Zheng Ruan, Ph. D.

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Education and Training

Van Andel Research Institute, Grand Rapids, Michigan, USA (Aug 2018 – Now)

Postdoctoral Research Fellow, Structural Biology

Advisor: Dr. Juan Du and Dr. Wei Lü

• University of Georgia (UGA), Athens, Georgia, USA (Aug 2012 -- Jul 2018)

Doctor of Philosophy, Bioinformatics

Dissertation: Functional annotation of oncogenic mutations of epidermal growth factor receptor kinase (EGFR)

Advisor: Dr. Natarajan Kannan

Huazhong Agricultural University (HZAU), Wuhan, Hubei, China (Sep 2008 – Jun 2012)

Bachelor of Science, Biotechnology

Thesis: Prediction and analysis of pentatricopeptide repeat (PPR) protein family in maize

Selected Award and Honors

- Graduate Student Excellence in Research Award 2019, University of Georgia, 2019
- Innovative and Interdisciplinary Research Grants for Doctoral Students (IIRG), University of Georgia Graduate School, 2017
- Grimes Family Distinguished Graduate Fellowship in Natural Sciences, Franklin College Grimes Award Committee, University of Georgia, 2015
- Monsanto Scholarship, Monsanto Company and Huazhong Agricultural University, 1st prize for 2010 & 2011
- National Scholarship, Ministry of Education of P.R. China, 2009

Current Extramural Research Funding

Postdoctoral Fellowship (American Heart Association 20POST35120556)

01/01/2020 -12/31/2021

Role: Principle Investigator

Structural and functional investigation of the pannexin 1 (PANX1) ATP release channel

Pending Extramural Research Funding

• NIH Pathway to Independence Awards (K99/R00)

07/01/2022 -06/30/2027

Role: Principle Investigator

Structural and Functional Studies on Proton-activated Chloride (PAC) Channel

Publications

Journal publications (Total citations: 458 and h-index: 11)

- Zheng Ruan*, Emery Haley*, Ian Orozco*, Rebecca Roth, Mark Sabat, Richard Myers, Wei Lu*, Juan Du*. Structures of TRPM5 channel elucidate mechanisms of activation and inhibition. *Nat Struct Mol Biol.* (2021) Doi: doi.org/10.1038/s41594-021-00607-4. (* Equal contribution)
- James Osei-Owusu, Junhua Yang, Ka Ho Leung, Zheng Ruan, Wei Lü, Yamuna Krishnan, Zhaozhu Qiu. Proton-activated chloride channel PAC regulates endosomal acidification and transferrin receptor-mediated endocytosis. *Cell Reports*. (2021) Jan 26: 34(4). Doi: 10.1016/j.celrep.2020.108683.
- 3. **Zheng Ruan***, James Osei-Owusu*, Juan Du, Zhaozhu Qiu*, Wei Lü*. Structures and pH sensing mechanism of proton-activated chloride channel. *Nature*. (2020) Nov 04: 588(7837): 350-354. Doi: 10.1038/s41586-020-2875-7. (* Equal contribution)
- 4. **Zheng Ruan**, Ian Orozco, Juan Du[#], Wei Lü[#]. Structures of human Pannexin 1 reveal ion pathways and mechanism of gating. *Nature*. (2020) Jun 03: 584(7822):646-651. Doi: 10.1038/s41586-020-2357-y.
- Wayland Yeung*, Zheng Ruan*, Natarajan Kannan. Emerging roles of the αC-β4 loop in protein kinase structure, function, evolution, and disease. *IUBMB Life*. (2020) Feb 26: 1-14. Doi: 10.1002/iub.2253. (* Equal contribution)
- 6. Yu-Yang Jiang, Wolfgang Maier, Ralf Baumeister, Gregory Minevich, Ewa Joachimiak, Dorota Wloga, **Zheng Ruan**, Natarajan Kannan, Stephen Bocarro, Anoosh Bahraini, Krishna Kumar Vasudevan, Karl Lechtreck,

