



Judith Frydman

Donald Kennedy Chair in the School of Humanities and Sciences and
Professor of Genetics
Biology

Bio

ACADEMIC APPOINTMENTS

- Professor, Biology
- Professor, Genetics
- Member, Bio-X
- Faculty Fellow, Sarafan ChEM-H
- Member, Stanford Cancer Institute
- Member, Wu Tsai Neurosciences Institute

PROGRAM AFFILIATIONS

- Center for Latin American Studies

LINKS

- Lab Website: <https://web.stanford.edu/group/frydman>

Research & Scholarship

CURRENT RESEARCH AND SCHOLARLY INTERESTS

The long term goal of our research is to understand how proteins fold in living cells. My lab uses a multidisciplinary approach to address fundamental questions about molecular chaperones, protein folding and degradation. In addition to basic mechanistic principles, we aim to define how impairment of cellular folding and quality control are linked to disease, including cancer and neurodegenerative diseases and examine whether reengineering chaperone networks can provide therapeutic strategies.

Teaching

COURSES

2024-25

- Biochemistry & Molecular Biology: BIO 83 (Aut)

2023-24

- Proteostasis: From Basic Principles to Aging and Neurodegeneration: BIO 211 (Win)

2022-23

- Proteostasis: From Basic Principles to Aging and Neurodegeneration: BIO 211 (Win)

2021-22

- Emergent and Re-Emergent Viruses as a Global Threat to Human Health: BIO 189, BIO 289 (Spr)
- Proteostasis: From Basic Principles to Aging and Neurodegeneration: BIO 211 (Win)
- Proteostasis: guarding the proteome in health and disease: BIOS 287 (Aut, Win)

STANFORD ADVISEES

Doctoral Dissertation Reader (AC)

Darren Lam, Zhuoran Li, Rahul Nagvekar, Micah Olivas, Eduardo Tassoni Tsuchida

Postdoctoral Faculty Sponsor

Fabian Morales Polanco, Natalia Moreira Barbosa, Sivan Pinto, Ivana Vujkovic Bukvin, Margaret Wangeline, Bowen Xu, Shuhao Zhang

Doctoral Dissertation Advisor (AC)

Korbin Kleczko

Doctoral (Program)

Korbin Kleczko

GRADUATE AND FELLOWSHIP PROGRAM AFFILIATIONS

- Biology (School of Humanities and Sciences) (Phd Program)
- Biophysics (Phd Program)
- Cancer Biology (Phd Program)

Publications

PUBLICATIONS

- **In situ analysis reveals the TRiC duty cycle and PDCD5 as an open-state cofactor.** *Nature*
Xing, H., Rosenkranz, R. R., Rodriguez-Aliaga, P., Lee, T. T., Majtner, T., Böhm, S., Turoňová, B., Frydman, J., Beck, M.
2024
- **Brain malformations and seizures by impaired chaperonin function of TRiC.** *Science (New York, N.Y.)*
Kraft, F., Rodriguez-Aliaga, P., Yuan, W., Franken, L., Zajt, K., Hasan, D., Lee, T. T., Flex, E., Hentschel, A., Innes, A. M., Zheng, B., Julia Suh, D. S., Knopp, et al
2024; 386 (6721): 516-525
- **A machine learning approach uncovers principles and determinants of eukaryotic ribosome pausing.** *Science advances*
Aguilar Rangel, M., Stein, K., Frydman, J.
2024; 10 (42): eado0738
- **Polyglutamine-mediated ribotoxicity disrupts proteostasis and stress responses in Huntington's disease.** *Nature cell biology*
Aviner, R., Lee, T., Masto, V. B., Li, K. H., Andino, R., Frydman, J.
2024
- **Impaired biogenesis of basic proteins impacts multiple hallmarks of the aging brain.** *bioRxiv : the preprint server for biology*
Di Fraia, D., Marino, A., Lee, J. H., Kelmer Sacramento, E., Baumgart, M., Bagnoli, S., Tomaz da Silva, P., Kumar Sahu, A., Siano, G., Tiessen, M., Terzibasi-Tozzini, E., Gagneur, J., Frydman, et al
2024
- **A hierarchical assembly pathway directs the unique subunit arrangement of TRiC/CCT.** *Molecular cell*
Betancourt Moreira, K., Collier, M. P., Leitner, A., Li, K. H., Lachapel, I. L., McCarthy, F., Opoku-Nsiah, K. A., Morales-Polanco, F., Barbosa, N., Gestaut, D., Samant, R. S., Roh, S., Frydman, et al
2023

