BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

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

These projects involve the coordinated usage of biochemical, structural and biophysics approaches to elucidate fundamental soluble tubulin biogenesis, tubulin dynamic polymerization regulatory and microtubule-based motor activation mechanisms. I and my group are well suited to carry out studies described in this proposal. The studies include biochemical reconstitution of multi-subunit complexes, structural studies using cryo-EM and single particle image analysis, reconstitution of complexes using single molecule fluorescence activity assays with dynamic microtubules *in vitro* in order to test structural models. I am an expert at combining these approaches which span across multiple resolution scales to extract mechanistic knowledge. I have over twenty years of experience in molecular biology, protein biochemistry, 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 microdiffraction x-ray crystallography, and high-resolution total internal reflection fluorescence (TIRF) microscopy to study dynamic microtubules. My group has very recently expanded towards high resolution single particle cryo-EM, as described in the preliminary data in this proposal. My group and I have developed systems incorporating all the above approaches to link atomic-level structural information to real-time functional readout on MT dynamics. Throughout my career, I have maintained successful collaborations and demonstrated high productivity in working with other groups. For the proposed work, I have established a network of long-term collaborations with three Cell biology experts with common goals using *in vivo* models.

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 minisymposium "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 Associated Proteins and Kinesin Motors: My research career started with a focus on 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 their novel bipolar organizations and mechanism in sliding apart antiparallel microtubules (Scholey et al 2014). We also determined the unique mechanism microtubule -motility directionality reversal in yeast kinesin-5 motors such as Cin8 (Shapira et al 2017). We recently described structural studies recently described the mechanism of disassembly of microtubule severing enzymes, Katanins (Nithianantham et al 2018).

- **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.

- Nithianantham S, McNally FJ, and **Al-Bassam J* "**Structural Basis for Disassembly of Katanin Heterododecamers" *J Biol Chem*. 2018. 293:10590-10605. PMCID: PMC6036222
- 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 M, Gaska I, Pandey H, Bodrug T, Inagaki , Major J, Brouhard GJ, Gheber L, Rosenfeld S, Forth S, Hendricks AG, **Al-Bassam J*** "The mechanochemical origins of the microtubule sliding motility within the kinesin-5 domain organization. BioRxiv 2021.10.12.463902; doi: https://doi.org/10.1101/2021.10.12.463902

2. Biochemical and Structural studies of Microtubule Polymerases: 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 αβ-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 microtubule stabilizing rescue factor (Al-Bassam et al 2010, 2012). In Summary, our work in this area has fundamentally set the current knowledge area for how microtubules are polymerization is regulated. My group recently fundamentally transformed this field with rigorous biochemical and x-ray crystallographic studies describing the transitions of TOG arrays:αβ-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
- Nithiananatham 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

3. 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 maintain their intracellular concentration. We reconstituted tubulin chaperones and Arl2 and demonstrate their shared role as cage-like multi-subunit machines that manipulate αβ-tubulin polymerization through regulation of GTP hydrolysis (Nithiananatham et al 2015).

- Nithiananatham 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. *Molecular Biology of the Cell*. 2017 28(3);359-363. doi: 10.1091/mbc.E15-10-0694. PMCID: PMC5341719

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

Ongoing Research Support

National Institutes of Health (5R01-GM110283) 1/1/2015-12/31/2024
"Mechanisms of Tubulin Dimer Regulatory Pathways and Their Impact on Microtubule Function"
Role : PI