

BIOGRAPHICAL SKETCH

NAME: Stagno, Jason R.

POSITION TITLE: Associate Scientist

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	END DATE	FIELD OF STUDY
National Cancer Institute, Center for Cancer Research, Frederick, MD	Postdoctoral Fellow	2012	Macromolecular Crystallography
University of California Irvine, Irvine, CA	PHD	2009	Molecular Biology
University of Maryland Baltimore County, Baltimore, MD	BS	2004	Biochemistry

A. Personal Statement

As a structural biologist, my research has focused on structure determination, primarily by X-ray crystallography, of proteins, nucleic acids, and their complexes to elucidate structure-function relationships. In the Center for Structural Biology, Protein-Nucleic Acid Interactions Section, we employ a diverse set of biophysical techniques, including nuclear magnetic resonance (NMR), small-angle X-ray scattering (SAXS), atomic force microscopy, X-ray crystallography, and cryo electron microscopy (cryoEM) to study RNA structure and dynamics. This multidisciplinary approach using complementary methods allows us to address significant biological questions more completely and more accurately at the molecular level. Such information is highly valuable for understanding the important roles RNA molecules play in various cellular processes. My current work includes structure determination and design of RNA devices for cancer immunotherapy, RNA conformational space and structural dynamics, and conformational switching mechanisms of riboswitches.

1. Stagno JR, Liu Y, Bhandari YR, Conrad CE, Panja S, Swain M, Fan L, Nelson G, Li C, Wendel DR, White TA, Coe JD, Wiedorn MO, Knoska J, Oberthuer D, Tuckey RA, Yu P, Dyba M, Tarasov SG, Weierstall U, Grant TD, Schwieters CD, Zhang J, Ferré-D'Amaré AR, Fromme P, Draper DE, Liang M, Hunter MS, Boutet S, Tan K, Zuo X, Ji X, Barty A, Zatsepin NA, Chapman HN, Spence JC, Woodson SA, Wang YX. Structures of riboswitch RNA reaction states by mix-and-inject XFEL serial crystallography. *Nature*. 2017 Jan 12;541(7636):242-246. PubMed Central PMCID: PMC5502819.
2. Stagno JR, Ma B, Li J, Altieri AS, Byrd RA, Ji X. Crystal structure of a plectonemic RNA supercoil. *Nat Commun*. 2012 Jun 12;3:901. PubMed Central PMCID: PMC3518024.
3. Stagno JR, Altieri AS, Bubunenko M, Tarasov SG, Li J, Court DL, Byrd RA, Ji X. Structural basis for RNA recognition by NusB and NusE in the initiation of transcription antitermination. *Nucleic Acids Res*. 2011 Sep 1;39(17):7803-15. PubMed Central PMCID: PMC3177189.
4. Stagno J, Aphasizheva I, Aphasizhev R, Luecke H. Dual role of the RNA substrate in selectivity and catalysis by terminal uridylyl transferases. *Proc Natl Acad Sci U S A*. 2007 Sep 11;104(37):14634-9. PubMed Central PMCID: PMC1976215.

B. Positions, Scientific Appointments and Honors

Positions and Scientific Appointments

2014 - Present Associate Scientist, Center for Structural Biology, Center for Cancer Research, National Cancer Institute, Frederick, MD

2012 - 2014 Health Science Policy Analyst, Office of Science Policy, Office of the Director, National Institutes of Health, Bethesda, MD