- **High-resolution mapping reveals the mechanism and contribution of genome insertions and deletions to RNA virus evolution.** *Proceedings of the National Academy of Sciences of the United States of America*
Aguilar Rangel, M., Dolan, P. T., Taguwa, S., Xiao, Y., Andino, R., Frydman, J.
2023; 120 (31): e2304667120
- **Novel Mode of nanoLuciferase Packaging in SARS-CoV-2 Virions and VLPs Provides Versatile Reporters for Virus Production.** *Viruses*
Gullberg, R. C., Frydman, J.
2023; 15 (6)
- **Nuclear and cytoplasmic spatial protein quality control is coordinated by nuclear-vacuolar junctions and perinuclear ESCRT.** *Nature cell biology*
Sontag, E. M., Morales-Polanco, F., Chen, J. H., McDermott, G., Dolan, P. T., Gestaut, D., Le Gros, M. A., Larabell, C., Frydman, J.
2023
- **Structural visualization of the tubulin folding pathway directed by human chaperonin TRiC/CCT.** *Cell*
Gestaut, D., Zhao, Y., Park, J., Ma, B., Leitner, A., Collier, M., Pintilie, G., Roh, S. H., Chiu, W., Frydman, J.
2022; 185 (25): 4770-4787.e20
- **A campaign targeting a conserved Hsp70 binding site uncovers how subcellular localization is linked to distinct biological activities.** *Cell chemical biology*
Shao, H., Taguwa, S., Gilbert, L., Shkedi, A., Sannino, S., Guerriero, C. J., Gale-Day, Z. J., Young, Z. T., Brodsky, J. L., Weissman, J., Gestwicki, J. E., Frydman, J.
2022
- **Ageing exacerbates ribosome pausing to disrupt cotranslational proteostasis** *Nature*
Stein, K. C., Morales-Polanco, F., Leinden, J. v., Rainbolt, K. T., Frydman, J.
2022
- **Cotranslational prolyl hydroxylation is essential for flavivirus biogenesis** *NATURE*
Aviner, R., Li, K. H., Frydman, J., Andino, R.
2021
- **CryoEM reveals the stochastic nature of individual ATP binding events in a group II chaperonin.** *Nature communications*
Zhao, Y., Schmid, M. F., Frydman, J., Chiu, W.
2021; 12 (1): 4754
- **Cryo-electron tomography provides topological insights into mutant huntingtin exon 1 and polyQ aggregates.** *Communications biology*
Galaz-Montoya, J. G., Shahmoradian, S. H., Shen, K., Frydman, J., Chiu, W.
2021; 4 (1): 849
- **Structural and functional dissection of reovirus capsid folding and assembly by the prefoldin-TRiC/CCT chaperone network** *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA*
Knowlton, J. J., Gestaut, D., Ma, B., Taylor, G., Seven, A., Leitner, A., Wilson, G. J., Shanker, S., Yates, N. A., Prasad, B., Aebersold, R., Chiu, W., Frydman, et al
2021; 118 (11)
- **Principles of dengue virus evolvability derived from genotype-fitness maps in human and mosquito cells.** *eLife*
Dolan, P. T., Taguwa, S., Rangel, M. A., Acevedo, A., Hagai, T., Andino, R., Frydman, J.
2021; 10
- **Proteostasis in Viral Infection: Unfolding the Complex Virus-Chaperone Interplay** *COLD SPRING HARBOR PERSPECTIVES IN BIOLOGY*
Aviner, R., Frydman, J.
2020; 12 (3)
- **Differentiation Drives Widespread Rewiring of the Neural Stem Cell Chaperone Network.** *Molecular cell*
Vonk, W. I., Rainbolt, T. K., Dolan, P. T., Webb, A. E., Brunet, A. n., Frydman, J. n.
2020
- **THE CHAPERONIN TRiC/CCT ASSOCIATES WITH PREFOLDIN THROUGH A CONSERVED ELECTROSTATIC INTERFACE ESSENTIAL FOR CELLULAR PROTEOSTASIS**
Gestaut, D., Roh, S., Ma, B., Pintilie, G., Joachimiak, L., Leitner, A., Walzotheni, T., Aebersold, R., Chiu, W., Frydman, J.

