

BIOGRAPHICAL SKETCH

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NAME: JOGL, GERWALD

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

POSITION TITLE: Associate Professor of Biology

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)	Completion Date MM/YYYY	FIELD OF STUDY
Karl Franzens Universität Graz, Austria	Mag. rer. nat.	05/1994	Chemistry/Crystallography
Karl Franzens Universität Graz, Austria	Dr. rer. nat.	12/1999	Chemistry/Protein Cryst.
Columbia University, New York	Post-Doc	08/2004	Structural Biology

A. Personal Statement

The course of my professional training reflects my overall goal to contribute to the development of new drugs for the treatment of human disease. My undergraduate research in chemistry and small molecule crystallography focused on the structure of cob(II)alamin, the radical species of coenzyme B12. My graduate research extended this work to structure-function studies of coenzyme B12 binding enzymes. During my postdoctoral training, I contributed to the structural biology of enzymes in central metabolic pathways (eg. triose phosphate isomerase) as well as enzymes in fatty acid metabolism that are potential drug targets for the treatment of obesity (eg. carnitine acetyl transferase, acetyl Co-A synthetase, carnitine palmitoyl transferase). Overall, I acquired substantial expertise in X-ray crystallography and neutron crystallography that provides a strong foundation for our current work. After I moved to Brown University, I began a collaboration with Dr. Steven Gregory. Our long-term vision from the very beginning was to build a collaborative research team to leverage our combined expertise in genetics and structural biology to study ribosome structure and function. In the past years, we succeeded in independently reproducing well-diffracting crystals of *Thermus thermophilus* 70S ribosomes carrying base substitutions in ribosomal RNA or even deletions of ribosomal proteins. Recently, we began using cryo-EM in collaboration with Dr. Reza Khayat to study antibiotic-dependent mutant ribosomes. Insights from this work will contribute to the molecular understanding of decoding by the ribosome.

- Demirci H., Murphy IV F.V., Murphy E., Gregory S.T., Dahlberg A.E., Jogl G. (2013). A structural basis for streptomycin-induced misreading of the genetic code. *Nature Comms.* 4, 1355. PMCID: PMC3552334
- Demirci H., Wang L., Murphy IV F.V., Murphy E.L., Carr J.F., Blanchard S.C., Jogl G., Dahlberg A.E., Gregory S.T. (2013). The central role of protein S12 in organizing the structure of the decoding site of the ribosome. *RNA* 19(12), 1791-801. PMCID: PMC3884664
- Demirci, H., Murphy IV F.V., Murphy E.L., Connetti J.L., Dahlberg A.E., Jogl G., Gregory S.T. (2014). Structural analysis of base substitutions in *Thermus thermophilus* 16S ribosomal RNA conferring streptomycin resistance. *Antimicrob. Agents Chemotherapy* 58(8), 4308-17. PMC: PMC4136021.
- Gregory S.T., Connetti J.L., Carr J.F., Jogl G., Dahlberg A.E. (2014). Phenotypic interactions among mutations in a *Thermus thermophilus* 16S rRNA gene detected with genetic selections and experimental evolution. *J. Bact.* 196(21), 3776-83. PMC: PMC4248807.

B. Positions and Honors

Positions and Employment

- 2011 – present Associate Professor of Biology, Brown University
2004 – 2011 Assistant Professor of Biology, Brown University.

Professional Memberships and Other Experience

- 2004 – present Member, American Crystallographic Association
2006 – present Member, American Society for Biochemistry and Molecular Biology
2008 – present Member, RNA Society
2010 National Science Foundation major research instrumentation review panelist
2012 - present Ad hoc referee for Acta Crystallographica, Biochemical Journal, Biochemistry, Biomed Central Structural Biology, Biomed Central Microbiology, FEBS Journal, Journal of Bacteriology, Journal of Molecular Biology, Nucleic Acids Research, PLoS One, RNA
2012 - present Ad hoc grant proposal reviewer for the Biotechnology and Biological Sciences Research Council, UK, the Czech Science Foundation, the Universities of Vienna and of Graz, Austria
2012 - 2015 Lecturer for the RapiData data collection and structure solving course at the NSLS I.
2014 NIH ad hoc reviewer study section ZRG1 IDM S02.
2015 NIH ad-hoc reviewer study section Macromolecular Structure and Function C.
2016 NIH ad-hoc reviewer study section Macromolecular Structure and Function B.
2017 NIH ad-hoc reviewer study section Macromolecular Structure and Function B.

