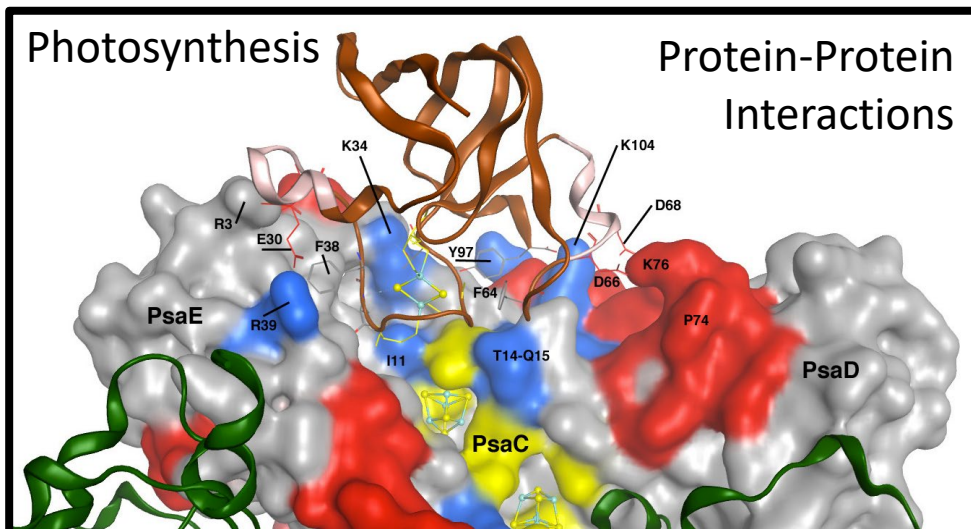
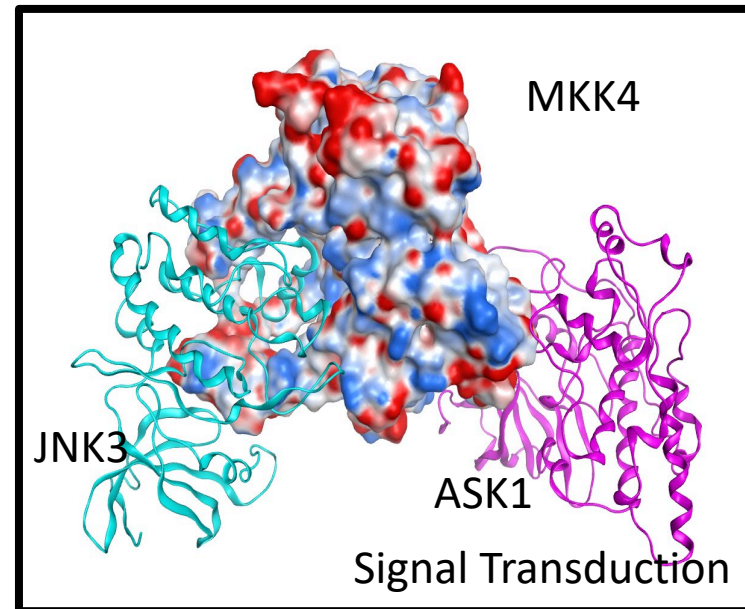
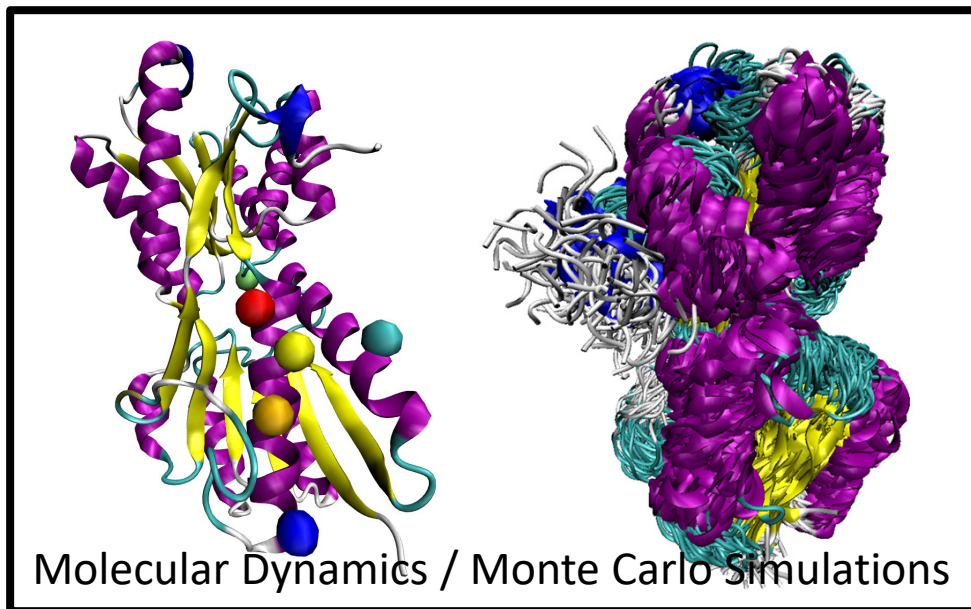


