

Dr. STÉPHANE LOUIS BENOIT, Ph.D.**Senior Research Scientist**

Department of Microbiology, University of Georgia

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OBJECTIVES

- ✓ To apply my knowledge and skills in microbiology, biochemistry and molecular biology,
- ✓ To educate aspiring scientists,
- ✓ To make a difference in the lives of people and animals, in the United States and around the world.

EDUCATION

1995-1999 **Ph.D. Biochemistry**, INSA Lyon, Villeurbanne, France (Dr. Mandrand-Berthelot).
Thesis: “*the aerobic formate dehydrogenase of Escherichia coli: physiological role, topological study and transcriptional analysis of the fdoGHI operon*”

PROFESSIONAL EXPERIENCE

2018-Present **Senior Research Scientist**, University of Georgia (PI: R.J. Maier).
2012-2018 Associate Research Scientist, University of Georgia (PI: R.J. Maier).
2005-2012 Assistant Research Scientist, University of Georgia (PI: R.J. Maier).
2003-2004 **Industry R&D Team Leader**, BioMérieux, Marcy L’Etoile, France.
2001-2003 Post-doctoral associate, University of Georgia (PI: R.J. Maier).
1999-2001 Post-doctoral associate, University of Georgia (PI: F.C. Gherardini).

2019-Present **Editorial Board Member** for (*Nature*) **Scientific Reports** (25-30 papers/year)

2009-Present *ad hoc* reviewer for *J. Bacteriol.*, *Mol. Microbiol.*, *FEBS Letters*, *Microbiology*, *Scientific Reports*, *Nature Microbiology*, *BMC CAM*, *BMC MICRO*, *Metallomics*, *P.N.A.S.*, *Chem. Comm.*, *Frontiers in Microbiology*, *Food & Function*.

CURRENT RESEARCH PROJECTS

- ♦ **Antimicrobial nickel chelation therapy** in Enterobacteriaceae (*Salmonella enterica* Typhimurium, *Infantis* and *Reading*; *Klebsiella pneumoniae*) and campylobacters (*C. jejuni*, *C. concisus*).
- ♦ **Hydrogenases and anaerobic respiratory pathways in helicobacters** (*H. pylori*, *H. hepaticus*) **and campylobacters** (*C. concisus*, *C. fetus*, *C. hyointestinalis*, *C. jejuni*, *C. ureolyticus*)
- ♦ **Oxidative stress resistance** through methionine sulfoxide recycling (*H. pylori*)
- ♦ **Iron-sulfur clusters maturation** (*H. pylori*)
- ♦ **Stepping outside microbiology**: using metal chelation to **inhibit Alzheimer’s β -amyloid aggregation**.

TEACHING AND MENTORING

Teaching

<u>Term</u>	<u>Course</u>	<u>Lectures</u>	<u>Students</u>
Fall 2021	UGA MIBO3500 (Intro Microbiology), Athens, GA.	21	197
Fall 2019	UGA MIBO3500 (Intro Microbiology), Costa Rica	26	5
Fall 2014	UGA MIBO3500 (Intro Microbiology), Athens, GA.	22	185
Spring 2012	UGA MIBO3000 (Intro Microbiology), Athens, GA. Coordinator for MIBO3000L (lab).	30	93

Mentoring

2001-Present	Mentoring of 13 undergraduate and 11 (Ph.D. and M.S.) graduate students, UGA.
2020-2022	Mentoring (STEM) of one minority middle school student during Covid pandemic.

PUBLICATIONS IN PEER-REVIEWED JOURNALS listed from most recent, with [link](#)

