Center for Alzheimer's and Neurodegenerative Diseases / Department of Biophysics UT Southwestern Medical Center NL10.116A / 5323 Harry Hines Blvd. / Dallas, Texas 75390-8813 Email: Lorena.saelicesgomez@utsouthwestern.edu Phone: (323) 847 9327

EDUCATION

Ph. D. Cum Laude in Biochemistry, University of Seville, Spain - 12/2010

Thesis title: "Structure-function relationship of glutamine synthetase in *Synechocystis* sp. 6803" Advisors: Francisco Javier Florencio Bellido and Maria Isabel Muro Pastor

Research Sufficiency Diploma (now called master's degree) in Biochemistry, University of Seville, Spain – 11/2007

Thesis title: "Protein-protein regulation of glutamine synthetase in *Synechocystis* sp. 6803" Advisor: Francisco Javier Florencio Bellido

BSc/MSc in Biology, University of Seville, Spain - 08/2005

Thesis: "Identification of genes in the *Neurospora* carotenoid pathway" Advisor: Francisco Javier Avalos Cordero

PROFESSIONAL EXPERIENCE:

Peter O'Donnell Jr. Brain Institute Investigator, UT Southwestern Medical Center, USA 03/2022 – present

Assistant Professor at UT Southwestern Medical Center, USA

06/2020 - present

Center for Alzheimer's and Neurodegenerative Diseases. My lab applies crystallography and cryoelectron microscopy to obtain atomic information of amyloid structures, which is later used to design tools for the clinic. Our attention is directed to transthyretin amyloidosis and Alzheimer's disease.

Associate Project Scientist at UCLA, USA

06/2018 - 05/2020

Advisor: Prof. David Eisenberg. We used cryo-electron microscopy to obtain structural information of amyloid fibrils extracted from amyloidosis patients.

Assistant Project Scientist at UCLA, USA

06/2015 - 05/2018

Advisor: Prof. David Eisenberg. Our project was focused on the structural and molecular understanding of protein aggregation, to developed new potential therapeutic strategies for transthyretin amyloidosis and Alzheimer's disease.

Marie-Curie Postdoctoral Fellow at ETH Zürich, Switzerland

06/2014 - 05/2015

Advisor: Prof. Roland Riek. We optimized and further characterized the previously developed structure-based inhibitor of amyloid-beta, whose aggregation is proposed to be the cause of Alzheimer's disease.

Marie-Curie Postdoctoral Fellow at UCLA, USA

06/2012 - 05/2014

Advisor: Prof. David Eisenberg. We developed novel potential therapeutic strategies for transthyretin amyloidosis and Alzheimer's disease, by the structure-based design of amyloid-aggregation inhibitors of transthyretin and amyloid-beta, respectively.

Postdoctoral Associate at University of Seville, Spain

12/2010 - 05/2012

Advisors: Profs. Francisco Javier Florencio Bellido and Maria Isabel Muro Pastor. We identified a three-amino acid core to be the binding interface of glutamine synthetase type I (GSI) of *Synechocystis* sp. PCC 6803, to the inactivating factors IF7 and IF17.

Ph. D. graduate student at University of Seville, Spain

09/2005 - 12/2010

Advisors: Profs. Francisco Javier Florencio Bellido and Maria Isabel Muro Pastor. We characterized the interaction of *Synechocystis* GSI and the inactivating factors IF7 and IF17. We found three conserved arginines on IF7 and IF17 that are critical for the inactivation.

Visiting Research Associate at UCLA, USA

08/2009 - 12/2009

Advisors: Profs. David Eisenberg and Duilio Cascio. We determined the x-ray structure of *Synechocystis* GSI and its variant N456K, which is a permanently active designed mutant.

Visiting Associate at the Institute of Biomedicine of Valencia, Spain

09/2007 - 12/2017

Advisor: Prof. Vicente Rubio. A short stay at the Rubio Lab provided an introduction to structural biology and x-ray crystallography.

