

Alison Schroer Vander Roest, PhD

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EDUCATION

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|---|-------------------------------|-----------|
| Vanderbilt University, Nashville, TN | PhD in Biomedical Engineering | 2011-2016 |
| Vanderbilt University, Nashville, TN | MS in Biomedical Engineering | 2011-2014 |
| University of Virginia, Charlottesville, VA | BS in Biomedical Engineering | 2008-2011 |

RESEARCH INTERESTS

Cardiovascular disease is the leading cause of death world-wide and is often associated with changing mechanics that influence cellular responses and progression of disease. In the heart, a main source of contractile forces are the β myosin motors responsible for cardiomyocyte contraction. Small alterations to myosin kinetics and functions can drive dramatic cellular and tissue remodeling (Vander Roest et al. 2021). Mechanical signals are transmitted through mechanosensitive protein complexes, many of which are involved in cell adhesion to the ECM and neighboring cells (Schroer and Merryman, 2015). Signaling downstream of these adhesions can alter cellular responses and initiate remodeling. Cellular and organ remodeling which occurs during disease alters the mechanical environment and can create feedback loops of cellular and tissue remodeling, such that it can be challenging to separate primary pathogenetic alterations from secondary adaptations. Computational models can be used to generate and refine hypotheses within systems of overlapping inputs, outputs, and feedback loops to better understand the links between cardiac mechanics and cellular responses. I believe that using a combination of *in vivo*, *in vitro*, and *in silico* modeling approaches can help untangle this complexity and allow us to develop a better understanding of the mechanisms of cardiac disease.

RESEARCH POSITIONS

Instructor, Department of Pediatrics, Stanford University School of Medicine 2022-Present

Postdoctoral Fellow, Microsystems, Spudich, Bernstein Labs, Stanford University 2017-2022

Investigating roles of sarcomeric protein mechanics in human induced pluripotent stem cell derived cardiomyocytes (iPSC-CMs) as model system for development and familial hypertrophic cardiomyopathy disease progression with beta-cardiac myosin (MYH7) mutations

Mentors: Beth Pruitt, PhD (2017-2018), James Spudich, PhD, Daniel Bernstein, MD (2018-present)

Collaborations: Sean Wu, Alex Dunn, Ken Campbell, Mike Regnier and AICS

Methods: Functional assessment of iPSC-CMs via live cell imaging and traction force microscopy and FRET tension sensors

CRISPR/Cas 9 gene editing – design of sgRNA, and ds and ssDNA homology regions

Microfabrication – microcontact printing and soft lithography of proteins

Computational modeling – kinetic models of myosin force generation

Graduate Researcher, Merryman Mechanobiology Laboratory, Vanderbilt University 2011-2016

Investigated mechanobiology of cardiac disease and fibrosis: focus on fibroblast activation, mechanotransduction through cellular adhesions, and remodeling after myocardial infarction

Thesis: Mechanobiology of Cardiac Disease and Fibrosis: a Novel Role for Cadherin-11

Mentor: W. David Merryman, PhD

Method: *in vitro* cell analysis techniques – cell culture, western blot, immunostaining, qPCR, etc.

in vivo mouse models – animal husbandry, injections, echocardiogram assessment, etc.

atomic force microscopy, Bruker Biocatalyst system – scanning live cells and tissue sections

computational modeling – cell signaling networks, 2D finite element models, Hill-type model

Research Assistant, Multiscale Muscle Mechanics Laboratory, University of Virginia 2009-2011
 Studied passive mechanics of skeletal muscle, using experimental and computational approaches
Mentor: Silvia Blemker, PhD

GRANTS AND FELLOWSHIP

Current:

1. Pathway to Independence K99/R00 (PI: **Alison S Vander Roest**). NIH NHLBI: "Modeling myosin mechanobiology towards understanding the mechanisms of hypertrophic cardiomyopathy" A1 1K99HL153679-01A1 08/2021-07/2023, \$166,320.
2. Stanford Child Health Research Institute (MCHRI) Instructor K-awards Support Program (PI: **Alison S Vander Roest**). "Modeling myosin mechanobiology towards understanding the mechanisms of hypertrophic cardiomyopathy" 01/2022-07/2023, \$50,000.
3. Collaborative Program Grant for Multidisciplinary teams – RM1 (PIs: James Spudich, Daniel Bernstein, Sean Wu, Beth Pruitt, Michael Regnier, Alexander Dunn, and David Mack) role: trainee contributed preliminary data and writing 20% of grant. NIH-NIGMS: "From proteins to cells to tissues: A multiscale assessment of biomechanical regulation by the myosin molecular motor." (1RM1GM131981-01), 05/2019-04/2024), \$9,400,000.