Honors

- 1992 Erasmus, EU Student Research Scholarship with Glaxo-Wellcome Protein Structure Group, London, UK
1994 M.Sc. Thesis Award, Austrian Chemical Society.
2018 Brown University Elizabeth Leduc Award of Excellence in Teaching in the Life Sciences

C. Contributions to Science

1. Coenzyme B12. My early work in this field focused on the significance of corrin ring flexing motions for the reactivity of coenzyme B12 in enzyme catalyzed reactions. To address this question, we determined neutron crystal structures of the radical coenzyme B12 species cob(II)alamin with a vacant sixth coordination site at the central cobalt atom. Neutron crystallography required the synthesis of this radical B12 coenzyme and the production of up to 5mm long crystals in an oxygen-free environment. This work was complemented by structural studies of two coenzyme B12-dependent enzymes using X-ray crystallography and EXAFS. Our data showed that corrin ring dynamics contribute less to enzyme catalysis than had been anticipated in the field.

1. Langan P., Lehmann M., Wilkinson C., Jogl G., Kratky C. (1998). Neutron Laue diffraction studies of coenzyme cob(II)alamin. Acta Cryst. D 55, 51-59. PMID: 10089394
2. Reitzer R., Gruber K., Jogl G., Wagner U.G., Bothe H., Buckel W., Kratky C. (1999). Glutamate mutase from *Clostridium cochlearium*: the structure of a coenzyme B₁₂-dependent enzyme provides new mechanistic insights. Structure 7, 891-902. PMID: 10467146
3. Champloy F., Jogl G., Reitzer R., Buckel W., Bothe H., Michalowicz A., Meyer-Klaucke W., Kratky C. (1999). EXAFS data support a short axial cobalt-nitrogen bond of the B₁₂ cofactor in the two coenzyme B₁₂-dependent enzymes glutamate mutase and 2-methyleneglutarate mutase. J. Amer. Chem. Soc. 121, 11780-11789. DOI: 10.1021/ja990349q.
4. Jogl G., Wang X., Mason S.A., Kovalevsky A., Mustyakimov M., Fisher Z., Hoffman C., Kratky C., Langan P. (2011). High-resolution neutron crystallographic studies of the hydration of the coenzyme cob(II)alamin. Acta Cryst. D 67, 584-591. PMC: PMCID 3107055.

2. Fatty Acid metabolism. My work in this field defined for the first time the structural biology of fatty acid transfer onto carnitine, a fundamental step in fatty acid catabolism. Structural and biochemical studies of four carnitine acyltransferases, crucial enzymes in fatty acid metabolism, explored the potential of these enzymes as drug targets for the treatment of obesity.

1. Jogl G. & L. Tong. (2003) Crystal structure of carnitine acetyltransferase and implications for the catalytic mechanism and fatty acid transport. *Cell* 112, 113-122. PMID: 12526798.
2. Jogl G. & L. Tong. (2004) Crystal structure of yeast acetyl-coenzyme A synthetase in complex with AMP. *Biochemistry* 43, 1425-1431. PMID: 14769018.
3. Hsiao Y., Jogl G., Tong L. (2004). Structural and biochemical studies of the substrate selectivity of carnitine acetyltransferase. *J. Biol. Chem.* 279, 31584-31589 (2004). PMID: 15155726.
4. Jogl G., Hsiao Y., Tong L. (2005). Crystal structure of mouse carnitine octanoyltransferase and molecular determinants of substrate selectivity. *J. Biol. Chem.* 280, 738-744. PMID: 15492013.