Dr. Derek Cashman

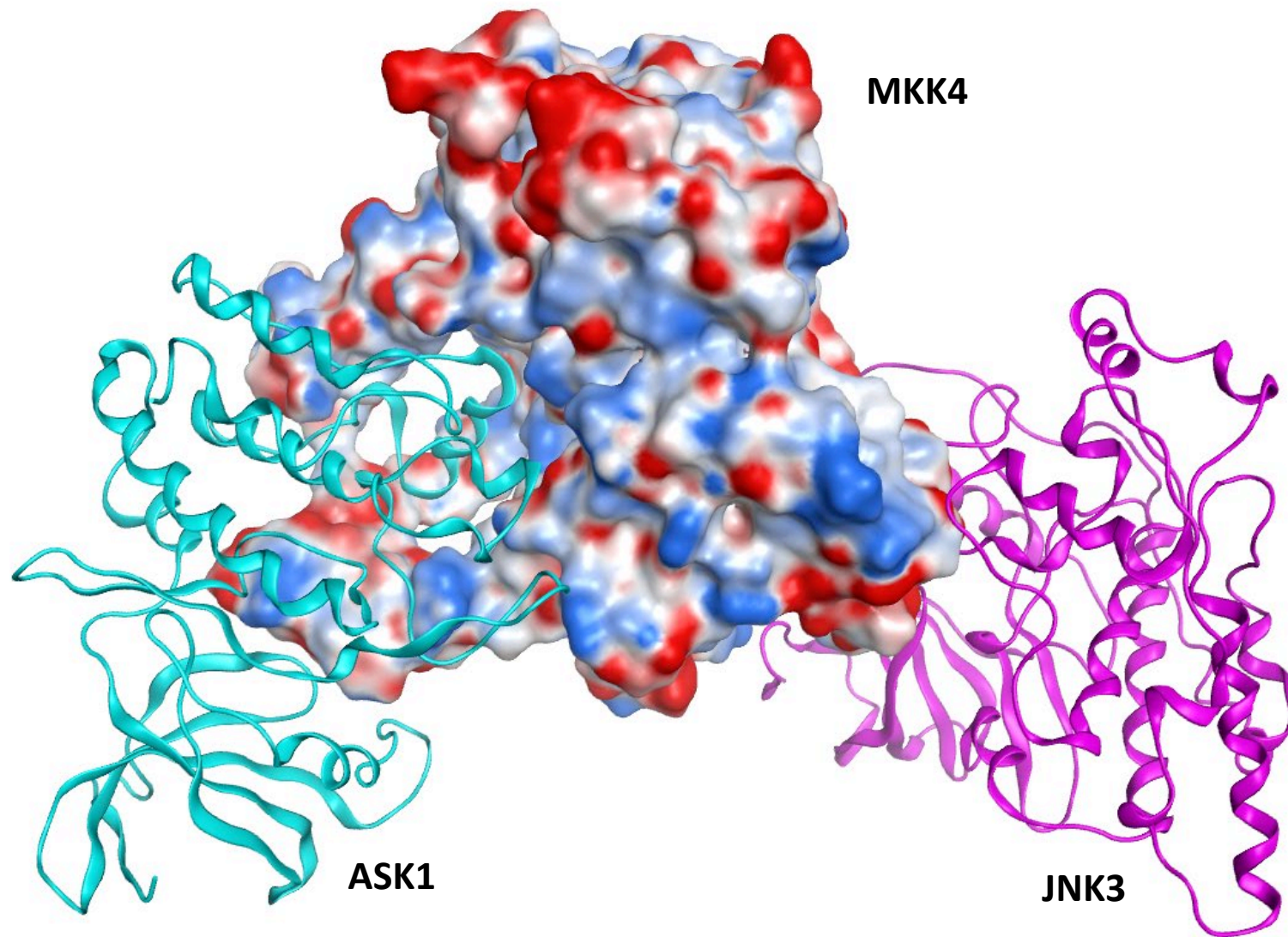
Computational Biophysical Chemistry

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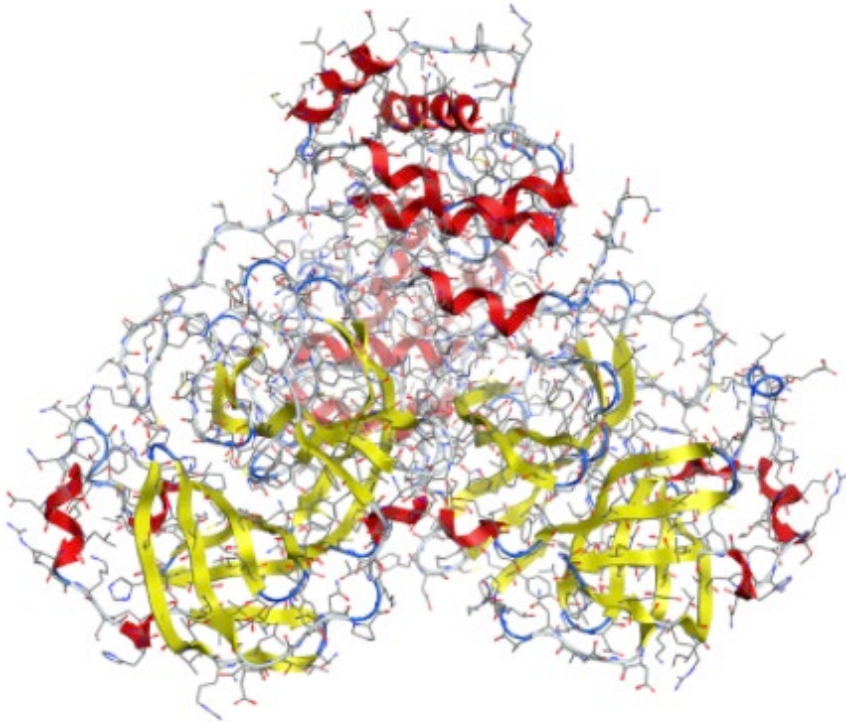


