BIOGRAPHICAL SKETCH

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NAME: Fanning, Sean William

eRA COMMONS USER NAME (credential, e.g., agency login): SFANNING1

POSITION TITLE: Assistant Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	END DATE MM/YYYY	FIELD OF STUDY
Virginia Tech	BS	05/2008	Biochemistry
Northern Illinois University	PHD	05/2012	Chemistry and Biochemistry
University of Chicago	Postdoctoral Fellow	05/2016	Cancer Biology

A. Personal Statement

I am a Tenure Track Assistant Professor of Cancer Biology. My research is focused on understanding how changes to protein structures impact oncogenic or therapeutic activities in hormone-dependent cancers. I have extensive background in the fields of structural biology, pharmacology, and cancer biology. My specific expertise centers on understanding how small molecule drugs and clinically important mutations affect the structure and cellular activities of estrogen receptor alpha in breast cancer. My research has helped lay the foundation for the clinical deployment of next generation antiestrogens to treat drug-resistant metastatic breast cancer. However, our understanding of how ligands influence estrogen receptor pharmacology remains incomplete. A major focus of our laboratory is to improve our understanding of estrogen receptor allostery drives functional complex formation and transcriptional reprogramming. We are highly collaborative by using our structural biology and biochemistry expertise to help other PIs in the cancer biology field and contributing to their peer-reviewed publications. As a member of the Department of Cancer Biology at Loyola University Chicago, I train graduate students, postdoctoral researchers, and medical students. We have the track-record and infrastructure needed to successfully complete the proposed studies.

Ongoing and recently completed projects I would like to highlight include:

National Institutes of Health, National Cancer Institute 1R37CA279341-01
Fanning (PI)
04/01/2023 – 03/31/2030
Structural-Transcriptional Relationships that Improve Y537S Estrogen Receptor Antagonism

Department of Defense BCRP, BC230282
Xu (PI), Fanning (co-I)
09/01/2023 – 08/31/2025
Development of New Agents for Treatment of Hormone Receptor +/HER2+ Breast Cancer

Susan G. Komen, CCR19608597
Fanning (PI)
08/26/2019 – 08/25/2023
Developing new treatments for drug-resistant ER+ metastatic breast cancer

1. Young KS, Hancock GR, Fink E, Zigrossi A, Flowers B, Cooper DA, Nguyen VT, Martinez M, Mon KS, Bosland M, Zak D, Runde A, Sharifi MN, Kastrati I, Minh DDL, Kregel S, **Fanning SW**. Targeting Unique Ligand Binding Domain Structural Features Downregulates DKK1 in Y537S *ESR1* Mutant Breast Cancer Cells. Breast Cancer Research 2025;27(1):10. doi: 10.1186/s13058-024-01945-z.
2. Hancock GR, Young KS, Hosfield DJ, Joiner C, Sullivan EA, Yildiz Y, Lainé M, Greene GL, **Fanning SW**. Unconventional isoquinoline-based SERMs elicit fulvestrant-like transcriptional programs in ER+

breast cancer cells. NPJ Breast Cancer. 2022 Dec 14;8(1):130. PubMed Central PMCID: PMC9748900.

3. Hosfield DJ, Weber S, Li NS, Sauvage M, Joiner CF, Hancock GR, Sullivan EA, Ndukwe E, Han R, Cush S, Lainé M, Mader SC, Greene GL, **Fanning SW**. Stereospecific lasofoxifene derivatives reveal the interplay between estrogen receptor alpha stability and antagonistic activity in *ESR1* mutant breast cancer cells. Elife. 2022 May 16;11 PubMed Central PMCID: PMC9177151.
4. **Fanning SW**, Mayne CG, Dharmarajan V, Carlson KE, Martin TA, Novick SJ, Toy W, Green B, Panchamukhi S, Katzenellenbogen BS, Tajkhorshid E, Griffin PR, Shen Y, Chandarlapaty S, Katzenellenbogen JA, Greene GL. Estrogen receptor alpha somatic mutations Y537S and D538G confer breast cancer endocrine resistance by stabilizing the activating function-2 binding conformation. Elife. 2016 Feb 2;5 PubMed Central PMCID: PMC4821807.