Honor Collaborator at the Department of Genetics of the University of Seville, Spain

08/2005 - 08/2006

Advisor: Prof. Francisco Javier Ávalos Cordero. We completed the characterization of the synthesis pathway of the xanthophyll neurosporaxanthin in *Neurospora crassa*, and identified the gene responsible for torulene cleavage in the *Neurospora* carotenoid pathway.

Undergraduate researcher at the University of Seville, Spain

07/2003 - 08/2005

Advisor: Prof. Francisco Javier Ávalos Cordero. We studied the genetic pathway of synthesis of the xanthophyll neurosporaxanthin in *Neurospora crassa*.

Undergraduate researcher at the University of Seville, Spain

09/2007 - 12/2007

Advisor: Prof. Aurelio Serrano. We were interested in the engineering of the central pathway in the metabolism of carbon in bacteria and yeast.

SCIENCE AND TECHNOLOGY SPECIALTIES

Scientific interests: amyloid diseases, neurodegenerative diseases, transthyretin amyloidosis, cardiac amyloidosis, structural biology methods, and cryo-electron microscopy advances.

Technical skills: Biochemical analysis of proteins and nucleic acids, cell biology, structure determination and analysis by x-ray crystallography, NMR, and cryo-electron microscopy, transmission electron microscopy imaging, peptide design, amyloid fibril extraction, tissue staining (immunohistochemistry and die staining), fluorescence and confocal microscopy imaging, and animal research.

PATENTS AND PUBLICATIONS

PATENTS:

International Patent - Application No. PCT/US17/40103. "Inhibition of the aggregation of transthyretin by specific binding of peptides to aggregation-driving segments". Inventors: Eisenberg DS, **Saelices L**

Provisional Application No. 63/352,521. "Structure-based probe for detection of transthyretin amyloid fibrils and aggregates". Inventors: **Saelices L**, Pedretti R.

RESEARCH ARTICLES: *Corresponding author

- Li L, Nguyen B, Mullapudi V, Saelices L, Joachimiak LA. (2023) Disease-associated patterns of acetylation stabilize tau fibril formation. Preprint available on bioRxiv. 2023.01.10. doi: <u>https://doi.org/10.1101/2023.01.10.523459</u>
- Balana AT, Mahul-Mellier AL, Nguyen BA, Horvath M, Javed A, Hard ER, Jasiqi Y, Singh P, Afrin S, Pedretti R, Singh V, Lee V, Luk KC, Saelices L, Lashuel HA, Pratt MR (2023) O-GlcNAc modification forces the formation of an a-Synuclein amyloid-strain with notably diminished seeding activity and pathology. Preprint available on *bioRxiv*. 2023.03.08; doi: <u>https://doi.org/10.1101/2023.03.07.531573</u>

- 3. Nguyen BA, Afrin S, Singh V, Ahmed Y, Pedretti R, Fernandez-Ramirez M, Benson MD, Sawaya MR, Cao Q, Boyer D, Pope A, Wydorski PM, Chhapra F, Eisenberg DS, Saelices L* (2022). Structural polymorphism of amyloid fibrils in cardiac ATTR amyloidosis revealed by cryo-electron microscopy. Preprint available on *bioRxiv* 2022.06.21.496949; doi: <u>https://doi.org/10.1101/2022.06.21.496949</u>
- 4. Cao Q, Boyer DR, Sawaya MR, Abskharon R, Saelices L, Nguyen BA, Lu J, Lin H, Kandeel F, Eisenberg DS (2021) Cryo-EM structures of hIAPP fibrils seeded by patient-extracted fibrils reveal new polymorphs and conserved fibril cores. Nat. Struc. Mol. Biol. 28(9):724-730.
- 5. Tayeb-Fligelman E, Cheng X, Tai C, Bowler JT, Griner S, Sawaya MR, Seidler PM, Jiang YW, Lu J, Rosenberg GM, Salwinski L, Abskharon R, Zee C, Hou K, Li Y, Boyer DR, Murray KA, Falcon G, Anderson DH, Cascio D, Saelices L, Damoiseaux R, Guo F, Eisenberg DS (2021) Inhibition of amyloid formation of the Nucleoprotein of SARS-CoV-2.