Honors

2022 Invited Lecture, BioXFEL International Conference

2021 Sigma Xi Inductee, Sigma Xi, The Scientific Research Honor Society

2021	Invited Lecture, European Advanced Materials Congress
2018	Poster Award, International Conference on the Crystallization of Biological Macromolecules
2018	Invited Lecture, Tsinghua University, School of Life Sciences
2018	Invited Lecture, Shanghai Jiao Tong University, School of Life Sciences and Biotechnology
2017	Promotion to Associate Scientist, NCI Center for Cancer Research
2017	PDB Molecule of the Month, Protein Data Bank
2016	Research Highlight in CCR Milestones, NCI Center for Cancer Research
2016	Certificate of Special Recognition for Mentoring, NCI Werner H. Kirsten Student Intern Program
2015	Best Abstract, NCI CCR Staff Scientists Staff Clinicians Retreat
2012	Outstanding Poster Award, NCI Frederick National Lab Spring Research Festival
2012	NIH Fellows Award for Research Excellence, National Institutes of Health
2012	Travel Award, American Crystallographic Association
2012	Young Investigator Award, Southeast Regional Collaborative Access Team
2007	William D. Redfield Graduate Fellowship Award, University of California Irvine
2005	Excellence in Science Award, American Association for the Advancement of Science

C. Contribution to Science

1. Structural basis for ligand-induced conformational switching of RNA riboswitches.
 - a. Wilt HM, Yu P, Tan K, Wang YX, Stagno JR. Tying the knot in the tetrahydrofolate (THF) riboswitch: A molecular basis for gene regulation. *J Struct Biol.* 2021 Mar;213(1):107703. PubMed Central PMCID: PMC7981257.
 - b. Wilt HM, Yu P, Tan K, Wang YX, Stagno JR. FMN riboswitch aptamer symmetry facilitates conformational switching through mutually exclusive coaxial stacking configurations. *J Struct Biol X.* 2020;4:100035. PubMed Central PMCID: PMC7573352.
 - c. Ding J, Swain M, Yu P, Stagno JR, Wang YX. Conformational flexibility of adenine riboswitch aptamer in apo and bound states using NMR and an X-ray free electron laser. *J Biomol NMR.* 2019 Sep;73(8-9):509-518. PubMed Central PMCID: PMC6817744.
 - d. Stagno JR, Liu Y, Bhandari YR, Conrad CE, Panja S, Swain M, Fan L, Nelson G, Li C, Wendel DR, White TA, Coe JD, Wiedorn MO, Knoska J, Oberthuer D, Tuckey RA, Yu P, Dyba M, Tarasov SG, Weierstall U, Grant TD, Schwieters CD, Zhang J, Ferré-D'Amaré AR, Fromme P, Draper DE, Liang M, Hunter MS, Boutet S, Tan K, Zuo X, Ji X, Barty A, Zatsepin NA, Chapman HN, Spence JC, Woodson SA, Wang YX. Structures of riboswitch RNA reaction states by mix-and-inject XFEL serial crystallography. *Nature.* 2017 Jan 12;541(7636):242-246. PubMed Central PMCID: PMC5502819.
2. Time-resolved crystallography of adenine riboswitch using an X-ray free electron laser.
 - a. Ramakrishnan S, Stagno JR, Conrad CE, Ding J, Yu P, Bhandari YR, Lee YT, Pauly G, Yefanov O, Wiedorn MO, Knoska J, Oberthür D, White TA, Barty A, Mariani V, Li C, Brehm W, Heinz WF, Magidson V, Lockett S, Hunter MS, Boutet S, Zatsepin NA, Zuo X, Grant TD, Pandey S, Schmidt M, Spence JCH, Chapman HN, Wang YX. Synchronous RNA conformational changes trigger ordered phase transitions in crystals. *Nat Commun.* 2021 Mar 19;12(1):1762. PubMed Central PMCID: PMC7979858.
 - b. Ding J, Swain M, Yu P, Stagno JR, Wang YX. Conformational flexibility of adenine riboswitch aptamer in apo and bound states using NMR and an X-ray free electron laser. *J Biomol NMR.* 2019 Sep;73(8-9):509-518. PubMed Central PMCID: PMC6817744.
 - c. Stagno JR, Bhandari YR, Conrad CE, Liu Y, Wang YX. Real-time crystallographic studies of the adenine riboswitch using an X-ray free-electron laser. *FEBS J.* 2017 Oct;284(20):3374-3380. PubMed Central PMCID: PMC6309305.
 - d. Stagno JR, Liu Y, Bhandari YR, Conrad CE, Panja S, Swain M, Fan L, Nelson G, Li C, Wendel DR, White TA, Coe JD, Wiedorn MO, Knoska J, Oberthuer D, Tuckey RA, Yu P, Dyba M, Tarasov SG,

Weierstall U, Grant TD, Schwieters CD, Zhang J, Ferré-D'Amaré AR, Fromme P, Draper DE, Liang M, Hunter MS, Boutet S, Tan K, Zuo X, Ji X, Barty A, Zatsepin NA, Chapman HN, Spence JC, Woodson SA, Wang YX. Structures of riboswitch RNA reaction states by mix-and-inject XFEL serial crystallography. *Nature*. 2017 Jan 12;541(7636):242-246. PubMed Central PMCID: PMC5502819.