ASK1/MKK4/JNK3 Docking Complex

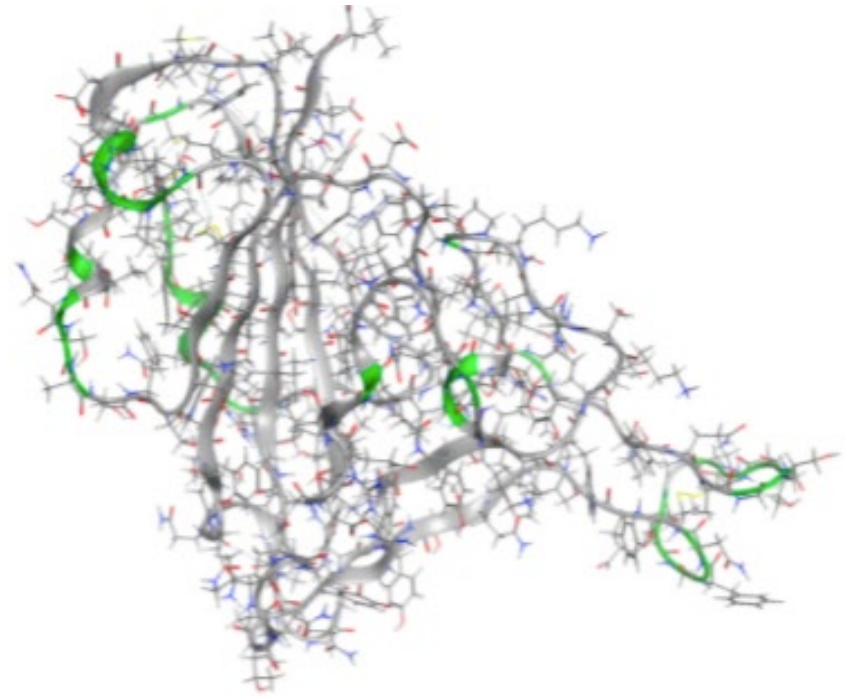


Docking calculations performed on ClusPro Server by Cameron Davis.