- 45-** Yu B, Choudhury M, Yang X, **Benoit SL**, Womack E, Lyles K, Acharya A, Kumar A, Yang C, Pavlova A, Zhu M, Yuan Z, Gumbart J, Boykin D, Maier RJ, Eichenbaum Z, Wang B.
Restoring and enhancing the potency of existing antibiotics against drug-resistant Gram-negative bacteria through the development of potent small-molecule adjuvants. *ACS Infectious Diseases*, July 8, **2022**. [Link](#).
- 44-** **Benoit SL**, Maier RJ.
Copper toxicity towards *Campylobacter jejuni* is enhanced by the nickel chelator dimethylglyoxime. *Metallomics*, Dec 28, **2021**. [Link](#).
- 43-** **Benoit SL**, Agudelo S, Maier RJ.
A two-hybrid system reveals previously uncharacterized protein-protein interactions within the *Helicobacter pylori* NIF iron-sulfur maturation system. *Scientific Reports*, May 24, **2021**. [Link](#).
- 42-** **Benoit SL**, Maier RJ.
The nickel-chelator dimethylglyoxime inhibits human Amyloid Beta peptide *in vitro* aggregation. *Scientific Reports*, March 23, **2021**. [Link](#).
- 41-** Zhu L, Pearson DW, **Benoit SL**, Xie J, Yang Y, Mondal, Howe JY, Vidal JE, Maier RJ, Zhao Y.
Highly efficient antimicrobial activity of Cu_xFe_yO_z nanoparticles against important human pathogens. *Nanomaterials*, 10(2294). November 20, **2020**. [Link](#).
- 40-** Duma J, Nothhaft H, Weaver D, Fodor C, Linton D, **Benoit SL**, Scott NE, Maier RJ, Szymanski CM.
Influence of protein glycosylation on *Campylobacter fetus* physiology. *Frontiers in Microbiology*, June 17, **2020**. [Link](#).
- 39-** **Benoit SL**, Maier RJ, Sawers, GR, Greening C.
Molecular hydrogen metabolism: a widespread trait of pathogenic bacteria and protists. *Microbiology and Molecular Biology Reviews*, January 29, **2020**. [Link](#).
- 38-** **Benoit SL**, Schmalstig AA, Glushka J, Maier SE, Edison AS, Maier RJ.
Nickel chelation therapy as an approach to combat multi-drug resistant enteric pathogens. *Scientific Reports*, September 21, **2019**. [Link](#).

- 37- Maier RJ, **Benoit SL**.
Role of nickel in microbial pathogenesis. *Inorganics* 7(7). June 26, 2019. [Link](#).
- 36- **Benoit SL**, Maier RJ.
Site-directed mutagenesis of *Campylobacter concisus* respiratory genes provides insight into the pathogen's growth requirements.
Scientific Reports, September 21, 2018. [Link](#).
- 35- Schmalstig AA, **Benoit SL**, Misra SK, Sharp JS, Maier RJ.
A non-catalytic antioxidant role for *Helicobacter pylori* urease.
Journal of Bacteriology, Vol. 200, e00124-18, 2018. [Link](#).
- 34- **Benoit SL**, Holland, A. A., Johnson, M. K., Maier RJ.
Iron-sulfur protein maturation in *Helicobacter pylori*: identifying a Nfu-type cluster carrier protein and its iron-sulfur protein targets. *Molecular Microbiology*, Vol. 108, p. 379-396, 2018. [Link](#).
- 33- De La Cruz LKC, **Benoit SL**, Pan Z, Yu B, Maier RJ, Ji X, Wang B.
Click, release, and fluoresce: a chemical strategy for a cascade prodrug system for codelivery of carbon monoxide, a drug payload, and a fluorescent reporter.
Organic Letters, Vol. 20, p. 897-900, 2018. [Link](#).
- 32- Blum FC, Hu HQ, Servetas SL, **Benoit SL**, Maier RJ, Maroney MJ, Merrell DS.
Structure-function analyses of metal-binding sites of HypA reveal residues important for hydrogenase maturation in *Helicobacter pylori*. *PLOS One*, August 15, 2017. [Link](#).
- 31- **Benoit SL**, Maier RJ.
Helicobacter catalase devoid of catalytic activity protects the bacterium against oxidative stress.
The Journal of Biological Chemistry, Vol. 291, p. 23366-23373, 2016. **Top 1% of JBC**. [Link](#).
- 30- Wang G, Romero-Gallo J, **Benoit SL**, Piazuolo MB, Dominguez RL, Morgan DR, Peek RM, Maier RJ.
Hydrogen metabolism in *Helicobacter pylori* plays a role in gastric carcinogenesis through facilitating CagA translocation. *mBio*, August 16, 2016. [Link](#).
- 29- Kuhns LG, **Benoit SL**, Bayyareddy K, Johnson D, Orlando R, Evans A, Waldrop G, Maier RJ.
Carbon fixation driven by molecular hydrogen results in chemolithoautotrophic-enhanced growth of *Helicobacter pylori*. *Journal of Bacteriology*, Vol. 198, p. 1423-1428, 2016. [Link](#).
- 28- Lamichhane-Khadka R, Miller-Parks, EF, **Benoit SL**, Maier RJ.
Host hydrogen rather than that produced by the pathogen is important for *Salmonella enterica* serovar Typhimurium virulence. *Infection and Immunity*, Vol. 83, p. 311-316, 2015. [Link](#).
- 27- **Benoit SL**, Maier RJ.
Twin-arginine translocation system in *H. pylori*: TatC, but not TatB, is essential for viability.
mBio, January 21, 2014. [Link](#).
- 26- Lamichhane-Khadka R, **Benoit SL**, Maier S, Maier RJ.
A link between gut community metabolism and pathogenesis: molecular hydrogen-stimulated glucarate catabolism aids *Salmonella* virulence. *Open Biology*, December 4, 2013. [Link](#).
- 25- **Benoit SL**, Bayyareddy K, Mahawar M, Sharp JS, Maier RJ.
Alkyl hydroperoxide reductase repair by *Helicobacter pylori* methionine sulfoxide reductase.
Journal of Bacteriology, Vol. 195, p. 5396-5401, 2013. [Link](#).