3. Solid-to-solid phase transitions in RNA crystals induced by ligand binding.

- a. Lee HK, Conrad CE, Magidson V, Heinz WF, Pauly G, Yu P, Ramakrishnan S, Stagno JR, Wang YX. Developing methods to study conformational changes in RNA crystals using a photocaged ligand. *Front Mol Biosci*. 2022;9:964595. PubMed Central PMCID: PMC9424638.
- b. Ramakrishnan S, Stagno JR, Heinz WF, Zuo X, Yu P, Wang YX. The mechanism driving a solid-solid phase transition in a biomacromolecular crystal. *IUCrJ*. 2021 Jul 1;8(Pt 4):655-664. PubMed Central PMCID: PMC8256710.
- c. Ramakrishnan S, Stagno JR, Magidson V, Heinz WF, Wang YX. Dependence of phase transition uniformity on crystal sizes characterized using birefringence. *Struct Dyn*. 2021 May;8(3):034301. PubMed Central PMCID: PMC8248999.
- d. Ramakrishnan S, Stagno JR, Magidson V, Heinz WF, Wang YX. A combined approach to characterize ligand-induced solid-solid phase transitions in biomacromolecular crystals. *J Appl Crystallogr*. 2021 Jun 1;54(Pt 3):787-796. PubMed Central PMCID: PMC8202036.

4. Substrate selectivity and catalysis by trypanosomal terminal uridylyl transferases.

- a. Rajappa-Titu L, Suematsu T, Munoz-Tello P, Long M, Demir Ö, Cheng KJ, Stagno JR, Luecke H, Amaro RE, Aphasizheva I, Aphasizhev R, Thore S. RNA Editing TUTase 1: structural foundation of substrate recognition, complex interactions and drug targeting. *Nucleic Acids Res*. 2016 Dec 15;44(22):10862-10878. PubMed Central PMCID: PMC5159558.
- b. Stagno J, Aphasizheva I, Bruystens J, Luecke H, Aphasizhev R. Structure of the mitochondrial editosome-like complex associated TUTase 1 reveals divergent mechanisms of UTP selection and domain organization. *J Mol Biol*. 2010 Jun 11;399(3):464-75. PubMed Central PMCID: PMC2916031.
- c. Stagno J, Aphasizheva I, Aphasizhev R, Luecke H. Dual role of the RNA substrate in selectivity and catalysis by terminal uridylyl transferases. *Proc Natl Acad Sci U S A*. 2007 Sep 11;104(37):14634-9. PubMed Central PMCID: PMC1976215.
- d. Stagno J, Aphasizheva I, Rosengarth A, Luecke H, Aphasizhev R. UTP-bound and Apo structures of a minimal RNA uridylyltransferase. *J Mol Biol*. 2007 Feb 23;366(3):882-99. PubMed Central PMCID: PMC1850106.

5. Structural basis for RNA recognition in initiation of transcription antitermination in bacteria.

- a. Stagno JR, Ma B, Li J, Altieri AS, Byrd RA, Ji X. Crystal structure of a plectonemic RNA supercoil. *Nat Commun*. 2012 Jun 12;3:901. PubMed Central PMCID: PMC3518024.
- b. Stagno JR, Altieri AS, Bubunenko M, Tarasov SG, Li J, Court DL, Byrd RA, Ji X. Structural basis for RNA recognition by NusB and NusE in the initiation of transcription antitermination. *Nucleic Acids Res*. 2011 Sep 1;39(17):7803-15. PubMed Central PMCID: PMC3177189.

