BIOGRAPHICAL SKETCH

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NAME: Jawdat MH Al-Bassam

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

POSITION TITLE: Associate Professor, Molecular Cellular Biology Department, College of Biological Sciences University of California, Davis

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
California State University, Long Beach	B.S.	09/1998	Biochemistry
Scripps Research Institute	Ph.D.	4/2004	Molecular Biophysics
Harvard Medical School; Boston, MA	Postdoctoral	04/2011	Molecular Biophysics and Structural Biology

A. Personal Statement

This project involves the coordinated use of biochemical, structural, and biophysical approaches to elucidate fundamental soluble ab-tubulin biogenesis and MT regulatory mechanisms. My group is well-suited to carry out the studies described in this proposal. The studies include biochemical reconstitution of multi-subunit complexes, single-particle cryo-EM structural studies, and reconstitution of assemblies using single-molecule fluorescence assays with dynamic microtubules in vitro to test structural models. I am an expert at combining these approaches, which span across multiple resolution scales, to extract mechanistic knowledge. I have twenty-three years of experience in molecular biology, protein biochemistry, and structural biology using both x-ray crystallography and cryo-EM. I am an expert in studying microtubules, motors, and their regulation mechanisms using a variety of biophysical and biochemical techniques. I am an established investigator with significant expertise in combining biochemical reconstitution with structural biology and total internal reflection fluorescence (TIRF) microscopy to study dynamic microtubules. My group is fully equipped to utilize high-resolution single-particle cryo-EM. We have built computational setups and established data collection systems utilizing in-house cryo-EM setups and national cryo-EM data collection facilities (NCATT, PNCC) based on standing time proposals. I have also established a network of long-term collaborations with two established cell biology experts with common goals using in vivo models for ab-tubulin biogenesis and microtubule dynamics.

B. Positions and Honors

Employment

1998-2004 Graduate student, Molecular Cellular Structure and Chemistry Program
Cell Biology Dept., The Scripps Research Institute, La Jolla, CA

2003-2011 Postdoctoral Fellow, Biological Chemistry and Molecular Pharmacology Dept., Harvard Medical School, Boston, MA

5/1/2011-5/1/2018 Assistant Professor, Molecular Cellular Biology Dept,
College of Biological Sciences, University of California, Davis, CA

5/2/2018-present Associate Professor, Molecular Cellular Biology Dept,
College of Biological Sciences, University of California, Davis, CA

Honors:

1995-1998 California State University, Long Beach President's scholarship
1995 California State University Long Beach, Spyros Pathos IV Memorial Award in Chemistry
1997 American Heart Association Undergraduate Summer Research Fellowship

1998 California State University, Long Beach, Robert Henderson Memorial Award in Biochemistry
1998 California State University Long Beach College of Natural Sciences and Mathematics, Outstanding graduate of the year
2000-2003 American Heart Association Pre-Doctoral Fellow
2000 The Scripps Research Institute Society of Fellows Travel Award
2001 The Scripps Research Institute Graduate Program Award
2002 American Society of Cell Biology Student Travel Award
2003 Invited speaker, 47th annual biophysical society meeting in San Antonio
2005-2008 American Cancer Society Postdoctoral Fellow
2009 Invited speaker, Gordon Research conference in "motile and contractile systems"
2013 Invited speaker, Gordon Research conference in "motile and contractile systems"
2014 Hellman Foundation fellow
2014 Invited speaker, European Molecular Biology Laboratory conference on "Microtubules"
2014 Invited speaker Gordon Research Conference in "Cytoskeletal motor proteins"
2015 Invited speaker Gordon Research conference in "motile and contractile systems"
2016 Invited speaker, European Molecular Biology Laboratory conference on "Microtubules"
2018 Invited speaker Gordon Research Conference in "Cytoskeletal motor proteins"
2018 Invited speaker, American Society for Cell biology Mini-symposium "Cytoskeleton Tracks"
2019 Invited speaker, Gordon Research Conference in "Cytoskeletal motor proteins"
2020 Invited speaker, European Molecular Biology Laboratory conference on "Microtubules"

Scientific Appointments

2019 Invited member, NIH study section panel ZGM1 TWD-7 KR
2020 Invited member, NIH study section panel ZGM1 TWD-7 MK
2021 Invited member, NIH study section panel MSFC
2021 Invited member, NIH study section panel ZGM1 TWD-7 MK
2022 Invited member, NIH study section panel ZGM1 TWD-7 MK

Professional Memberships

2000-present Member, American Society for Cell Biology
2003-present Member, American Biophysical Society