- 24- Gilbreath JJ, Pich OQ, **Benoit SL**, Besold AN, Cha JH, Maier RJ, Michel SL, Maynard EL, Merrell DS. Random and site-specific mutagenesis of the *Helicobacter pylori* uptake regulator provides insight into Fur structure-function relationships. Molecular Microbiology, Vol. 89, p. 304-323, **2013**. [Link](#).
- 23- **Benoit SL**, Miller E, Maier RJ.
Helicobacter pylori stores nickel to aid its host colonization.
Infection and Immunity, Vol. 81, p. 580-584, **2013**. [Link](#).
- 22- **Benoit SL**, Seshadri S, Lamichhane-Khadka R, Maier RJ.
Helicobacter hepaticus NikR controls urease and hydrogenase activities via the NikABDE and HH0418 putative nickel import proteins. Microbiology, Vol. 159, p. 136-146, **2013**. [Link](#).
- 21- Kuhns LG, Mahawar M, Sharp JS, **Benoit SL**, Maier RJ.
Role of *Helicobacter pylori* methionine sulfoxide reductase in urease maturation.
Biochemical Journal, Vol. 450, p. 141-148, **2013**. [Link](#).
- 20- **Benoit SL**, McMurry JL, Hill SA, Maier RJ.
Helicobacter pylori hydrogenase accessory protein HypA and urease accessory protein UreG compete with each other for UreE recognition.
BBA gen. subjects, Vol.1820, p. 1519-1525, **2012**. [Link](#).
- 19- **Benoit SL**, Maier RJ.
Mua (HP0868) is a nickel-binding protein that modulates urease activity in *Helicobacter pylori*.
mBio, April 19, **2011**. [Link](#).
- 18- Carpenter BM, Gancz H, **Benoit SL**, Evans S, Olsen C, Michel SL, Maier RJ, Merrell DS.
Mutagenesis of conserved amino acids of *H. pylori* Fur reveals residues important for function.
Journal of Bacteriology, Vol. 192, p. 5037-5052, **2010**. [Link](#).
- 17- Shi R, Munger C, Assinas A, **Benoit SL**, Miller E, Matte A, Maier RJ, Cygler M.
Crystal Structures of Apo and Metal-Bound Forms of the UreE Protein from *Helicobacter pylori*; Role of multiple metal binding sites. Biochemistry, Vol. 49, p. 7080-7088, **2010**. [Link](#).
- 16- Brahmachary P, Wang G, **Benoit SL**, Weinberg MV, Maier RJ, Hoover TR.
The human gastric pathogen *Helicobacter pylori* has a potential acetone carboxylase that enhances its ability to colonize mice. BMC Microbiology, Jan 23, p. 8-14, **2008**. [Link](#).
- 15- **Benoit SL**, Zbell AL, Maier RJ.
Nickel enzyme maturation in *Helicobacter hepaticus*: roles of accessory proteins in hydrogenase and urease activities. Microbiology, Vol. 153, p. 3748-3756, **2007**. [Link](#).
- 14- Zbell AL, **Benoit SL**, Maier RJ.
Differential expression of NiFe uptake-type hydrogenase genes in *Salmonella enterica* serovar Typhimurium. Microbiology, Vol. 153, p. 3508-3516, **2007**. [Link](#).
- 13- Seshadri S, **Benoit SL**, Maier RJ.
Roles of His-rich Hpn and Hpn-like proteins in *Helicobacter pylori* nickel physiology.
Journal of Bacteriology, Vol. 189, p. 4120-4126, **2007**. [Link](#).
- 12- **Benoit SL**, Mehta N, Weinberg M, Maier C, Maier RJ.
Interaction between the *Helicobacter pylori* accessory proteins HypA and UreE is needed for urease maturation. Microbiology, Vol. 153, p. 1474-1482, **2007**. [Link](#).

