

Jonathan Ipsaro, Ph.D.

Principal Scientist – Atavistik Bio, Cambridge, Massachusetts, USA

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Summary

- Broadly-trained researcher with 15 years of experience in structure determination, biophysics, biochemistry, and computation
- Accomplished structural biologist that has successfully utilized X-ray, cryo-EM, and NMR for an array of targets (RNA interference machinery, cytoskeletal complexes, nucleosomes bound to chromatin remodelers, transcription factors, metabolic enzymes, etc.)
- Extensive experience with protein and nucleic acid biochemistry
- Effective project manager comfortable with CRO management, in-house collaboration, and independent work
- Ambitious to tackle human health issues using integrated structural and computational methods

Experience

2025 – Current Principal Scientist (Structural Biology) – Atavistik Bio, Cambridge, MA

2023 – 2025 Senior Scientist (Structural Biology) – Atavistik Bio, Cambridge, MA

About: Atavistik Bio is a small-molecule drug discovery company focused on targeting allosteric pockets for precision oncology therapeutics

Responsibilities:

- Design, management, and evaluation of macromolecular structure determination (X-ray crystallography, cryo-EM, and NMR) workflows for multiple concurrent projects by CRO partners
- Evaluation and communication of structural data to inform structure-based drug design for modelers, chemists, and biologists
- Biophysical assay design, implementation, and evaluation for hit-to-lead progression
- Development and deployment of computational tools to nominate new targets, automate assay data analysis, and predict macromolecular structure
- Training and mentorship for interns and junior scientists

2019 – 2023 Howard Hughes Medical Institute / Cold Spring Harbor Laboratory – Research Investigator

Primary Project: Structural studies of epigenetic regulatory machinery

Collaborations: Molecular characterization of cancer drivers; Structure determination of chromatin remodelers in plants; Protein/enzyme engineering for mass spectrometry biotechnology tools

Responsibilities:

- Execution of structure determination workflows for 4-6 concurrent projects
- Designing and cloning of constructs for protein and nucleic acid production
- Expression of targets in multiple recombinant systems (*E. coli*, insect cells, etc.)
- Protein purification, biochemical analysis, and biophysical characterization (including binding analyses of multi-component complexes)
- Determination of macromolecular and multi-subunit complex structures by X-ray crystallography and cryo-EM (data collection, processing, model building, refinement, and deposition)
- Preparation and analysis of next-gen sequencing libraries including custom bioinformatic pipeline coding and implementation
- Training and supervision of multiple graduate students, junior post-docs, and technicians
- Training for users, maintenance of, and basic repairs for numerous biochemical and biophysical apparatus (e.g. ITC, SPR, MALLS)

2010 – 2019 Cold Spring Harbor Laboratory – Post-doctoral Fellow

Primary Project: Structural studies of epigenetic regulatory machinery

Advisor: Leemor Joshua-Tor

Skills

Structural biology:	X-ray crystallography & cryo-EM (sample preparation, crystallization/freezing, data collection, processing, model building, refinement)
	NMR (sample preparation, basic analysis of protein samples)
Molecular biology:	Construct design (protein and nucleic acid), cloning, protein expression and purification, RNA transcription and purification
Biophysics:	Analytical ultracentrifugation (AUC), circular dichroism (CD), fluorescence polarization (FP), surface plasmon resonance (SPR), small-angle X-ray scattering (SAXS), multi-angle light scattering (MALLS)
Biochemistry:	Nucleic acid labeling and detection, enzymatic activity assays with various readouts (gels, TLC, MS), SHAPE, Next-generation sequencing
Computation:	Python, Web development HTML/PHP/SQL/JavaScript, Bash, R

Education

2004 – 2009	Ph.D., Northwestern University – Department of Biochemistry, Molecular Biology & Cell Biology <i>Thesis: Biophysical characterization and structural elucidation of the spectrin-ankyrin interaction</i> Advisor: Alfonso Mondragón, Ph.D.
2000 – 2004	B.S., Case Western Reserve University – Department of Biochemistry (with Honors); minor in Physics B.A, Case Western Reserve University – Department of Modern Languages and Literature (Spanish)