Completed:

4. Postdoctoral Fellowship (PI: **Alison S Vander Roest**). American Heart Association: "Investigating myosin mechanobiology in human induced pluripotent stem cell-derived cardiomyocyte" (AHA20POST35211011), 01/2020-08/2021, \$129,352.
5. Predoctoral Fellowship (PI: **Alison K Schroer**). American Heart Association: "Investigating the role of cadherin-11 in myocardial remodeling after myocardial infarction" (AHA15PRE25710333), 07/01/2015-12/18/2016, \$52,000.00.
6. Graduate Research Fellowship (PI: **Alison K Schroer**). NSF "Modeling integrin mechanotransduction and myofibroblast differentiation" (NSF DGE-0909667), 06/01/2012-05/31/2016, \$121,500.

SELECTED HONORS

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| <i>Research Training in myocardial biology at Stanford</i> – T32 Fellow | 2017-2019 |
| <i>Thomas Harris Graduate Fellowship</i> | 2011-2012 |
| Graduated <i>summa cum laude</i> , University of Virginia | 2011 |
| Rodman Scholar University of Virginia | 2008-2011 |

TEACHING EXPERIENCE AND TRAINING

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| Stanford University, Co-instructor for CTS225 – Stem Cells in CV Reg. Medicine | Spring 2021 |
| Participating in ~30 hours of Scientific Teaching Series Workshops and EDUC courses | 2020-2021 |
| Stanford University, Co-instructor for ME342A – Methods in Mechanobiology | Summer 2017 |
| BME Department, Teaching Assistant for BME 101 (Biomechanics) | Fall 2011 |
| Vanderbilt BME Department, Teaching Assistant for BME (Cellular models) | Spring 2012 |
| ***Awarded departmental Teaching Assistant award | |

PUBLICATIONS

In preparation or submitted

1. Pardon G, Lewis H, **Vander Roest AS**, Castillo EA, Wilson R, Denisin AK, Blair CA, Birnbaum F,

Holbrook C, Koleckar K, Chang ACY, Pruitt BL, Blau HM “Insights into single hiPSC-derived cardiomyocytes phenotypes and maturation using ContraX, an efficient pipeline for tracking contractile dynamics”, 2020 bioRxiv, doi: <https://doi.org/10.1101/2021.03.18.436014>

2. Pardon G, Birnbaum F, **Vander Roest AS**, Pruitt BL, Blau HM “Altered cellular compliance and myofibril organization in single hiPSC-cardiomyocytes with DMD mutations (in preparation).
3. **Vander Roest AS**, Dunn A, Ruppel KM, Spudich JA, Pruitt BL, Bernstein DB, “Myosin mutations and myosin inhibitors alter hiPSC-CM contractility: linking force and hypertrophy” (in preparation).