Complete List of Published Work in My Bibliography:

<https://www.ncbi.nlm.nih.gov/myncbi/jason.stagno.1/bibliography/public/>

Invited Talks

2022	BioXFEL International Conference
2021	European Advanced Materials Congress
2018	Tsinghua University, School of Life Sciences
2018	Shanghai Jiao Tong University, School of Life Sciences and Biotechnology

Selected Bibliography (since 2012)

* Denotes co-first author or co-corresponding author.

1. **Stagno, J.R.**, Li, J., Altieri, A.S., Byrd, R.A., Ji, X. Crystal Structure of a Plectonemic RNA Supercoil. *Nature Commun.* 3(901), 2012. PMCID: PMC3518024
2. Zhao, J., **Stagno, J.R.**, Varticovski, L., Nimako, E., Rishi, V., McKinnon, K., Akee, R., Shoemaker, R.H., Ji, X., Vinson, C. P6981, an arylstibonic acid that inhibits the DNA binding of CREB with an IC₅₀ of 5 nM. *Mol. Pharmacol.* 82(5):814-823, 2012. PMCID: PMC3477234
3. Fang, X, Stagno J.R., Bhandari, YR, Zuo X, Wang, Y.-X. Modeling RNA topological structures using small angle X-ray scattering. *Curr Opin Struct Biol.* 30, 147-60, 2015. PMCID: PMC6676907
4. Liu, Y., Holmstrom, E., Zhang, J., Yu, P., Wang, J., Dyba, M., Chen, D., Ying, J., Lockett, S., Nesbitt, D.J., Ferré-D'Amaré, A.R., Sousa, R., **Stagno, J.R.**, Wang, Y.-X. Synthesis and applications of RNAs with position-selective labelling and mosaic composition. *Nature* 522, 368-72, 2015. PMCID: PMC4800989
5. Liu, Y., Yu, P., Dyba, M., Sousa R., **Stagno J.R.**, Wang Y.-X. Applications of PLOR in labeling large RNAs at specific sites. *Methods* 103:4-10, 2016. PMID: 27033177
6. Bhandari, Y.R., Jiang, W., Stahlberg, E.A., **Stagno, J.R.**, Wang, Y.-X. Modeling RNA topological structures using small angle X-ray scattering. *Methods* 103, 18-24, 2016. PMID: 27090001
7. Rajappa-Titu, L., Suematsu, T., Munoz-Tello, P., Long, M., Demir, O., Cheng, K., **Stagno, J.R.**, Luecke, H., Amaro, R., Aphasizheva, I., Aphasizhev, R., Thore, S. RNA Editing TUTase 1: structural foundation of substrate recognition, complex interactions and drug targeting. *Nucleic Acids Res.* 44(22):10862-10878, 2016. PMCID: PMC5159558
8. **Stagno, J.R.**, Liu, Y., Bhandari, Y.R., Conrad, C.E., Panja, S., Swain, M., Fan, L., Nelson, G., Li, C., Wendel, D.R., White, T.A., Barty, A., Coe, J.D., Wiedorn, M.O., Knoska, J., Oberthur, D., Tuckey, R.A., Yu, P., Dyba, M., Tarasov, S.G., Weierstall, U., Zatsepin, N.A., Grant, T.D., Schwieters, C.D., Zhang, J., Ferré-D'Amaré, A.R., Fromme, P., Draper, D.E., Tan, K., Chapman, H., Zuo, X., Hunter, M.S., Boutet, S., Ji, X., Spence, J.C.H., Woodson, S.A., Wang, Y.-X. Structures of riboswitch RNA reaction states by mix-and-inject XFEL serial crystallography. *Nature.* 541(7636):242-246, 2016. PMCID: PMC5502819
9. **Stagno, J.R.**, Bhandari, Y.R., Conrad, C.E., Liu, Y., Wang, Y.-X. Real-time crystallographic studies of the adenine riboswitch using an X-ray free electron laser. *FEBS* 284(20):3374-3380, 2017. PMCID: PMC5693684
10. Bhandari, Y.R., Jiang, W., Stahlberg, E.A., **Stagno, J.R.**, Wang, Y.-X., Topological Structure Determination of RNA Using Small-Angle X-ray Scattering. *J. Mol. Biol.* (24;429(23):3635-3649, 2017. PMID: 28918093.
11. Liu, Y., Holmstrom, E., Yu, P., Tan, K., Zuo, S., Nesbitt, D.J., Sousa, R., **Stagno, J.R.**, Wang, Y.-X. Incorporation of isotopic, fluorescent, and heavy-atom modified nucleotides into RNAs by position-selective labeling of RNA. *Nature Protocols* 13(5):987-1005, 2018. PMID: 29651055.
12. **Stagno, J.R.**, Bhandari, Y.R., Conrad, C.E., Grant, T., Fromme, P., Hunter, M.S., Boutet, S., Tan, K., Zuo, X., Ji, X., Zatsepin, N.A., Chapman, H.N., Spence, J.C.H., Wang, Y.-X. Using X-ray free-electron laser to capture intermediate states. *Acta Crystallogr A: Foundations and Advances.* 74(a1):a15, 2018. DOI:10.1107/S010876731809984.