Preprint available on *bioRxiv* 2021.03.05.434000; doi: <u>https://doi.org/10.1101/2021.03.05.434000</u>

6. Cao Q, Anderson DH, Liang WY, Chou J, Saelices L* (2019) The inhibition of cellular toxicity of amyloid-beta by dissociated transthyretin. The Journal of Biological Chemistry, August 7;jbc.RA120.013440

Preprint available on *bioRxiv* (2019) doi: <u>https://doi.org/10.1101/852715</u>

- Work featured on:
 - <u>ASBMBToday</u>
 - <u>ScienceDaily</u>
 - <u>New Medical Life Science</u>
 - <u>CAND Website</u>
 - UTSW website
- 7. Saelices L, Nguyen BA, Chung K, Wang Y, Ortega A, Lee JH, Coelho T, Bijzet J, Benson MD, Eisenberg DS (2019) A pair of peptides inhibits seeding of the hormone transporter transthyretin into amyloid fibrils. The Journal of Biological Chemistry 294(15):6130-6141 Preprint available on bioRxiv (2018) doi: <u>https://doi.org/10.1101/354555</u>
- 8. Saelices L*, Pokrzywa M, Pawelek K, Eisenberg DS. (2018) Assessment of the effects of transthyretin peptide inhibitors in Drosophila models of neuropathic ATTR. Neurobiology of Disease 120:118-125. - Recognized as one of most influential studies by Journal. Preprint available on bioRxiv (2018) <u>https://doi.org/10.1101/354555</u>
- **9. Saelices L,** Chung K, Lee JH, Cohn W, Whitelegge JP, Benson MD, Eisenberg DS (2018) Amyloid seeding of transthyretin by ex vivo cardiac fibrils and its inhibition. *Proceedings of the National Academy of Sciences* 115(29):E6741-E6750
- **10. Saelices L,** Sievers SA, Sawaya MR, Eisenberg, DS (2018) Crystal structures of amyloidogenic segments of human transthyretin. *Protein Science* 27(7):1295-1303
- Krotee P, Griner SL, Sawaya MR, Cascio D, Rodriguez JA, Shi D, Philipp S, Murray K, Saelices L, Lee J, Seidler P, Glabe CG, Jiang L, Gonen T, Eisenberg DS (2018) Common fibrillar spines of amyloid-β

and human islet amyloid polypeptide revealed by microelectron diffraction and structure-based inhibitors. *The Journal of Biological Chemistry* 293(8):2888-2902.

- Pantoja-Uceda D, Neira JL, Saelices L, Robles-Rengel R, Florencio FJ, Muro-Pastor MI, Santoro J (2016) Dissecting the Binding between Glutamine Synthetase and Its Two Natively Unfolded Protein Inhibitors. Biochemistry, 55(24), 3370-3382.
- **13. Saelices L,** Johnson LM, Liang WY, Sawaya MR, Cascio D, Ruchala P, Whitelegge J, Jiang L, Riek R, Eisenberg DS (2015) Uncovering the Mechanism of Aggregation of Human Transthyretin. *The Journal of Biological Chemistry* 290: 28932-28943.

Work featured on:

- F1000 <u>f1000.com/prime/725851054</u>
- EUROPA: Research Information Centre
- UCLA-DOE website
- 14. Saelices L, Robles-Rengel R, Muro-Pastor MI, Florencio FJ (2015) A core of three amino acids at the carboxyl-terminal region of glutamine synthetase defines its regulation in cyanobacteria. *Molecular Microbiology* 96(3):483-96
- **15. Saelices L**, Galmozzi CV, Florencio FJ, Muro-Pastor MI, Neira JL (2011) The inactivating factor of glutamine synthetase IF17 is an intrinsically disordered protein, which folds upon binding to its target. *Biochemistry* 50(45):9767-78.
- 16. Saelices L, Galmozzi CV, Florencio FJ, Muro-Pastor MI (2011) Mutational analysis of the inactivating factors, IF7 and IF17 from Synechocystis sp. PCC 6803: critical role of arginine amino acid residues for glutamine synthetase inactivation. *Molecular Microbiology* 82(4):964-75
- 17. Galmozzi CV, Saelices L, Florencio FJ, Muro-Pastor MI (2010) Posttranscriptional regulation of glutamine synthetase in the filamentous Cyanobacterium Anabaena sp. PCC 7120: differential expression between vegetative cells and heterocysts. Journal of Bacteriology 192, 4701-11
- 18. Saelices L, Youssar L, Holdermann I, Al-Babili S, Avalos J (2007) Identification of the gene responsible for torulene cleavage in the Neurospora carotenoid pathway. Molecular Genetics and Genomics 278, 527-37

REVIEWS:

1. Hood CJ, Hendren NS, Pedretti R, Roth LR, **Saelices L**, Grodin JL (2022) Update on Disease-Specific Biomarkers in Transthyretin Cardiac Amyloidosis. *Curr Heart Fail Rep.* Online ahead of print.

BOOK CHAPTERS:

 Saelices L, Galmozzi CV, Florencio FJ, Muro-Pastor MI (2011) Chapter of the book "Avances en el metabolismo del nitrógeno. Aproximación molecular al estudio del ciclo del nitrógeno en la biosfera y sus repercusiones agronómicas y medioambientales". Servicio de Publicaciones de la Univ. de Córdoba.

STRUCTURES PUBLISHED ON PDB:

Full-length transthyretin variants: 6E71, 6E75, 6E76, 4TLU, 4TNF, 4TNG, 4TKW, 4TL4, 4TL5, 4TLK, 4TLS, 4TLT, 4TM9, 4TNE

Full-length transthyretin variants with stabilizing ligands: 6E6Z, 6E70, 6E72, 6E74, 6E73, 6E77, 6E78 Peptides in their amyloid state: 6C3F, 6C3G, 6C3S, 6C3T, 6C4O, 6C88, 5VOS, 4XFN, 4XFO Glutamine synthetase: 3NG0

TEACHING AND MENTORING

09/2005 – present: Mentoring and supervision

- Rocio Robles (2 months) Germany, biotech company
- Wilson Liang (14 months) UCSD, pharmacy school
- Joshua Chou (7 months) San Diego, biotech company
- Priscilla Dietrich (4 months) ETH Zurich, graduate school
- Kevin Chung (36 months) Yale University, graduate school
- Ji H. Lee (30 months) UC Davis, Master's in criminology
- Stephen Yu (7 months) Los Angeles, biotech company
- Shannon Esswein (2 months) Caltech, MD-PhD
- Nikita Bhat (6 months)
- Yifei Wang (24 months) Duke University, master's in biochemistry
- Alfredo Ortega (17 months)
- Tai Michaels (3 months) Yale University, biomedical engineering major.
- Qiongfang Zhang (12 months) Graduate student at Columbia University
- Li-Uen Lin (12 months) currently applying to medical school and Ph.D. programs
- Timothy Kramer (12 months)
- Binh A. Nguyen, Ph.D. (2 years at UCLA + September 2020-present at UTSW) <u>current</u> Instructor in my laboratory
- Rose Pedretti (February 2021) <u>current</u> graduate student in my laboratory
- Pawel Wydorski (1.5 months) graduate student at UTSW
- Alexander Pope (1.5 months) graduate student at UTSW
- Shumaila Afrin, Ph.D. (February 2021-present) <u>current</u> postdoctoral student in my laboratory
- Maria del Carmen Fernandez Ramirez (June 2021-present) <u>current</u> postdoctoral student in my laboratory
- Yasmin Ahmed (October 2021-present) <u>current</u> Research Technician in my laboratory
- Farzeen Chhapra (4 months) Research Assistant in my laboratory
- Justyna Kurleto (1.5 months) rotation student in my laboratory
- Jacob Canepa (1.5 months) rotation student in my laboratory
- Alex Wosztyl (1.5 months) rotation student in my laboratory
- Virender Singh (February 2022-present) <u>current</u> postdoctoral student in my laboratory
- Preeti Singh (June 2022-present) <u>current</u> Research Technician in my laboratory
- Lanie Wang (June 2022-present) <u>current</u> Research Technician in my laboratory
- Anna Yakubovska (June 2022-present) <u>current</u> BioLab Fulbright graduate assistant in my laboratory
- Devin Keely (January 2023-present) <u>current</u> Research Assistant in my laboratory
- Luis Cabrera Hernandez (January 2023-present) <u>current</u> graduate student in my laboratory

