



INTRODUCTION

Welcome to the inaugural edition of the Center for Molecular Interactions in Cancer (CMIC) newsletter. I am writing to you just beyond the one-year anniversary of when we submitted our Centers of Biomedical Research Excellence (COBRE) application (1P20GM152281-01). We are still waiting for the final word on that massive tome we pounded into existence during the last half of 2022. After some “administrative delays”, I was recently told by the NIH Grants Management Specialist overseeing our application that they are working on a start date in the second half of February. Hopefully, we will have some good (and definitive) news soon.

I am excited about what is ahead and thrilled by the prospect of working with such a talented team. Together, I know we can build a community and research infrastructure that will help scientists at UAMS study molecules and pathways involved in cancer with atomic-level resolution.

Be on the lookout for email updates from me about plans for the upcoming year. Until next time...

Cheers,

Robert L. Eoff, PhD
Professor of Biochemistry &
Molecular Biology
CMIC Director



OUR MISSION

Cancer affects the health of millions of Americans. Studying molecular mechanisms that endow cells with malignant properties is an essential component of advancing pre-clinical studies and a key part of efforts to improve patient outcomes. The purpose of this NIH COBRE grant is to establish the CMIC at the UAMS. The mission of the CMIC is to study molecular features and functional properties of biomolecules that drive cancer. The unifying theme of research among Center members is the coupling of structural biology and high-resolution imaging with precise, quantitative analysis of biochemical and cellular processes to understand how molecular interactions govern the initiation, progression and treatment of cancer. Our long-term goal is to leverage faculty mentoring, strategic recruitment, and cutting-edge core resources to develop a critical mass of investigators that will support a self-sustaining center in which research advances our knowledge of cancer through precise and comprehensive analyses of molecular events that impact malignant pathogenesis.

CENTER NEWS & UPDATES

The past months have seen many notable accomplishments by the CMIC Research Project Leaders (RPLs) and their teams. New grants are listed below and publications are listed on page 2. *Well done!*

GRANTS

- Congratulations to Adam Wolfe, MD/PhD, for being awarded a prestigious grant from the American Cancer Society! The grant entitled “Targeting the KRAS-USP7-RAD18 Axis” will study how KRAS and USP7 coordinate DNA repair pathways, focusing on models of pancreatic ductal adenocarcinoma. The four-year award is a huge achievement for Dr. Wolfe and his team.

Project number: ASTRO-CSDG-23-1037280-01-CDP

Total Award Amount (including Indirect Costs): \$583,200

- Congratulations to Dr. Mohammad Rahman, who was the recipient of an award from the Arkansas Breast Cancer Research Program (ABCRP) for his project entitled “Manipulating RNA splicing as a targeted approach in breast cancer.”

- A big shout of congrats to Dr. Eric Enemark, Director of the CMIC Structural Biology Core, who has secured \$159,634 in funds through an Arkansas INBRE supplement to purchase a cryo-EM GPU/storage system.

ANNOUNCEMENTS & OTHER NEWS

- Dr. Tudor Moldoveanu worked very hard to assemble and submit a Major Research Instrumentation grant to the NSF entitled “Acquisition of Glacios cryo-TEM in Arkansas”. This award would bring state-of-the-art instrumentation for structure determination by cryo-EM to UAMS.

- If you are interested in developing structural biology projects, then please reach out to Dr. Enemark to discuss how the CMIC team can help you get started. He has an ongoing collaboration with the Pacific Northwest Center for Cryo-EM and can help you get your projects going.

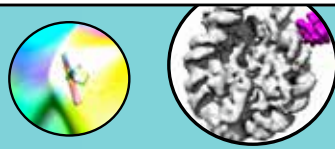
- For those new to structural biology, check out PDB101 from the Protein Data Bank: <https://pdb101.rcsb.org/>

UPCOMING EVENTS

- The Oklahoma COBRE in Structural Biology is organizing a free workshop on using Phenix Software for Macromolecular Structure Determination. The in-person event will be held March 18-19 (2024) at the University of Oklahoma Stephenson Life Sciences Center. To register for this free event, visit:

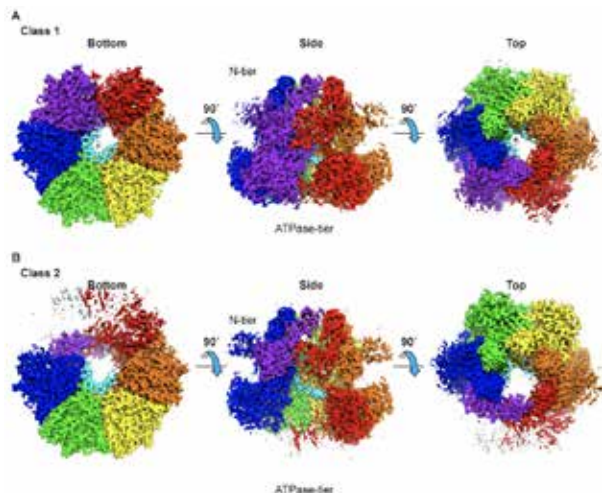
<https://www.ou.edu/structuralbiology/events>

- If you have any additional news or updates to share with the CMIC team, then please let Robert know.



