BIOGRAPHICAL SKETCH

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NAME: Stroupe, M. Elizabeth

eRA COMMONS USER NAME (credential, e.g., agency login): stroupepi

POSITION TITLE: Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	END DATE MM/YYYY	FIELD OF STUDY
Wake Forest University, Winston-Salem, NC	BS	05/1997	Chemistry
The Scripps Research Institute, La Jolla, CA	PHD	12/2002	Structural Biology
The Scripps Research Institute, La Jolla, CA	Postdoctoral Fellow	08/2003	Structural Biology
Brandeis University, Waltham, MA	Postdoctoral Fellow	06/2009	Cryogenic Electron Microscopy

A. Personal Statement

The overarching goal of my research is to understand the structural basis for complex biological systems. How do multi-domain enzymes that result from gene fusion events during evolution, like Mycoplasma penetrates methionine tRNA synthetase or Salmonella typhimurium siroheme synthase, function? What is the molecular basis for sulfur reduction by the enzyme sulfite reductase? How do NADPH-dependent sulfite reductases differ from their ferredoxin-dependent homologs? How do different bacteria synthesize heme and heme-like molecules? How does the cell assemble ribosomes? These are some examples of questions that the Stroupe laboratory aims to understand using a combination of X-ray crystallography, 3D cryogenic electron microscopy, and biochemistry.

1. Rai J, Parker MD, Huang H, Choy S, Ghalei H, Johnson MC, Karbstein K, Stroupe ME. An open interface in the pre-80S ribosome coordinated by ribosome assembly factors Tsr1 and Dim1 enables temporal regulation of Fap7. RNA. 2021 Feb;27(2):221-233. PubMed Central PMCID: PMC7812869.
2. Pennington JM, Kemp M, McGarry L, Chen Y, Stroupe ME. Siroheme synthase orients substrates for dehydrogenase and chelatase activities in a common active site. Nat Commun. 2020 Feb 13;11(1):864. PubMed Central PMCID: PMC7018833.
3. Johnson MC, Ghalei H, Doxtader KA, Karbstein K, Stroupe ME. Structural Heterogeneity in Pre-40S Ribosomes. Structure. 2017 Feb 7;25(2):329-340. PubMed Central PMCID: PMC5314460.
4. Stroupe ME, Leech HK, Daniels DS, Warren MJ, Getzoff ED. CysG structure reveals tetrapyrrole-binding features and novel regulation of siroheme biosynthesis. Nat Struct Biol. 2003 Dec;10(12):1064-73. PubMed PMID: 14595395.

B. Positions, Scientific Appointments and Honors

Positions and Scientific Appointments

2021 - Professor, Florida State University, Tallahassee, FL
2016 - 2021 Associate Professor (with tenure), Florida State University, Tallahassee, FL
2009 - 2016 Assistant Professor, Florida State University, Tallahassee, FL

Honors

1993 - 1997 Presidential Scholarship in Music, Wake Forest University
2018 Developing Scholar Award, Florida State University
2014 Undergraduate Research Mentor Award, Florida State University
2010 First Year Assistant Professor Award, Florida State University
2004 Howard Hughes Medical Institute Fellow, Life Sciences Research Foundation

1997	Predoctoral Fellow, National Science Foundation
1996	Undergraduate Award for Excellence in Chemistry, Iota Sigma Pi
1996	National Science Foundation Undergraduate Research Fellowship, Wake Forest School of Medicine
1996	Undergraduate Researcher Award, American Institutes of Chemists
1995	National Science Foundation Undergraduate Research Fellowship, Wake Forest University
1994	Freshman Chemistry Achievement Award, CRC Press

C. Contribution to Science

1. Structural biology of ribosome biogenesis: Gene expression turns DNA sequence into a transient copy made of RNA. If the gene codes for a protein, the RNA is then translated by the ribosome, which is a large macromolecule composed of RNA and protein. Cells spend considerable energy making ribosomes – they are the majority of the cell's dry mass. To protect the cell from making mistakes in generating ribosomes, there are proofreading steps along the way, controlled by a large number of assembly factors that transiently associate with the evolving molecules. The Karbstein group at The Scripps Research Institute (Florida) has the unique expertise to isolate intermediate steps along the way, focusing on the small subunit, called the 40S subunit in eukaryotes. Our collaborative research program has allowed us to determine the cryo-EM structure of the pre-40S ribosome as well as an essential proof-reading 80S-like intermediate.

    a. Rai J, Parker MD, Huang H, Choy S, Ghalei H, Johnson MC, Karbstein K, Stroupe ME. An open interface in the pre-80S ribosome coordinated by ribosome assembly factors Tsr1 and Dim1 enables temporal regulation of Fap7. RNA. 2021 Feb;27(2):221-233. PubMed Central PMCID: PMC7812869.
    b. Johnson MC, Ghalei H, Doxtader KA, Karbstein K, Stroupe ME. Structural Heterogeneity in Pre-40S Ribosomes. Structure. 2017 Feb 7;25(2):329-340. PubMed Central PMCID: PMC5314460.
    c. Khoshnevis S, Askenasy I, Johnson MC, Dattolo MD, Young-Erdos CL, Stroupe ME, Karbstein K. The DEAD-box Protein Rok1 Orchestrates 40S and 60S Ribosome Assembly by Promoting the Release of Rrp5 from Pre-40S Ribosomes to Allow for 60S Maturation. PLoS Biol. 2016 Jun;14(6):e1002480. PubMed Central PMCID: PMC4900678.
    d. Ghalei H, Schaub FX, Doherty JR, Noguchi Y, Roush WR, Cleveland JL, Stroupe ME, Karbstein K. Hrr25/CK1δ-directed release of Ltv1 from pre-40S ribosomes is necessary for ribosome assembly and cell growth. J Cell Biol. 2015 Mar 16;208(6):745-59. PubMed Central PMCID: PMC4362465.

