BIOGRAPHICAL SKETCH

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NAME: ALIREZA GHANBARPOUR

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POSITION TITLE: Postdoctoral Associate

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	END DATE MM/YYYY	FIELD OF STUDY
Shahid Beheshti University	BS	08/2008	05/2012	Chemistry
Sharif University of Technology	MS	08/2012	05/2014	Inorganic Chemistry
Michigan State University	PhD	08/2014	03/2019	Chemistry
Yale University (NRSA F32 Postdoctoral Fellow)	-	04/2019	09/2021	Cell Biology
MIT (Postdoc Associate)	-	10/2021	Present	Structural Biology/Biochemistry

A. Personal Statement

My new lab studies how adaptors and anti-adaptors alter the specificity of AAA proteases and therefore define the proteome profile according to cellular needs. I am interested in uncovering mechanistic details of these processes through high resolution cryo-EM structures, phenotypic assays, and pulse-labeling mass spectrometry. This multidisciplinary approach will offer a platform for rational design of therapeutics aiming at pathogenic bacteria or human diseases associated with dysregulation of the mitochondrial AAA proteases.

In addition to advancing my research, I am also highly committed to training a new generation of scientists from different backgrounds and disseminating my training and science to a broader community to advance biomedical research. I am devoted to promoting diversity and inclusion in both the classroom and the research lab, as I believe these are essential elements of academic success. I am committed to working with students and colleagues of diverse ethnicities, religions, sexual orientations, social classes, abilities, languages, and countries of origin. I was a postdoc representative in Biology Department DEI council to further promote these values. My former and future mentorship experiences will equip me to train my lab members in a diverse, welcoming, and productive environment.

1. **Ghanbarpour, A**; Kenaya, N.; Turke, M.; Pinger, C.; Kemp, C.; Studzinski, E.; Vasileiou, C.; Borhan, B.; Geiger, J.H.; Exploiting β-strand "Phase" and disulfide locking to mechanically manipulate domain-swapped protein structures, ***Structure***, under revision. (2023)
2. **Ghanbarpour, A.***; Fei. X.*; Baker, Tania A.; Davis, J. H.; Sauer, R. T.; The SspB adaptor drives structural changes in the AAA+ ClpXP protease during ssrA-tagged substrate delivery. ***PNAS**,120,* e2219044120 *(*2023). *Equal Contributors
3. **Ghanbarpour, A.***; Valverde D. P.*; Melia, T. J.; Reinisch, K. M., A Model: Lipid Transfer Proteins and Scramblases Partner in Membrane Expansion and Organelle Biogenesis. ***PNAS**, 118, e2101562118 (2021).* *Equal Contributors,
4. **Ghanbarpour, A.**; Pinger, C.; Xiangshu, J.; Assar, Z., Santos, E.; Nosrati, M.; Pawlowski, K.; Spence, D.; Vasileiou, C.; Borhan, B.; Geiger, J. H. Engineering the hCRBPII Domain-Swapped Dimer into a New Class of Protein Switches, ***J. Am. Chem. Soc.,*** 141, 43, 17125-17132 (2019)

B. Positions and Honors

Positions

TITLE/POSITION	START DATE	END DATE	FIELD	INSTITUTION	SUPERVISOR
Graduate Student Teaching and Research Assistant	08/2014	03/2019	Chemistry	Michigan State University	Prof. James H. Geiger
Postdoctoral Associate/Fellow	04/2019	09/2021	Cell Biology	Yale University	Prof. Karin M. Reinisch
Postdoctoral Associate	10/2021	08/2024	Biology	Massachusetts Institute of Technology	Profs. Robert T. Sauer and Joseph H. Davis
Assistant Professor	08/2024	Present	Biochemistry and Molecular Biophysics	Washington University School of Medicine	-

Other Experience and Professional Memberships

2022-present Postdoc representative in DEI council, Department of Biology, MIT
2020-2021 Hindawi publication honorary lead editor
2014-2015 Reviewer for Crystal Engineering Communications journal (RSC publication)

Honors and Awards

2021 Poster Presentation Award, Molecular Membrane Biology Conference, GRC (online)
2020 National Research Service F32 Postdoc Award (Grant number 1F32GM137568-01)
2018 Ph.D. Continuation Fellowship, Faculty of Natural Science, Michigan State University.
2018 Education Merit Award for Excellence in Teaching (Superb Award), Department of Chemistry, Michigan State University
2018 Travel Award Fellowship, Biophysical Society Conference, Spring 2018
2017 Ph.D. Continuation Fellowship, Faculty of Natural Science, Michigan State University