2020/2021 Governor's School for Emerging Technologies



SARS-CoV-2 Main Protease

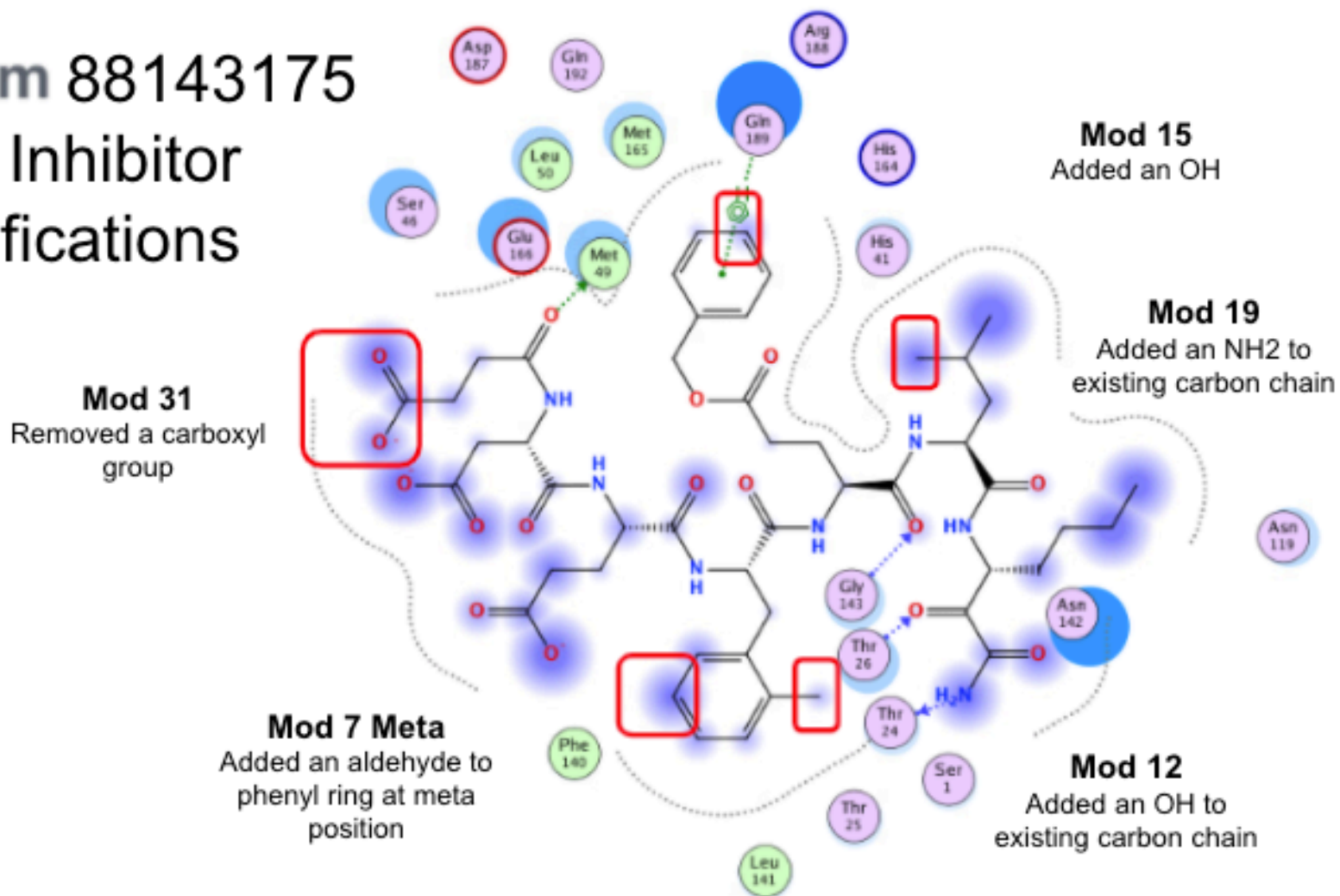


SARS-CoV-2 Receptor-Binding Domain

Thank you to research mentors: Cory Rogers, Rachel Paris and Allison Adams who assisted with this project.

