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the

Sobrado Lab

Annual Newsletter



Happy 2016!!

2015 was a year of great accomplishments by current and former members of the Lab. Congrats to all!!!

Best wishes for 2016!!!!

Greetings from Fralin 107!

In this newsletter you will find a short summary of activities of current and former members of the Sobrado Lab. Enjoy learning what your friends are doing now!



Content

Highlights

Page 2

Structure of NbtG, Dr. Robinson, NSF Grant, Heba at the SEC.

Publications

Page 3

JBC, JOC, Nature, and more

Current Members

Page 4

News from members the team

From the Alumni

Page 5-6

Information from lab alumni

An Unprecedented NADPH Domain Conformation in Lysine Monooxygenase NbtG Provides Insights into Uncoupling of Oxygen Consumption from Substrate Hydroxylation

Received for publication, December 2, 2014, and in revised form, March 20, 2015. Published, JBC Papers in Press, March 23, 2015, DOI: 10.1074/jbc.M114.629485. Claudia Binda^{1,1}, Reeder M. Robinson^{1,1}, Julia S. Martin del Campo², Nicholas D. Keul¹, Pedro J. Rodriguez², Howard H. Robinson¹, Andrea Mattevi¹, and Pablo Sobrado^{1,1}. From the ¹Department of Biology and Biotechnology, University of Pavia, Pavia 27100, Italy, ²Department of Biochemistry, Virginia Tech, Blacksburg, Virginia 24061, and ³Biology Department, Brookhaven National Laboratory, Upton, New York 11973

Background: Flavin-dependent lysine monooxygenases are involved in siderophore biosynthesis and are promising bacterial drug targets.
Result: Biochemical and structural characterization of lysine monooxygenase from *Nocardia farcinica* (NbtG) is presented.
Conclusion: An unprecedented domain conformation blocks the proper binding of NAD(P)H in the active site, which explains the high level of uncoupling observed in NbtG.
Significance: The structural and biochemical data should aid in drug design.



Highlights

....some highlights of 2015

Structure of Lysine Monooxygenase

The structure of the first lysine monooxygenase was obtained after many years of hard work by Reeder and our collaborations in the Mattevi lab in Pavia, Italy. The structure was solved by Dr. Claudia Binda and it was published in JBC. The paper also includes the biochemical characterization of this enzyme. Julia And Pedro also contributed to this work. This is publication #50!

Dr. Reeder Robinson!!!!

Reeder defended his doctoral dissertation and became the 2nd doctoral student from the Sobrado Lab. Reeder's accomplishments include Best Graduate Student in the Biochemistry Department, receiving the Vince Massey Award, and more than 10 peer-reviewed publications. Congrats!!!!

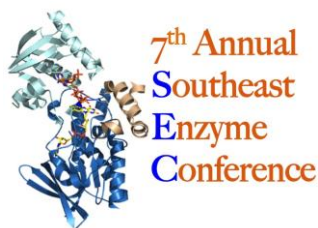
Founding from NSF!!!



Our project on the characterization of chemical reactions catalyzed by atypical flavoproteins was funded by the National Science Foundation (3-years grant). This is a project in collaboration with Prof. Tanner and his group at the University of Missouri, Columbia. Special thanks to Drs. Yumin Dai and Karina Kizjakina for their hard work on 2-haloacrylate

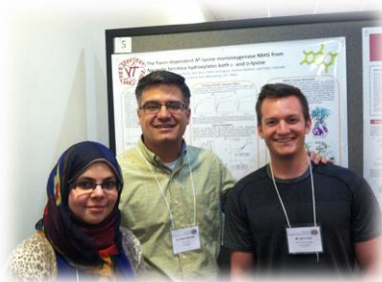
Heba presented her work at the SEC 2015!!!

Heba Abdelwahab delivered a fantastic seminar at the 6th Southeast Enzyme Conference in Atlanta, GA. Heba is a visiting student from Egypt. We also met with Nick Keul (former undergraduate). Nick is now a PhD student at UGA.