Funding & Academic Honors

2011 – 2013	NIH Ruth L. Kirschstein National Research Service Award
2010	Harvey L. Karp Discovery Award, Cold Spring Harbor Laboratory
2008	Northwestern University Graduate School Conference Travel Award
2006 – 2009	Cellular and Molecular Basis of Disease NIH Training Grant (NIH 5 T32 GM008061-24), Northwestern University, Evanston IL
2005 – 2006	Neil Welker Interdepartmental Biological Sciences Teaching Assistant Award, Northwestern University, Evanston IL
2004 – 2005	Rappaport Fellow, Northwestern University, Evanston IL

Recent Invited Talks

Apr. 2025	American Society for Biochemistry and Molecular Biology Annual Meeting – Chicago, IL
Nov. 2020	RNA Interest Group – Student Invited Speaker – University of Utah, UT
May 2020	Regulatory and Non-Coding RNAs Meeting – Cold Spring Harbor Laboratory, NY
Aug. 2019	New York Structural Biology Discussion Group – New York City, NY

Publications (most recent first; 12 first author)

1. Aktan A*, Ipsaro JJ*, Skopelitis D*, Pal S, Chung FS, Carpenter S, Desmarais JJ, Wu XS, Chang K, DiMare MT, Harten E, Bergman S, Kinney JB, Engelman JA, Bhang HC, Joshua-Tor L, Vakoc CR. Structural Basis of DNA-Dependent Coactivator Recruitment by the Tuft Cell Master Regulator POU2F3. 2025. *Cell Reports*. 44(11): 116572. PMID: 41260223
2. Blanco MJ, Buskes MJ, Govindaraj RG, Ipsaro JJ, Prescott-Roy JE, Padyana AK. Allostery Illuminated: Harnessing AI and Machine Learning for Drug Discovery. 2024. ACS Med. Chem. Lett. doi: 10.1021/acsmedchemlett.4c00260
3. Baumgartner L, Ipsaro JJ, Hohmann U, Handler D, Schleiffer A, Duchek P, Brennecke J. Evolutionary adaptation of an HP1-protein chromodomain integrates chromatin and DNA sequence signals. 2024. *eLife*. 13:RP93194. PMID: 38995818
4. Qian Z, Song D, Ipsaro JJ, Bautista C, Joshua-Tor L, Yeh JT-H, Tonks NK. Manipulating PTPRD function with ectodomain antibodies. 2023. *Genes Dev*. 37(15-16):743-759. PMID: 37669874
5. Lee SC*, Adams DW*, Ipsaro JJ*, Cahn J*, Lynn J, Kim HS, Berube B, Major V, Calarco JP, LeBlanc C, Bhattacharjee S,