08/2022: "Scientific Writing and Reading" for the UTSW Graduate School Core Course
08/2021: "Scientific Writing and Reading" for the UTSW Graduate School Core Course
08/2020 - 09/2020: Teaching Literature Discussion for the UTSW Graduate School Core Course
05/2018 - 05/2020: Mentor for the student exchange program of the UCLA-DOE Center for Global

Mentoring in collaboration with the Vietnam National University, Ho Chi Minh City"

- Binh A. Nguyen, Ph.D.
- 2018: Teaching SRP99
- Nikita Bhat
- Yifei Wang

2018: Teaching SRP199 (upper-division research course)

- Kevin Chung
- Qiongfang Zhang
- Li-Uen Lin

2016: Volunteer in the CNSI at UCLA High School Nanoscience Program for high school teachers.

2015: Created a video lesson for high school students followed by a Q&A online session

09/2014 – 02/2015: Teaching assistant in Physical Chemistry, ETH Zürich, Switzerland

09/2014 – 02/2015: Teaching assistant in General Chemistry, ETH Zürich, Switzerland

2006 – 2010: Teaching assistant in Biochemistry and Molecular Biology of Plants, University of Seville, Spain

2006 – 2010: Teaching assistant in Biochemistry, University of Seville, Spain

09/2005 – 02/2006: Teaching assistant in Genetics, University of Seville, Spain

2003 – 2005: Tutor in Genetics and Biochemistry

INVITED TALKS

2023: Brain Injury and Dementia Symposium – UT Southwestern Medical Center, Dallas, USA

 Structural and molecular study of the neuroprotection of transthyretin over amyloid-beta aggregation

2022: International Society for Amyloidosis (ISA) meeting – Heidelberg, Germany

 Cryo-EM study of cardiac ATTR fibrils. Structure-based development of anti-seeding inhibitors and detection probes

2022: USC, Los Angeles, USA

 Cryo-electron microscopy study of structural polymorphism of amyloid fibrils in ATTR amyloidosis

2022: COBRE Symposium in Structural Biology, Oklahoma, USA

Learning from structures of amyloid assemblies to develop clinical tools in amyloidosis

2022: SURF/AMGEN Seminar, UTSW, Dallas, USA

 Structural variability of amyloid fibrils revealed by cryo-electron microscopy and translated into potential clinical tools **2022:** National Centers for Cryo-Electron Microscopy seminar series "CryoEM Current Practices Webinar". NCCAT CryoEM Center hosting

 Cryo-EM study of cardiac ATTR fibrils and structure-based design of clinical tools for ATTR amyloidosis

2022: Universidad Central del Caribe (UCC) School of Medicine in Puerto Rico. Online.