Pablo was selected as the Chair of the 2016 Southeast Enzyme Conference

<http://sec.gsu.edu/>





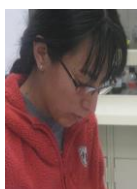
From current members of the Lab:



Pablo Sobrado. Pablo was able to participate in several excellent conferences in 2015. With his family, he visited several cities on the east coast and Toronto, Canada.



Isabel Da Fonseca, postdoc. Isabel took the leading role as mentor of undergraduate students. She was busy mentoring several students in the summer and fall.



Julia S. Martin Del Campo, postdoc. Julia continues her work on HTS assays with SidA. She was able to identify a natural product that inhibits *A. fumigatus* growth *in vitro*. She is now moving to identifying inhibitors of UGM.



Heba Abdelwahab, graduate student. Heba has made great progress in her research. She has found several interesting mutants of NbtG involved in coenzyme selectivity. She has also characterized a rifampicin monooxygenase- she has lots of kinetic data and with Prof. Tanner's group she has solved the structure of this enzyme.



Mynor Medrano, graduate student. Mynor continues working on an ornithine monooxygenase and will complete his MS degree in the spring of 2016.



Benedicta Farson, graduate student. Benedicta joined the lab in the spring of 2015 from the Biochemistry program. She is working on a two-component flavin monooxygenases.



Maddie Marcus, Undergraduate. Maddie is working on a flavin dependent hydratase. She is interested in determine if the reduced FAD functions as an acid/base.

Irene Jenkins, continued her work on plant mutases. **Jendaya O'Grady** worked with SidA mutants and **McKay Hanna** with some UGM mutants.

Rotation Students: We were very happy to work with Kendra Bufkin and Yu Pan from the Biochemistry program during their rotation projects.



Heba's big day!

Heba has been working in the lab on several projects and she has accumulated a tremendous amount of data. She also got engaged and planned her wedding!!! We wish them lots of love and happiness!

Publications:

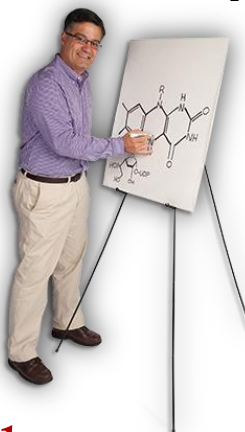
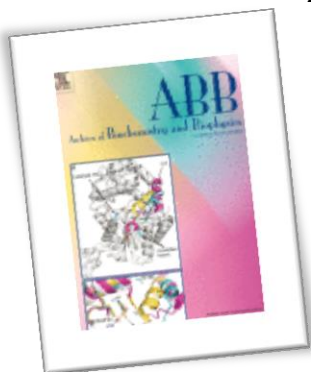
1. Sohrabi, R., Huh, JH, **Badieyan, S.**, Harinantenaina, L., Kingston DGI, Kliebensten, D., Sobrado, P., and Tholl, D., (2015) In Planta Variation of Volatile Biosynthesis: An alternative Biosynthetic Route to the Formation of the Pathogen-Induced Volatile Homoterpene DMNT via Triterpene Degradation in *Arabidopsis* Roots, *Plant Cell*, 27, 874-90.
2. **Badieyan, S**, Bach, R., and Sobrado, P. (2015) Mechanism of *N*-Hydroxylation Catalyzed by Flavin-dependent Monooxygenases . *J. Org. Chem.* 80, 2139-47.



3. Binda, C., **Robinson, R.**, Martin del Campo, J.S., Keul, N., **Rodriguez, P.**, Robinson, H.H., Mattevi, A., and Sobrado, P. (2015) An unprecedented NADPH-domain conformation in Lysine Monooxygenase NbtG provides insights into uncoupling of oxygen consumption from substrate hydroxylation. *J. Biol. Chem.* 290:12676-88.