WILEY.2019: 44

- **Dual Role of Ribosome-Binding Domain of NAC as a Potent Suppressor of Protein Aggregation and Aging-Related Proteinopathies** *MOLECULAR CELL*
Shen, K., Gamerding, M., Chan, R., Gense, K., Martin, E. M., Sachs, N., Knight, P. D., Schloemer, R., Calabrese, A. N., Stewart, K. L., Leiendecker, L., Baghel, A., Radford, et al
2019; 74 (4): 729-+
- **The Chaperonin TRiC/CCT Associates with Prefoldin through a Conserved Electrostatic Interface Essential for Cellular Proteostasis** *CELL*
Gestaut, D., Roh, S., Ma, B., Pintilie, G., Joachimiak, L. A., Leitner, A., Walzthoeni, T., Aebersold, R., Chiu, W., Frydman, J.
2019; 177 (3): 751-+
- **The ATP-powered gymnastics of TRiC/CCT: an asymmetric protein folding machine with a symmetric origin story.** *Current opinion in structural biology*
Gestaut, D., Limatola, A., Joachimiak, L., Frydman, J.
2019; 55: 50–58
- **The ATP-powered gymnastics of TRiC/CCT: an asymmetric protein folding machine with a symmetric origin story** *CURRENT OPINION IN STRUCTURAL BIOLOGY*
Gestaut, D., Limatola, A., Joachimiak, L., Frydman, J.
2019; 55: 50–58
- **Proteostasis in Viral Infection: Unfolding the Complex Virus-Chaperone Interplay.** *Cold Spring Harbor perspectives in biology*
Aviner, R., Frydman, J.
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- **Zika Virus Dependence on Host Hsp70 Provides a Protective Strategy against Infection and Disease.** *Cell reports*
Taguwa, S., Yeh, M., Rainbolt, T. K., Nayak, A., Shao, H., Gestwicki, J. E., Andino, R., Frydman, J.
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- **Nascent Polypeptide Domain Topology and Elongation Rate Direct the Cotranslational Hierarchy of Hsp70 and TRiC/CCT.** *Molecular cell*
Stein, K. C., Kriel, A. n., Frydman, J. n.
2019
- **Distinct proteostasis circuits cooperate in nuclear and cytoplasmic protein quality control.** *Nature*
Samant, R. S., Livingston, C. M., Sontag, E. M., Frydman, J.
2018; 563 (7731): 407-411
- **Hsp90 shapes protein and RNA evolution to balance trade-offs between protein stability and aggregation** *NATURE COMMUNICATIONS*
Geller, R., Pechmann, S., Acevedo, A., Andino, R., Frydman, J.
2018; 9: 1781
- **Lysosome activation clears aggregates and enhances quiescent neural stem cell activation during aging** *SCIENCE*
Leeman, D. S., Hebestreit, K., Ruetz, T., Webb, A. E., McKay, A., Pollina, E. A., Dulken, B. W., Zhao, X., Yeo, R. W., Ho, T. T., Mahmoudi, S., Devarajan, K., Passegue, et al
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- **An information theoretic framework reveals a tunable allosteric network in group II chaperonins.** *Nature structural & molecular biology*
Lopez, T., Dalton, K., Tomlinson, A., Pande, V., Frydman, J.
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- **Structure and Dynamics of the Huntingtin Exon-1 N-Terminus: A Solution NMR Perspective.** *Journal of the American Chemical Society*
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- **Mechanisms and Functions of Spatial Protein Quality Control.** *Annual review of biochemistry*
Sontag, E. M., Samant, R. S., Frydman, J.
2017
- **Control of the structural landscape and neuronal proteotoxicity of mutant Huntingtin by domains flanking the polyQ tract** *ELIFE*
Shen, K., Calamini, B., Fauerbach, J. A., Ma, B., Shahmoradian, S. H., Lachapei, I. L., Chiu, W., Lo, D. C., Frydman, J.