- Exploiting atomic structures to develop clinical tools in amyloidosis. Recent advances using cryo-electron microscopy
- 2022: 16th International Conference on Alzheimer's & Parkinson's Diseases (AD/PD) Barcelona, Spain
 - Amyloid seeding emerges as a potential target for the treatment of amyloidosis.
- 2021: Plenary talk at the 2021 Cajal Xmas Meeting Madrid, Spain
 - The dissociation of transthyretin as a neuroprotective strategy to inhibit amyloid-beta aggregation in Alzheimer's Disease.
- **2021:** The FASEB Protein Aggregation Conference: Function, Dysfunction, and Disease, online.
 - Could amyloid seeding represent a therapeutic approach for late-stage transthyretin amyloidosis?
- 2021: VA/UCLA Grand Rounds, UCLA, Los Angeles, USA.
 - Impostor Syndrome: Common Profiles, Causes and Solutions.
- 2021: WISE group, UCLA, Los Angeles, USA.
 - Impostor Syndrome and its implications for women in academia.
- **2020:** Boston University, online.
 - Structures to defeat transthyretin amyloidosis.
- 2020: UTSW Graduate School, Dallas, USA.
 - Impostor Syndrome.
- 2019: Center for Alzheimer's and Neurodegenerative Diseases, UTSW, Dallas, USA.
 - Blocking an unforeseen fundamental route to transthyretin amyloidosis
- 2019: Institute for Neurodegenerative Diseases, UCSF, San Francisco, USA.
 - Understanding the molecular basis of transthyretin amyloid aggregation
- 2019: FASEB SRC, Snowmass, Colorado, USA.
 - "Amyloid seeding of human transthyretin"
- 2019: FASEB NextGen Seminar, Snowmass, Colorado, USA.
 - "Amyloid seeding of transthyretin and its inhibition"
- 2018: Seminar Series, Department of Biological Chemistry, UCLA, Los Angeles, USA.
 - " "Amyloid seeding of transthyretin by ex-vivo cardiac fibrils: inhibition and implications"

2017: ADRx, Thousand Oaks, USA.

- "Inhibition of seeding caused by disease-related amyloid fibrils of transthyretin"
- 2015: ADRx, Thousand Oaks, USA.
 - "Design of peptide inhibitors for amyloid proteins. Amyloid-beta and transthyretin"
- 2015: Center for Translational Exosome Research in Neurodegenerative Disease EXPOSIUM
 - "TTR-derived peptide inhibitors of Amyloid-beta aggregation and cytotoxicity"
- 2014: UCLA Alzheimer's Research Center, Los Angeles, USA.
 - "Amyloid Beta Toxicity Inhibition"
- 2013: The Scripps Research Institute. San Diego, USA.
 - "Inhibition of transthyretin amyloid fibril formation"
- 2010: National Meeting on Metabolism of Nitrogen. Benalauría, Málaga, Spain.
 - "Structural and functional study of the glutamine synthetase type I of Synechocysts sp. 6803"
- 2009: IBVF Symposium. Seville, Spain.
 - "Regulation of glutamine synthetase activity in cyanobacteria. Identification of the regions involved in the protein-protein interaction between GS and IFs"

FELLOWSHIPS, HONORS AND AWARDS

- 2022: Welch Foundation Research Award
- 2021: Izasa Scientifica Award for best Plenary Talk at the Xmas Cajal Meeting
- 2021: NIH-NHLBI DP2 New Innovator Award
- 2021: American Heart Association Career Development Award
- 2021: Distinguished Researcher Award from the President's Research Council
- 2019: UCLA Molecular Biology Institute Productivity Award
- 2019: FASEB NextGen Award
- 2019: The Company of Biologist Award for Scientific Meetings to organize the 2019 FASEB NextGen
- 2018: Travel Award for The XVIth International Society of Amyloidosis 2018 Symposium.
- 2018: UCLA Clinical and Translational Science Institute (CTSI) Voucher Award
- 2017: Amyloidosis Foundation David C. Seldin, MD, PhD Memorial Research Grant, 2017 and 2018
- 2016: Presentation Prize at The XVth International Society of Amyloidosis 2016 Symposium.
- 2016: Travel Award for The XVth International Society of Amyloidosis 2016 Symposium.
- 2016: Amyloidosis Foundation Research Grant, 2016
- **2016:** The Company of Biologist Award for Scientific Meetings to organize the 2016 Gordon Research Seminar