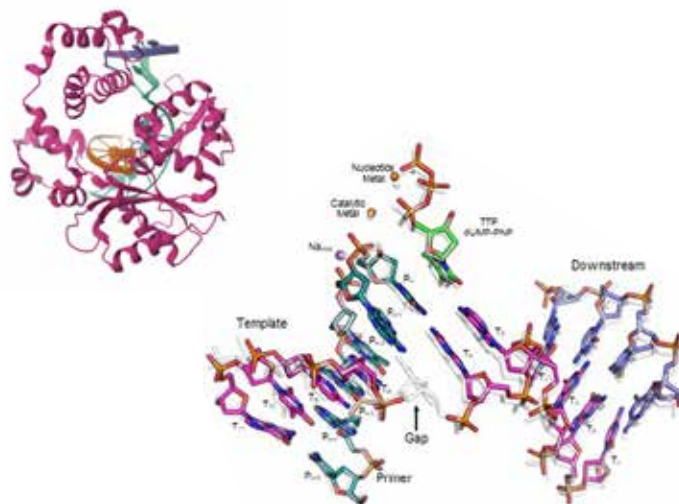
NEW STRUCTURES

The Enemark lab published an elegant series of structures of the SsoMCM hexameric helicase (Meagher M. et al. 2022 Int J Mole Sci, 23, 14678).



PDB codes: 8EAF, 8EAG, 8EAH, 8EAI, 8EAJ, 8EAK, 8EAL, 8EAM

Dr. Jamsen published an exciting structure of the repair enzyme polymerase lambda (Pol λ) in his most recent NSMB article (Chandramouly G. et al. 2023 Nat Struct Mol Biol, 30, 107-114).



PDB code: 2PFO

RECENT PUBLICATIONS

(RPL publications from January 2023-January 2024)

Chandramouly G, **Jamsen J**, Borisonnik N, Tyagi M, Calber ML, Tredinnick T, Ozdemir AY, Kent T, Demidova EV, Arora S, Wilson SH, Pomerantz RT (2023) "Pol λ promotes microhomology-mediated end-joining" *Nat Struct Mol Biol*, 30, 107-114 (PMCID: PMC10197178).

Alam J, Huda MN, Tackett AJ, **Miah S** (2023) "Oncogenic signaling-mediated regulation of chromatin during tumorigenesis" *Cancer Metastasis Rev*, 42, 409-425.

Islam MR, Nagar P, Neetole ST, Wan L, **Rahman MA** (2023) "RNA splicing in cancer and targeted therapies" *Genes*, 14, 2020 (PMCID: PMC10671003).

Farshadyeganeh P, Nazim M, Zhang R, Ohkawara B, Nakajima K, **Rahman MA**, Nasrin F, Ito M, Takeda JI, Ohe K, Miyasaka Y, Ohno T, Masuda A, Ohno K (2023) "Splicing regulation of GFPT1 muscle-specific isoform and its roles in glucose metabolisms and neuromuscular junction" *iScience*, 26, 107746 (PMCID: PMC10514471).

Nagar P, Islam MR, **Rahman MA** (2023) "Nonsense-mediated mRNA decay as a mediator of tumorigenesis" *Genes*, 14, 357 (PMCID: PMC9956241).

THE STRUCTURE OF DETERMINATION

The All Blacks rugby team from New Zealand is one of the most successful sports teams in the world. They've achieved (and sustained) greatness on the pitch by creating a culture of intentionality and commitment, where self-discipline and teamwork are prioritized. Members of the legendary All Blacks follow a shared set of principles to guide their training and gameplay. James Kerr distilled these principles down into 15 mantras in his book *Legacy*:

Mantra #1: "sweep the sheds"

In other words, "never be too big to do the small things that need to be done." This is one way that the All Blacks stay humble, keeping their egos in check, while also being incredibly successful. If you take pride in your performance, no matter the size of the task, then quality will manifest in everything you set out to do.

For more reading, check out the article by Christine Kininmonth summarizing the book *Legacy* by James Kerr: <https://www.thegrowthfaculty.com/blog/summaryLegacyAllBlacksJamesKerrbook>