B. Positions, Scientific Appointments and Honors

2025 -	Member of the Annual Steering Committee of the Endocrine Society
2024 -	Member of the Integrative Biomedical Sciences Doctoral Program admission committee
2024 -	Ad hoc member of the NIH NCI DMPC study section
2024 -	Member of the Endocrine Cancers Steering Committee of the Endocrine Society
2024 -	Member of the Research Affairs Core Committee of the Endocrine Society
2024 -	Editorial Board Member Scientific Reports
2023	Junior Scientist of the Year, Loyola University Chicago Stritch School of Medicine
2023 -	Co-Chair NR IMPACT Thinktank
2023 -	Invited Guest Editor *Cells*
2022	Invited Guest Editor *Frontiers in Endocrinology*
2022 – 2023	NIH Early Career Reviewer
2022	DOD BCRP Study Section Member
2022 -	Member of the Loyola University of Chicago Technology Transfer Committee
2022 -	Member NR IMPACT Thinktank
2022 - 2024	Member of the Research Funding Committee at Loyola University Chicago
2021 -	Member Scientific Advisory Board, Olema Oncology, San Francisco, CA
2020 -	Assistant Professor of Cancer Biology, Loyola University Chicago, Stritch School of Medicine, Maywood, IL
2016 - 2020	Pathways to Independence Instructor, University of Chicago, Ben May Department for Cancer Research, Chicago, IL
2013 - 2016	Postdoctoral Fellow (Independently Funded), University of Chicago, Ben May Department for Cancer Research, Chicago, IL
2012 - 2013	Postdoctoral Scholar (Salary Support from Postdoctoral Mentor), University of Chicago, Ben May Department for Cancer Research, Chicago, IL
2010 - 2012	Graduate Research Assistant , Northern Illinois University, Department of Chemistry and Biochemistry, DeKalb, IL
2008 - 2010	Graduate Teaching Assistant, Northern Illinois University, Department of Chemistry and Biochemistry, DeKalb, IL

Honors

2023	Junior Faculty of the Year, Loyola University Chicago, Stritch School of Medicine
2021	Member Scientific Advisory Board, Olema Oncology

C. Contribution to Science

1. Acquired resistance to antiestrogen therapies represents a significant clinical barrier that blocks complete disease remission for a significant population of breast cancer patients. In order to develop improved antiestrogens we need to understand the molecular basis for how cancers become resistant to these therapies. Activating *ESR1* somatic mutations Y537S and D538G enable hormone therapy resistance in many patients. We found that these mutations confer constitutive transcriptional activity and the inhibitory

potency of antiestrogens were reduced. Next, we revealed the molecular basis for how the Y537S and D538G estrogen receptor alpha (ERalpha) somatic mutations confer antiestrogen resistance using biophysical, structural biology, and computational studies. Importantly, we showed that these two mutations act by stabilizing a loop preceding helix 12, the key molecular switch that governs estrogen receptor alpha activity. This new conformation keeps helix 12 in the active state, aberrantly exposing the activating function-2 cleft, such that coregulator can bind in the absence of hormone thereby promoting transcription of ERalpha-mediated target genes. This further reduces the binding affinity of tamoxifen, a widely administered endocrine therapy. The potency of tamoxifen is also reduced because these mutations circumvent the influence of the drug on conformation of the receptor.

a. **Fanning SW**, Mayne CG, Dharmarajan V, Carlson KE, Martin TA, Novick SJ, Toy W, Green B, Panchamukhi S, Katzenellenbogen BS, Tajkhorshid E, Griffin PR, Shen Y, Chandarlapaty S, Katzenellenbogen JA, Greene GL. Estrogen receptor alpha somatic mutations Y537S and D538G confer breast cancer endocrine resistance by stabilizing the activating function-2 binding conformation. Elife. 2016 Feb 2;5PubMed PMID: 26836308; PubMed Central PMCID: PMC4821807.

b. Toy W, Shen Y, Won H, Green B, Sakr R, Will M, Li Z, Gala K, **Fanning SW**, King T, others. ESR1 ligand-binding domain mutations in hormone-resistant breast cancer. Nature genetics. 2013; 45(12):1439.

