## BIOGRAPHICAL SKETCH

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NAME: Lauren Parker Jackson

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

POSITION TITLE: Assistant Professor of Biological Sciences & Biochemistry

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 |
|---|---|---|---|
| Vanderbilt University | B.S. | 05/2003 | Chemistry |
| MRC Laboratory of Molecular Biology & Trinity College, University of Cambridge | Ph.D. | 01/2008 | Structural Biology |
| Cambridge Institute for Medical Research | Postdoctoral | 11/2013 | Biochemistry |

### A. Personal Statement

The goal of my laboratory is to understand the cellular roles of important protein complexes that initiate cellular trafficking pathways by forming coats around vesicles or tubules at specific membranes. We focus on the retromer, adaptor protein 4 (AP4), and coat protein complex I (COPI) complexes and the roles they undertake in both fundamental cell biology and human disease. Each coat functions as a "hub" to coordinate large protein networks that drive the regulated formation of vesicles or tubules at precise locations. We use biochemical, biophysical, and structural methods to address at the molecular level how coats interact with protein and lipid partners to regulate coat assembly and to sort important cargoes to different destinations. We use our mechanistic data to address functional relevance of coat protein complexes in cultured cell lines or in model systems, including budding yeast. Ultimately, we aim to identify new binding partners and cargoes for these coats and to characterize molecular mechanisms of coat protein assembly and regulation. We propose to extend our work to address the "moonlighting" roles of trafficking proteins in cell division.

A. Frazier MN, Davies AK, Voehler M, Kendall AK, Borner GHH, Chazin WJ, Robinson MS, and **Jackson LP**. (2016). Molecular basis for the interaction between Adaptor Protein Complex 4 (AP4) β4 and its accessory protein, tepsin. *Traffic* 17: 400-415. PMCID: PMC4805503.

B. **Jackson LP**. (2014). Structure and mechanism of COPI vesicle biogenesis. *Curr Opin Cell Biol* **29C**, 67-73. PMCID not available. (Invited review.)

C. **Jackson LP**†, Kümmel D†, Reinisch K, and Owen DJ. (2012). Structures and mechanisms of vesicle coat components and multisubunit tethering complexes. *Curr Opin Cell Biol* **24,** 475-483. (†corresponding authors). PMCID: PMC3425711.

**B. Employment, Honors, & Service**

**Employment**

2014-present Assistant Professor, Dept. of Biological Sciences, Vanderbilt University, Nashville, TN, USA
2016-present Assistant Professor, Dept. of Biochemistry, Vanderbilt University School of Medicine
2009-2013 Postdoctoral Research Associate, Cambridge Institute for Medical Research, Cambridge, UK
2009-2013 Supervisor, Natural Sciences Part IA, Jesus College, Cambridge, UK (teaching experience)
2007-2009 Junior Consultant, The Boston Consulting Group, London, UK

**Honors**

2016 Pew Scholar
2016 Provost Research Studio for faculty development, Vanderbilt University
2016 Littlejohn Faculty Fellow, Vanderbilt Undergraduate Summer Research Program
2013 Gordon Research Conference travel award (Molecular Membrane Biology)
2012 Keystone Symposia Future of Science Fund Scholarship (Structural Biology of Cellular Processes)
2011 Protein Society Young Investigator Travel Grant/Finn Wold Travel Award
2010 Gordon Research Conference travel award (Lysosomes and Endocytosis)
2004 Academy of Achievement International Achievement Summit, Chicago, IL
2003 MRC Laboratory of Molecular Biology Student Scholarship
2003 Trinity College Honorary External Research Studentship
2003 National Science Foundation Fellowship (declined)
2003 Gates Cambridge Scholarship (declined)
2003 Founder's Medalist, College of Arts & Science, Vanderbilt University
2003 Phi Beta Kappa, Vanderbilt University
2003 Joel Tellinghuisen Award for Undergraduate Research, Phi Beta Kappa, Vanderbilt University
2003 Outstanding Senior in Chemistry, Vanderbilt University Dept. of Chemistry
2003 Donald E Pearson Award for Undergraduate Research, Vanderbilt University Dept. of Chemistry

