

David Li, Ph.D.

American Liver Foundation Postdoctoral Research Fellow

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Interested in the mechanobiological pathways, diagnosis, and treatment of lipid crystals causing disease.

EDUCATION and RESEARCH EXPERIENCE

University of Pennsylvania

2021 – present

Postdoctoral Researcher, Division of Gastroenterology and Hepatology

PI: **Dr. Rebecca G. Wells**

- Discovered that **lipid crystals of cholesterol and cholesterol esters** are formed in the rat liver during high fat and cholesterol (HFHC) diets, and that these **crystals are sufficient to stiffen the fatty liver and promote fibrosis**
- Measured **liver tissue mechanical properties** using rheometry, magnetic resonance elastography, and demarcated microindentation-visualization
- Characterized **solid and liquid lipid crystal presence, accumulation, organization, and shape** in the HFHC liver using polarized light microscopy, confocal microscopy, cryo-SEM, and cryo-FIB/SEM
- **Isolated lipid crystals from tissue** and embedded them within **fibrin matrices** to measure isolated mechanical effects on model systems
- Determined lipid content of liver tissue using **lipidomics** and **synthesized artificial lipid crystals** from lipidomic standards matching the composition and structure of crystals found in the HFHC liver
- **Perfused tissues** with drugs to rapidly remove crystals (<2h) from the HFHC liver for therapeutics
- Loaded primary human hepatocytes and Huh7 cells with cholesterol to **generate crystals within cells**
- Determined that simple steatosis (fat accumulation) caused liver softening in a genetic mouse model
- Developed a novel technique to **directly associate histological features with local tissue stiffness**
- Fabricated micropillars of polyacrylamide gel with high aspect ratio using **photolithography** to assess the effects of vascular stiffness on fibrotic development

This work was awarded the American Liver Foundation Postdoctoral Research Fellowship Award and an NRSA T32 Postdoctoral Fellowship Award from the NIDDK.

Carnegie Mellon University

2014 – 2020

Received Ph.D. in Biomedical Engineering, 2020

PI: **Dr. Yu-li Wang**

- Discovered the **novel cell response** to follow the tails of retreating cells in **collective migration**, termed “contact following of locomotion”
- Fabricated a **micropatterned substrate with alternating soft and stiff regions** using 3D printing of polyacrylamide gel to observe how cells collectively segregated off of soft regions onto stiff regions
- Determined **traction forces and cell-cell forces of collectives**, and used photolithography, soft lithography, microcontact printing, local drug delivery and cellular microsurgery to investigate cellular coordination during migration.

This work resulted in a first-author publication in PNAS, which was recommended x3 in F1000 Prime.

Boston University

2012 – 2014

Received M.S. in Biomedical Engineering, 2014

PI: **Dr. Joyce Y. Wong**

- **Developed and fabricated a microfluidic device** w/ biomimetic shear and ion gradients to spin silk
- Generated a computational fluid flow model for microfluidic silk spinning devices
- Measured silk fiber mechanical properties using a uniaxial tensile tester
- Characterized protein **secondary structure of crystalline silk fibers** using ATR-FTIR

This work was awarded the Graduate Assistance in Areas of National Need Fellowship and resulted in a first-author publication in Biofabrication.