2. Selective estrogen receptor degraders (SERDs) show improved activities in models of ER+ hormone resistant breast cancers. SERDs act by disrupting the c-terminal helix, helix 12, on the ligand binding domain of estrogen receptor alpha. We showed that the experimental compound OP-1074 showed potent SERD activity in preclinical models of primary and hormone-insensitive breast cancers. Interestingly, OP-1154 and OP-1156 did induce degradation like OP-1074 even though they were chemically identical except for the inclusion or orientation of a single methyl group. We found that this stereo-specific methyl group was sufficient to disorder helix 12 and confer SERD activity onto OP-1074. Next, to further explore whether SERD activity played a role in therapeutic efficacy, we examined the efficacy of the mixed SERM/SERD bazedoxifene (BZA) in breast cancer cells that possess WT, Y537S, and D538G *ESR1*. We chose BZA because it is already clinically approved for use in hormone therapies and possesses significant anticancer activities in luminal breast cancer cells. We found that BZA possessed improved potency compared to tamoxifen and this potency is improved when CDK4/6 inhibitor is added. Comprehensive structural and biochemical assays showed that the SERD activity of BZA enables its potency for the Y537S and D538G *ESR1* mutations.

a. **Fanning SW**, Hodges-Gallagher L, Myles DC, Sun R, Fowler CE, Plant IN, Green BD, Harmon CL, Greene GL, Kushner PJ. Specific stereochemistry of OP-1074 disrupts estrogen receptor alpha helix 12 and confers pure antiestrogenic activity. Nat Commun. 2018 Jun 18;9(1):2368. PubMed PMID: 29915250; PubMed Central PMCID: PMC6006285.

b. **Fanning SW**, Jeselsohn R, Dharmarajan V, Mayne CG, Karimi M, Buchwalter G, Houtman R, Toy W, Fowler CE, Han R, Lainé M, Carlson KE, Martin TA, Nowak J, Nwachukwu JC, Hosfield DJ, Chandarlapaty S, Tajkhorshid E, Nettles KW, Griffin PR, Shen Y, Katzenellenbogen JA, Brown M, Greene GL. The SERM/SERD bazedoxifene disrupts ESR1 helix 12 to overcome acquired hormone resistance in breast cancer cells. Elife. 2018 Nov 29;7PubMed PMID: 30489256; PubMed Central PMCID: PMC6335054.

3. *ESR1* Y537S and D538G activating somatic mutations enable hormone-therapy resistance and contribute to mortality. While next generation SERDs have been deployed to the clinic to address these mutations, it was unclear as to whether the ER-degrading/downregulating activities of these molecules was required to antagonize the mutant receptors. We studied how a panel of SERMs, SERM/SERDs, and SERDs engaged WT, Y537S, and D538G ERα in breast cancer cells. These studies showed that the mutants can differentially how antiestrogens affect receptor degradation and oncogenic transcriptional activities. Importantly, a subset of structurally diverse SERMs and SERDs showed improved antagonistic potencies in breast cancer cells expressing Y537S ERα. High-resolution x-ray crystal structures of these SERMs and SERDs in complex with WT and Y537S ERα showed that the most effective molecules engaged a new hydrogen bond to favor the receptor antagonist conformation.

a. Hosfield DJ, Weber S, Li N-S, Suavage M, Joiner CF, Hancock GR, Sullivan EA, Nduwke E, Han R, Cush S, Lainé M, Mader SC, Greene GL, **Fanning SW**. Stereospecific lasofoxifene derivatives reveal the interplay between estrogen receptor alpha stability and antagonistic activity in ESR1 mutant breast cancer cells. eLife. 2022;11:e72512. doi: 10.7554/eLife.72512.

4. Chemical manipulation of multiple ER structural motifs can elicit unique structure-transcriptional relationships. The SERM/SERD elacestrant possesses an unconventional chemical structure compared to other SERMs and SERDs. A high-resolution x-ray crystal structure showed that elacestrant adopts a unique ligand binding pose within the hormone binding pocket. To further explore structure activity relationships of ER, we developed a series of isoquinoline-based SERM as a structural hybrid of elacestrant and conventional SERMs and SERDs. Through comprehensive structure-activity relationship studies, we developed T6I-29. This new ligand uniquely showed SERM-like effects on ER in the breast cancer cell but fulvestrant-like effects on the transcriptome. These studies also showed that ER ligands can induce the expression of SUMO1 in breast cancer cells whereas it was only previously known that these ligands can induce the modification of ER by SUMO. We have also shown that this SERM has desirable pharmaceutical properties and anti-tumoral activities in Y537S *ESR1* breast cancer cells. Importantly, we have found that this SERM uniquely downregulates the expression and secretion of DKK1 in these cells, a secreted glycoprotein that is associated with metastatic burden in multiple cancers. We also found that DKK1 levels are significantly elevated in a large proportion of ER+ breast cancer patients compared to healthy controls.

