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Computational Chemistry and Bioinformatics Research Core (CCBRC)

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Computational Chemistry and Bioinformatics Research CORE (CCBRC)

Glycoscience Center of Research Excellence
AT THE UNIVERSITY OF MISSISSIPPI

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THE UNIVERSITY of MISSISSIPPI
DEPARTMENT OF BIOMOLECULAR SCIENCES

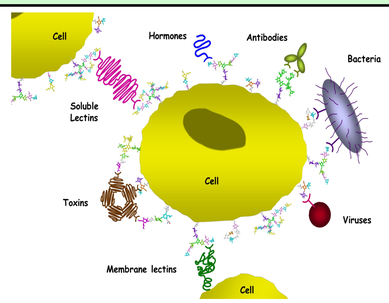
CCBRC

- The Glycoscience Center of Research Excellence (GlyCORE) is a NIH COBRE Phase 1 center.
- GlyCORE seeks to develop, support and foster glycoscience research throughout the Mid-South region of USA (including Mississippi, Alabama, Arkansas, Louisiana, Tennessee, Kentucky and Missouri).
- The CCBRC is a core facility of GlyCORE which focuses on computational glycoscience and provides training, access to hardware and software, and collaboration to help solve scientific problems.

Why Glycoscience?

Protein–Glycan Interactions

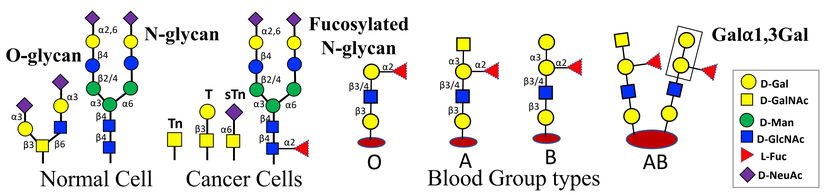
Glycosylation is the most common post-translational modification. Protein–glycan interactions are involved in many biological processes including cell signalling, immune response, and cell–cell adhesion [1-2]. Cancer cells frequently go though altered glycosylation, and these modifications are unique for cancer cells or cancer types [3].



Protein-glycan interactions are key to numerous physiological and pathological processes (Fig[2])

Such modified glycans are known as tumor-associated carbohydrate antigens (TACAs). Furthermore, exposure to non-self type glycans can result in an immunological response in humans. For example, blood group antigens A, B or non-human antigen Galα1,3Gal or Neu5Gc can trigger a severe allergic reaction [4-6]. Thus it is essential not only to understand protein–glycan interactions but also to design recognition molecules to detect glycan patterns with high specificity.

Glycoantigens and Glycomarkers



Services

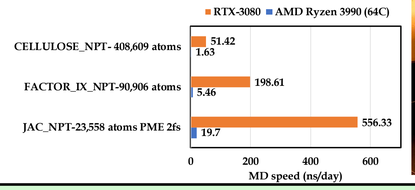
- ❑ Providing all sorts of computational support for GlyCORE Jis, PPPIs.
- ❑ Research on computational glycosciences.
- ❑ Performing computations as part of service or collaboration.
- ❑ Consultation on glycoscience research.
- ❑ Providing access to high performance and GPU computing resources.
- ❑ Providing access to software for molecular modeling.
- ❑ Training and workshops on computational glycosciences.

CORE Facilities

Hardware:

- GAG: 8x A5000 GPUs, 384 GB memory, 40 TB storage
- High end GPU workstations: Nvidia RTX 308024T GPUs, 40 cores, 196 GB memory, 24 TB storage
- GPU workstations: 24 cores, 32 GB memory, RTX 3080/A5000 GPUs
- Storage server: 80 TB of storage (6x 16 TB; RAID5)

NVIDIA RTX 3080 RTX A5000



Licensed software:

- Schrödinger Drug Discovery Platform
- Flex, Flare Forge (Cresset Group)
- Amber20, Desmond
- PyMOL v.2

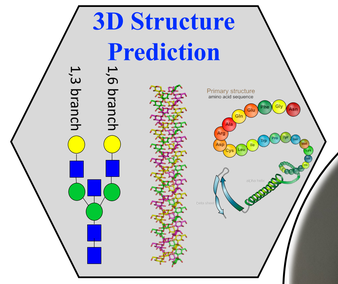
Other software:

- Molecular Dynamics: Amber20, NAMD
- Docking: AutoDock Vina, Vina-Carb, MGLTools
- Structure Prediction: MODELLER, ROSETTA
- Binding Free-energy Calculation: Sire, FESetup
- Molecular Viewers: VMD, PyMOL, Maestro
- Sequencing: Guppy, Flye, PycoQC, Flitlong, etc.