- 2012: Marie-Curie Fellowship for Postdoctoral Studies from People Programme (Marie Curie Actions) of the European Union's Seventh Framework Programme (FP7/2007-2013)
- 2009: Travel Fellowship for PhD studies, awarded by the Government of Spain
- 2007: Travel Fellowship for PhD studies, awarded by the Government of Spain
- 2006: FPI Fellowship for PhD studies, awarded by the Government of Spain
- 2005: Honorary Collaborator of the Dept. of Genetics of University of Seville, Spain
- 2004: Fellowship for Undergraduate Research Training, awarded by the Government of Spain
- 2001-2005: Yearly Scholarships for Undergraduate Studies, awarded by the Government of Spain

RESEARCH SUPPORT (last 6 years)

Current Research Support

NIH NHLBI / 1R01HL160892-01A1 07/01/2022-06/30/2027

Identifying subclinical transthyretin cardiac amyloidosis in asymptomatic carriers of the V122I TTR allele

This project aims to identify evidence of cardiac amyloid progression prior to hereditary ATTR cardia disease onset in V122I mutation carriers.

NIH NIA / 1RF1AG078888-01

08/15/2022-07/31/2025

(PI: Lukasz Joachimiak, Role: Co-I)

(PI: Justin Grodin, Role: Co-I)

J-domain protein conformational selectivity for tau in disease

This project aims to identify how the diverse family of JDP molecular chaperones discriminate and bind different tau conformations.

Welch Foundation Research Grant - I-2121-20220331 6/1/2022-5/31/2025

Cryo-electron microscopy study of the conformational switch of monomeric tau that drives its amyloid aggregation

This study aims to identify the local structures that define this conformational switch under both anti-and pro- amyloidogenic conditions of tau and determine their structures by cryo-electron microscopy aided by a recently developed scaffolding system and conformational-specific nanobodies to be developed in our laboratory.

NIH NHLBI / DP2 HL163810-01 09/01/2021-08/31/2026

Closing the gap between structural biology and translational science for amyloid diseases

This project aims to establish a multidisciplinary high-risk program to obtain atomic information about amyloid fibrils using cryo-electron microscopy, to analyze their pathological role in a co-culture cell system to be developed in our laboratory, and to design structure-specific tools to use in the clinic.

(PI: Lorena Saelices Gomez)

(PI: Lorena Saelices Gomez)

(PI: Saelices/Eisenberg)

UT Southwestern Start-up Funds 06/08/2020 - 06/07/2028

The study of structural and mechanistic basis for self-assembling amyloid proteins.

 This study aims to better define amyloid structures associated with ATTR and Alzheimer's disease and apply this understanding to develop tools to advance our knowledge about the biology of protein aggregation.

American Heart Association Career Development Award 07/01/2021 - 06/30/2024

Study of the phenotypic variability of cardiac amyloidosis to develop peptide-based diagnostic tools.

In this study, we will obtain atomic information of fibers extracted from systemic amyloidosis patients using cryo-electron microscopy to evaluate a potential association between different fibril forms and disease manifestation. We will also design peptides to detect these fibrils in blood and biopsies from patients with amyloidosis.

Completed Research Support

Distinguished Researcher Award from the President's Research Council (PI: Lorena Saelices Gomez) 06/01/2021 - 05/31/2022

Biological Mechanisms of Transthyretin Amyloidosis.

 This study aims to develop a novel cell-based system to study the impact of structural polymorphism in cell and tissue toxicity in systemic amyloidosis.

NIH NIA RF1AG048120

(PI: David Eisenberg; Role: Project Scientist)

04/2019 - 03/2024

Development of inhibitors and diagnostics for amyloid diseases.

 This project aims to develop inhibitors and diagnostics for systemic amyloidoses, including Alzheimer's, transthyretin and light chain amyloidoses. I assisted and coordinated the application for this R01. My role was scientist.