4. Bai, Y., McCoy, J., Levin, E., **Sobrado, P.**, Rajashankar, K., Fox, B.G., and Zhang, M. (2015) X-ray Structure of Mammalian Stearoyl-CoA desaturase. *Nature*. 524:252-6.

5. **Robinson R**, Qureshi IA, **Klancher CA**, **Rodriguez PJ**, Tanner JJ, Sobrado P. Contribution to catalysis of ornithine binding residues in ornithine N5-monooxygenase. *Arch Biochem Biophys.* 2015 Nov 1;585:25-31.



In the news:

The research from our group was highlighted in the Virginia Tech Magazine.
Check it out!

<http://www.vtmag.vt.edu/winter15/professors.html>

Also, see the announcement of our new grant from NSF:

<https://www.vtnews.vt.edu/articles/2015/08/081215-fralin-enzymes.html>

From the Alumni

Dr. Reeder Robinson, graduate student (2010-2015). Reeder became the second PhD from the lab. He is the expert on N-hydroxylating flavin monooxygenases. After he completed his PhD, he moved to the Medical University of South Carolina with his fiancée, Meg. Reeder is now a postdoc in the lab of Prof. Nate Dolloff at MUSC. He is characterizing drugs against melanoma. Reeder and Meg live in Charleston and will move to their new house in 2016!.



Catherine Klancher, undergraduate (2013-2015). Catherine worked on several projects all related to flavin monooxygenases. She is a co-author on a paper published in ABB early in 2015. Catherine spent the summer backpacking in Europe. She visited Copenhagen, Amsterdam, Prague, Budapest, Vienna, and Berlin.

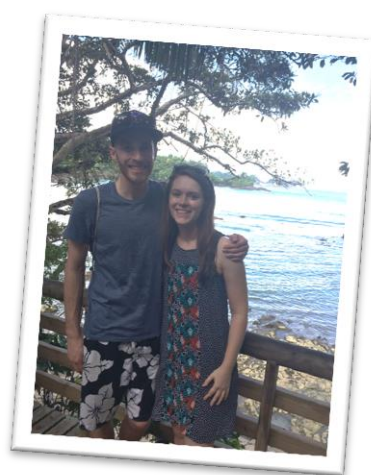


Catherine is currently a graduate student in the Microbiology program at Indiana University. She is working on gene regulation of chitin metabolism in the lab of Dr. Ankur Dalia.



Dr. Karina Kizjakina, potdoc (2011-2013). 2016 will be a very exciting year from Karina. She is getting married in February and moving to a new house in April. She sent us a picture from Lebanon with her fiancée, Tony.

Lauren Kraft, undergraduate (summer 2012). Lauren was a NSF-REU fellow from Lehigh University. She is now a graduate student at Northwestern in the Interdisciplinary Biological Sciences program working in the lab of Prof. Laura Lackner. In the summer of 2015, she visited Costa Rica with her family (see the picture at the famous Manuel Antonio National Park).



From the Alumni

Jun Qi, postdoc (2010-2011). Jun was recently promoted to Associate Research Scientist at Dow. He took his two daughters to Disney and experienced the long lines!! Look at Jun and Congwen beautify girls- Summer and Mili!



Juan Moliva, undergraduate (summer 2011). Juan was a NSF-REU from Penn State that spent a summer in our lab. He is now a PhD student at Ohio State University in the Immunology program. In 2015 he published a review article in Vaccine and another in Journal of Infectious Disease



Jacob Ellerbrock, undergraduate (2012-2014). Jacob worked with the UGMs and flavin dependent monooxygenases. He was a co-author in several papers. In 2015, Jacob traveled to Key West and then to Las Vegas- needless to say he had a great time. In the summer, he moved to Richmond, VA, to start Pharmacy School at VCU!