   a. Hancock GR, Young KS, Hosfield DJ, Joiner C, Sullivan EA, Yildiz Y, Lainé M, Greene GL, **Fanning SW**. Unconventional isoquinoline-based SERMs elicit fulvestrant-like transcriptional programs in ER+ breast cancer cells. NPJ Breast Cancer. 2022 Dec 14;8(1):130. PubMed Central PMCID: PMC9748900.
   b. Young KS, Hancock GR, Fink E, Zigrossi A, Flowers B, Cooper DA, Nguyen VT, Martinez M, Mon KS, Bosland M, Zak D, Runde A, Sharifi MN, Kastrati I, Minh DDL, Kregel S, **Fanning SW**. Targeting Unique Ligand Binding Domain Structural Features Downregulates DKK1 in Y537S *ESR1* Mutant Breast Cancer Cells. Breast Cancer Research 2025;27(1):10. doi: 10.1186/s13058-024-01945-z.

5. Our lab helps others out in understanding how their molecules affect estrogen receptor alpha structure. We also help them develop new technologies to understand estrogen receptor cellular activities. This includes synthetic peptide-based inhibitors that directly block coregulator binding. It also includes new small molecules that can bind to estrogen receptor in new and unique ways to elicit novel therapeutic activities.

   a. Speltz TE, Qiao Z, Swenson CS, Shangguan X, Coukos JS, Lee CW, Thomas DM, Santana J, **Fanning SW,** Greene GL, Moellering RE. Targeting MYC with modular synthetic transcriptional repressors derived from bHLH DNA-binding domains. Nat Biotechnol. 2022 Oct 27; PubMed PMID: 36302987.
   b. Montgomery JE, Donnelly JA, **Fanning SW**, Speltz TE, Shangguan X, Coukos JS, Greene GL, Moellering RE. Versatile Peptide Macrocyclization with Diels-Alder Cycloadditions. J Am Chem Soc. 2019 Oct 16;141(41):16374-16381. PubMed PMID: 31523967.
   c. Speltz TE, Mayne CG, **Fanning SW**, Siddiqui Z, Tajkhorshid E, Greene GL, Moore TW. A "cross-stitched" peptide with improved helicity and proteolytic stability. Org Biomol Chem. 2018 May 23;16(20):3702-3706. PubMed PMID: 29725689; PubMed Central PMCID: PMC5993042.
   d. Boudreau MW, Duraki D, Wang L, Mao C, Kim JE, Henn MA, Tang B, **Fanning SW**, Kiefer J, Tarasow TM, Bruckheimer EM, Moreno R, Mousses S, Greene GL, Roy EJ, Park BH, Fan TM, Nelson ER, Hergenrother PJ, Shapiro DJ. A small-molecule activator of the unfolded protein response eradicates human breast tumors in mice. Sci Transl Med. 2021 Jul 21;13(603). doi: 10.1126/scitranslmed.abf1383. PubMed PMID: 34290053; PubMed Central PMCID: PMC8456366.

Complete List of Published Works:

https://www.ncbi.nlm.nih.gov/myncbi/16g8kbxuzLG55/bibliography/public/

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
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NAME: Fink, Emma

eRA COMMONS USER NAME (credential, e.g., agency login): emmafink

POSITION TITLE: Graduate Student

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	START DATE MM/YYYY	COMPLETION DATE MM/YYYY	FIELD OF STUDY
Providence College, Providence, RI	BS	07/2018	05/2022	Biochemistry
Providence College, Providence, RI	BS	07/2018	05/2022	Computer Science
Loyola University Chicago, Maywood, IL	PHD	08/2022	05/2027	Biochemistry