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- **Cotranslational signal-independent SRP preloading during membrane targeting** *NATURE*
Chartron, J. W., Hunt, K. C., Frydman, J.
2016; 536 (7615): 224-?
- **Delayed emergence of subdiffraction-sized mutant huntingtin fibrils following inclusion body formation.** *Quarterly reviews of biophysics*
Sahl, S. J., Lau, L., Vonk, W. I., Weiss, L. E., Frydman, J., Moerner, W. E.
2016; 49
- **Defining Hsp70 Subnetworks in Dengue Virus Replication Reveals Key Vulnerability in Flavivirus Infection.** *Cell*
Taguwa, S., Maringer, K., Li, X., Bernal-Rubio, D., Rauch, J. N., Gestwicki, J. E., Andino, R., Fernandez-Sesma, A., Frydman, J.
2015; 163 (5): 1108-1123
- **Local slowdown of translation by nonoptimal codons promotes nascent-chain recognition by SRP in vivo.** *Nature structural & molecular biology*
Pechmann, S., Chartron, J. W., Frydman, J.
2014; 21 (12): 1100-1105
- **Local slowdown of translation by nonoptimal codons promotes nascent-chain recognition by SRP in vivo** *NATURE STRUCTURAL & MOLECULAR BIOLOGY*
Pechmann, S., Chartron, J. W., Frydman, J.
2014; 21 (12): 1100-1105
- **The Structural Basis of Substrate Recognition by the Eukaryotic Chaperonin TRiC/CCT** *CELL*
Joachimiak, L. A., Walzthoeni, T., Liu, C. W., Aebersold, R., Frydman, J.
2014; 159 (5): 1042-1055
- **The structural basis of substrate recognition by the eukaryotic chaperonin TRiC/CCT.** *Cell*
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2014; 26: 139-146
- **Spatial sequestration of misfolded proteins by a dynamic chaperone pathway enhances cellular fitness during stress.** *Nature cell biology*
Escusa-Toret, S., Vonk, W. I., Frydman, J.
2013; 15 (10): 1231-1243
- **Spatial sequestration of misfolded proteins by a dynamic chaperone pathway enhances cellular fitness during stress** *NATURE CELL BIOLOGY*
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- **Principles of cotranslational ubiquitination and quality control at the ribosome.** *Molecular cell*
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- **Evolutionary conservation of codon optimality reveals hidden signatures of cotranslational folding.** *Nature structural & molecular biology*
Pechmann, S., Frydman, J.
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- **Evolutionary conservation of codon optimality reveals hidden signatures of cotranslational folding** *NATURE STRUCTURAL & MOLECULAR BIOLOGY*
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2013; 20 (2): 237-243
- **The Cotranslational Function of Ribosome-Associated Hsp70 in Eukaryotic Protein Homeostasis** *CELL*
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- **TRiC's tricks inhibit huntingtin aggregation.** *eLife*
Shahmoradian, S. H., Galaz-Montoya, J. G., Schmid, M. F., Cong, Y., Ma, B., Spiess, C., Frydman, J., Ludtke, S. J., Chiu, W.
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- **A Gradient of ATP Affinities Generates an Asymmetric Power Stroke Driving the Chaperonin TRiC/CCT Folding Cycle** *CELL REPORTS*
Reissmann, S., Joachimiak, L. A., Chen, B., Meyer, A. S., Nguyen, A., Frydman, J.
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- **Systematic Functional Prioritization of Protein Posttranslational Modifications** *CELL*
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- **The Molecular Architecture of the Eukaryotic Chaperonin TRiC/CCT** *STRUCTURE*
Leitner, A., Joachimiak, L. A., Bracher, A., Moenkemeyer, L., Walzthoeni, T., Chen, B., Pechmann, S., Holmes, S., Cong, Y., Ma, B., Ludtke, S., Chiu, W., Hartl, et al
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- **Defining the Specificity of Cotranslationally Acting Chaperones by Systematic Analysis of mRNAs Associated with Ribosome-Nascent Chain Complexes** *PLOS BIOLOGY*
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- **A ribosome-anchored chaperone network that facilitates eukaryotic ribosome biogenesis** *JOURNAL OF CELL BIOLOGY*
Albanese, V., Reissmann, S., Frydman, J.
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- **Mechanism of folding chamber closure in a group II chaperonin** *NATURE*
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- **Misfolded proteins partition between two distinct quality control compartments** *NATURE*