- 11- Maier RJ, **Benoit SL**, Seshadri S.
Nickel-binding and accessory proteins facilitating Ni-enzyme maturation in *Helicobacter pylori*. *Biometals*, Vol. 20, p. 655-664, **2007**. [Link](#).
- 10- **Benoit SL**, Mehta NS, Mysore J, Maier RJ.
In vitro and *in vivo* characterization of alkyl hydroperoxide reductase mutant strains of *Helicobacter hepaticus*. *Biochimica et Biophysica Acta*, Vol.1770, p. 257-65, **2007**. [Link](#).
- 9- Boylan JA, Hummel C, **Benoit S**, Garcia-Lara J, Treglown J, Crane III E, Gherardini FC.
Borrelia burgdorferi bb0728 encodes a coenzyme A disulphide reductase whose function suggests a role in intracellular redox and the oxidative stress response. *Molecular Microbiology*, Vol. 59, p. 475-86, **2006**. [Link](#).
- 8- Mehta NS, **Benoit S**, Mysore J, Sousa RS, Maier RJ.
Hydrogenase mutants of *Helicobacter hepaticus* are deficient in amino acid uptake and in causing hepatic inflammation in A/J mice. *Infection and Immunity*, Vol. 73, p. 5311-5318, **2005**. [Link](#).
- 7- **Benoit S**, Mehta N, Wang G, Gatlin M, Maier RJ.
Requirement of *hydD*, *hydE*, *hypC* and *hypE* genes for hydrogenase activity in *Helicobacter pylori*. *Microbial Pathogenesis*, Vol. 36, p. 153-157, **2004**. [Link](#).
- 6- Wang G, Conover RC, **Benoit S**, Olczak AA, Olson JW, Johnson MK, Maier RJ.
Role of a bacterial organic hydroperoxide detoxification system in preventing catalase inactivation. *The Journal of Biological Chemistry*, Vol. 279, p. 51908-51914, **2004**. [Link](#).
- 5- Mehta N, **Benoit S**, Maier RJ.
Roles of conserved nucleotide-binding domains in accessory proteins, HypB and UreG, in the maturation of nickel-enzymes required for efficient *Helicobacter pylori* colonization. *Microbial Pathogenesis*, Vol. 35, p. 229-234, **2003**. [Link](#).
- 4- **Benoit S**, Maier RJ.
Dependence of *Helicobacter pylori* urease activity on the nickel-sequestering ability of the UreE accessory protein. *Journal of Bacteriology*, Vol. 185, p. 4787-4795, **2003**. [Link](#).
- 3- **Benoit S**, Posey JE, Chenoweth MR, Gherardini FC.
Treponema pallidum 3-phosphoglycerate mutase is a heat-labile enzyme that may limit the maximum growth temperature for the spirochete. *Journal of Bacteriology*, Vol. 183, p.4702-4708, **2001**. [Link](#).
- 2- **Benoit S**, Abaibo, H, Mandrand-Berthelot M-A.
Topological analysis of the aerobic membrane-bound formate dehydrogenase of *Escherichia coli*. *Journal of Bacteriology*, Vol. 180, p.6625-6634, **1998**. [Link](#).
- 1- Abaibou H, Pommier J, **Benoit S**, Giordano G, Mandrand-Berthelot M-A.
Expression and characterization of the *Escherichia coli* *fdo* locus and a possible physiological role for aerobic formate dehydrogenase. *Journal of Bacteriology*, Vol. 177, p.7141-7149, **1995**. [Link](#).

