BIOGRAPHICAL SKETCH

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NAME: Ruan, Jianbin

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

POSITION TITLE: Assistant Professor of Immunology

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)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Science and Technology of China, Hefei, China	B.S.	07/2007	Biotechnology
University of Science and Technology of China, Hefei, China	Ph.D.	07/2012	Structural Biology
Boston Children's Hospital, Boston, MA	Postdoc	08/2019	Structural Biology and Immunology

A. Personal Statement

The long-term research program in my lab focuses on structural and biochemical studies of innate immune signaling and host-pathogen interactions. I am currently the assistant professor in the Department of Immunology at the University of Connecticut Health Center. Over the past ten years we have made significant contributions to our understanding of the structures and functions of the inflammasome signaling pathways, from upstream receptors (AIM2 and NLRs/) and adaptors (ASC) to downstream effectors including inflammatory caspases (caspases-1) and Gasdermin proteins. Our current projects are aiming to elucidate the molecular mechanisms of how non-canonical inflammasome is activated upon sensing its cytosolic ligands; to elucidate the structural basis of programmed cell deaths that are executed by pore-forming proteins including GSDMs, MLKL and NINJ1; and to elucidate the mechanism of how pathogens escape host immune responses by targeting the pyroptosis signaling pathway. We will take a multidisciplinary approach that combines innovative experimental techniques including biochemical and biophysical characterization, biochemical reconstitution, X-ray crystallography, electron microscopy, structure-based mutagenesis, and cellular experiments.

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

R01 AI158435, National Institute of Allergy and Infectious Diseases
Jianbin Ruan (PI)
03/17/21-02/28/26
Structural and mechanistic elucidation of non-canonical inflammasome signaling

Charles A. King Trust Postdoctoral Research Fellowship
Jianbin Ruan (PI)
09/01/17-09/01/19
The killer protein gasdermin D: activation mechanism and a new potential therapeutic target

Citations

1. Wang C, Shivcharan S, Tian T, Wright S, Ma D, Chang JY, Li K, Song K, Xu C, Rathinam VA, **Ruan J**. Structural basis for GSDMB pore formation and its targeting by IpaH7.8. ***Nature***. 2023 Mar 29; DOI: 10.1038/s41586-023-05832-z, PMID: 36991122, PMCID: PMC10115629.

2. Xia S, Zhang Z, Magupalli VG, Pablo JL, Dong Y, Vora SM, Wang L, Fu TM, Jacobson MP, Greka A, Lieberman J, **Ruan J**[#], Wu H[#]. Gasdermin D pore structure reveals preferential release of mature interleukin-1. ***Nature***. 2021 Apr 21;. doi: 10.1038/s41586-021-03478-3. **# Co-corresponding author,** PubMed PMID: 33883744.
3. **Ruan J**, Xia S, Lieberman J, Wu H. Cryo-EM structure of the Gasdermin A3 membrane pore. ***Nature***. 557:62-7 (2018). PMID: 29695864, PMCID: PMC6007975
4. Evavold C, **Ruan J**, Tan Y, Xia S, Wu H, Kagan J. The Pore-Forming protein Gasdermin D regulates interleukin-1 secretion from living macrophages. ***Immunity***. 48:35-44 (2018). PMID: 29195811, PMCID: PMC5773350
5. Liu X[#], Zhang Z[#], **Ruan J**[#], Pan Y, Magupalli VG, Wu H, Lieberman J. Inflammasome-activated gasdermin D causes pyroptosis by forming membrane pores. ***Nature*** 535:153-8 (2016). **# co-first author,** PMID: 27383986, PMCID: PMC5539988

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

2019 – Present	Assistant Professor, Department of Immunology, University of Connecticut School of Medicine, Farmington, CT
2012 – 2019	Postdoctoral Research Fellow, Program in Cellular and Molecular Medicine, Boston Children's Hospital, Department of Biological Chemistry and Molecular Pharmacology, Harvard Medical School, Boston, MA
2007 – 2012	Graduate Research Assistant, University of Science and Technology of China, Hefei, China
2006 – 2007	Research Assistant, Guangzhou Institute of Biomedicine and Health, Chinese Academy of Sciences, Guangzhou, China

Honors

2017	Charles A. King Trust Postdoctoral Research Fellowship Society
2012	"Zhuliyuehua" Scholarship for Excellent Doctoral Student of Chinese Academy of Sciences
2004	Second Prize of Excellent Undergraduate Scholarship