C. Contribution to Science

Undergraduate studies (2008-2012)

As an undergraduate student, I worked under the supervision of Professor Amini and Professor Khavasi at Shahid Beheshti University. In the Amini lab, I became acquainted with the synthesis of novel lead (II) complexes and their characterizations using X-ray crystallography. My work during the 18 months in his lab led to five publications in *Acta E journal*. I continued my interest in the crystallography of small molecules and crystal engineering in the Khavasi laboratory, where my focus centered on elaborating the key interactions driving the crystal packing of amidic ligands. The main purpose of that research, which involved crystal engineering, was to gain insight into the rules governing the crystal packing of these compounds and then employ this knowledge to construct novel crystals with the desired chemical and physical properties. I synthesized the amidic ligand with different halogen substituents and determined with atomic resolution structures that the halogen…halogen interaction is essential in directing the crystal packing of the amidic ligand, even in the presence of stronger interactions, such as hydrogen bonding. Furthermore, I demonstrated that by making a subtle structural change and using quinoline instead of naphthalene in the ligand backbone, the halogen…halogen interaction could be altered to a halogen…π interaction, tuning the supramolecular interactions in the crystal lattice. I collaborated with analytical chemists to employ a metal-organic framework for applications such as ion separation and absorbing trace amount of lead (II) ions from water samples.

1. Khavasi, H. R.; **Ghanbarpour, A.;** Tehrani, A. A. Synthon crossover between halogen-π and halogen-halogen interaction. *Cryst. Eng. Comm*. **2014**, *16*, 749-752.
2. Salarian, M.; **Ghanbarpour, A.;** Behbahani, M.; Bagheri, S.; Begheri, A. Analytical application of metal-organic framework sustained by nanosized Ag_{12} cuboctahedral node as a novel sorbent for selective solid-phase extraction of ultra-traces lead ions. *Microchemica Acta*., **2014**, *181*, 999-1007.
3. Mohammadnezhad, G.; **Ghanbarpour, A.**, Amini M. M., Ng, S. W.; Di-μ-azido-κ4*N*1:*N*1-bis[(1,10-phenanthroline-κ2*N*,*N*')(thiocyanato-κ*N*)lead(II)] ***Acta Cryst.***, E66, m1120 (2010).

4. Mohammadnezhad, G.; **Ghanbarpour, A.**; Amini, M.M.; Ng, S.W; *catena*-Poly[[(1,10-phenanthroline-2*N*,*N*')lead(II)]–azido-2*N*1:*N*3–nitrito-3*O*,*O*':*O*'-[(1,10-phenanthroline-2*N*,*N*')lead(II)]-di–azido-4*N*1:*N*1, ***Acta Cryst.***, E66, m821 (2010).

Master's studies (2012-2014)

I continued my research as a master's student in the field of catalysis at Sharif University of Technology in Dr. Bagherzadeh's lab, where I finished two key projects. First, I synthesized new Mn (II) complexes, which were structurally characterized by X-ray crystallography for the aerobic epoxidation of olefins. This method developed a greener and cheaper system for producing epoxides with various industrial interests. Second, I determined the effects of supramolecular interactions, such as the halogen….halogen interaction, in governing the crystal packing of inorganic compounds, such as Mn(II) complexes based on amidic ligands.

1. Khavasi, H. R.; **Ghanbarpour, A.,** Tehrani, A. A. The role of intermolecular interactions involving halogens in the supramolecular architecture of a series of Mn (II) coordination compounds. *RSC Advances*, **2016**, *6*, 2422-2430
2. Bagherzadeh, M.**; Ghanbarpour, A.;** Khavasi, H. R. Highly efficient aerobic epoxidation of cyclic olefins in mild conditions by a novel binuclear manganese (II) complex containing *N*-(4-nitrophenyl) picolinamide ligand. *Catalysis Communications,* **2015**, *65*, 72-75.
3. Bagherzadeh, M.; Haghdoost, M. M.; **Ghanbarpour, A.**; Payab, M.; Khavasi, H. R.; Ellern, A.; Woo, L. K. New Molybdenum (VI) Catalyst for the Epoxidation of Alkenes and Oxidation of Sulfides: an Experimental and Theoretical Study. ***Inorg. Chim. Acta.***, *411*, 62-66 (2014).