BOOK CHAPTERS

- 2- **Benoit SL**, Maier RJ.
Role of Nickel ions in biological systems.
In Encyclopedia of metalloproteins, **2013**, Kretsinger, R. H., Permakyov, E. A., Uversky, V. N. Springer. New York. [Link](#).

1- Benoit SL, Maier RJ.

Hydrogen and Nickel metabolism in *Helicobacter* species.

In Incredible anaerobes: from physiology to genomics to fuel, 2008, Vol. 1125, p.242-251. Wiegel, J., Maier, R. J., Adams, M. W, Eds.

Annals of the New York Academy of Sciences. New York. [Link](#).

PRESENTATIONS AND SEMINARS (listed from most recent)

17- Benoit SL

Campylobacter concisus: report of first mutants and a new animal model. [Oral presentation](#), *Campylobacter, Helicobacter and related organisms (CHRO)*, [Belfast, UK](#), 2019.

16- Benoit SL

Site-directed mutagenesis of *Campylobacter concisus* respiratory genes provides insight into the pathogen's growth requirements. [Oral presentation](#), Univ. of Georgia, [Athens, GA](#), 2019.

15- Benoit S

NIF system and iron-sulfur clusters network in *Helicobacter pylori*.

[Oral presentation](#), 11th International Biometals Symposium, [Ottawa, Canada](#), 2018.

14- Benoit SL, Holland, AA, Johnson, MK, Maier RJ.

The Nif system of *Helicobacter pylori*: identifying a Nfu-type carrier protein and its iron-sulfur targets. [Poster](#), 117th ASM general meeting, [New Orleans, LA](#), 2017.

13- Benoit SL, Maier RJ.

The gastric pathogen *Helicobacter pylori* can store nickel to aid colonization of the host.

[Poster](#), 8th International Biometals Symposium, [Brussels, Belgium](#), 2012.

12- Benoit SL, Maier RJ.

Mua (HP0868) is a nickel-binding protein that modulates urease activity in *Helicobacter pylori*

[Poster](#), 111th ASM general meeting, [New Orleans, LA](#), 2011.

11- Benoit SL

The quest for nickel in *Helicobacter pylori*.

[Oral presentation](#), Microbiology Department Fall seminars, Univ of Georgia, [Athens, GA](#), 2010.

10- Benoit SL, Maier, RJ.

Link between hydrogen use and cholesterol metabolism in *Helicobacter pylori*.

[Poster](#), 9th International Hydrogenase Conference, [Uppsala, Sweden](#), 2010.

9- Carpenter BM, Gancz H, Benoit SL, Evans S, Michel SL, Maier RJ, Merrell DS.

Analysis of site specific amino acid mutations in the ferric uptake regulator of *Helicobacter pylori*.

[Poster](#), 110th ASM general meeting, [San Diego, CA](#), 2010.

8- Benoit SL, Maier RJ.

Construction and characterization of *Helicobacter pylori* *tatB* and *tatC* mutants.

[Poster](#), 109th ASM general meeting, [Philadelphia, PA](#), 2009.

7- Zbell A, Benoit SL, Maier RJ.

Salmonella typhimurium uptake-type hydrogenases are differentially expressed *in vivo*.

[Poster](#), 8th International Hydrogenase Conference. [Breckenridge, CO](#), 2007.

6- Benoit SL, Zbell A, Maier RJ.

Nickel supplementation cannot restore nickel-enzyme activities in *Helicobacter hepaticus* accessory protein disruption strains. [Poster](#), 106th ASM general meeting, [Orlando, FL](#), 2006.

5- Boylan J, Benoit S, Garcia-Lara J, Gherardini FC.

The regulation and functional characterization of *Borrelia burgdorferi* NADH oxidase.

[Poster](#), 105th ASM general meeting, [Atlanta, GA](#), 2005.

4- Benoit S, Maier RJ.

Dependence of *Helicobacter pylori* urease activity on the nickel-sequestering ability of the UreE accessory protein. Poster, 103rd ASM general meeting, Washington DC, 2003.