2. Siroheme biosynthesis: Siroheme is the specialized iron-containing tetrapyrrole used by sulfite and nitrite reductases in catalyzing the conversion of sulfite to sulfide. It is evolutionarily ancient and in some microorganisms that lack the canonical heme biosynthetic machinery, it is also a precursor to protoporphyin IX hemes. Siroheme is synthesized from the common tetrapyrrole precursor uroporphyrinogen III through three steps. Different organisms use different combinations of two or three enzyme modules: a methyltransferase, a dehydrogenase, a ferrochelatase, or a bifunctional dehydrogenase/ferrochelatase. In proteobacteria, the methyltransferase and bifunctional dehydrogenase/ferrochelatase are expressed as a chimeric, multifunctional enzyme. I solved the first structure of the siroheme synthase from Salmonella typhimurium in 2003 and showed that the enzyme module form an asymmetric homodimer with two methyltransferase active sites and two dehydrogenase/chelatase active sites. Now, we have determined the structure of the dehydrogenase/chelatase module bound to each of its substrates and products. We are currently working to understand the molecular determinants that distinguish bifunctional dehydrogenase/chelatases from their monofunctional dehydrogenase homologs.

    a. Pennington JM, Kemp M, McGarry L, Chen Y, Stroupe ME. Siroheme synthase orients substrates for dehydrogenase and chelatase activities in a common active site. Nat Commun. 2020 Feb 13;11(1):864. PubMed Central PMCID: PMC7018833.
    b. Stroupe M, Warren MJ.. Encyclopedia of Inorganic and Bioinorganic Chemistry. Johnson MK, Scott RA., editors. Online ISBN: 9781119951438: John Wiley & Sons, Inc.; 2017. p.1-6.

c. Stroupe ME, Leech HK, Daniels DS, Warren MJ, Getzoff ED. CysG structure reveals tetrapyrrole-binding features and novel regulation of siroheme biosynthesis. Nat Struct Biol. 2003 Dec;10(12):1064-73. PubMed PMID: 14595395.

3. Structural Biology of Sulfite Reductase: Sulfur is an essential building block of biological molecules, found in the amino acids cysteine and methionine as well as cofactors like biotin and glutathione. Additionally, some organisms use sulfate for anaerobic respiration. The multimeric oxidoreductase sulfite reductase (SiR) is the central redox enzyme in the bio-geo sulfur cycle, reducing sulfite to sulfide by six electrons, either for metabolism (assimilatory SiR) or in anaerobic respiration (dissimilatory SiR). Diverse organisms from bacteria to plants have assimilatory SiRs. Sulfate-reducing prokaryotes that use dissimilatory SiR are found in multiple phyla and include members of the human microbiome. Research in my laboratory has elucidated the basis for subunit association in assimilatory SiR from Escherichia coli, as well as the mechanism for coupled proton/electron transfer, both of which are essential for in vivo activity. SiR's cofactors fuel catalysis: electrons from an NADPH molecule pass through FAD and FMN cofactors bound to SiR's reductase subunit, a cytochrome p450 reductase homolog. Electrons then move to SiR's oxidase subunit, a metalloenzyme with an iron-sulfur cluster that shares a ligand with the iron of a porphyrinoid called siroheme. The evolving substrate, bound at the other face of the siroheme, accepts electrons along with six protons to balance the reaction: $SO3^{2-} + 6H^{+} + 6e^{-} \rightarrow S^{2-} + 3H{\sim}2{\sim}O$. Despite SiR's centrality in biology and a history of interest in its structure and function, questions remain about how SiR's subunits assemble, how electrons move through the complex, and how its metal center is formed. Long-term, I aim to learn how SiR's superstructure drives electron transfer and to understand the differences between NADPH- and ferredoxin-dependent SiR homologs across phyla.

   a. Murray DT, Walia N, Weiss KL, Stanley CB, Randolph PS, Nagy G, Stroupe ME. Neutron scattering maps the higher-order assembly of NADPH-dependent assimilatory sulfite reductase. Biophys J. 2022 May 17;121(10):1799-1812. PubMed Central PMCID: PMC9199090.
   b. Murray DT, Weiss KL, Stanley CB, Nagy G, Stroupe ME. Small-angle neutron scattering solution structures of NADPH-dependent sulfite reductase. J Struct Biol. 2021 Jun;213(2):107724. PubMed PMID: 33722582.
   c. Tavolieri AM, Murray DT, Askenasy I, Pennington JM, McGarry L, Stanley CB, Stroupe ME. NADPH-dependent sulfite reductase flavoprotein adopts an extended conformation unique to this diflavin reductase. J Struct Biol. 2019 Feb 1;205(2):170-179. PubMed PMID: 30654136.
   d. Askenasy I, Murray DT, Andrews RM, Uversky VN, He H, Stroupe ME. Structure-Function Relationships in the Oligomeric NADPH-Dependent Assimilatory Sulfite Reductase. Biochemistry. 2018 Jul 3;57(26):3764-3772. PubMed PMID: 29787249.