Ph.D. studies (2014-2019)

At Michigan State University (MSU), I shifted my research interests from inorganic chemistry to structural biology and protein engineering, under the supervision of Professor Geiger. I employed a "protein redesign" strategy to develop a model system to mimic microbial rhodopsin isomerization in a single crystal using human cellular retinoic acid binding protein II as a template. A long-standing question was how rhodopsins manage the photoisomerization of retinal selectively around one double bond, given that the photoisomerization of retinal in solution leads to a broad distribution of isomers. I created a new protein-based model system that could drive photoisomerization of retinal from all-*trans* to 13-*cis* and dark isomerization back to all-*trans* retinal in a single crystal and solution. I also discovered a novel protein photo-switch that does not require chromophore isomerization. Instead, the conformation of a single amino acid alters upon irradiation inside the binding cavity, leading to a pK_a change in the chromophore and subsequent shifting of the absorption wavelength by more than 100 nm. In a second study, I generated a new class of allosterically regulated metalloproteins by redesigning the domain-swapped dimer of human cellular retinol binding protein II to allow that triggering by ligand binding or the reduction potential of the environment. In this study, I created a new allosteric protein and confirmed all of the changes and engineering steps by atomic resolution structures, CD spectroscopy, and binding assays. I also discovered that some variants of hCRBPII can generate a domain-swapped trimer. I devised a novel method to control the folding pathway in domain-swapped proteins by installing a strategic disulfide bond. This work was highlighted on the front cover of *ChemBioChem*. In a third project, I investigated the role of amino-acid insertion in the hinge loop region on the overall conformations of domain-swapped dimers of human cellular retinol binding protein II. Since in 3D domain swapping, the swapped region adopts its native conformation, the only part of the domain-swapped structure that undergoes a large structural change is the "hinge loop" region that links the two structurally similar domains. I demonstrated that small changes in the hinge loop sequence can have profound effects on the resulting structure, illustrating the potential for creating significantly altered protein structures with small changes in sequence. During my work as a Ph.D. student, I mentored nine undergraduate MSU students and two high school students (in local STEM programs), which allowed me to further develop my mentorship and leadership skills. I also was a teaching assistant for several chemistry courses at MSU, which enabled me to hone my teaching skills in preparation for my future career.

1. Santos, M.*; Sheng, W.*; Salmani, R. E.; Nick, S.T., **Ghanbarpour, A.**, Gholami, H.; Vasileiou, C.; Geiger, J.; Borhan, B. Design of Large Stokes Shift Fluorescent Proteins Based on Excited State Proton Transfer of an Engineered Photobase, ***J. Am. Chem. Soc.***, 143, 15091 (2021). *Equal Contributors
2. **Ghanbarpour, A.**; Santos, E. M.; Pinger, C.; Assar, Z.; Hossaini Nasr, S.; Vasileiou, C.; Spence, D.; Borhan, B.; Geiger, J. H. Human Cellular Retinol Binding Protein II Forms a Domain-Swapped

Trimer Representing a Novel Fold and a New Template for Protein Engineering, ***ChemBioChem***, 21, 3192-3196. (2020). ***Highlighted on the cover.***

3. **Ghanbarpour, A.**; Pinger, C.; Xiangshu, J.; Assar, Z., Santos, E.; Nosrati, M.; Pawlowski, K.; Spence, D.; Vasileiou, C.; Borhan, B.; Geiger, J. H. Engineering the hCRBPII Domain-Swapped Dimer into a New Class of Protein Switches, ***J. Am. Chem. Soc.,*** 141, 43, 17125-17132 (2019).
4. **Ghanbarpour, A.**; Nairat, M.; Nosrati, M.; Santos, E. M.; Vasileiou, C.; Dantus, M.; Borhan, B.; Geiger, J. H. Mimicking Microbial Rhodopsin Isomerization in a Single Crystal. ***J. Am. Chem. Soc.,*** 141,1735-1741 (2019).

