BIOGRAPHICAL SKETCH

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NAME: Fangwei Leng

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

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.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Sichuan University, Chengdu, China	B.S	06/2009	Biotechnology
Institute of Biophysics, Chinese Academy of Sciences, Beijing, China	PH.D	01/2016	Structural Biology and Biochemistry
Harvard Medical School	Post-doctoral fellow		Structural Biology and Biochemistry

A. Personal Statement

I am a biochemist and structural biologist, who is interested in molecular mechanisms of proteins involved in the innate immune system. As a PhD student, working under the guidance of Drs. Dacheng Wang and Can Xie, I studied NOD-like receptors (NLRs) in the innate immune system. We identified LPS as a ligand of NLRP6 and explored the structural information of NLRP6-LPS complex. As a post-doctoral fellow in the Hur lab, my research focuses on The Forkhead family transcription factor FOXP3 is a master regulator in the development and functions of the Tregs.

B. Positions and Honors

07/2016-current Post-doctoral fellow, Harvard Medical Schol & Boston Children's Hospital Boston (Hur Lab)

C. Contributions to Science

1. My Ph.D project focused on investigating the structure and activation mechanism of NLRs using a combination of X-ray crystallography and electron microscopy (EM). After a series of efforts in optimizing the expression and purification strategies, I was able to successfully purify the NLRP6 monomer to homogeneity. Using size-exclusion chromatography analysis and negative stain EM, we found that Lipopolysaccharide (LPS) is able to bind NLRP6 monomer directly and induce it's global conformational change and dimerization. The NLRP6 homodimer can further assemble into a linear molecular platform via ATP stimulation. Using live cell imaging, we also found that LPS is able to induce aggregation and co-localization of NLRP6 and ASC in Hela cells, suggesting a step-by-step mechanism of a potential LPS-induced inflammasome initiation.

Leng F*, Yin H*, Qin S, Zhang K, Guan Y, Fang R, Wang H, Li G, Jiang Z, Sun F, Wang D& Xie C." NLRP6 self-assembles into a linear molecular platform following LPS binding and ATP stimulation". Sci Rep. 2020 Jan 13;10(1):198.

2. Besides NLRP6, my research also included mechanistic dissection of NLRP10, which is distinct from other NLRs in that it lacks the leucine-rich repeats domain. My work suggests that the full-length NLRP10 is susceptible to proteolysis in cells, and often accumulates PYD-truncated mutants. The PYD-truncation mutants of NLRP10 induce the formation of NLRP10 oligomers. These analyses suggest that the PYD domain protects NLRP10 from aberrant oligomerization and activation. We expect that our findings as well as the optimize protocols for NLRP10 purification would help future analysis of NLRP10.

Leng F *, Xie C, Wang D. "Structure and self-assembly of NLRP10". ***PROG BIOCHEM BIOPHYS***. 2015,42(12):1112~1118.

3. In the Sun hur lab, I am focusing on the transcription factor FoxP3 which plays a key role in development and maintenance of regulatory T (Treg) cells. Previous study has reported the domain-swapped dimer structure of FOXP3 Forkhead domain. However, our crystal structure of FOXP3 with longer truncation turns out to be a head-to-head dimer. We found that FOXP3 head-to-head dimer can form into filament on some targets, indicating a novel molecular organization of FOXP3-DNA complex.

Fangwei Leng*, Wenxiang Zhang*, Ricardo N. Ramirez, Juliette Leon, Yi Zhong, Lifei Hou, Koichi Yuki, Joris van der Veeken, Alexander Y. Rudensky, Christophe Benoist and Sun Hur. The transcription factor FoxP3 can fold into two dimerization states with divergent implications for regulatory T cell function and immune homeostasis. Immunity. 2022 Aug 9;55(8):1354-1369. (Cover article).

4. I have also worked on a project on Nebrodeolysin. It's a novel hemolysin isolated from the edible mushroom Pleurotus nebrodensis, exhibiting remarkable hemolytic activity towards rabbit erythrocytes. Nebrodeolysin shows strong cytotoxicity against Lu-04, Bre-04, HepG2, L929, and HeLa cells. And It was also found that this hemolysin can induce apoptosis in L929 and HeLa cells.

Lv H, Kong Y, Yao Q, Zhang B, **Leng F**, Bian H, Balzarini J, Damme E, Bao J. Nebrodeolysin, a novel hemolytic protein from mushroom Pleurotus nebrodensis with apoptosis-inducing and anti-HIV-1 effects. ***PHYTOMEDICINE*** 16, 198 (Mar, 2009)

5. reviews.

a. **LENG F**, The Recent Progress of Non-coding RNA and RNomics. ***PROG BIOCHEM BIOPHYS*** (sep, 2010)
b. **LENG F**, The Recent Progress of Genomics Research in China. ***PROG BIOCHEM BIOPHYS*** (Nov, 2010)
c. **LENG F**, The Recent Progress of Carbon Cycle Research in East Asian. ***PROG BIOCHEM BIOPHYS*** (sep, 2011)
d. **Leng F**, Recent progress of immunology research in China. ***SCI CHINA LIFE SCI*** 54, 1068 (Nov, 2011)
e. **Leng F**, Build a two-way road for health industry: the current circumstance of translational medicine in China. ***SCI CHINA LIFE SCI*** 55, 931 (Oct, 2012)
f. **Leng F**, On Ca(2+) signalling research. ***SCI CHINA LIFE SCI*** 55, 744 (Aug, 2012)
g. **Leng F**, Opportunity and challenge: ten years of proteomics in China. ***SCI CHINA LIFE SCI*** 55, 837 (Sep, 2012)

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

Completed Research Support

National Natural Science Foundation of China (31370740, 31070127 to C.X.), 973 National Basic Research Plan of China (2011CB100704 to C.X, 2011CB910304 to D-C.W.), and the Strategic Priority Research Program of the Chinese Academy of Sciences (XDB08020200 to D-C.W.)

NIH grants (R01AI154653 and R01AI111784 to S.H; AI150686 to C.B.; P30 CA008748 and R01 AI034206 to A.R.).