**Professional Service & Memberships**

Editorial board member, *Traffic*, 2017-present
Guest Editor, *Traffic* review series ("Trafficking at atomic resolution"), spring 2019
Member, Planning Committee, 2018 Pew Annual Meeting
Chair, Science Session I, 2018 Pew Annual Meeting
F1000 contributing faculty member, Cell Signaling & Trafficking Structures, 2018-present
*Ad hoc* reviewer, NIH Membrane Biology & Protein Processing (MBPP) study section
*Ad hoc* reviewing for *Nature Struct Mol Biol, eLife, J Cell Biology*, *Structure*, *PNAS*, *Nat Chem Biology*
*Ad hoc* reviewer, book chapter in "Biomolecular and Bioanalytical Techniques: Theory, Methodology and Applications", Wiley (UK)
*Ad hoc* reviewing for Stanford Synchrotron Radiation Light Source (SSRL)
*Ad hoc* reviewing for Deutsche Forschungsgemeinschaft (DFG) funding body
Member, American Society for Cell Biology, 2015-present
Member, Biophysical Society, 2017-present

**C. Contributions to Science**

Publication list
http://www.ncbi.nlm.nih.gov/myncbi/browse/collection/48006064/?sort=date&direction=descending

1. Molecular mechanisms of vesicular and tubular coat assembly

My work on key coat protein complexes has provided insight into how vesicles and tubules form at specific membranes. Clathrin-mediated endocytosis at the plasma membrane has long served as a paradigm for understanding coated vesicle formation. However, the field lacked mechanistic information about how clathrin and its adaptor complex, AP2, recognized cargo in the context of the membrane. My postdoctoral work revealed how AP2 is recruited to membranes by a specific phosphoinositide, where it then undergoes a substantial conformational change to bind linear motifs found in the C-termini of cargo molecules. Subsequent

work by other groups showed how this conformational change is required for clathrin recruitment and is likely conserved in related coats like AP1 and COPI. More recent work focuses on the mostly uncharacterized AP4 coat. We have provided the first mechanistic glimpse into how AP4 interacts with its only known accessory protein, tepsin, and we have determined structures and evolutionary pattern of both the ENTH and VHS-like domains in tepsin. Our work provides a foundation for understanding AP4 coat assembly and ultimately how AP4 impacts brain function. Finally, on endosomes, retromer sorts cargoes to at least two destinations, the plasma membrane and *trans*-Golgi network (TGN). A major question is how retromer can specifically sort protein cargoes to distinct destinations. Identification of a new retromer binding partner called VARP linked an ancestral SNARE protein, VAMP7, to retromer for the first time. The retromer/VARP/VAMP7 protein network may help partition endosomes so that relevant cargoes are sent specifically to the plasma membrane, where VAMP7 can drive fusion events. Ongoing work in the lab aims to uncover the structural basis for retromer assembly.

A. **Jackson LP***, Kelly BT*, McCoy AJ, Gaffry T, James LC, Collins BM, Höning S, Evans PR, Owen DJ. (2010). A large scale conformational change couples membrane recruitment to cargo binding in the AP2 clathrin adaptor complex. *Cell* 141, 1220-29, (*joint first authors), PMCID: PMC3655264.

B. Archuleta TA, Frazier MN, Monken A, Kendall AK, Harp J, McCoy AJ, Creanza N, and **Jackson LP**. (2017). Structure and evolution of ENTH and VHS/ENTH-like domains in tepsin. *Traffic* 18: 590-603.

C. Frazier MN, Davies AK, Voehler M, Kendall AK, Borner GHH, Chazin WJ, Robinson MS, and **Jackson LP**. (2016). Molecular basis for the interaction between Adaptor Protein Complex 4 (AP4) β4 and its accessory protein, tepsin. *Traffic* 17: 400-415.