PubChem 88143175

Best Inhibitor Modifications



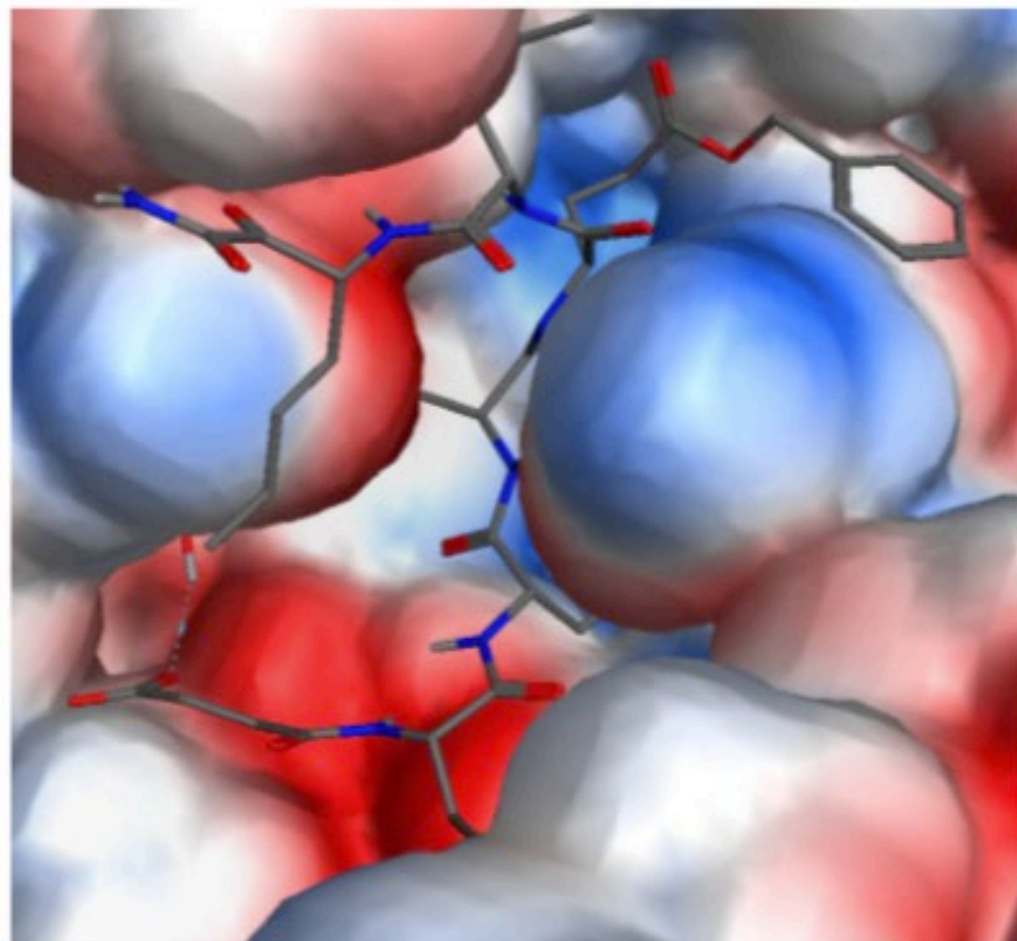
PubChem 88143175

Modification	Change	Grid Score ¹	Grid VDW Energy	Grid ES Energy	Molec Weight	LogP	No. Rotatable Bonds	H-Bond Donors	H-Bond Acceptors
Mod 12	Moved C + OH meta	-100.07	-95.6	-4.47	1039.08	1.66	45	9	18
Mod 31	Removed a carboxyl	-96.24	-90.86	-5.38	982.054	2.23	42	12	13
Mod 15	Added OH para	-91.17	-90.34	-0.82	1055.08	1.17	46	14	14
Mod 7 Meta	Added OH meta	-90.49	-86.37	-4.13	1021.07	2.85	42	11	15
Mod 19	Replaced C with NH ₂	-88.85	-86.78	-2.07	1040.07	0.23	47	14	14

1. Grid Energies in kcal/mol; 2. Molec. Weight in g/mol

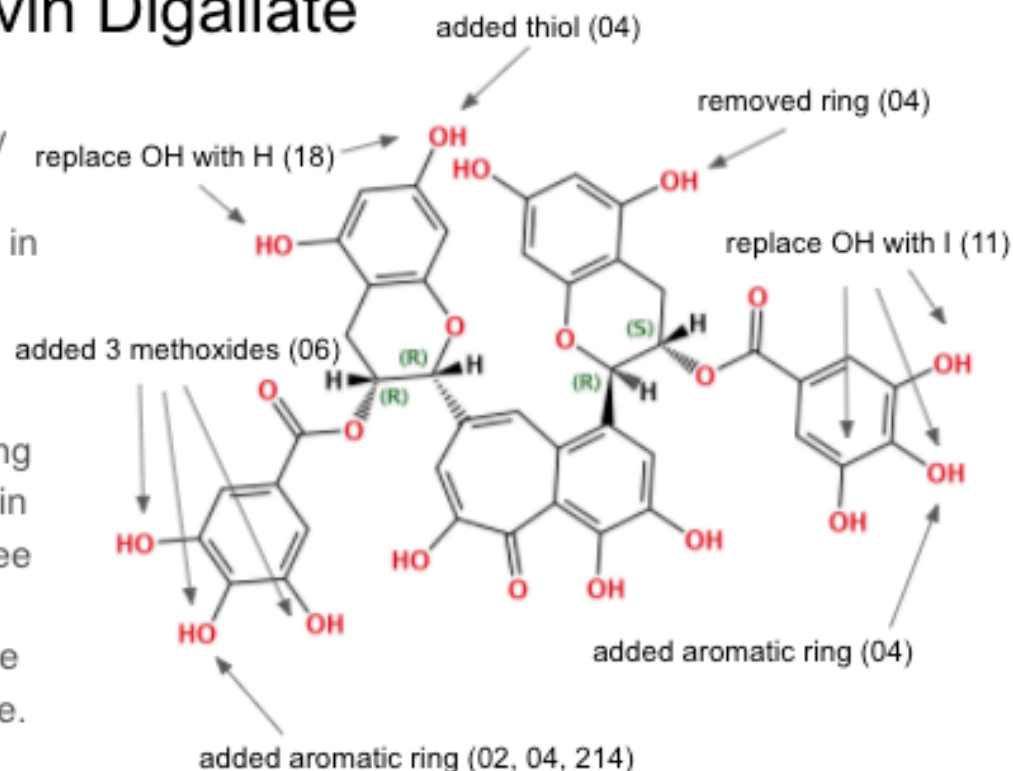
Electrostatic Docking Map of PubChem 88142175 (mod 12)

Modification:	Moved C + OH to Meta
Grid Score:	-100.07 kcal/mol
Grid VDW Energy:	-95.6 kcal/mol
Grid ES Energy :	-4.47 kcal/mol
Molecular Weight:	1059.08 g/mol
LogP:	1.66
Rotatable Bonds:	45
H-Bond Donors:	9
H-Bond Acceptors:	18



Theaflavin Digallate

- Scientists at North Carolina State University found that certain chemical compounds in green tea could inhibit a particular protease in the SARS-CoV-2 virus.
- Researched, analyzed, and docked three compounds from green tea.
- The most successful modification was adding an oxygen and aromatic ring to the theaflavin digallate base, which produced a binding free energy (ΔG_{Bind}) of -8.99 kcal/mol.
- ADME properties of theaflavin digallate were unfavorable regarding Lipinski's Rule of Five.