13. Van Beek, H., Handing, K., Gualtier, E., **Stagno, J.R.**, Wang, Y.-X., Ramsey, L. Sensitive detection of RNA microcrystals using SONICC imaging. *Acta Crystallogr A: Foundations and Advances*. 73(a1):a201, 2017. DOI: 10.1107/S0108767317098026.
14. **Stagno, J.R.**, Yu, P., Dyba, M.A., Wang, Y.-X., Liu, Y. Heavy-atom labeling of RNA by PLOR for de novo crystallographic phasing. *PLoS ONE* 14(4): e0215555, 2019. PMID: 30986270.
15. Ding, J., Swain, M., Yu, P., **Stagno, J.R.**, Wang, Y.-X. Conformational flexibility of adenine riboswitch aptamer in apo and bound states using NMR and an X-ray free electron laser. *J Biomol NMR*. Sep;73(8-9):509-518, 2019. PMID: 31606878.
16. Jones, C.P., Tran, B., Conrad, C., **Stagno, J.R.**, Trachman III, R., Fischer, P., Meents, A., Ferré-D'Amaré, A. Co-crystal structure of the *Fusobacterium ulcerans* ZTP riboswitch using an X-ray free-electron laser. *Acta Crystallogr F Struct Biol Commun*, 2019. PMID: 31282869.
17. Trachman III, R., **Stagno, J.R.**, Conrad, C., Jones, C.P., Fischer, P., Meents, A., Wang, Y.-X., Ferré-D'Amaré, A. Co-crystal structure of the iMango-III fluorescent RNA aptamer using an X-ray free-electron laser. *Acta Crystallogr F Struct Biol Commun*, 2019. PMID: 31397326.
18. Majumder, P., Zhang, Y., Iglesias, M., Fan, L., Kelley, J.A., Andrews, C., Patel, N., **Stagno, J.R.**, Oh, B.C., Furtmüller, G.J., Lai, C.C., Wang, Y.-X., Brandacher, G., Raimondi, G., Schneider, J.P. Multiphase Assembly of Small Molecule Microcrystalline Peptide Hydrogel Allows Immunomodulatory Combination Therapy for Long-Term Heart Transplant Survival. *Small*. Sep;16(38):e2002791, 2020. PMID: 32812339
19. Wilt, H.M., Yu, P., Tan, K., Wang, Y.-X., **Stagno, J.R.** FMN riboswitch aptamer symmetry facilitates conformational switching through mutually exclusive coaxial stacking configurations. *Journal of Structural Biology X*. Volume 4, 2020. PMID: 33103111
20. Wilt, H.M., Yu, P., Tan, K., Wang, Y.-X., **Stagno, J.R.** Tying the knot in the tetrahydrofolate (THF) riboswitch: A molecular basis for gene regulation. *Journal of Structural Biology*. Volume 213, 2021. PMID: 33571639
21. Ramakrishnan, S. *, **Stagno, J.R.***, Conrad, C.E., Ding, J., Yu, P., Bhandari, Y.R., Lee, Y.T., Pauly, G., Yefanov, O., Wiedorn, M.O., Knoska, J., Oberthur, D., White, T.A., Barty, A., Mariani, V., Li, C., Brehm, W., Heinz, W.F., Magidson, V., Lockett, S., Hunter, M.S., Boutet, S., Zatsepin, N.A., Zuo, X., Grant, T.D., Pandey, S., Schmidt, M., Spence, J.C.H., Chapman, H.N., Wang, Y.-X. Synchronous RNA conformational changes trigger ordered phase transitions in crystals. *Nat Commun*. **12**(1): 1762, 2021. PMID: **33741910**