Published

1. Ranjbarvaziri S, Ellenberger M, Kooiker K, Fajardo G, Zhao M, **Schroer AK**, Koyano TK, Fong R, Woldeyes RA, Ma N, Lei T, Traber GM, Chan FP, Perrino J, Reddy S, Chiu W, Wu JC, Woo YJ, Ruppel K, Spudich JA, Snyder M, Contrepolis K, and Bernstein D; “Altered cardiac energetics and mitochondrial dysfunction in hypertrophic cardiomyopathy” (in Press: *Circulation*)
2. **Vander Roest AS***, Liu C*, Morck M, Kooiker KB, Jung G, Song D, Dawood A, Pardon G, Jhingran A, Vaziri S, Fajardo G, Zhao M, Campbell K, Pruitt BL, Ruppel KM, Spudich J, Bernstein D; “Hypertrophic cardiomyopathy β -myosin mutation (P710R) leads to hypercontractility by disrupting super-relaxed state: multiscale measurements and computational modeling”, *PNAS* 118 (24) e2025030118; 2021.
3. **Schroer AK**, Pardon G, Castillo E, Blair C, Pruitt B, “Engineering hiPSC cardiomyocyte in vitro model systems for functional and structural assessment”, *Progress in Biophysics and Molecular Biology*, 144; 3-15, 2019.
4. **Schroer AK**, Bersi MR, Clark CR, Zhang Q, Sanders LH, Hatzopoulos AK, Lal H, Force TL, Merryman WD, “Cadherin-11 blockade reduces inflammation-driven fibrotic remodeling and improves outcomes after myocardial infarction”, *JCI Insight*, 4(18):e131545, 2019.
5. Manalo AW, **Schroer AK**, Fenix A, Coogan J, Broisma T, Merryman WD, Bader D, “Loss of CENP-F Results in Dilated Cardiomyopathy with Severe Disruption of Cardiac Myocyte Architecture”, *Scientific Reports*, 8: 7546, 2018.
6. **Schroer AK**, Shotwell MS, Sidorov VY, Wikswa JP, and Merryman WD, “I-wire heart-on-a-chip II: Biomechanical analysis of contractile 3D cardiomyocyte tissue constructs”, *Acta Biomaterialia*. 48:79-87, 2017.
7. West JD, Carrier EJ, Bloodworth NC, **Schroer AK**, Chen P, Ryzhova LM, Gladson S, Shay S, Hutcheson JD, and Merryman WD, “Serotonin 2B antagonism prevents heritable pulmonary arterial hypertension”, *PLoS ONE*, Vol. 11(2):e0148657, 2016.
8. **Schroer AK** and Merryman WD, “Mechanobiology of myofibroblast adhesion in fibrotic cardiac disease”, *Journal of Cell Science*, Vol. 128(10):1865-75, 2015.
9. **Schroer AK** and Merryman WD, “Network modeling approach to myofibroblast differentiation”, *Cellular and Molecular Bioengineering*, Vol. 7(3): 446-59, 2014.
10. Rehorn MR, **Schroer AK**, Blemker SS. “The passive properties of muscle fibers are velocity dependent.” *Journal of Biomechanics*, Vol. 47(3): 687-93, 2013.

SELECTED PRESENTATIONS

Invited Presentations:

1. **Vander Roest AS**, “Cardiac mechanobiology: Modeling altered cardiac biomechanics across scales to understand mechanisms of disease” University of Louisville Biomedical Engineering Departmental Seminar, **Invited Seminar** (01/2022)
2. **Vander Roest AS**, “Modeling Altered Biomechanics of Myosin with Disease Causing Mutations Across Molecular and Cellular Scales” University of Washington Muscle Research Seminar-**Invited Seminar** (03/2020)
3. **Schroer AK**, Kooiker K, Adhikari A, Ruppel K, Bernstein D, Spudich J, Pruitt B. “human induced pluripotent stem cell derived cardiomyocytes as models for the mechanobiology of cardiomyopathy at the single cell level” 6th International Conference on Stem Cell Engineering, **Invited Talk**, presented on behalf of Beth Pruitt (12/2018).

4. **Schroer AK**, “*Studying mechanobiology of cardiac disease outside and in: roles for cadherin-11 and beta cardiac myosin*”, **Invited Seminar, Purdue University** (10/2018)

Conference Presentations:

5. **Vander Roest AS**, Liu C, Dunn A, Ruppel KM, Spudich JS, Pruitt BL, “ *β -myosin Biomechanics and Cardiomyocyte Mechanobiology: Modeling Hypertrophic Cardiomyopathy*” BMES Annual Meeting – Podium presentation (10/2021).
6. **Vander Roest AS**, Kooiker KB, Liu C, Adhikari A, Morck MM, Pruitt BL, Ruppel KM, James Spudich JS, Daniel Bernstein D; “*Modeling Biomechanical Effects of Hypertrophic Cardiomyopathy Mutations in β -Myosin Across Scales*”. BMES Annual Meeting – On demand presentation (10/2020).
7. **Schroer AK**, Kooiker K, Jung G, Vaziri S, Adhikari A, Song D, Lui C, Ruppel KM, Pruitt BL, Spudich J, Bernstein D; “*HCM mutations in β -myosin have divergent biomechanical effects in molecular and cellular models*”, BMES Annual Meeting – Podium Presentation (10/2019).
8. **Schroer AK**, Kooiker K, Jung G, Vaziri S, Adhikari A, Song D, Lui C, Ruppel KM, Wu S, Pruitt BL, Spudich J, Bernstein D; “*Hypertrophic cardiomyopathy mutations with opposite effects on β -myosin biomechanics show similar structural and biomechanical phenotypes in human induced pluripotent stem cell derived cardiomyocytes (hiPSC-CMs)*”, AHA Basic Cardiovascular Science – published abstract and Poster Presentation (07/2019)
9. **Schroer AK**, Kooiker K, Adhikari A, Jung G, Ruppel KM, Spudich JA, Bernstein D, Pruitt B; “*Substrate patterning and stiffness affect dynamics of cell spreading, contraction, and myofibril stability in iPSC-cardiomyocytes with hypercontractile myosin mutations*”, World Congress of Biomechanics – Podium Presentation (07/2018)
10. **Schroer AK**, Kooiker K, Adhikari A, Jung G, Ruppel KM, Spudich JA, Bernstein D, Pruitt B; “*Mechanobiology of myosin mutations and myofibril remodeling in iPSC-cardiomyocytes*”, Biophysical Society Annual Meeting – Published abstract and Poster Presentation (01/2018)
11. **Schroer AK**, Pardon G, Wilson R, Denisin A, Castillo E, Kooiker K, Adhikari A, Ang YS, Spudich J, Bernstein D, Conklin B, Srivastava D, Wu S, Ribeiro A, Pruitt B; “*Studying mechanobiology of myosin mutation and myofibril remodeling in iPSC-cardiomyocytes*”, NIH/AIMBE meeting – Poster Presentation (05/2017).
12. **Schroer AK**, Clark CH, Lal H, Force TL, Merryman WD; “*Cadherin-11 blocking antibody treatment improves outcomes in mice after myocardial infarction*”, International Society for Applied Cardiovascular Biology Biannual meeting – Poster Presentation (09/2016).
13. **Schroer AK**, Clark CH, Lal H, Force TL, Merryman WD; “*Cadherin-11 Exacerbates Maladaptive Remodeling After Myocardial Infarction*”, Summer Biomechanics, Bioengineering and Biotransport Conference - Podium Presentation (07/2016). *** **won PhD paper competition**
14. **Schroer AK**, Merryman WD; “*Finite Element Modeling of Cell Specific Cytoskeletal Mechanics and Focal Adhesion Forces*”, World Congress for Biomechanics - Poster Presentation (7/2014).
15. **Schroer AK**, Rhyzhova, LM, Merryman WD; “*Integrin-focal adhesion coupling and substrate stiffness affect smooth muscle alpha actin expression in fibroblasts*”, ASME Summer Bioengineering Conference - Podium Presentation (6/2012).

PROFESSIONAL SOCIETY MEMBERSHIPS

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| <i>Biophysical Society (BPS)</i> | 2017-Present |
| <i>American Heart Association (AHA)</i> | 2015-Present |
| <i>Biomedical Engineering Society (BMES)</i> | 2012-Present |

SERVICE, OUTREACH AND DEI EXPERIENCES

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| Participating in BME Faculty UNITE meetings | 2020-2021 |
| Mentoring high school student in Stanford Institutes of Medicine Summer Research Program | 2021 |
| Serving on Pediatrics Department Postdoc committee | 2019-2021 |
| Mentored undergraduate student in Stanford CVI and SSRP summer research program | 2019 and 2021 |
| Reviewing manuscripts for several journals, including Biophysical Journal. | 2011-Present |