- Ramu U, Grimanelli D, Jacob Y, Voigt P, Joshua-Tor L, Martienssen RA. 2023. Chromatin remodeling of histone H3 variants underlies epigenetic inheritance of DNA methylation. *Cell.* 186(19): 4100-4116.e15. PMID: 37643610
6. Gao Y, He X, Wu XS, Huang Y, Toneyan S, **Ipsaro JJ**, Ha T, Koo PK, Egeblad M, Joshua-Tor L. 2023. ETV6 dependency in Ewing sarcoma by antagonism of EWS-FLI1-mediated enhancer activation. *Nat. Cell Biology.* 25(2):298-308. PMID: 36658219
 7. Wu XS, Huang Y, **Ipsaro JJ**, He X, Preall JB, Ng D, Shue YT, Sage J, Egeblad M, Joshua-Tor L, and Vakoc CR. 2022. C11orf53/OCA-T is a tuft cell-specific coactivator of OCT11. *Nature.* 607(7917):169-175. PMCID: PMC9419707
 8. **Ipsaro JJ[†]**, Joshua-Tor L. Developmental Roles and Molecular Mechanisms of Asterix/Gtsf1. 2022. *WIREs RNA.* doi: 10.1002/wrna.1716. PMID: 35108755. [†]**Corresponding author**
 9. **Ipsaro JJ**, O'Brien PA, Bhattacharya S, Palmer AG 3rd, Joshua-Tor L. 2021. Asterix/Gtsf1 links tRNAs and piRNA silencing of retrotransposons. *Cell Reports.* 34(13):108914. PMID: 33789107
 10. Wilson JP*, **Ipsaro JJ***, Del Giudice SN, Turna NS, Gauss CM, Dusenbury KH, Marquart K, Rivera KD, Pappin DJ. 2020. Tryp-N: A Thermostable Protease for the Production of N-terminal Argininyl and Lysinyl Peptides. *J Proteome Res.* 19(4):1459-1469. PMCID: PMC7842235
 11. Stein CB, Genzor P, Mitra S, Elchert AR, **Ipsaro JJ**, Benner L, Sobti S, Su Y, Hammell M, Joshua-Tor L, Haase AD. 2019. Decoding the 5' nucleotide bias of PIWI-interacting RNAs (piRNAs). *Nat. Commun.* 10(1):828. PMCID: PMC6381166
 12. **Ipsaro JJ**, Shen C, Arai E, Xu Y, Kinney JB, Joshua-Tor L, Vakoc CR, Shi J. 2017. Rapid generation of drug-resistance alleles at endogenous loci using CRISPR-Cas9 indel mutagenesis. *PLoS One.* 12(2):e0172177. PMCID: PMC5322889
 13. Shen C, **Ipsaro JJ**, Shi J, Milazzo JP, Wang E, Roe JS, Suzuki Y, Pappin DJ, Joshua-Tor L, Vakoc CR. 2015. NSD3-Short Is an Adaptor Protein that Couples BRD4 to the CHD8 Chromatin Remodeler. *Mol. Cell.* 60(6):847-59. *Selected for journal cover.* PMCID: PMC4688131
 14. **Ipsaro JJ**, Joshua-Tor L. 2015. From guide to target: molecular insights into eukaryotic RNA-interference machinery. *Nat. Struct. Mol. Biol.* 22(1):20-8. PMCID: PMC4450863
 15. **Ipsaro JJ***, Haase AD*, Knott SR, Joshua-Tor L, Hannon GJ. 2012. The structural biochemistry of Zucchini implicates it as a nuclease in piRNA biogenesis. *Nature.* 491(7423):279-83. PMCID: PMC3493678
 16. Yasunaga M, **Ipsaro JJ**, Mondragón A. 2012. Structurally similar but functionally diverse ZU5 domains in human erythrocyte ankyrin. *J. Mol. Biol.* 417(4):336-50. PMCID: PMC3312341
 17. Strauch RC, Mastarone DJ, Sukerkar PA, Song Y, **Ipsaro JJ**, Meade TJ. 2011. Reporter protein-targeted probes for magnetic resonance imaging. *J. Am. Chem. Soc.* 133(41):16346-9. PMCID: PMC3203639
 18. **Ipsaro JJ**, Harper SL, Messick TE, Marmorstein R, Mondragón A, and Speicher DW. 2010. Crystal structure and functional interpretation of the erythrocyte spectrin tetramerization domain complex. *Blood.* 115(23):4843-52. *Selected for journal cover.* PMCID: PMC2890174
 19. **Ipsaro JJ** and Mondragón A. 2010. Structural basis for spectrin recognition by ankyrin. *Blood.* 115(20):4093-101. *Selected for journal cover.* PMCID: PMC2875089
 20. **Ipsaro JJ**, Huang L, and Mondragón A. 2009. Structures of the spectrin-ankyrin interaction binding domains. *Blood.* 113(22):5385-93. PMCID: PMC2689041
 21. **Ipsaro JJ***, Huang L*, Gutierrez L, and MacDonald RI. 2008. Molecular Epitopes of the Ankyrin-Spectrin Interaction. *Biochemistry.* 47(28):7452-64. PMCID: PMC3280509
 22. Wuchty S, **Ipsaro JJ**. 2007. A draft of protein interactions in the malaria parasite *P. falciparum*. *J. Proteome Res.* 6(4):1461-70. PMID: 1730018

Patents

Pappin DJ, Wilson JP, **Ipsaro JJ**. 2017. Proteases for the production of N-terminal argininyl- and lysinyl-peptides and methods of use in protein analysis. U.S. Patent 9,719,078. Filed June 15, 2014 and issued August 01, 2017.

Organizations

2012 – 2015 Post-doc Liaison Committee, CSHL

Peer-elected group of post-docs chosen to facilitate interactions between post-docs and administrators