

Center for Alzheimer's and Neurodegenerative Diseases
UT Southwestern Medical Center
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EDUCATION

Ph. D. Cum Laude in Biochemistry, University of Seville, Spain - December 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 - November 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 - August 2005

Thesis: "Identification of genes in the *Neurospora* carotenoid pathway"

Advisor: Francisco Javier Avalos Cordero

PROFESSIONAL EXPERIENCE:

Assistant Professor at UT Southwestern Medical Center, USA

06/2020 – present

Center for Alzheimer's and Neurodegenerative Diseases. My lab applies crystallography and cryo-electron 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 are currently using 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.

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**

RESEARCH ARTICLES:

1. 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*, Submitted
***Corresponding author**
Preprint available on *bioRxiv* (2019) doi: <https://doi.org/10.1101/852715>
2. **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: <https://doi.org/10.1101/354555>
3. **Saelices L***, Pokrzywa M, Pawelek K, Eisenberg DS. (2018) [Assessment of the effects of transthyretin peptide inhibitors in Drosophila models of neuropathic ATTR](#). ***Corresponding author**
Neurobiology of Disease 120:118-125. - Recognized as one of most influential studies by *Journal*.
Preprint available on *bioRxiv* (2018) <https://doi.org/10.1101/354555>
4. **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
5. **Saelices L**, Sievers SA, Sawaya MR, Eisenberg, DS (2018) [Crystal structures of amyloidogenic segments of human transthyretin](#). *Protein Science* 27(7):1295-1303
6. 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- \$\beta\$ and human islet amyloid polypeptide revealed by microelectron diffraction and structure-based inhibitors](#). *The Journal of Biological Chemistry* 293(8):2888-2902.
7. 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.

8. **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 [f1000.com/prime/725851054](https://doi.org/10.1002/f1000.com/prime/725851054)
 - EUROPA: Research Information Centre
 - UCLA-DOE website
9. **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
10. **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.
11. **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
12. 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
13. **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

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

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) – Accepted by UCI and Columbia University for graduate school
- Li-Uen Lin (12 months) – currently applying to medical school
- Timothy Kramer (12 months)
- Binh A. Nguyen, Ph.D. (2 years) – UCLA

2018 – present: 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

TALKS

2019: Personal invitation. Center for Alzheimer's and Neurodegenerative Diseases, UTSW, USA.

- Blocking an unforeseen fundamental route to transthyretin amyloidosis

2019: Personal invitation. Online presentation. Institute for Neurodegenerative Diseases, UCSF, 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, USA.

- "Amyloid seeding of transthyretin by ex-vivo cardiac fibrils: inhibition and implications"

2017: Personal invitation. ADRx, Thousand Oaks, USA.

- "Inhibition of seeding caused by disease-related amyloid fibrils of transthyretin"

2015: Personal invitation. ADRx, Thousand Oaks, USA.

- "Design of peptide inhibitors for amyloid proteins. Amyloid-beta and transthyretin"

2015: Invited speaker. Center for Translational Exosome Research in Neurodegenerative Disease EXPOSIUM

- "TTR-derived peptide inhibitors of Amyloid-beta aggregation and cytotoxicity"

2014: Personal invitation by Gregory Cole and Sally Frautschy. UCLA Alzheimer's Research Center, Los Angeles, USA.

- "Amyloid Beta Toxicity Inhibition"

2013: Personal invitation by Prof. Jeffery Kelly. 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

- 2019: FASEB NextGen Award
- 2019: The Company of Biologist Award for Scientific Meetings to organize the 2019 FASEB NextGen
- 2018: Recognized for outstanding Research and Contributions in the Subject of Neurobiology of Disease
- 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 5 years)

Current Research Support

UT Southwestern Start-up Funds (PI: Lorena Saelices)
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.

Completed Research Support

NIH NIA R01AG048120 (PI: David Eisenberg)
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 (PI: David Eisenberg)
06/2014 - 05/2019

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

(PI: Saelices/Eisenberg)

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.

Amyloidosis Foundation David C. Seldin Memorial Research Grant

(PI: Saelices)

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

PI: Saelices)

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: Saelices)

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:

06/2019: Chair of the first FASEB Next Generation Seminar on Protein Aggregation. Colorado, USA

2017 – present: Consultant and Advisor, ADRx Inc

2017 – present: Member of the International Society of Amyloid

2017 – present: Member of the American Heart Association

08/2016: Chair of the Neurobiology of Brain Disorders Gordon Research Seminars. Girona, Spain.

2015 – present: Member of the American Society for Biochemistry and Molecular Biology

07/2014: Ph.D. Committee Chair, Candidate: Guillermo Rodríguez Bey, University of Cadiz, Spain.

2010 – present: Ad-hoc reviewer (Nature Communications, PlosOne, Journal of Neuroscience, Amyloid, Therapeutics and Clinical Risk Management)