A. Personal Statement

Throughout my academic career, I have pursued a rigorous and interdisciplinary training path. I earned my Bachelor of Science in Biochemistry and Computer Science from Providence College while competing as a Division I volleyball player. Research became the perfect bridge between my disciplines, allowing me to integrate my love for both computational and biochemical approaches to discovery. My undergraduate research experiences ranged from protein biochemistry to computational biophysics, which provided me with a diverse skill set that I now apply to my graduate research. Notably, during my time in the Stack Lab at Providence College, I used sequence similarity networks to classify distinct subgroups of azoreductases resulting in a co-author publication. While in the Dickson Lab at Michigan State University, I gained a valuable introduction to molecular dynamics simulations. As a third-year Ph.D. candidate in the Biochemistry and Molecular Cancer Biology program at Loyola University Chicago I conduct research in Dr. Sean Fanning's laboratory. Dr. Fanning is a highly trained cancer biologist, biochemistry, structural biologist and an outstanding mentor. In our lab, we study how estrogen receptor structure can be manipulated with small molecules to reach therapeutic endpoints in breast cancer. My project focuses on the ligand-specific structural mechanisms of estrogen receptor (ER) transcriptional reprogramming to enhance our understanding of ER pharmacology employing single-particle cryo-electron microscopy (cryo-EM) and molecular dynamics simulations. Through his extensive network of collaborators, Dr. Fanning has connected me with other leading researchers, fostering valuable opportunities for collaboration and professional growth. With Dr. Wei Xu's lab at the University of Wisconsin-Madison, I have worked on the structural characterization of heat shock protein 90 (HSP90) with a novel inhibitor which holds promise as a novel cancer therapy. Collaboration with Dr. Donald McDonnell's lab at Duke University expanded the scope of my nuclear receptor studies to include androgen receptor and estrogen-related receptor alpha (ERRα). The work on AR resulted in a co-author publication and the work on ERRα is currently being prepared for submission as a first-author publication in the coming months. Additionally, a collaboration with Olema Pharmaceuticals contributed to a co-first author publication which is expected to be submitted in the next month, further expanding the impact of my research and reinforcing the translational potential of my work. My commitment to advancing cancer research extends beyond the laboratory. As a graduate student mentor, I support first-year students in navigating their transition into graduate school, fostering an inclusive and collaborative research environment. Additionally, my active involvement in professional organizations such as the Endocrine Society has provided me with opportunities to present my work at national conferences like ENDO, where I have honed my ability to communicate complex scientific findings to diverse audiences. Furthermore, I am one of three students leading the establishment of a Colleges Against Cancer chapter at the Loyola Health Sciences Campus, an ACS-affiliated group dedicated to cancer awareness, advocacy and fundraising. This initiative allows me to contribute to the broader cancer research and patient support community beyond my academic work. The NCI F31 fellowship will help me complete my dissertation research and further my training in structural and computational biology. With this support, I will generate high-resolution structural data to inform the rational design of next-generation ER-targeting therapeutics. Furthermore, the mentorship and training opportunities afforded by this fellowship will be instrumental in preparing me for a career as an independent investigator in cancer drug discovery.

5. Safi R, Wardell SE, Watkinson P, Qin X, Lee M, Park S, Krebs T, Dolan EL, Blattler A, Tsuji T, Nayak S, Khater M, Fontanillo C, Newlin MA, Kirkland ML, Xie Y, Long H, Fink EC, Fanning SW, Runyon S, Brown M, Xu S, Owzar K, Norris JD, McDonnell DP. Androgen receptor monomers and dimers regulate opposing biological processes in prostate cancer cells. Nat Commun. 2024 Sep 3;15(1):7675. PubMed Central PMCID: PMC11371910.
6. Long AR, Mortara EL, Mendoza BN, Fink EC, Sacco FX, Ciesla MJ, Stack TMM. Sequence similarity network analysis of drug- and dye-modifying azoreductase enzymes found in the human gut microbiome. Arch Biochem Biophys. 2024 Jul;757:110025. PubMed Central PMCID: PMC11295148.

B. Positions and Honors

Positions and Scientific Appointments

2022 -	Graduate Student, Loyola University Chicago, Maywood IL, IL
2021 - 2021	Undergraduate Research Assistant, Dickson lab, Michigan State University, East Lansing, MI
2020 - 2022	Undergraduate Research Assistant, Stack lab, Providence College, Providence, RI

Honors

2018 - 2022	Dean's Honor List, Providence College
2018 - 2022	St. Catherine of Siena Scholarship, Providence College
2025	Acceptance to the Single Particle Cryo-EM workshop, Cold Spring Harbor Laboratory
2024	Conference Travel Award, Cardinal Bernardin Cancer Center, Loyola University Chicago
2024	Acceptance to the 62nd Hands0on Workshop on Computational Biophysics, Auburn University