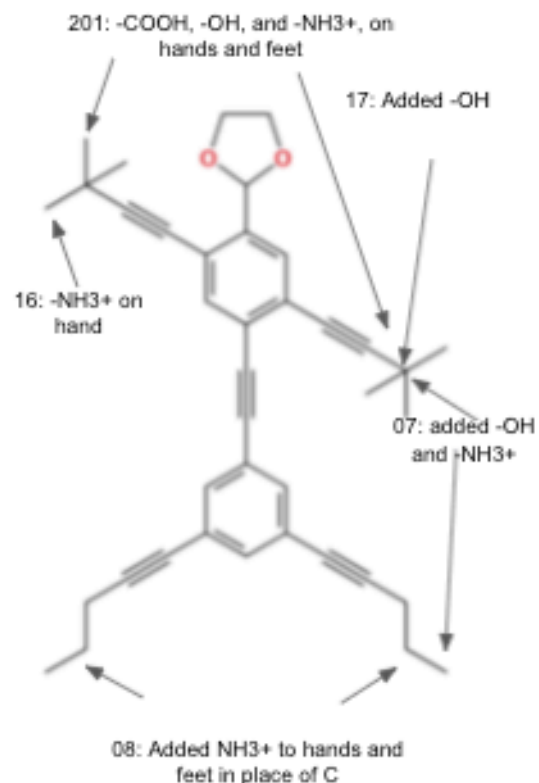


Top 7 Theaflavin Digallate Analogs

Molecule	ΔG Bind (kcal/mol)	Log P	Mol. Weight (g/mol)	H-bond acceptors	H-bond donors	Toxic?	Notes
TNTECH 2021-02	-8.99	4.59	960.81	18	13	no	Highest overall
TNTECH 2021-04	-8.70	6.02	1052.9	14	10	no	
TNTECH 2021-06	-8.60	4.05	910.79	18	11	no	
TNTECH 2021-11	-8.41	-0.56	1210.36	18	13	no	Extremely high molecular weight
TNTECH 2021-214	-8.07	5.05	944.81	17	12	no	
TNTECH 2021-18	-8.04	8.38	832.81	10	5	no	Lower molecular weight, high logP
TNTECH 2021-31	-7.6	2.97	868.71	18	13	no	Lead compound

Top Five NanoKid Analogs

<u>Compound/Modification</u>	ΔG_{bind} (kcal/mol)	<u>logP</u>	<u>Molecular Weight</u> (g/mol)	<u># H-bond acceptors</u>	<u>H-bond donors</u>	<u>Toxic?</u>
TNTECH 2021-07	-8.58	-10.31	718.62	15	10	no
TNTECH 2021-08	-8.48	-17.70	597.6	8	6	no
TNTECH 2021-16	-8.07	-12.53	599.64	8	7	no
TNTECH 2021-17	-8.05	-14.52	721.65	15	11	no
TNTECH 2021-201	-8.05	-18.4	601.64	8	8	no
NanoKid	-7.93	12.18	542.76	2	0	no



