OMB No. 0925-0001 and 0925-0002 (Rev. 11/16 Approved Through 10/31/2018)

BIOGRAPHICAL SKETCH

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NAME: Wang, Longfei

eRA COMMONS USER NAME (credential, e.g., agency login): longfei\_wang

POSITION TITLE: Research Fellow

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.)

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| --- | --- | --- | --- |
| INSTITUTION AND LOCATION | DEGREE(if applicable) | Completion DateMM/YYYY | FIELD OF STUDY |
| Huazhong Agricultural University, Wuhan, China | B.S. | 07/2005 | Biology |
| Institute of Biophysics, Beijing, China | Ph.D. | 07/2011 | Biochemistry and Molecular Biology |
| Harvard Medical School, Boston, MA | Research Fellow  | 09/2011-04/2017 | Biochemistry and Pharmacology |

**A. Personal Statement**

I obtained my expertise in membrane proteins biochemistry in Prof. Wenrui Chang’s laboratory, where my PhD work focused on light-harvesting complexes of plants. I then briefly worked in Dr. Zhenfeng Liu’s laboratory and solved the crystal structure of a trimeric intracellular cation (TRIC) channel. At Harvard Medical School, I extended my research skills and performed drug screenings of an onco-target called LIN28 and obtained a number of hit compounds. The screening assay I developed as well as the lead compounds was then licensed to Twentyeight-seven Therapeutics as one of their core pipelines. Under Dr. Hao Wu’s mentorship at Boston Children’s Hospital, I focused on the study of human TRPM2 channel. I was able to purify full-length human TRPM2 whereas our competing group revealed in their recent paper in *Nature* that they were not able to purify human TRPM2 and instead work on a zebrafish ortholog. I determined the cryo-EM structures of human TRPM2 in three distinct states. Based on my background, I am fully competent to lead the proposed project.

**B. Positions and Honors**

Positions and Employment

2011-2011 Research Associate, Institute of Biophysics, Beijing, China

2011-2017 Research Fellow, Department of Biological Chemistry & Molecular Pharmacology, Harvard Medical School, Boston, MA

2017- Research Fellow, Program in Cellular and Molecular Medicine, Boston Children’s Hospital, Boston, MA

Other Experience and Professional Memberships

2011-2012 Software Curator, SBGrid Consortium

2015-2016 Data Science, Harvard Extension School

Honors

2001-2004 Outstanding Student, Huazhong Agricultural University

2002 Honghua Scholarship, Huazhong Agricultural University

**C. Contributions to Science**

1. **Revealing LIN28-mediated regulation in stem cell and cancers and developing LIN28-targeted cancer therapies.** LIN28 is an RNA binding protein that plays crucial roles in embryonic development, pluripotency, glucose metabolism, tissue regeneration, and tumorigenesis. I identified that ZKD domain of LIN28 recruits TUTase and initiate let-7 degradation pathway by oligouridylation. I then determined the human LIN28/let-7 complex structure. Based on the structure, I developed a sensitive screening assay and performed drug screening targeting LIN28. Several lead compounds were identified from the screening that inhibits LIN28 with micro-molar potency in cells.

1. **Wang, L.**, Nam, Y., Lee, A.K., Yu, C., Roth, K., Chen, C., Ransey, E.M. and Sliz, P., 2017. LIN28 zinc knuckle domain is required and sufficient to induce let-7 oligouridylation. ***Cell reports***, 18(11), pp.2664-2675. PMC in progress.
2. **Wang, L.**, Rowe, R.G., Jaimes, A., Yu, C., Nam, Y., Pearson, D.S., Zhang, J., Xie, X., Marion, W., Heffron, G.J. and Daley, G.Q., 2018. Small-Molecule Inhibitors Disrupt let-7 Oligouridylation and Release the Selective Blockade of let-7 Processing by LIN28. ***Cell reports***, 23(10), pp.3091-3101. PMC in progress.
3. **Wang, L.**, Yang, Q., Jaimes, A., Wang, T., Strobelt, H., Chen, J. and Sliz, P., 2018. MightyScreen: an open-source visualization application for screening data analysis. ***SLAS DISCOVERY: Advancing Life Sciences R&D***, 23(2), pp.218-223. PMC in progress.
4. Zhang, J., Ratanasirintrawoot, S., Chandrasekaran, S., Wu, Z., Ficarro, S.B., Yu, C., Ross, C.A., Cacchiarelli, D., Xia, Q., Seligson, M. and Shinoda, G., Xie W.,Cahan P., **Wang L.**, …, 2016. LIN28 regulates stem cell metabolism and conversion to primed pluripotency. ***Cell Stem Cell***, 19(1), pp.66-80. PMC in progress.

2. **Structure of anti-tumor peptide rBTI.** BWI-1 (buckwheat trypsin inhibitor), a member of the potato inhibitor I family, suppresses the growth of T-acute lymphoblastic leukemia cells and induces apoptosis in human solid tumor cell lines. I determined crystal structure of rBTI alone and rBTI in complex with trypsin. The structures reveal a novel conformation change of P8 position residue.

1. **Wang, L.**, Zhao, F., Li, M., Zhang, H., Gao, Y., Cao, P., Pan, X., Wang, Z. and Chang, W., 2011. Conformational changes of rBTI from buckwheat upon binding to trypsin: implications for the role of the P8′ residue in the potato inhibitor I family. ***PloS one***, 6(6), p.e20950. PMCID:PMC3115953.

3. **The crystal structure of a trimeric intracellular cation (TRIC) channel.** Trimeric intracellular cation (TRIC) channels are crucial for Ca2+ handling in eukaryotes and are involved in K+ uptake in prokaryotes. I determined the crystal structure of Sulfolobus solfataricus (SsTRIC) channel in the presence of potassium.  The structure revealed a Velcro-like plug-pore interacting model which serves as a unified framework for the gating mechanisms of prokaryotic and eukaryotic TRIC channels.

1. Ou, X., Guo, J., **Wang, L.**, Yang, H., Liu, X., Sun, J. and Liu, Z., 2017. Ion-and water-binding sites inside an occluded hourglass pore of a trimeric intracellular cation (TRIC) channel. ***BMC biology***, 15(1), p.31. PMCID:PMC5401562.

 **Complete list of published work in MyBibliography**

https://www.ncbi.nlm.nih.gov/sites/myncbi/1Lkpw4Jce-GkCd/bibliography/56583926/public/?sort=date&direction=ascending

**D. Research Support:**

**Ongoing: None**

**Completed: None**