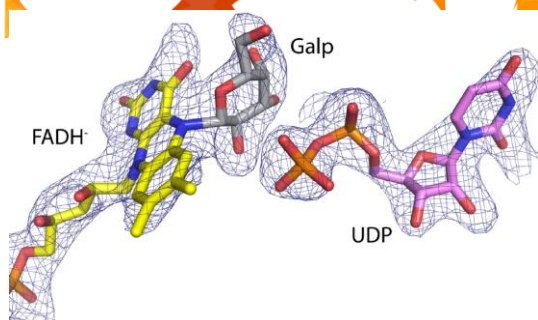
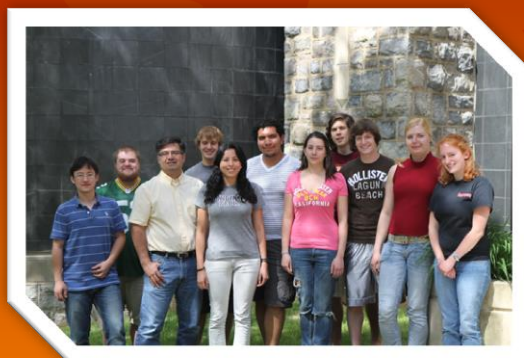
Dr. Somaye Badieyan, postdoc (2012-2013). Somaye is now a postdoc in the laboratory of Prof. Neil Marsh at the University of Michigan. Somaye was our computational chemist. She helped us understand the role of protein/cofactor motion in SidA. She also determined the chemical mechanism of SidA using DFT.



Karishma Tolani, undergraduate (2011-2013). Karishma performed high throughput screening with UGM and SidA. After graduating from VT she obtained a MS in Biomedical Sciences at Drexel University. In 2014, she spent 3-weeks traveling through India. Then she entered a Medical School in St. George University, Grenada, West Indies. In the summer of 2015, she traveled with her sisters to Europe- visiting 12 countries!!!!. She will be moving to NY for her clinical rotations.



ALUMNI CONTACT INFORMATION



FLAVINS!!!!

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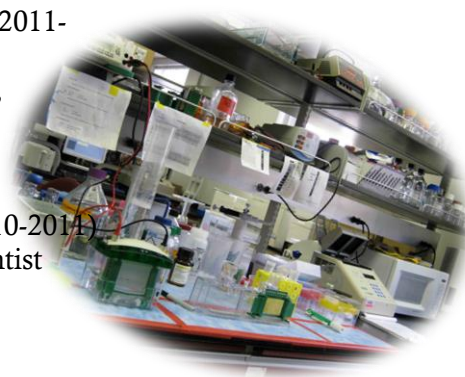
2. **Dr. Jun Qi**, Postdoc (2010-2011)
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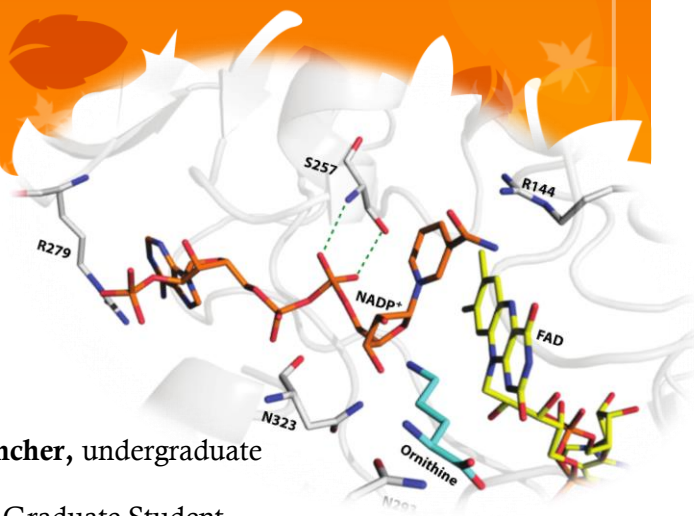
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ALUMNI CONTACT INFORMATION



FLAVINS!!!!



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