D. Hesketh GG*, Pérez-Dorado I*, **Jackson LP**, Wartosch L, Schäfer IB, Gray SR, McCoy AJ, Zeldin OB, Garman EF, Harbour ME, Evans PR, Seaman MN, Luzio JP, Owen DJ. (2014). VARP is Recruited Onto Endosomes by Direct Interaction with Retromer, Where Together They Function in Export to the Cell Surface. *Dev Cell* 29, 591-606 (*joint first authors), PMCID: PMC4059916.

E. Davies AK, Itzhak DN, Edgar JR, Archuleta TL, Hirst J, **Jackson LP**, Robinson MS, and Borner GHH. (2018). AP-4 vesicles contribute to spatial control of autophagy via RUSC-dependent peripheral delivery of ATG9A. *Nature Commun* 27: 3958.

2. Cargo recognition by vesicle coat proteins

The identification and sorting of protein cargoes to specific destinations lie at the heart of membrane trafficking. Recognition of linear motifs by the clathrin coat machinery was well-understood in the field, but there were no molecular data on how the COPI coat interacted with any of its important cargoes in the retrograde pathway. Our structural work elucidated how two COPI subunits could interact with dilysine motifs found in retrograde cargoes, which in turn implied that COPI coats assemble differently from clathrin-based coats. A second major question was how SNARE proteins are sorted as cargo back to their steady-state destination following a fusion event. Our work on the lysosomal SNARE protein, VAMP7, provided one of the first two structural examples of how coats package SNAREs into forming vesicles in a non-competitive way. Instead of linear motifs, SNAREs instead use folded structural domains to interact specifically with a single adaptor protein, and loss of important residues in these domains have important implications for mis-sorting. My recent work at Vanderbilt has built upon and combined these two interests. In collaboration with Todd Graham's lab, we uncovered the biochemical basis for recognition of a ubiquitinated SNARE protein by COPI. This work highlighted that ubiquitin can act as a retrieval signal for a SNARE.

A. **Jackson LP**†, Lewis M, Kent HM, Edeling MA, Evans PR, Duden R, and Owen DJ†. (2012). Molecular basis for recognition of dilysine trafficking motifs by COPI. *Dev Cell* **23**, 1-8 (†corresponding authors), PMCID: PMC3521961.

B. Pryor PR, **Jackson LP**, Gray SR, Edeling MA, Thompson A, Sanderson CM, Evans PR, Owen DJ, Luzio JP. (2008). Molecular basis for the sorting of the SNARE VAMP7 into endocytic clathrin-coated vesicles by the ArfGAP Hrb. *Cell* 134, 817-27, PMCID: PMC2648964.

C. Xu P, Hankins HM, Macdonald C, Erlinger SJ, Frazier MN, Diab NS, Piper RC, **Jackson LP**, MacGurn JA, and Graham TR. (2017). COPI mediates recycling of an exocytic SNARE from endosomes by recognition of a ubiquitin sorting signal. *eLife* 2017; 6:e28342. DOI:10.7554/eLife.28342.

3. Structural studies of filamentous plant viruses

Filamentous plant viruses are important models for understanding helical virus assembly and in agricultural disease; potyviruses alone account for more than half the viral crop damage world-wide. Because of their filamentous nature, these viruses do not crystallize. As an undergraduate, I helped develop methods for making filamentous virus samples of the potexvirus, potato virus X (PVX), and the potyvirus, wheat streak mosaic virus (WSMV). Our fiber diffraction data on PVX provided the first estimates of helical symmetry for the virus, while our work on WSMV was one of the first examples of potyvirus fiber diffraction. Subsequently, the combination of structural techniques like EM and STEM was used together with our fiber diffraction data to produce a more detailed analysis of PVX structure.

**Parker L**, Kendall A, Berger, PH, Shiel, PJ, and Stubbs, G. (2005). Wheat streak mosaic virus— Structural parameters for a *Potyvirus*. *Virology* 340, 64-69. (featured on cover)

Stubbs G, **Parker L**, Junn J, and Kendall, A. (2005). Flexible filamentous virus structures from fiber diffraction. *Fiber Diffraction Review* 13, 38-42.