3- Benoit S, Posey JE, Chenoweth MR, Gherardini FC.

Preliminary characterization of a temperature-sensitive glycolytic enzyme, 3-phosphoglycerate mutase (Gpm) from *T. pallidum*. Poster, 100th ASM general meeting, Los Angeles, CA, 2000.

2- Benoit S, Abaibou H, Mandrand-Berthelot M.A.

Modèle topologique de la formiate déshydrogénase membranaire aérobie chez *Escherichia coli*. Oral presentation, 25th meeting of the young researchers, Quebec, Canada, 1998.

1- Benoit S, Abaibou H, Mandrand-Berthelot M-A.

Membrane topology of the aerobic formate dehydrogenase of *Escherichia coli*.

Poster, Anaerobic metabolism and electrons transfer systems meeting, Marseille, France, 1997.

TECHNICAL EXPERTISE

- **More than 20 years of experience working with the following BSL-2 microorganisms:**
 - ◆ Spirochetes
 - *Borrelia burgdorferi* (Lyme disease); **among the first to generate mutants in *Bb*** ([Link.](#))
 - *Treponema pallidum* (syphilis)
 - ◆ Gamma-proteobacteria (food poisoning, intestinal diseases)
 - *Salmonella enterica* serovar Typhimurium (including MDR strains)
 - *Klebsiella pneumoniae* (including MDR strains such as NDM- 1 positive)
 - *Shigella flexneri*
 - *Acinetobacter baumannii*
 - ◆ Epsilon-proteobacteria / Campylobacterales
 - *Helicobacter pylori* (human gastric ulcers and cancers)
 - *Helicobacter hepaticus* (murine liver cancers)
 - *Campylobacter concisus* (human oral-gastro-intestinal pathogen; Crohn's disease); **First mutants generated in *C. concisus*** ([Link.](#))
 - *Campylobacter jejuni* (food poisoning, campylobacteriosis)
 - Other *Campylobacter spp.*: *C. hyointestinalis*, *C. fetus*, *C. ureolyticus*.
- **DNA and protein sequence analysis** using BIOCYC, Genbank, Geneious, KEGG, Uniprot.
- **DNA and RNA purification** from various bacterial species, using kits and homemade protocols.
- **Gene cloning, PCR, RT-PCR, qRT-PCR, EMSA, Primer extension, Southern and Northern blot.**
- **Protein expression and purification** (affinity, ion-exchange, hydrophobic, SEC, ÄKTA purification)
- Native and denaturing electrophoresis, Western blot, ELISA, immunoprecipitation.
- **Immunology-based diagnostic assays** (R&D team leader at BioMérieux for one year)
- Handling of radioisotopes (¹³C, ³⁵S, ³²P, ⁶³Ni).
- Atomic absorption spectrophotometry (Shimadzu AA-6701F) knowledge, usage and maintenance.
- **Experience with animals** (*G. mellonella* insect model; mouse and chicken models). **Knowledge of mouse and chicken anatomy.** Experience with euthanasia, organ harvest, gut sample processing.

PATENTS

Nickel chelation therapy. **Benoit, SL** and Maier, RJ. International application number: PCT/US2020/030483

MEMBERSHIPS

American Society of Microbiology (since 2003).
International Biometals Society (since 2011).

LANGUAGES AND CITIZENSHIP

English: fluent (writing, reading, speaking)
French: mother language, fluent (writing, reading, speaking)
American and French dual citizenship.
German and Spanish: basic knowledge.

REFERENCES

1. Dr. Robert J. **Maier**, Ph.D. (Professor, **Georgia Research Alliance Eminent Scholar, current employer**)
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2. Dr. Scott **Merrell**, Ph.D. (Professor and EID Program director, **collaborator**)
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Email: douglas.merrell@usuhs.edu
3. Dr. Binghe **Wang**, Ph.D. (Regents’ Professor, Georgia Research Alliance Eminent Scholar, **collaborator**)
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Email: bwang31@gsu.edu
4. Dr. Aaron **Mitchell**, Ph.D. (Professor, **Head of UGA Microbiology department**)
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5. Dr. Timothy R. **Hoover**, Ph.D. (Professor, UGA **colleague and collaborator**)
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