C. Contributions to Science

1. Biochemical and Structural studies of Microtubule Regulators with TOG domain arrays: During my postdoctoral research at Harvard Medical School and as an independent investigator at UC Davis, I discovered two families of regulators share arrays of Tumor Overexpressed Gene (TOG) domains to recruit soluble ab-tubulins to polymerize or stabilize microtubules (Al-Bassam et al. 2006), determined the first TOG domain x-ray structure, and described their tubulin binding mechanism (Al-Bassam et al. 2007). I and my group have reconstituted the fission yeast versions of these proteins with dynamic microtubules, showing that Alp14, the XMAP215 ortholog, is a microtubule plus-end directed microtubule polymerase, while a CLASP ortholog is a microtubule rescue factor stabilizing growing states (Al-Bassam et al., 2010, 2012). In summary, our work in this area has fundamentally set the current knowledge area for how microtubule polymerization is regulated. My group recently fundamentally transformed this field with rigorous biochemical and x-ray crystallographic studies describing the transitions of TOG arrays:ab-tubulin complexes as microtubule polymerases, leading to a novel mechanistic model (Nithianantham et al, 2018; Cook et al, 2019).

Al-Bassam J, van Breugel M, Harrison SC, Hyman A. Stu2p binds tubulin and undergoes an open-to-closed conformational change. *J Cell Biol*. 2006 Mar 27; 172(7):1009-22. PMCID: PMC2063759

Al-Bassam J, Larsen NA, Hyman AA, Harrison SC. Crystal structure of a TOG domain: conserved features of XMAP215/Dis1-family TOG domains and implications for tubulin binding. *Structure*. 2007; 15(3): 355-62.

Brouhard G, Stear J, Notzel T, **Al-Bassam J**, Kinoshita K, Harrison SC, Howard J, Hyman AA, XMAP215 is a processive microtubule polymerase that catalyzes both growth and shrinkage, *Cell*. 2008, 132:79-88.

Al-Bassam J*, Kim H, Brouhard G, van Oijen A, Harrison SC, Chang F*. CLASP promotes microtubule rescues by recruiting tubulin dimer to the microtubule". *Developmental Cell, 2010. 19: 245-258. PMCID: PMC3156696*

Al-Bassam J*, Kim H, Flor-Parra I, Lal N, Velji H, Chang F. " Fission yeast Alp14 is a dose dependent microtubule polymerase ". *Molecular Biology of the Cell.* 2012. 15:2878-90. PMCID: PMC3408415

Al-Bassam J*, Chang F * ” Regulation of Microtubule Dynamics by TOG domain proteins XMAP215/Dis1 and CLASP”. *Trends in Cell Biology*. 2011. 21: 604-614

Al-Bassam J. ”Reconstituting Dynamic Microtubule Polymerization Regulation by TOG Domain Proteins”. Methods in Enzymology. 2014. 540: 131-148

Nithianantham S, Cook BD, Beans M, Guo, F, Chang FC, **Al-Bassam J.** “Structural Basis of tubulin recruitment and assembly by microtubule polymerases with Tumor Overexpressed Gene (TOG) domain arrays” *eLife*. pii: e38922. doi: 10.7554/eLife.38922. PMCID: PMC6251626

Cook BD, Chang FC, Flor-Parra I, **Al-Bassam J*** “Microtubule polymerase and processive plus-end tracking activities arise from unique tubulin recruitment and self-organization by arrays of TOG domains” *Mol Biol Cell. 2019. 30:1490-1504.* PMCID: PMC6724690

Biochemical and Structural Studies of Tubulin Biogenesis and Microtubule Severing Proteins: My group has uncovered a fundamental molecular mechanism for soluble αβ-tubulin biogenesis and degradation processes modulated by five tubulin chaperones and Arl2 GTPase to maintain their intracellular concentration. We reconstituted tubulin chaperones and Arl2 and demonstrated their shared role as cage-like multi-subunit machines that manipulate αβ-tubulin polymerization through the regulation of GTP hydrolysis (Nithianantham et al., 2015). We described structural studies on the mechanism of disassembly of microtubule-severing enzymes, Katanins (Nithianantham et al. 2018). We have recently determined cryo-EM structures for the tubulin cofactor assemblies in complex with αβ-tubulin in the pre-catalytic and TBCC-bound post-catalytic states using single particle cryo-EM structural methods, revealing the mechanism of tubulin biogenesis and catalytic transitions altering the tubulin heterodimer organization (Taheri et al., 2024).

