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: Hurley, James H.

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

POSITION TITLE: Judy C. Webb Chair, Professor of Biochemistry, Biophysics and Structural Biology

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
San Francisco State University	B.A.	05/1984	Physics
San Francisco State University	M.S.	05/1986	Physics
University of California, San Francisco	Ph.D.	05/1990	Biophysics
University of Oregon	Postdoctoral	05/1992	Structural Biology

A. Personal Statement

My research program focuses on the fundamental mechanisms of protein sorting to lysosomes by the endosomal and multivesicular body pathways and by autophagy. I became fascinated with autophagy in the late 2000s. By then, it had become clear how profoundly important autophagy is for maintaining cellular health, not just in starvation, but in normal physiology as well. I realized at that time how little was known about the structure and function of the core autophagy machinery, and that the basic mechanisms of autophagosome biogenesis were almost completely obscure. This seemed like an ideal problem for my lab, which has pioneered the integration of structural biology with yeast cell biology and *in vitro* reconstitution of membrane remodeling. I continue to believe that this trio of approaches is the ideal toolkit to dissect the basic mechanisms of conserved membrane remodeling processes such as the biogenesis of multivesicular bodies and autophagosomes. Autophagy mechanism has already become the most exciting topic in my lab. My lab has made pivotal discoveries by elucidating the double crescent structure of Atg17, the first structure of a member of the PROPPIN family of autophagic PI(3)P receptors, and the first structure of an autophagic PI 3-kinase complex. This last complex includes the Beclin-1 subunit that is implicated as a central player in cancer genetics, and we are keen to apply our mechanistic insights to clarifying its role in regulating tumor induction and progression. These discoveries, the scientific momentum they have provided, and the technologies that we bring to bear, position the lab to lead the way in elucidating fundamental mechanisms in autophagy.

B. Positions and Honors

Positions and Employment

1987 Guest Scientist, Fermi National Accelerator Laboratory, Batavia IL
1990-1992 Postdoctoral Fellow, Institute of Molecular Biology, University of Oregon, Eugene OR
1992-1997 Tenure Track Investigator, LMB, NIDDK, NIH, Bethesda MD
1997-2013 Chief, Section on Structural Biology and Cell Signaling, LMB, NIDDK, NIH, Bethesda MD
July 2013- Professor, Dept. of Molecular & Cell Biology, University of California, Berkeley
2014- Faculty Affiliate, Molecular Biophysics and Integrated Bioimaging Division, Lawrence Berkeley National Laboratory

Selected Professional Service

1997-1998 X-ray Biology Panel, National Synchrotron Light Source
1997-2002 Instructor, FAES Graduate School at NIH

1998-2001 Scientific Advisory Committee, HHMI Synchrotron X4 Beamlines
1999-2003 Editorial Committee, *Annual Reviews of Biophysics and Biomolecular Structure*
1999- Editorial Boards: *Structure* (1999-), *Developmental Cell* (2005-), *Cell* (2009-), *Protein Science* (2015-), *Journal of Cell Biology* (2017-), *Journal of Molecular Biology* (2017-)
2009 Co-chair, Annual Meeting of the American Society of Biochemistry and Molecular Biology
2010 Co-organizer, ASBMB Special Symposium, "BIochemistry and Cell Biology of ESCRTs in Health and Disease," Snowbird UT, October 14-17, 2010
2011-2012 Scientific Advisory Board, NIGMS AIDS-related Structural Biology Centers
2014-2016 Spokesperson, UC PRT Beamline 8.3.1, Advanced Light Source
2015-2019 Member, AIDS-related Molecular and Cell Biology (AMCB) study section, NIH CSR
2015- Chair, Biophysics Graduate Program, UC Berkeley

Honors

1984 Phi Beta Kappa and Phi Kappa Fellowship
1987-1988 University Fellowship, University of California, San Francisco
1988-1990 University of California Regents' Fellowship
1991-1992 American Cancer Society Postdoctoral Fellowship
1998 Maryland's Outstanding Young Scientist & Allan C. Davis Medal
2009 SER-CAT Outstanding Science Award
2012 Chiron Lectures, University of California, Berkeley
2014 Han Neurath Award, Protein Society