C. Contribution to Science

6. 1 in 8 women will be diagnosed with breast cancer in their lifetime. Over 70% of these cases are driven by the expression of estrogen receptor alpha (ERα). Fanning lab studies ER pharmacology to develop improved breast cancer therapeutics that maximize anti-cancer efficacy while limiting side effects. Previous studies in the Fanning lab identified a lead antiestrogenic compound, T6I-29, from a library of compounds designed to combine functional groups from existing therapeutic molecules. This compound was created to target the mutation commonly found in recurrent breast cancer. An in vivo comparative study with T6I-29 and the standard of care, fulvestrant, was performed. We found that T6I-29 had anti-tumoral effects. However, ICI was more efficacious overall. Interestingly, RNA-seq suggests that T6I-29 uniquely downregulates dickkopf-1 (DKK1), which is a secreted glycoprotein known to be pathogenic in breast cancer. This finding was supported by an upregulation of DKK1 in ERα+ patients compared to healthy controls when looking at human plasma samples using ELISA. Follow-up studies on the role DKK1 plays in mutant metastatic breast cancer progression and evaluating it as a new potential target are ongoing in the lab. My contribution to this project was assisting in the in vivo study. I handled the mice, tracked weights and tumor sizes, performed IVIS imaging and daily injections. At the end of the study, I helped sacrifice the animal and harvest organs for immunohistochemistry. I reviewed the manuscript and provided minor edits.
    a. Young KS, Hancock GR, Fink EC, Zigrossi A, Flowers B, Cooper DA, Nguyen VT, Martinez MC, Mon KS, Bosland M, Zak DR, Runde AP, Sharifi MN, Kastrati I, Minh DDL, Kregel S, Fanning SW. Targeting unique ligand binding domain structural features downregulates DKK1 in Y537S ESR1 mutant breast cancer cells. Breast Cancer Res. 2025 Jan 17;27(1):10. PubMed Central PMCID: PMC11742495.
7. Prostate cancer is the second-leading cause of cancer death in American men. Most prostate cancers express the androgen receptor which becomes activated by low levels of endogenous androgens to fuel tumor growth and progression. Historically, inhibition of androgen activation through ablation of androgen synthesis or inhibitors that outcompete the native ligand have been used to treat the disease. However, high dose androgens have also been shown to be effective treatment strategies for late-stage disease. This manuscript explores the mechanistic pathway differentiating high and low dose androgen activation. It was found that different AR effects stem from receptor oligomerization. Low dose androgens favor the monomer population that activates mTOR to drive cancer progression, while high dose androgens form dimers that suppress the oncogene, c-MYC, expression. The findings in this paper provide a better understanding of androgen receptor action in prostate cancer and can provide doctors with more information to base their decisions on androgen therapies for their patients. My contribution to this work

was in purifying recombinant AR LBD from E. coli and performing mass photometry experiments. We evaluated the oligomerization of the LBD in solution in response to different AR ligands. A concentration curve showed the AR LBD transition from a dimer to higher order species as we increase the concentration of protein which supports the claim that changes in the concentration of activated AR change the oligomerization state.

a. Safi R, Wardell SE, Watkinson P, Qin X, Lee M, Park S, Krebs T, Dolan EL, Blattler A, Tsuji T, Nayak S, Khater M, Fontanillo C, Newlin MA, Kirkland ML, Xie Y, Long H, Fink EC, Fanning SW, Runyon S, Brown M, Xu S, Owzar K, Norris JD, McDonnell DP. Androgen receptor monomers and dimers regulate opposing biological processes in prostate cancer cells. Nat Commun. 2024 Sep 3;15(1):7675. PubMed Central PMCID: PMC11371910.