CORE Competencies

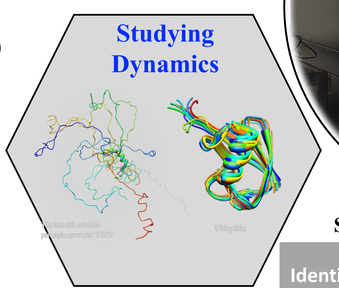
- Glycam-web
- Homology modeling
- *ab Initio: Rosetta*
- Machine learning based
- Replica Exchange MD

3D Structure Prediction



- Molecular dynamics (MD)
- Replica Exchange MD
- Steered MD
- Metadynamics
- Umbrella sampling

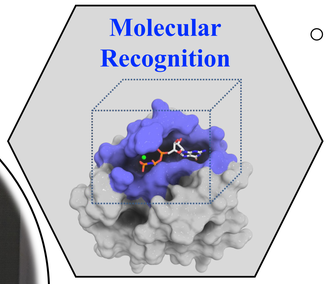
Studying Dynamics



GPU Cluster

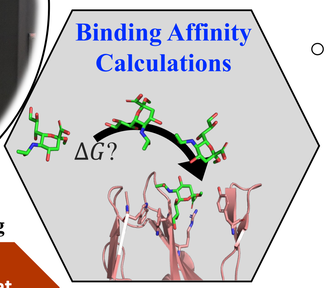
Structure Guided Drug Designing

Molecular Recognition



- Docking
  - Protein–protein
  - Protein–ligand
  - Protein–glycan
  - Protein–glycosaminoglycan

Binding Affinity Calculations



- Binding-energy calculation
  - Scoring functions
  - End-point approaches
  - Alchemical approaches
  - Potential of Mean Force

Recent Publications of CCBRC:

1. Shofolawe-Bakare, O. T.; de Mel, J. U.; **Mishra, S. K.**; Hossain, M.; Hamadani, C. M.; Pride, M. C.; Dasanayake, G. S.; Monroe, W.; Roth, E. W.; Tanner, E. E. L.; **Doerksen, R. J.**; Smith, A. E.; Werfel, T. A. ROS-Responsive Glycopolymeric Nanoparticles for Enhanced Drug Delivery to Macrophages. *Macromol. Biosci*, e2200281.
2. Nagae, M.; Hirata, T.; Tateno, H.; **Mishra, S. K.**; Manabe, N.; Osada, N.; Tokoro, Y.; Yamaguchi, Y.; **Doerksen, R. J.**; Shimizu, T.; Kizuka, Y. Discovery of a Lectin Domain That Regulates Enzyme Activity in Mouse N-Acetylglucosaminyltransferase-IVa (MGAT4A). *Commun. Biol.* **2022**, *5* (1), 1–11.
3. Vibhute, A. M.; Tanaka, H.; **Mishra, S. K.**; Osuka, R. F.; Nagae, M.; Yonekawa, C.; Korekane, H.; **Doerksen, R. J.**; Ando, H.; Kizuka, Y. Structure-Based Design of UDP-GlcNAc Analogs as Candidate GnT-V Inhibitors. *Biochim. Biophys. Acta BBA - Gen. Subj.* **2022**, *1866* (6), 130118.
4. Khaje, N. A.; Eletsky, A.; Biehn, S. E.; Mobley, C. K.; Rogals, M. J.; Kim, Y.**; Mishra, S. K.**; **Doerksen, R. J.**; Lindert, S.; Prestegard, J. H.; Sharp, J. S. Validated Determination of NRG1 Ig-like Domain Structure by Mass Spectrometry Coupled with Computational Modeling. *Commun. Biol.* **2022**, *5* (1), 1–8.
5. Kim, S. B.; Zoepfl, M.; **Samanta, P.**; Zhang, F.; Xia, K.; Thara, R.; Linhardt, R. J.; **Doerksen, R. J.**; McVoy, M. A.; Pomin, V. H. Fractionation of Sulfated Galactan from the Red Alga Botryocladia Occidentalis Separates Its Anticoagulant and Anti-SARS-CoV-2 Properties. *J. Biol. Chem.* **2022**, *298*.
6. Dwivedi, R.; **Samanta, P.**; Sharma, P.; Zhang, F.; **Mishra, S. K.**; Kucheryavy, P.; Kim, S. B.; **Aderibigbe, A. O.**; Linhardt, R. J.; Tandon, R.; **Doerksen, R. J.**; Pomin, V. H. Structural and Kinetic Analyses of Holothurian Sulfated Glycans Suggest Potential Treatment for SARS-CoV-2 Infection. *J. Biol. Chem.* **2021**, 297(4) 101207.

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[2] D. Solis, N. V. Bovin, A. P. Davis, J. Jiménez-Barbero, et al., *Biochim. Biophys. Acta.* **1850**, 186–235 (2015).
[3] N. Taniguchi, Y. Kizuka, *Advances in Cancer Research*, (eds. Drake, R. R. & Ball, L. E.) **126**, 11–51 (Academic Press, 2015).
[4] C. Yu, K. Gao, L. Zhu, W. Wang, L. Wang, F. Zhang, C. et al., *Sci. Rep.* **6**, 20029 (2016).
[5] S. Cunningham, E. Starr, I. Shaw, J. Glavin, M. Kane, L. Joshi, *Anal. Chem.* **85**, 949–955 (2013).
[6] H. Clausen, S. Hakomori, *Vox Sang.* **56**, 1–20 (1989).

Acknowledgements

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