C. Contributions to Science

1. Elucidating the molecular mechanism of pyroptosis caused by Gasdermins (GSDMs). GSDMs are recently identified pore-forming effector proteins that cause membrane permeabilization and pyroptosis, a lytic pro-inflammatory type of cell death. GSDMs contain a cytotoxic N-terminal pore-forming domain (GSDM-NT), a C-terminal repressor domain, and a flexible linker in between. Proteolytic cleavage of the linker liberates GSDM-NT, allowing it to insert into cell membranes and form gigantic pores, which causes pyroptosis. I unveiled the molecular mechanism of pyroptosis induced by GSDMs using cryo-EM combined with biochemistry and cell biology assays.
    a. Xia S, Zhang Z, Magupalli VG, Pablo JL, Dong Y, Vora SM, Wang L, Fu TM, Jacobson MP, Greka A, Lieberman J, **Ruan J**[#], Wu H[#]. Gasdermin D pore structure reveals preferential release of mature interleukin-1. ***Nature***. 593:607-11 (2021). PMID: 33883744, PMCID: PMC8588876. **# Co-corresponding author**
    b. **Ruan J**, Xia S, Lieberman J, Wu H. Cryo-EM structure of the Gasdermin A3 membrane pore. ***Nature***. 557:62-7 (2018). PMID: 29695864, PMCID: PMC6007975
    c. Evavold C, **Ruan J**, Tan Y, Xia S, Wu H, Kagan J. The Pore-Forming protein Gasdermin D regulates interleukin-1 secretion from living macrophages. ***Immunity***. 48:35-44 (2018). PMID: 29195811, PMCID: PMC5773350

d. Liu X[#], Zhang Z[#], **Ruan J[#]**, Pan Y, Magupalli VG, Wu H, Lieberman J. Inflammasome-activated gasdermin D causes pyroptosis by forming membrane pores. ***Nature*** 535:153-8 (2016). **# co-first author,** PMID: 27383986, PMCID: PMC5539988

2. Elucidating assembly and activation mechanisms of ASC-dependent inflammasomes. The inflammasome is a multiprotein intracellular complex that detects pathogenic microorganisms and sterile stressors, and that activates the highly pro-inflammatory cytokines interleukin-1β (IL-1β) and IL-18. Addressed the assembly mechanisms for AIM2, NLRPs, and NAIP2-NLRC4 inflammasomes using *in vitro* reconstitution, electron microscopy (EM), and polymerization assays. Knowledge of those mechanisms is the key to the development of therapeutic drugs that can target inflammasomes.

   a. Hollingworth LR, David L, Li Y, Griswold AR, **Ruan J**, Sharif H, Fontana P, Orth-He EL, Fu TM, Bachovchin DA, Wu H. Mechanism of filament formation in UPA-promoted CARD8 and NLRP1 inflammasomes. ***Nature Communications.*** 12:189 (2021). PMID: 33420033, PMCID: PMC7794386

   b. Shen C, Lu A, Xie W, **Ruan J**, Negro R, Egelman E, Fu TM, Wu H. Molecular Mechanism for NLRP6 Inflammasome Assembly and Activation. ***Proceedings of the National Academy of Sciences.*** 116: 2052-7 (2019), PMID: 30674671, PMCID: PMC6369754

   c. Zhang L, Chen S, **Ruan J**, Wu J, Tong AB, Yin Q, Li Y, David L, Lu A, Wang WL, Marks C, Ouyang Q, Zhang X, Mao Y, Wu H. Cryo-EM structure of the activated NAIP2-NLRC4 inflammasome reveals nucleated polymerization. ***Science***. 350:404-9 (2015). PMID: 26449474, PMCID: PMC4640189

   d. Lu A[#], Magupalli VG[#], **Ruan J[#]**, Yin Q, Atianand MK, Vos MR, Schröder GF, Fitzgerald KA, Wu H, Egelman EH. Unified polymerization mechanism for the assembly of ASC-dependent inflammasomes. ***Cell.*** 156:1193-206 (2014). **# co-first author**, PMID: 24630722, PMCID: PMC4000066

3. Elucidation of selectivity mechanisms of histone modification reader proteins. Post-translational modifications (PTM) of histone proteins are central to the regulation of chromatin structure, playing vital roles in regulating the activation and repression of gene transcription. The actions of PTM to govern DNA transcription are mediated by "readers." I revealed the molecular mechanism of the substrate selectivity by solving the crystal structures of reader proteins Sgf29, Cbx3, and G9a and their complexes with histone peptides harboring different modification states.

   a. Bian C[#], Xu C[#], **Ruan J[#]**, Lee KK[#], Burke TL[#], Tempel W, Barsyte D, Li J, Wu M, Zhou BO, Fleharty BE, Paulson A, Allali-Hassani A, Zhou JQ, Mer G, Grant PA, Workman JL, Zang J, Min J. Sgf29 binds histone H3K4me2/3 and is required for SAGA complex recruitment and histone H3 acetylation. ***The EMBO journal.*** 30:2829-42 (2011). **# co-first author.** PMID: 21685874, PMCID: PMC3160252

   b. **Ruan J[#]**, Ouyang H[#], Amaya MF, Ravichandran M, Loppnau P, Min J, Zang J. Structural basis of the chromodomain of Cbx3 bound to methylated peptides from histone h1 and G9a. ***PloS one***. 7:e35376 (2012). **# co-first author.** PMID: 22514736, PMCID: PMC3325965

   c. Li J, Li Z, **Ruan J**, Xu C, Tong Y, Pan PW, Tempel W, Crombet L, Min J, Zang J. Structural basis for specific binding of human MPP8 chromodomain to histone H3 methylated at lysine 9. ***PloS one***. 6:e25104 (2011). PMID: 22022377 PMCID: PMC3192050

Complete List of Published Work in MyBibliography:
https://www.ncbi.nlm.nih.gov/myncbi/1VOZ7ADHMskQy/bibliography/public/