8. Understanding how a drug will be metabolized by the gut is an important property to consider in personalized medicine. The diversity in individual microbiomes leads to varied drug metabolism from activation to toxification of drugs. Current methods do not take into account the individual's gut microbiome which leads to poorer therapeutic outcomes. Azoreductase (AzoR) is a protein commonly found in the gut best known for its role in reducing the anticolitic prodrug sulfasalazine. However, the AzoR protein family is diverse with many variants expressed at low levels. We classified distinct subgroups of the family to understand how different AzoRs might contribute to drug metabolism by computing a sequence similarity network. This was followed by chemically guided functional profiling to focus on representative proteins prevalent in the NIH Human Microbiome Project dataset. To understand the substrate specificity of these enzymes, a comprehensive structure-function relationship of this enzyme was performed to improve predictive power for azo-bond reduction. Classifying AzoR family members will provide a workflow for other prevalent drug-modifying enzymes in the gut microbiome to work towards a better understanding of personalized treatments. My role in this work was computing the sequence similarity network with the help of Dr. Stack and I reviewed the literature to compile the initial list of azoreductase data that had been previously published. I reviewed the manuscript and provided minor edits.
   a. Long AR, Mortara EL, Mendoza BN, Fink EC, Sacco FX, Ciesla MJ, Stack TMM. Sequence similarity network analysis of drug- and dye-modifying azoreductase enzymes found in the human gut microbiome. Arch Biochem Biophys. 2024 Jul;757:110025. PubMed Central PMCID: PMC11295148.
9. A major obstacle to immunotherapy for the treatment of breast cancer is the immune-suppressive tumor microenvironment that is maintained by myeloid immune cells and regulatory T cells. Cholesterol homeostasis and metabolism are known to regulate the immune system with a metabolite, 27-hydroxycholesterol (27HC), working through myeloid cells to impair T cell function. Cholesterol can be metabolized into bile acids which activate a feedback loop starting with liver x receptor (LXR) which activates farnesoid x receptor to upregulate NROB2. The nuclear receptor, NR0B2, regulates myeloid cells by reducing inflammasome activity and IL1β production. This limits the expansion of immune-suppressive regulatory T cells (Tregs). NR0B2 is identified as a promising therapeutic target in metastatic breast cancer. My contribution to this work was purifying recombinant NR0B2 and LXR ligand binding domain (LBD) and performing a thermal shift assay to assess binding of the ligand DSHN and compound 6 to NR0B2 and 27HC to LXR LBD. We concluded that a shift in the melting temperature as a result of ligand addition relative to vehicle control indicates the ligand binds NR0B2 and LXR, respectively.
   a. Vidana Gamage HE, Shahoei SH, Wang Y, Jacquin E, Weisser E, Bautista RO, Henn MA, Schane CP, Nelczyk AT, Ma L, Das Gupta A, Bendre SV, Nguyen T, Tiwari S, Tjoanda E, Krawczynska N, He S, Albright ST, Farmer R, Smith AJ, Fink EC, Chen H, Sverdlov M, Gann PH, Boidot R, Vegran F, Fanning SW, Hergenrother PJ, Apetoh L, Nelson ER. NR0B2 re-educates myeloid immune cells to reduce regulatory T cell expansion and progression of breast and other solid tumors. Cancer Lett. 2024 Aug 10;597:217042. PubMed Central PMCID: PMC11892351.
   b. Gamage HEV, Shahoei SH, Albright ST, Wang Y, Smith AJ, Farmer R, Fink EC, Jacquin E, Weisser E, Bautista RO, Henn MA, Schane CP, Nelczyk AT, Ma L, Gupta AD, Bendre SV, Nguyen T, Tiwari S, Krawczynska N, He S, Tjoanda E, Chen H, Sverdlov M, Gann PH, Boidot R, Vegran F, Fanning SW, Apetoh L, Hergenrother PJ, Nelson ER. Re-education of myeloid immune cells to reduce regulatory T cell expansion and impede breast cancer progression. bioRxiv. 2023 Aug 14; PubMed Central PMCID: PMC10462080.