Nithianantham S, Le S, Seto E, Ti S, Yue A, Jia W, Leary J, Corbett KD, Moore JK, **Al-Bassam J***. “Tubulin cofactors and Arl2 are cage-like chaperones that regulate the soluble αβ-tubulin pool for microtubule dynamics”. *eLife.* 2015 Jul 24;4. doi: 10.7554/eLife.08811. PMCID: PMC4574351

Al-Bassam J*. Revisiting the tubulin cofactors and Arl2 in the regulation of soluble aß-tubulin pools and their effect on microtubule dynamics. *Mol Biol Cell*. 2017 28(3);359-363. doi: 10.1091/mbc.E15-10-0694. PMCID: PMC5341719

Nithianantham S, McNally FJ, and **Al-Bassam J* “**Structural Basis for Disassembly of Katanin Heterododecamers” *J Biol Chem*. 2018. 293:10590-10605. PMCID: PMC6036222

Taheri A, Wang Z, Singal B, Guo F, **Al-Bassam J***. Cryo-EM Structures of the Tubulin cofactors Reveal The Molecular Basis for The Biogenesis of alpha/beta-tubulin. *bioRxiv [Preprint].* 2024 Jan 31:2024.01.29.577855. doi: 10.1101/2024.01.29.577855. PMID: 38405852;

3. Biochemical and structural studies of microtubule-associated proteins and kinesin motors: My research career started with a focus on the structural mechanisms of microtubule-associated proteins in neurons and studies of monomeric kinesin-3 motor proteins. I described the first cryo-EM structure of the microtubule-associated proteins, MAP2, and tau, in binding along MT protofilaments and described their mechanism in stabilizing microtubule organization (Al-Bassam et al., 2002). I also used biochemistry and cryo-EM to describe a structural basis for the monomeric kinesin-3 motor proteins to activate into dimerization (Al-Bassam et al., 2003). In 2011, I initiated new studies of the bipolar tetrameric kinesin-5 motor to understand its novel bipolar organizations and mechanism for sliding apart antiparallel microtubules (Scholey et al. 2014). We also determined the unique mechanism of microtubule-motility directionality reversal in yeast kinesin-5 motors such as Cin8 (Shapira et al., 2017). We recently determined the mechanism of the kinesin-5 tail for motor regulation and its impact on microtubule sliding (Bodrug et al., 2020). We also determined that the minifilament bipolar assembly domains and the tail region are the origins of the kinesin-5 microtubule sliding motility (Nithianatham et al 2023).

Al-Bassam J., Ozer R.S., Safer D., Halpain S., Milligan R.A.; MAP2 and tau bind along the outer ridges of microtubule protofilaments. 2002. *J. Cell Biol.* 157: 1187-1196. PMCID: PMC2173547

Al-Bassam J., Cui Y., Klopheinstein D., Carragher, B.O., Vale R.D., Milligan, R.A. Distinct Conformations of the Kinesin Unc104 Neck Regulate a Monomer-to-Dimer Motor Transition, *J. Cell Biol.* 2003. 163: 743-753.

Roger. B*, **Al-Bassam J*,** Milligan R.A., Halpain S. MAP2, but not tau, repeats bind and bundle f-actin, *Current Biol*. 2004. 14:363-371; PMID: 15028210.

Scholey JE, Nithianantham S, Scholey JM, **Al-Bassam J***. ”Structural Basis for the assembly of the mitotic motor Kinesin-5 into bipolar tetramers” *eLife,* 2014. 3:e02217. doi: 10.7554/elife.02217

Shapira, O, Goldstein, A, **Al-Bassam J***, and Gheber L*. (2017). “A potential physiological role for bidirectional motility and motor clustering of mitotic kinesin-5 Cin8 in yeast mitosis”. *J Cell Sci* 130, 725-734. *Co-corresponding.

Singh SK, Pandey H, Al-Bassam J, Gheber L. “Bidirectional motility of kinesin-5 motor proteins: structural determinants, cumulative functions, and physiological roles” *Cell Mol Life Sci.* 2018 May;75(10):1757-1771. doi: 10.1007/s00018-018-2754-7. PMID: 29397398

Al-Bassam J*, Nithianantham S. Malleable folding of coiled-coils regulates kinesin-3 dimerization. *Proc Natl Acad Sci U S A.*

2018; 115:12845-12847. doi: 10.1073/pnas.1818758115.

Bodrug T, Wilson-Kubalek E, Thompson A, Major J, Alfieri A, Gaska I, Nithianantham S, Debs G, Gutierrez P, Gheber L, McKenney R, Sindelar C, Milligan R, Stumpff J, Forth S, Rosenfeld S, **Al-Bassam J*.** "The Kinesin-5 Tail Domain Directly Modulates the Mechanochemical Cycle of the Motor for Anti-Parallel Microtubule Sliding", *eLife*. 2020 Jan 20;9:e51131. doi: 10.7554/eLife.51131. **Corresponding author*

Nithianantham S, Iwanski MK, Gaska I, Pandey H, Bodrug T, Inagaki S, Major J, Brouhard GJ, Gheber L, Rosenfeld SS, Forth S, Hendricks AG, **Al-Bassam J***. The kinesin-5 tail and bipolar minifilament domains are the origin of its microtubule crosslinking and sliding activity. *Mol Biol Cell*. 2023 Oct 1;34(11):ar111. doi: 10.1091/mbc.E23-07-0287. Epub 2023 Aug 23. PMID: 37610838; PMCID: PMC10559304. * **Corresponding author*