NIH - R01 AG048120 06/2014 - 05/2019 (PI: David Eisenberg: Role: Project Scientist)

Plus, two associated administrative supplements R01AG048120-03S1 and R01AG048120-04S1 Development of inhibitors for systemic amyloid diseases.

The goal of this project was to develop inhibitors for systemic amyloidosis, including transthyretin and light chain amyloidoses. During this grant, we have designed inhibitors of the aggregation of transthyretin. We designed the inhibitor against the structure of the aggregation-driving segments and tested them *in vitro*. I assisted with the application for this R01. My role was scientist.

National Center for Advancing Translational Sciences

UCLA CTSI Grant UL1TR001881

07/2018 – 03/2019

Evaluation of anti-amyloid peptide inhibitors of transthyretin fibril formation in a mouse model of ATTR

 The goal of this grant is to evaluate peptide inhibitors of transthyretin amyloidosis in a mouse model of the disease.

(PI: Lorena Saelices Gomez)

(PI: Lorena Saelices Gomez)

(PI: Lorena Saelices Gomez)

Amyloidosis Foundation David C. Seldin Memorial Research Grant Project number 20170827 01/2017 – 12/2019

Inhibition of transthyretin aggregation in Drosophila by modified peptide inhibitors (Renewal)

 The goal of this grant is to evaluate peptide inhibitors of transthyretin amyloidosis in a disease model of *Drosophila*, in combination with transthyretin stabilizers such as tafamidis (marketed by Pfizer in Europe).

Amyloidosis Foundation Research Grant 01/2016 – 12/2016

Inhibition of transthyretin aggregation in Drosophila by modified peptide inhibitors.

 The goal of this grant is to evaluate peptide inhibitors of transthyretin amyloidosis in a disease model of *Drosophila melanogaster*, the fruit fly.

FP7/2007-2013 Marie-Curie IOF Postdoctoral Fellowship(PI: Lorena Saelices Gomez)06/2012 - 05/2015

Structural biology of amyloid fibrils and design of structure specific therapeutics

 During this grant, we identified two segments of transthyretin that drive protein aggregation, causing the abnormal deposition that causes transthyretin amyloidosis. We determined the crystal structure of these segments in their amyloid form.

OTHER ACTIVITIES:

- 2025: Elected co-chair of the 2025 FASEB Protein Aggregation Conference
- **2023:** Ph.D. Committee Chair, Candidate: Jaime Vaquer-Alicea (Laboratory of Marc Diamond), UT Southwestern.
- 2023: Elected co-organizer of the 2023 FASEB Protein Aggregation Conference
- 2022: Session Chair at the 16th International Conference on Alzheimer's & Parkinson's Diseases (AD/PD)
- **2021:** Chair of the Diversity and Inclusion workshop at the 2021 FASEB Protein Aggregation Conference: Function, Dysfunction, and Disease.
- **2021-present:** Ph.D. Committee Chair, Candidate: Carla Madrid (Laboratory of Kendra Frederick), UT Southwestern.
- **2021-present:** Ph.D. Committee Chair, Candidate: Sofia Bali (Laboratory of Lukasz Joachimiak), UT Southwestern.
- 2019: Chair of the first FASEB Next Generation Seminar on Protein Aggregation. Colorado, USA
- 2017 2020: Consultant and Advisor, ADRx Inc
- 2017 present: Member of the International Society of Amyloid
- 2017 present: Member of the American Heart Association
- 2016: Chair of the Neurobiology of Brain Disorders Gordon Research Seminars. Girona, Spain.
- 2015 present: Member of the American Society for Biochemistry and Molecular Biology
- 2014: Ph.D. Committee Chair, Candidate: Guillermo Rodríguez Bey, University of Cadiz, Spain.
- **2010 present:** Ad-hoc reviewer (Journal of Biophysics, Biochemistry, Nature Communications, PlosOne, Journal of Neuroscience, Amyloid, Brain Sciences, Biophysics Journal, Therapeutics and Clinical Risk Management)