D. Scholastic Performance

Scholastic Performance

YEAR	COURSE TITLE	GRADE
	PROVIDENCE COLLEGE	
2018	Prin. of Economics- Macro	T
2018	Conceptual Physics	T
2018	AP English Lang & Comp	T
2018	AP English Lit & Comp	T
2018	AP US History	T
2018	Calc-Analytical Geometry I	T
2018	Intermediate Spanish II	T
2018	Introduction Public Speaking	A-
2018	Introductory Chemistry I	A
2018	Introductory Chemistry I Lab	LB
2018	Introduction to Biochemistry	A
2018	DWC I: Ancient Civilizations	AH
2018	DWC I Seminar	NG
2018	Calc- Analytical Geometry II	A
2019	General Biology II	A-
2019	General Biology II Lab	LB
2019	Introductory Chemistry II	A-
2019	Introductory Chemistry II Lab	LB
2019	DWC II: Middles Ages & Renaissance	A-H
2019	DWC II: Seminar	NG
2019	Growth in Christian Life	A-
2019	Introduction to Philosophy	A
2019	Organic Chemistry I	A-
2019	Organic Chemistry I Lab	LB
2019	General Physics I	A
2019	General Physics I Lab	LB
2019	DWC III: Emergence Modern Era	A-H
2019	DWC III: Seminar	NG
2020	Organic Chemistry II	A
2020	Organic Chemistry II Lab	LB
2020	General Physics II	B+
2020	General Physics II Lab	LB
2020	DWC IV: The Wester and the World	B+H
2020	DWC IV: Seminar	NG
2020	Ethics, Moral Leadership and the Common Good	A-
2020	General Biology I	A
2020	General Biology I Lab	LB
2020	Biochemistry I	B+
2020	Advanced Analytical Chemistry I	A-
2020	Advanced Analytical Chemistry I Lab	LB
2020	Chemistry Seminar	P
2020	Music Appreciation	A
2021	Cell Bio & Molecular Genetics	A
2021	Biochemistry Lab	A-
2021	Biochemistry Lab	LB

2021	Physical Chemistry I	A
2021	Physical Chemistry I Lab	B+
2021	Chemistry Seminar	A-
2021	Research	A
2021	Thinking & Writing About History	A
2021	Chemistry Seminar	P
2021	Inorganic Chemistry	A
2021	Inorganic Chemistry Lab	LB
2021	Genetics	A
2021	Genetics Lab	A
2021	Diversity in Latin American Religous History	B?
2022	Biochemistry II	A
2022	Chemistry Seminar	P
2022	Research	A
2022	Honors- Intro to Sociology	AH
2022	Colloquium: The Human Brain	AH
	PROVIDENCE COLLEGE	
2022	Algorithms	A
2022	Algorithms Lab	P
2022	Computer Security	A
2018	Computer Science I	T
2019	Computer Science II	A
2019	Computer Science II Lab	P
2019	Discrete Data Structure	A
2019	Discrete Data Structure Lab	P
2020	Computer Architecture	A
2020	Computer Architecture Lab	P
2020	Discrete Mathematics	A-
2020	Introduction to Statistics	A
2020	Operating Systems	A
2021	Computer Networks	A
2021	Database Management Systems	A
2021	Artificial Intelligence	A
	LOYOLA UNIVERSITY CHICAGO	
2022	Ethics in Biomedical Science	A
2022	Biochemistry & Molecular Biology	A
2022	Cell Biology	A
2022	Methods Biomedical Science	A
2022	Research	A
2023	Molecular Biology	B
2023	Research in Molecular Biology	A
2023	Molecular Biology Journal Club	P
2023	Seminar in Molecular Biology	P
2023	Molecular Biology of Oncogenesis	A-
2023	Statistical Methods for Biomedical Science	A
2023	Presentation Skills	P
2023	Doctoral Study-Summer	P
2023	Research in Molecular Biology	A
2023	Molecular Biology Journal Club	P
2023	Seminar in Molecular Biology	P

2023	Special Topics in Oncology	A
2023	Signal Transduction	A
2023	Current Topics Pharm & Epid Disease	A-
2024	Special Topics Molecular Biology	A
2024	Research in Molecular Biology	A
2024	Molecular Biology Journal Club	P
2024	Seminar in Molecular Biology	P
2024	Molecular Basis of Disease/Therapeutics	A
2024	Doctoral Study-Summer	P
2024	Research in Molecular Biology	A
2024	Molecular Biology Journal Club	P
2024	Seminar in Molecular Biology	P
2024	Dissertation Supervision	P

Transfer credit denoted with a "T" indicates courses taken at Lyons Township High School. Courses at Providence College and Loyola University Chicago are graded on an A-F scale with honors classes taken at Providence College noted with an "H". Chemistry labs were assigned "LB" as they were factored into the associated course grade, but computer science labs were denoted as "P" or "F" for pass/fail. Chemistry Seminar, Dissertation Supervision, Doctoral Study-Summer, Molecular Biology Journal Club, Presentation Skills, and Seminar in Molecular Biology are graded on a pass "P" or fail "F" scale.