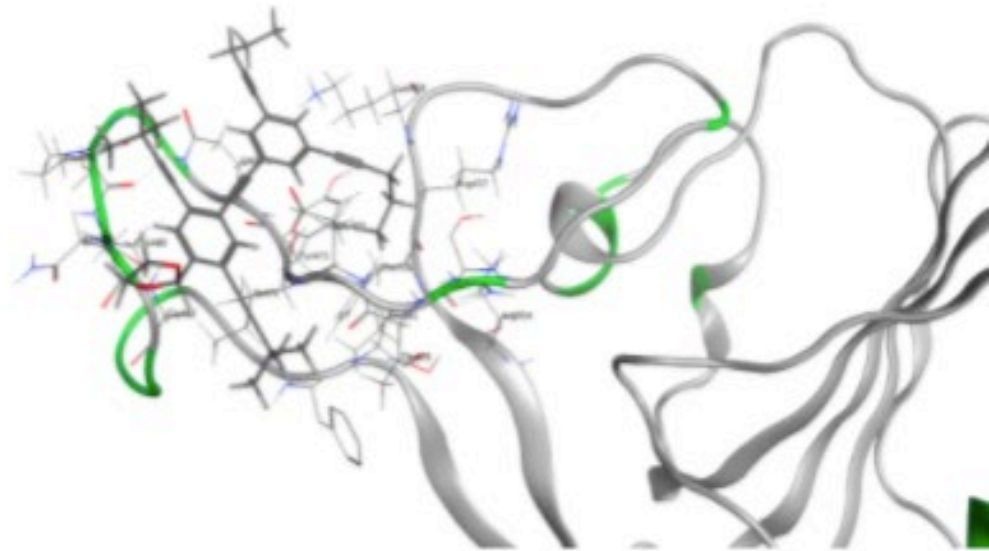
NanoKid Modification Process

Takeaways from lead compound NanoKid:

- Extremely hydrophobic
- Relatively low molecular weight
- Impressive starting binding energy
- Binds to the frustrated area in the SARS-CoV-2 spike protein

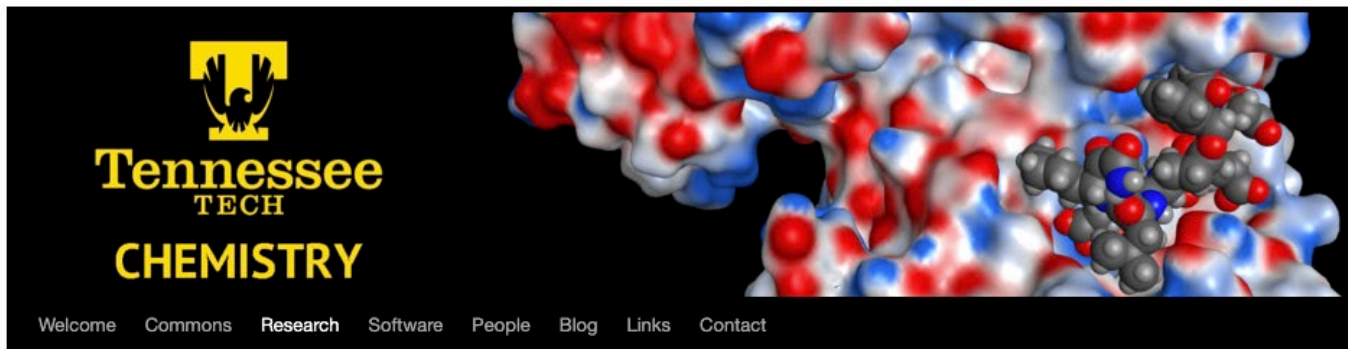
Goals and initial thoughts:

- Improve bind and decrease score
 - Add polar functional groups
- Make hydrophilic
 - Add to preexisting structures on nanokid
- Keep molecular weight low
 - Add to preexisting structures on nanokid
- Avoid toxicity



Ligand interactions between SARS-CoV-2 spike protein and lead compound NanoKid

Tennessee Tech Chemistry Computer Resources



Research Computing



Computer modeling labora

TTU HPC Cluster

- Approximately 35 teraFLOPS
- 36 non-GPU compute nodes, 3 GPU nodes
- 28 Xeon CPU cores per node (> 1,000 CPUs total)
- 128 GB RAM per compute node
- Each compute node is connected to the campus network via 1 GB ethernet and each node is connected to other nodes via 56 GB InfiniBand
- 200 GB local HD space per node
- 175 TB total HD space

The computer modeling laboratory in the Labora
eight Linux workstations designed for a variety of scientific computing needs. Each

3D Printing With MOE 2020