Johns Hopkins University

2008 – 2012

Received B.S. in Biomedical Engineering, 2012

PUBLICATIONS

1. **Li D**, Janmey PA, Wells RG (2023) Local fat content determines global and local stiffness in fatty livers. *FASEB Bioadv* 5:251-261.
2. de Jong IEM, Hunt ML, Chen D, Du Y, Llewellyn J, Gupta K, **Li D**, Erxleben D, Rivas F, Hall AR, Furth EE, Naji A, Liu C, Dhand A, Burdick JA, Davey MG, Flake AW, Porte RJ, Russo PA, Gaynor JW, Wells RG (2023) A fetal wound healing program after intrauterine bile duct injury may contribute to biliary atresia. *J Hepatol* S0168-8278(23)05060-2.
3. Loneker AE, Alisafaei F, Kant A, **Li D**, Janmey PA, Shenoy VB, Wells RG (2023) Lipid droplets are intracellular mechanical stressors that impair hepatocyte function. *Proc Natl Acad Sci USA* 120:e2216811120.
4. Wang YL, **Li D** (2020) Creating Complex Polyacrylamide Hydrogel Structures Using 3D Printing with Applications to Mechanobiology. *Macromol Biosci* 20:2000082.
5. **Li D**, Wang YL (2020) Mechanobiology, Tissue Development and Tissue Engineering. Principles of Tissue Engineering, eds Lanza R, Langer R, Vacanti JP, Atala A (Academic Press, MA), pp 237-256.
6. **Li D**, Wang YL (2018) Coordination of cell migration mediated by site-dependent cell-cell contact. *Proc Natl Acad Sci USA* 115:10678–10683.
7. **Li D**, Jacobsen MM, Rim NG, Backman D, Kaplan DL, Wong JY (2017) Introducing biomimetic shear and ion gradients to microfluidic spinning improves silk fiber strength. *Biofabrication* 9:025025.
8. Jacobsen MM, **Li D**, Rim NG, Backman D, Smith ML, Wong JY (2017) Silk-fibronectin protein alloy fibres support cell adhesion and viability as a high strength, matrix fibre analogue. *Scientific Reports* 7:45653.
9. Lin S, Ryu S, Tokareva O, Gronau G, Jacobsen MM, Huang W, Rizzo DJ, **Li D**, Staii C, Pugno NM, Wong JY, Kaplan DL, Buehler MJ (2015) Predictive modelling-based design and experiments for synthesis and spinning of bioinspired silk fibres. *Nature Communications* 6:6892.
10. Tokareva O, Lin S, Jacobsen MM, Huang W, Rizzo DJ, **Li D**, Simon M, Staii C, Cebe P, Wong JY, Buehler MJ, Kaplan DL (2014) Effect of sequence features on assembly of spider silk block copolymers. *Journal of Structural Biology* 186:412-419.
11. Sunshine JC, Akanda MI, **Li D**, Kozielski KL, Green JJ (2011) Effects of base polymer hydrophobicity and end group modification on polymeric gene delivery. *Biomacromolecules* 12:3592-3600.

Manuscripts in Preparation / in Press

1. **Li D**, Loneker AE, Saifraou Y, Ford J, Mihelc E, Levental KR, Levental I, Sack I, Janmey PA, Wells RG (2024) Dietary cholesterol forms intrahepatic crystals and stiffens the steatotic liver. *BioRxiv* 2024.12.29.630682 [Preprint]. DOI: 10.1101/2024.12.29.630682.
2. Byfield FJ, Eftekhari B, Kaymak-Loveless K, Mandal K, **Li D**, Wells RG, Chen W, Brujic J, Bergamaschi G, Wuite GJL, Patteson AE, Janmey PA (2024) Metabolically intact nuclei are fluidized by the activity of the chromatin remodeling motor BRG1. *Biophysical Journal* (in press, available online)

FELLOWSHIPS

- American Liver Foundation Postdoctoral Research Fellowship Award 2023 – 2024
- Ruth L. Kirschstein Institutional Research Service Award T32 Fellowship (NIDDK) 2022 – 2024
- Graduate Assistance in Areas of National Need Fellowship 2013

AWARDS AND HONORS

- Research article recommended x3 by F1000 Prime, Faculty Opinions 2019
- BMES Annual Meeting Reviewer's Choice Award 2014

SCIENTIFIC PRESENTATIONS

PODIUM TALKS

1. "Increased liver cholesterol storage induces lipid crystal formation that stiffens the tissue." Oral presentation at 2024 BMES Annual Meeting, Baltimore, MD.
2. "Dietary cholesterol forms intrahepatic crystals and stiffens the steatotic liver." Oral presentation at 2024 Summer Biomechanics, Bioengineering, and Biotransport Conference, Lake Geneva, WI.