- Eduardo Orias, Jacek Gaertig. LF4/MOK and a CDK-related kinase regulate the number and length of cilia in Tetrahymena. *PLoS Genet.* (2019) Jul 24: 15(7). Doi: 10.1371/journal.pgen.1008099.
- 7. Yu-Yang Jiang*, Wolfgang Maier*, Ralf Baumeister, Ewa Joachimiak, **Zheng Ruan**, Natarajan Kannan, Diamond Clark, Panagiota Louka, Mayukh Guha, Joseph Frankel, Jacek Gaertig. Two antagonistic Hippo signaling circuits set the division plane at the medial position in the ciliate Tetrahymena. *Genetics*. (2019) Feb 1; 211(2) 651-663. doi: 10.1534/genetics.118.301889. (* Equal contribution)
- 8. Sam A. Jamieson*, **Zheng Ruan***, Abigail E. Burgess, Jack R. Curry, Hamish D. McMillan, Jodi Brewster, Anita K. Dunbier, Natarajan Kannan, Peter D. Mace. Substrate binding allosterically relieves autoinhibition of the pseudokinase TRIB1. **Sci Signal.** 2018 Sep 25; 11(549) doi: 10.1126/scisignal.aau0597. (* Equal contribution) Cover story of the issue
- Zheng Ruan, Natarajan Kannan. Altered conformational landscape and dimerization dependence underpins the activation of EGFR by αC-β4 loop insertion mutations. *PNAS*. 2018 Aug 13; 115 (35) E8162-E8171 doi: doi.org/10.1073/pnas.1803152115.
- 10. Liang-Chin Huang, Karen E. Ross, Harold Drabkin, Krzysztof J. Kochut, Zheng Ruan, Peter D'Eustachio, Daniel McSkimming, Cecilia Arighi, Chuming Chen, Darren Natale, Cynthia Smith, Pascale Gaudet, Cathy Wu, and Natarajan Kannan. High resolution annotation of protein kinase post-translational modifications and cancer-associated mutations through integration of domain-specific ontologies and protein resources. Sci Rep. 2018 Apr 25; 8:6518 doi: 10.1038/s41598-018-24457-1.
- Annie Kwon, Mihir John, Zheng Ruan, Natarajan Kannan. Coupled regulation by the juxtamembrane and sterile α motif (SAM) linker is a hallmark of Ephrin tyrosine kinase evolution. *J Biol Chem.* 2018 Apr 6; 293(14): 5102-5116 doi:10.1074/jbc.RA117.001296.
- Melody Fulton, Laura Hanold, Zheng Ruan, Sneha Patel, Aaron Beedle, Natarajan Kannan, Eileen J. Kennedy. Conformationally constrained peptides target the allosteric kinase dimer interface and inhibit EGFR activation. *Bioorg Med Chem.* 2018 Mar 15; 26(6): 1167-1173. doi: 10.1016/j.bmc.2017.08.051.
- 13. Yu-Yang Jiang, Wolfgang Maier, Ralf Baumeister, Gregory Minevich, Ewa Joachimiak, **Zheng Ruan**, Natarajan Kannan, Diamond Clarke, Joseph Frankel and Jacek Gaertig. The Hippo Pathway Maintains the Equatorial Division Plane in the Ciliate Tetrahymena. *Genetics*. 2017 Jun 1; 206(2):873-888. doi: 10.1534/genetics.
- 14. **Zheng Ruan**, Samiksha Katiyar, Natarajan Kannan. Computational and experimental characterization of patient derived mutations reveal an unusual mode of regulatory spine assembly and drug sensitivity in EGFR kinase. **Biochemistry**. 2017 Jan 10; 56(1): 22-32. doi: 10.1021/acs.biochem.6b00572.
- 15. Jonathan A Stefely, Floriana Licitra, Leila Laredj, Andrew G Reidenbach, Zachary A Kemmerer, Anais Grangeray, Tiphaine Jaeg-Ehret, Catherine E Minogue, Arne Ulbrich, Paul D Hutchins, Emily M Wilkerson, Zheng Ruan, Deniz Aydin, Alexander S Hebert, Xiao Guo, Elyse C Freiberger, Laurence Reutenauer, Adam Jochem, Maya Chergova, Isabel E Johnson, Danielle C Lohman, Matthew JP Rush, Nicholas W Kwiecien, Pankaj K Singh, Anna I Schlagowski, Brendan J Floyd, Ulrika Forsman, Pavel J Sindelar, Michael S Westphall, Fabien Pierrel, Joffrey Zoll, Matteo Dal Peraro, Natarajan Kannan, Craig A Bingman, Joshua J Coon, Philippe Isope, Hélène Puccio, David J Pagliarini. Cerebellar ataxia and coenzyme Q deficiency through loss of unorthodox kinase activity. Mol Cell. 2016 Aug 18; 63(4): 608-20. doi: 10.1016/j.molcel.2016.06.030.
- 16. Smita Mohanty, Krishnadev Oruganty, Annie Kwon, Dominic P Byrne, Samantha Ferries, Zheng Ruan, Laura E Hanold, Samiksha Katiyar, Eileen J Kennedy, Patrick A Eyers, Natarajan Kannan. Hydrophobic core variations provide a structural framework for tyrosine kinase evolution and functional specialization. *PLoS Genet.* 2016 Feb 29; 12(2): e1005885. doi: 10.1371/journal.pgen.1005885.
- 17. **Zheng Ruan**, Natarajan Kannan. Mechanistic insights into R776H mediated activation of epidermal growth factor receptor kinase. *Biochemistry*. 2015 Jul 14; 54(27): 4216-25. doi: 10.1021/acs.biochem.5b00444.
- Tuan Nguyen, Zheng Ruan, Krishnadev Oruganty, Natarajan Kannan. Co-Conserved MAPK features couple D-domain docking groove to distal allosteric sites via the C-terminal flanking tail. *PLoS One.* 2015; 10(3): e0119636. doi: 10.1371/journal.pone.0119636.
- 19. Timothy I Shaw, **Zheng Ruan**, Travis C Glenn, Liang Liu. STRAW: Species TRee Analysis Web server. **Nucleic Acids Res.** 2013 Jul; 41(Web Server issue): W238-W241. doi: 10.1093/nar/gkt377.