**Parker L**, Kendall A, and Stubbs, G. (2002). Surface Features of Potato Virus X from Fiber Diffraction. *Virology* 300, 291-29. (featured on cover)

**D. Research Support**

Current funding

1. NIH/NIGMS 1R35GM119525 09/01/2016 – 05/31/2021 Role: PI
"Molecular mechanisms of coat protein assembly and regulation in membrane trafficking"
The major goal of this project is to determine the molecular mechanisms by which vesicular and tubular coat protein complexes assemble and are regulated on cellular membranes.

2. Pew Charitable Trusts, Pew Scholars Award 08/01/2016 – 07/31/2020 Role: PI
"Coat protein function in membrane trafficking and human disease"
The major goal of this project is to elucidate molecular structures and functions of important non-clathrin coat protein complexes that initiate trafficking pathways at the Golgi and endosomes.

3. NIH/NIGMS R01 (PI: Todd Graham) 05/01/2016 – 04/30/2020 Role: Collaborator
"Mechanisms of protein transport between Golgi and endosomes"
The major goal of this project is to define the function of COPI and ubiquitin in recycling a SNARE protein from early endosomes to the Golgi.

Under review

1. NIH/NCI 1R01GM121421 (PI: Yashi Ahmed, Dartmouth; Vanderbilt PI: Ethan Lee) Role: Collaborator
"Targeting the Wnt Receptor Complex in APC-deficient Colorectal Cancers"
*Submitted February 2019*

# 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: Kendall, Amy

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

POSITION TITLE: Laboratory Manager

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) | END DATE MM/YYYY | FIELD OF STUDY |
|---|---|---|---|
| Vanderbilt University, Nashville , TN | BS | 05/1993 | Elementary Education / Natural Sciences |
| Vanderbilt Universtiy, Nashville, TN | MS | 05/2000 | Biological Sciences |

## A. Personal Statement

Beginning with my graduate work in the mid-nineties, I have always worked at the intersection of structural methods including x-ray fiber diffraction, negative stain and cryo-electron microscopy, and x-ray crystallography. My studies of flexible filamentous plant viruses eventually led to studies of disordered amyloid and prion filaments, and this work has prepared me well for structural studies of malleable membrane trafficking proteins including retromer. As a senior staff scientist, I have helped to drive the adoption of negative stain and cryoEM methods by our laboratory, and have served as the EM "point person" for more than 20 years. I have trained students in microscopy methods and written protocols for sample preparation, instrument use, image processing and validation, and publication production. I have attended workshops and conferences in order to remain up-to-date on current topics in microscopy, and have disseminated this information to our laboratory and others at Vanderbilt.


1. Tuttle MD, Comellas G, Nieuwkoop AJ, Covell DJ, Berthold DA, Kloepper KD, Courtney JM, Kim JK, Barclay AM, Kendall A, Wan W, Stubbs G, Schwieters CD, Lee VM, George JM, Rienstra CM. Solid-state NMR structure of a pathogenic fibril of full-length human α-synuclein. Nat Struct Mol Biol. 2016 May;23(5):409-15. PubMed PMID: 27018801; PubMed Central PMCID: PMC5034296.
2. Frazier MN, Davies AK, Voehler M, Kendall AK, Borner GH, Chazin WJ, Robinson MS, Jackson LP. Molecular Basis for the Interaction Between AP4 β4 and its Accessory Protein, Tepsin. Traffic. 2016 Apr;17(4):400-15. PubMed PMID: 26756312; PubMed Central PMCID: PMC4805503.
3. Kendall A, Williams D, Bian W, Stewart PL, Stubbs G. Barley stripe mosaic virus: structure and relationship to the tobamoviruses. Virology. 2013 Sep 1;443(2):265-70. PubMed PMID: 23725818.
4. Kendall A, McDonald M, Bian W, Bowles T, Baumgarten SC, Shi J, Stewart PL, Bullitt E, Gore D, Irving TC, Havens WM, Ghabrial SA, Wall JS, Stubbs G. Structure of flexible filamentous plant viruses. J Virol. 2008 Oct;82(19):9546-54. PubMed PMID: 18667514; PubMed Central PMCID: PMC2546986.