3. "Dietary cholesterol stiffens the steatotic liver." Oral presentation at 2023 BMES Annual Meeting, Seattle, WA.
4. "Dietary cholesterol alters lipid deposit organization and stiffens the steatotic liver." Seminar talk at PS-ON/CSBC Cell & Tissue Mechanics Group 2023, online.
5. "Local fat content determines global and local stiffness in fatty livers." Microsymposium talk at Cell Bio 2022 - An ASCB|EMBO Annual Meeting, Washington, DC.
6. "Anisotropic cues promote symmetry breaking to initiate migration of adherent cells." Microsymposium talk at 2019 ASCB|EMBO Annual Meeting, Washington, DC.
7. "Cell migration coordination by site-dependent cell-cell contact." Microsymposium talk at 2018 ASCB|EMBO Annual Meeting, San Diego, CA.

POSTER TALKS

1. "Local fat content determines global and local stiffness in fatty livers," Cell Bio 2022 – An ASCB|EMBO Annual Meeting, Washington DC.
2. "Local fat content determines global and local stiffness in livers with simple steatosis." 2022 NIH Center for Molecular Studies in Digestive and Liver Diseases Symposium, Philadelphia, PA.
3. "A microfabricated 3D model of vascular mechanics in tissues to probe cell responses to vascular pathologies." 2022 Penn-Stanford CVI Symposium, Philadelphia, PA.
4. "Anisotropic cues promote symmetry breaking to initiate migration of adherent cells." 2019 ASCB|EMBO Annual Meeting, Washington DC.
5. "Cell migration coordination by site-dependent cell-cell contact." 2018 ASCB|EMBO Annual Meeting, San Diego, CA.
6. "Location-dependent responses to epithelial cell-cell contact – tail following complements contact inhibition to facilitate collective migration." 2017 ASCB|EMBO Annual Meeting, Philadelphia, PA.
7. "Biomimetic modifications to microfluidic silk spinning." 2014 BMES Annual Meeting, San Antonio, TX.
8. "Effects of polymer/DNA self-assembly conditions on nanoparticle size and transfection efficacy." 2010 JHU BME Undergraduate Research Day, Baltimore, MD.
9. "Analysis of a combinatorial polymer library for gene delivery vectors." 2009 JHU BME Undergraduate Research Day, Baltimore, MD.

TEACHING EXPERIENCE

- Lecturer / lab instructor for CEMB Graduate Training Boot Camp 2024
- Lecturer / lab instructor for CEMB Summer Research Experience for Teachers Program 2022 – 2024
- Graduate of the Future Faculty Program from the Eberly Center for Teaching Excellence 2016 – 2020
- Teaching assistant and guest lecturer for Introduction to Biomedical Engineering Lab 2015 – 2016
- Teaching assistant for Principles and Applications of Tissue Engineering 2013 – 2014
- Guest instructor for BU UDesign Summer Camp 2013
- Teaching assistant for Biomaterials I and II 2011 – 2012

MENTORSHIP AND SERVICE

- Mentor for Belén Sirera Conca, an international PhD visiting student 2024
- Mentor for middle and high school teachers from underserved communities in Philadelphia 2024
- Ad hoc peer reviewer for Scientific Reports 2024
- Mentor for Zina Helal, a CEMB undergraduate researcher 2021 – 2022
- Graduate of the Mentor Training for Summer Researchers Program 2021
- Volunteer judge for the annual PJAS competition of local middle/high school students 2017 – 2018

PROFESSIONAL MEMBERSHIPS

Biomedical Engineering Society, American Society of Mechanical Engineers, American Society for Cell Biology, European Molecular Biology Organization, American Association for the Advancement of Science