Conference Abstracts

 Zheng Ruan, Orozco J Ian, Juan Du, Wei Lu. Structural and Functional Investigation on Human Pannexin 1 (PANX1) Reveals Novel Insight Into Channel Gating, Ion Permeation and Drug Inhibition. *Biophys. J.* 2021; 120(3):112a

- 2. James Osei-Owusu, **Zheng Ruan**, Juan Du, Wei Lu, Zhaozhu Qiu. Structures of Human Proton-Activated Chloride Channel (PAC) Reveal Mechanism of pH Sensing and Gating. **Biophys. J.** 2021; 120(3):192a
- Zheng Ruan, Samiksha Katiyar, Natarajan Kannan. Characterization of rare oncogenic mutations in the kinase domain of Epidermal Growth Factor Receptor (EGFR). FASEB J. 2016 Apr 1; 30 (1 Supplement), 665.4-665.4, doi: 10.1096/fj.1530-6860.
- 4. **Zheng Ruan**, Natarajan Kannan. 57 Activation mechanism of R776H mutation in Epidermal Growth Factor Receptor (EGFR). *J Biomol Struct Dyn.* 2015; 33 Suppl 1:38-9. doi: 10.1080/07391102.2015.1032673.

Scientific Presentations

- CryoEM Current Practices Webinar. Lessons learned from Sample Preparation and Structural Analysis of Three Membrane Channels. Aug 26, 2021.
- Biophysical Society Annual Meeting 2021: Biophysical Structural and Functional Investigation on Human Pannexin 1 (PANX1) Reveals Novel Insight Into Channel Gating, Ion Permeation and Drug Inhibition. Feb 24, 2021. Platform: Other Channels and Regulatory Mechanisms.
- Gordon Research Conference Proteins: Exploring the Role of Proteins as Cellular Organizers by Combining Experiment and Theory. June 18-23, 2017. Holderness, NH. Poster presentation and lightning talk: Experimental and Computational Analysis on Oncogenic Mutations in Epidermal Growth Factor Receptor (EGFR)
- 4. Invited talks: Mechanistic Insight into Oncogenic Mutations Using Molecular Dynamics Simulations. UGA Center for Simulational Physics. March 21, 2017. Athens, GA
- 5. EB 2016 (ASBMB annual meeting). April 2-6, 2016. San Diego, CA. Poster presentation: Characterization of rare oncogenic mutations in the kinase domain of Epidermal Growth Factor Receptor (EGFR)
- 6. Albany 2015: The 19th Conversation. June 9-13, 2015. Albany, NY. Poster Presentation: Activation mechanism of R776H mutation in Epidermal Growth Factor Receptor
- 7. State-of-the-Art Next Generation Sequence Symposium. April 8-9, 2013. Athens, GA. Poster Presentation: ErbB signaling network modeling

Paper Review Experiences

Ad hoc reviewer for Journal of Chemical Information and Modeling, Journal of Biological Chemistry, and Communications Biology.