22. Ramakrishnan, S. *, **Stagno, J.R.***, Magidson, V., Heinz, W.F., and Wang, Y.X. A combined approach to characterize solid-solid phase transitions in biomacromolecular crystals. *J Appl Crystallogr* **54**, 787-796, 2021. PMCID: PMC8202036
23. Ramakrishnan, S. *, **Stagno, J.R.***, Magidson, V., Heinz, W.F., and Wang, Y.X. The mechanism driving a solid-solid phase transition in a biomacromolecular crystal. *IUCrJ* **8**, 655-664, 2021. PMCID: PMC8256710
24. Ramakrishnan, S. *, **Stagno, J.R.***, Magidson, V., Heinz, W.F., and Wang, Y.X. Dependence of phase transition uniformity on crystal sizes characterized using birefringence. *Struct Dyn* **8**, 034301, 2021. PMCID: PMC8248999
25. **Stagno, J.R.**, Ramakrishnan, S., Spence, J.C.H., Chapman, H.N., Wang, Y.X. Ordered phase transitions triggered by synchronous conformational changes in riboswitch crystals. *Vid. Proc. Adv. Mater.*, Volume 2, 2108246, 2021. DOI: 10.5185/vpoam.2021.08246.
26. **Stagno, J.R.**, Ramakrishnan, S., Heinz, W.F., Magidson, V., Zuo, X., Yu, P., Wang, Y.X. Solid–solid phase transition in adenine riboswitch crystals driven by large conformational changes induced by ligand. *Acta Crystallogr A: Foundations and Advances*. **A77**, a74, 2021. DOI: 10.1107/S0108767321099256.
27. Lee, H.K., Conrad, C.E., Magidson, V., Heinz, W.F., Pauly, G., Yu, P., Ramakrishnan, S., **Stagno, J.R.***, Wang, Y.-X.* Photo-induced solid-to-solid phase transition in macromolecular crystals. *Frontiers in Molecular Biosciences*, 2022, doi.org/10.3389/fmolb.2022.964595.
28. **Stagno, J.R.**, Preparation of RNA microcrystals for serial crystallography. *RNA Structure and Dynamics Studies, Methods Mol Biol*, 2023;2568:233-242, 2022. doi: 10.1007/978-1-0716-2687-0_15.

29. **Stagno, J.R.**, Knoska, J., Chapman, H.N., Wang, Y.-X. RNA time-resolved crystallography experiments using an X-ray free electron laser (XFEL). *RNA Structure and Dynamics Studies, Methods Mol Biol*, 2023;2568:243-249, 2022. doi: 10.1007/978-1-0716-2687-0_15.
30. Ding, J., Lee, Y.T., Bhandari, Y.R., Fan L., Schwieters, C.D., Yu, P., Tarosov, S.G., **Stagno, J.R.**, Ma, B., Nussinov, R., Rein, A., Zhang, J., Wang, Y.-X. Visualizing RNA conformational and architectural heterogeneity in solution. *Nature Communications*. 14(1):714, 2023, doi: 10.1038/s41467-023-36184-x.
31. Lee, H.K., Wilt, H.M., Conrad, C.E., Yu, P., Fan, L., Zhang, J., Shi, G., Ji, X., Wang, Y.-X., **Stagno, J.R.**, Crystal structure of E. coli thiamine pyrophosphate-binding riboswitch in the apo state. 2022 (Structure, *in press*).