C. Contributions to Science

1. These papers, together with more than 30 other papers on the ESCRTs, underlie much of the current paradigm for the structure and mechanism of this unique pathway for reverse-topology membrane budding and scission.
    a. Wollert T, **Hurley JH** (2010). Molecular mechanism of multivesicular body biogenesis by ESCRT complexes. Nature, 464(7290):864-869. PMCID: PMC2851844.
    Research Highlight in Nat Rev Mol Cell Biol. 11:314 (2010), News & Views in Nat. Cell. Biol 12:422-423 (2010). Rated "Exceptional" by the Faculty of 1000.
    b. Wollert T, Wunder C, Lippincott-Schwartz J, **Hurley JH** (2009). Membrane scission by the ESCRT-III complex. Nature, 458(7235):172-177. PMCID: PMC2743992.
    News & Views in Nature, 458:159-160 (2009). Rated #1 paper in "All Biology" by the Faculty of 1000, March-April, 2009.
    c. Hierro A, Sun J, Rusnak AS, Kim J, Prag G, Emr SD, **Hurley JH** (2004). Structure of the ESCRT-II endosomal trafficking complex. Nature, 431(7005):221-225. PubMed PMID: 15329733.
    Highlighted in Structure Watch, Nat Rev Mol Cell Biol. 5:773 (2004), Dev Cell 7:457-463 (2004), and Stanford Research Laboratory Science Highlights, February, 2005.
    d. Kostelansky MS, Schluter C, Tam YY, Lee S, Ghirlando R, Beach B, Conibear E, **Hurley JH** (2007). Molecular architecture and functional model of the complete yeast ESCRT-I heterotetramer. Cell, 129(3):485-498. PMCID: PMC2065850.
    Highlighted in News & Views in Nature, 447:921-922 (2007), and in Cell Host & Microbe, 2:1-2 (2007).
2. The structures of the large multiprotein complexes responsible for macroautophagy have been elusive. Here, the Atg17 complex was the first of these larger structures to be reported, putting the earliest stage of autophagosome formation on the a mechanistic footing. This was followed with an electron microscopy structure of class III human phosphatidylinositol 3-kinase complex involved in autophagy. Together, these are seminal contributions to structural understanding of how autophagy begins
    a. Ragusa MJ, Stanley RE, **Hurley JH** (2012). Architecture of the Atg17 complex as a scaffold for autophagosome biogenesis. Cell, 151(7):1501-1512. PMCID: PMC3806636.
    Preview in Cell, 151:1403-1405 (2012).
    b. Baskaran S, Carlson LA, Stjepanovic G, Young LN, Kim do J, Grob P, Stanley RE, Nogales E, **Hurley JH** (2014). Architecture and dynamics of the autophagic phosphatidylinositol 3-kinase complex. Elife, e05115. doi:10.7554/eLife.05115. PMCID: PMC4281882.

3. Sixteen years apart, these papers bookmark pioneering structural insights into paradigmatic lipid second messenger receptor, protein kinase C.
    a. Leonard TA, Różycki B, Saidi LF, Hummer G, **Hurley JH** (2011). Crystal structure and allosteric activation of protein kinase C βII. Cell, 144(1):55-66. PMCID:PMC3104240.
    Preview in Structure, 19:144-146 (2011).
    b. Zhang G, Kazanietz MG, Blumberg PM, **Hurley JH** (1995). Crystal structure of the cys2 activator-binding domain of protein kinase C delta in complex with phorbol ester. Cell, 81(6):917-924. PMID: 7781068.
4. Central role in defining the structural basis for ubiquitin recognition.
    a. Prag G, Misra S, Jones EA, Ghirlando R, Davies BA, Horazdovsky BF, **Hurley JH** (2003). Mechanism of ubiquitin recognition by the CUE domain of Vps9p. Cell, 113(5):609-20. PMID: 12787502.
    Highlighted in Cell 113:554-556 (2003). Rated "Exceptional" by the Faculty of 1000.
    b. Lee S, Tsai YC, Mattera R, Smith WJ, Kostelansky MS, Weissman AM, Bonifacino JS, **Hurley JH** (2006). Structural basis for ubiquitin recognition and autoubiquitination by Rabex-5. Nat Struct Mol Biol. 13(3):264-271. PMCID: PMC1578505.
    Highlighted (with one other paper) in News & Views, Nat Struct Mol Biol. 13:1133-1136 (2006), and featured as "Article of the Month" in Nat Struct Mol Biol. March, 2006.
5. These papers build on more than a decade of work in the Hurley lab on regulation and recruitment of clathrin adaptors. The first paper answered a major question of more than 20-year's standing – how Arf1 activates heterotetrameric adaptor complexes. The second showed how the Nef protein of HIV uses the adaptor complex AP-2 to downregulate clathrin. The third used reconstitution and cryo-EM to show that AP-1, Arf1, and Nef can form a network of polygons whose geometry matches that of clathrin. The last paper was a stunning surprise that showed the AP-1 and Arf1 have coat-like properties by themselves, and that Nef hijacks clathrin in an astonishingly sophisticated manner.
    a. Ren X, Farías GG, Canagarajah BJ, Bonifacino JS, **Hurley JH** (2013). Structural basis for recruitment and activation of the AP-1 clathrin adaptor complex by Arf1. Cell 152(4):755-767. PMCID: PMC3913725.
    b. Ren X, Park SY, Bonifacino JS, **Hurley JH** (2014). How HIV-1 Nef hijacks the AP-2 clathrin adaptor to downregulate CD4. Elife 3:e01754. doi:10.7554/eLife.01754. PMCID: PMC3901399.
    c. Shen QT, Ren X, Zhang R, Lee IH, **Hurley JH** (2015). HIV-1 Nef hijacks clathrin coats by stabilizing AP-1:Arf1 polygons. Science. 350(6259):aac5137. PMCID: PMC4638387.