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- **Mechanism of lid closure in the eukaryotic chaperonin TRiC/CCT** *NATURE STRUCTURAL & MOLECULAR BIOLOGY*
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- **Essential function of the built-in lid in the allosteric regulation of eukaryotic and archaeal chaperonins** *NATURE STRUCTURAL & MOLECULAR BIOLOGY*
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- **Evolutionary constraints on chaperone-mediated folding provide an antiviral approach refractory to development of drug resistance** *GENES & DEVELOPMENT*
Geller, R., Vignuzzi, M., Andino, R., Frydman, J.
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- **Identification of the TRiC/CCT substrate binding sites uncovers the function of subunit diversity in eukaryotic** *MOLECULAR CELL*
Spiess, C., Miller, E. J., McClellan, A. J., Frydman, J.
2006; 24 (1): 25-37
- **The chaperonin TRiC controls polyglutamine aggregation and toxicity through subunit-specific interactions** *NATURE CELL BIOLOGY*
Tam, S., Geller, R., Spiess, C., Frydman, J.
2006; 8 (10): 1155-U211
- **Systems analyses reveal two chaperone networks with distinct functions in eukaryotic cells** *CELL*
Albanese, V., Yam, A. Y., Baughman, J., Parnot, C., Frydman, J.
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- **Protein quality control: chaperones culling corrupt conformations** *NATURE CELL BIOLOGY*
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- **Folding and quality control of the VHL tumor suppressor proceed through distinct chaperone pathways** *CELL*
McClellan, A. J., Scott, M. D., Frydman, J.
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- **Mechanism of the eukaryotic chaperonin: protein folding in the chamber of secrets** *TRENDS IN CELL BIOLOGY*
Spiess, C., Meyer, A. S., Reissmann, S., Frydman, J.
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- **Tumorigenic mutations in VHL disrupt folding in vivo by interfering with chaperonin binding** *MOLECULAR CELL*
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- **Closing the folding chamber of the eukaryotic chaperonin requires the transition state of ATP hydrolysis** *CELL*
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McCallum, C. D., Do, H., Johnson, A. E., Frydman, J.
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Thulasiraman, V., Yang, C. F., Frydman, J.
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Frydman, J., Hartl, F. U.
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Tilk, S., Frydman, J., Curtis, C., Petrov, D. A.
2024; 12
 - **Human tNeurons reveal aging-linked proteostasis deficits driving Alzheimer's phenotypes.** *Research square*
Chou, C. C., Vest, R., Prado, M. A., Wilson-Grady, J., Paulo, J. A., Shibuya, Y., Moran-Losada, P., Lee, T. T., Luo, J., Gygi, S. P., Kelly, J. W., Finley, D., Wernig, et al
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Gu, Y., Pope, A., Smith, C., Carmona, C., Johnstone, A., Shi, L., Chen, X., Santos, S., Bacon-Brenes, C. C., Shoff, T., Kleczko, K. M., Frydman, J., Thompson, et al
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 - **A structural vista of phospho-ubiquitin-like PhLP2A-chaperonin TRiC cooperation during the ATP-driven folding cycle.** *Nature communications*
Park, J., Kim, H., Gestaut, D., Lim, S., Opoku-Nsiah, K. A., Leitner, A., Frydman, J., Roh, S.
2024; 15 (1): 1007
 - **Human transdifferentiated neurons reveal lysosomal repair deficits in Alzheimer's disease**
Chou, C., Frydman, J.
ACADEMIC PRESS INC ELSEVIER SCIENCE.2024
 - **A lethal mitonuclear incompatibility in complex I of natural hybrids.** *Nature*
Moran, B. M., Payne, C. Y., Powell, D. L., Iverson, E. N., Donny, A. E., Banerjee, S. M., Langdon, Q. K., Gunn, T. R., Rodriguez-Soto, R. A., Madero, A., Baczenas, J. J., Kleczko, K. M., Liu, et al

2024

- **Transdifferentiation: A Novel Tool for Disease Modeling and Translational Applications in Alzheimer's Disease**
Chou, C., Vest, R., Prado, M. A., Wilson-Grady, J., Paulo, J. A., Shibuya, Y., Moran-Losada, P., Lee, T., Luo, J., Gygi, S. P., Kelly, J. W., Finley, D. P., Wernig, et al
WILEY.2023: S205-S206
- **SARS-CoV-2 Nsp1 regulates translation start site fidelity to promote infection.** *bioRxiv : the preprint server for biology*
Aviner, R., Lidsky, P. V., Xiao, Y., Tassetto, M., Zhang, L., McAlpine, P. L., Elias, J., Frydman, J., Andino, R.
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