3. Structural enzymology. A number of studies reflect my keen interest in understanding enzymatic function on a molecular and structural level. These publications characterize the structure and function of enzymes either important in eukaryotic cell function or involved in biosynthesis of antibiotic compounds.

1. Jogl G., Rozovsky S., McDermott A.E., Tong L. (2003) Optimal alignment for enzymatic proton transfer: Structure of the Michaelis complex of triosephosphate isomerase at 1.2 Å resolution. *Proc. Natl. Acad. Sci. USA* 100, 1, 50-55. PMCID: PMC140880.
2. Holmes W. & G. Jogl (2006). Crystal structure of inositol phosphate multikinase 2 and implications for substrate specificity. *J. Biol. Chem.* 281, 38109-38116. PMID: 17050532.
3. You Z., Omura S., Ikeda H., Cane D.E., Jogl G. (2007). Crystal structure of the non-heme iron dioxygenase PtlH in pentalenolactone biosynthesis. *J. Biol. Chem.* 282, 36552-36560. PMCID: PMC3010413.
4. Li H. & G. Jogl (2009). Structural and biochemical studies of TIGAR (*TP53*-Induced Glycolysis and Apoptosis Regulator). *J. Biol. Chem.* 284, 1748-1754. PMCID: PMC2615519.

4. Post-synthesis ribosome modification. Both ribosomal RNA and ribosomal proteins are post-transcriptionally and post-translationally modified on sites that are conserved from bacteria to humans. In contrast to tRNA modifications, the function of ribosomal modifications remains poorly understood. In collaboration with Steven Gregory, we studied a considerable number of ribosome methyltransferases. This work defined substrate recognition mechanisms of bacterial methyltransferases and contributed to understanding the significance of these modifications for ribosome function.

1. Demirci H., Gregory S.T., Dahlberg A.E., Jogl G. (2007). Recognition of ribosomal protein L11 by the protein trimethyltransferase PrmA. *EMBO J.* 26, 567-577. PMCID: PMC1783454
2. Demirci H., Belardinelli R., Seri E., Gregory S.T., Gualerzi C., Dahlberg A.E., Jogl G. (2009). Structural rearrangements in the active site of the *Thermus thermophilus* 16S rRNA methyltransferase KsgA in a binary complex with 5'-methylthioadenosine. *J. Mol. Biol.* 388, 271-282. PMCID: PMC2679894
3. Demirci H., Larsen H.G.L., Hansen T., Rasmussen A., Cadambi A., Gregory S.T., Kirpekar F., Jogl G. (2010). Multi-site specific 16S rRNA methyltransferase RsmF from *Thermus thermophilus*. *RNA* 16, 1584-1596. PMCID: PMC2905757.
4. Demirci H., Murphy IV F.V., Belardinelli R., Kelley A.C., Ramakrishnan V., Gregory S.T., Dahlberg A.E., Jogl G. (2010). Modification of 16S ribosomal RNA by the KsgA methyltransferase restructures the 30S subunit to optimize ribosome function. *RNA* 16, 2319-2324. PMCID: PMC2995393.

Complete List of Published Work in MyBibliography:

<http://www.ncbi.nlm.nih.gov/sites/myncbi/gerwald.jogl.1/bibliography/44156019/public/?sort=date&direction=ascending>

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

NIH 1R01GM094157 (MPI: Jogl G and Gregory ST)
NIH/NIGMS
Structural robustness of ribosome functional centers.

09/01/10 – 04/30/20

Role: Co-PI (contact author).

This project seeks to define the limits of structural variability (introduced by eg. antibiotic resistance mutations) of the major functional centers of the bacterial ribosome. Results from these studies will provide important insights into molecular mechanisms of antibiotic resistance and will further our understanding of ribosome function in general.

Brown University Seed Award (MPI: Deaconescu A and Jogi G) 5/1/18 – 4/30/19

Instrumentation for specimen vitrification for cryo-electron microscopy at Brown University

Completed Research Support (past three years)

Brown University Seed Award (MPI: Jogi G and Gregory ST) 5/1/15 – 4/30/17

Engineering orthogonal ribosomes to study ribosome function