Post-doctoral studies: Yale (2019-2021)

I joined Prof. Karin Reinisch's lab at Yale, where I was awarded an NRSA F32 fellowship to investigate how autophagosomes form at contact sites in the ER. ATG2A is a lipid-transfer protein tethering between the ER and autophagosomes and transferring bulk lipids between organelles. I determined that ATG2A does not work in isolation but is part of a larger machinery. Notably, I identified integral-membrane proteins present at contact sites, such as TMEM41B and VMP1 in the ER and ATG2 interactors. I determined that all these membrane proteins act as lipid scramblases, and along with another graduate student in the lab, proposed a model wherein ATG2, cooperating with the scramblases, transports lipids in bulk from the ER to the nascent autophagosome. ATG2 permits lipid transport from the ER to the seeding vesicle, with TMEM41B and VMP1 re-equilibrating the leaflets of the ER as lipids are extracted, and ATG9 in the acceptor seed scrambling ER lipids as they are inserted. My first-author *PNAS* paper describing this study has been cited 77 times. I also verified that bacterial homologs of TMEM41B and VMP1, containing the VTT domain, act as scramblases. This work led to assigning a new function to a relatively large and unknown family of membrane proteins carrying the VTT domain. Recently, it was shown that TMEM41B and VMP1 are essential for the formation of Flavivirus and coronavirus replication compartments. We speculated that the replication compartments for these viruses might also form *de novo*, resembling autophagosomes.

1. **Ghanbarpour, A.***; Valverde D. P.*; Melia, T. J.; Reinisch, K. M., A Model: Lipid Transfer Proteins and Scramblases Partner in Membrane Expansion and Organelle Biogenesis. ***PNAS**, 118, e2101562118 (2021).* *Equal Contributors, ***Recommended in Faculty Opinions.***
2. Huang, D.; Xu, B.; Liu, L.; Wu, L.; Zhu, Y.; **Ghanbarpour, A.**; Wang, Y.; Chen, F-J.; Lyu, J.; Hu, Y.; Kang, Y.; Zhou, W.; Wang, X.; Ding, W.; Li, X.; Jiang, Z.; Chen, J.; Zhang, X.; Zhou, H.; Zhong Li, J.; Guo, C.; Zheng, W.; Zhang, X.; Li, P.; Melia, T.; Reinisch, K.; Chen, X-W. TMEM41B acts as an ER scramblase required for lipoprotein biogenesis and lipid homeostasis**. *Cell Metabolism**, 33, 1, (2021).* *Equal Contributors

Post-doctoral studies: MIT (2021-2024)

I started my second postdoc in the Sauer and Davis labs at MIT in the Fall of 2021. During this time, I learned cryo-EM to investigate the molecular mechanisms by which the ClpXP proteolytic machine recognizes and engages specific protein substrates and adaptors. My primary focus at MIT was generating a library of structural information on the bacterial ClpXP AAA protease, complemented by biochemical experiments to probe molecular mechanisms. I determined cryo-EM structures for several substrate-free forms of ClpXP, a complex of ClpXP with the SspB adaptor and an ssrA-tagged substrate, and complexes of ClpXP with a cross-linked DHFR substrate. These structures demonstrate how ClpXP engages multiple polypeptides within its axial channel and contacts a fully engaged native substrate before unfolding. I submitted three first-author manuscripts during my postdoc: one was published in *PNAS*, another in *Nature Communications*, and a third one is under revision in *Nature Communications*.

1. **Ghanbarpour, A.**; *Sauer, R. T; Davis, J. H.; A proteolytic AAA+ machine poised to unfold a protein substrate, BioRxiv. Nat. Commun. (under revision).*

2. **Ghanbarpour, A.***; Fei. X.*; Baker, Tania A.; Davis, J. H.; Sauer, R. T.; The SspB adaptor drives structural changes in the AAA+ ClpXP protease during ssrA-tagged substrate delivery. *PNAS,120,* e2219044120 *(*2023). *Equal Contributors
3. **Ghanbarpour, A.**; Cohen, S.; Fei. X.; Bell, T.; Baker, Tania A.; Davis, J. H.; Sauer, R. T. A closed translocation channel in the substrate-free AAA+ ClpXP protease diminishes rogue degradation. *Nature Communication* (under revision). (2023) (BioRxiv)

Book Chapter

Kermani, A. A.; Agarwal, S., **Ghanbarpour, A.;** Advances in X-ray crystallography methods to study structural dynamics of macromolecules, *Academic Press.* Elsevier publication (2023).

Complete List of Published Work in My Bibliography:

https://www.ncbi.nlm.nih.gov/myncbi/1z7o7oIomKHwHx/bibliography/public/