## B. Positions and Honors

### Positions and Employment

1999 - 2002 Research Assistant II, Vanderbilt University, Nashville , TN
2002 - 2005 Research Assistant III, Vanderbilt University, Nashville, TN
2005 - Laboratory Manager, Vanderbilt University, Nashville, TN

### Other Experience and Professional Memberships

## Honors

## C. Contribution to Science

1. Structural studies of amyloid and prion proteins.

   Structural studies of self-propagating amyloids (prions) are essential to understand the mechanism of prion self-propagation and molecular toxicity, and structural studies of both prion and non-prion amyloids are required for the rational design of drugs to treat these diseases. We used x-ray fiber diffraction in combination with solid state NMR and negative stain electron microscopy to determine low resolution structures of Aβ, the amyloid implicated in Alzheimer's disease, and α-synuclein, the amyloid implicated in Parkinson's disease. We also used x-ray fiber diffraction to compare a number of different types of natural and synthetic PrP prions.

   a. Tuttle MD, Comellas G, Nieuwkoop AJ, Covell DJ, Berthold DA, Kloepper KD, Courtney JM, Kim JK, Barclay AM, Kendall A, Wan W, Stubbs G, Schwieters CD, Lee VM, George JM, Rienstra CM. Solid-state NMR structure of a pathogenic fibril of full-length human α-synuclein. Nat Struct Mol Biol. 2016 May;23(5):409-15. PubMed PMID: 27018801; PubMed Central PMCID: PMC5034296.
   b. Wan W, Wille H, Stöhr J, Kendall A, Bian W, McDonald M, Tiggelaar S, Watts JC, Prusiner SB, Stubbs G. Structural studies of truncated forms of the prion protein PrP. Biophys J. 2015 Mar 24;108(6):1548-1554. PubMed PMID: 25809267; PubMed Central PMCID: PMC4375555.
   c. McDonald M, Box H, Bian W, Kendall A, Tycko R, Stubbs G. Fiber diffraction data indicate a hollow core for the Alzheimer's aβ 3-fold symmetric fibril. J Mol Biol. 2012 Oct 26;423(3):454-61. PubMed PMID: 22903058; PubMed Central PMCID: PMC3462308.
   d. Wille H, Bian W, McDonald M, Kendall A, Colby DW, Bloch L, Ollesch J, Borovinskiy AL, Cohen FE, Prusiner SB, Stubbs G. Natural and synthetic prion structure from X-ray fiber diffraction. Proc Natl Acad Sci U S A. 2009 Oct 6;106(40):16990-5. PubMed PMID: 19805070; PubMed Central PMCID: PMC2761340.

2. Structural studies of filamentous plant viruses.

   Filamentous plant viruses have long been used as models for viral structure and assembly. Using a combination of x-ray fiber diffraction and cryo-electron microscopy, we determined the low resolution structures of a number of different flexible filamentous plant viruses including potato virus X and soybean mosaic virus, and the low resolution structure of a rigid filamentous plant virus, barley stripe mosaic virus. These low resolution structures allowed us to speculate about the relationships between the filamentous plant viruses and provided information that might be used to design modified coat proteins for peptide expression and conferral of resistance on host plants.

   a. Kendall A, Williams D, Bian W, Stewart PL, Stubbs G. Barley stripe mosaic virus: structure and relationship to the tobamoviruses. Virology. 2013 Sep 1;443(2):265-70. PubMed PMID: 23725818.
   b. Kendall A, McDonald M, Bian W, Bowles T, Baumgarten SC, Shi J, Stewart PL, Bullitt E, Gore D, Irving TC, Havens WM, Ghabrial SA, Wall JS, Stubbs G. Structure of flexible filamentous plant viruses. J Virol. 2008 Oct;82(19):9546-54. PubMed PMID: 18667514; PubMed Central PMCID: PMC2546986.

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