

COSTAS A LYSSIOTIS

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EDUCATION

The Scripps Research Institute, La Jolla, CA
Chemical Biology Ph.D. Candidate

Fall 2005 – Current

Graduate Thesis Research, Advisor – Professor Peter G. Schultz

My research focuses on the identification and characterization of chemicals that reprogram cell fate. In particular, we found that histone deacetylation is responsible for maintaining the lineage identity of oligodendrocyte precursor cells, where pharmacological inhibition of histone deacetylase activity reverts precursor cells back to the multipotent stem state (2). More recently, we have developed a small molecule screening platform to identify chemical complements for the reprogramming factors that induce pluripotency in somatic cells. Implementation of this strategy has led to the identification of compounds that can replace the reprogramming factors Klf4 and Sox2 (5). Current and future efforts with these compounds have begun to unravel the mechanisms at play during epigenome overhaul.

University of Michigan, Ann Arbor, MI
B.S. Chemistry & Biochemistry

December 2004

Graduated with distinction and highest honors in chemistry
Dean's List: Fall/Winter 2001, Winter 2002, Fall 2003, Fall/Winter 2004

Undergraduate Thesis Research, Advisor – Professor Gary D. Glick

My research focused on testing the in vitro activity of a new class of pro-apoptotic compounds with therapeutic properties in several models of autoimmunity. Aspects of this work included combination studies to determine what properties are necessary for selectivity, elucidating the cellular mechanism of action (3,6) and enhancing efficacy (1).

PUBLICATIONS

8. Hu XV, **Lyssiotis CA**, Tao H, Baker RK, Rodrigues TMA, Miraglia L, Orth AP, Lyons GE, Wu X & Schultz PG. (2009) A Functional Genomics Screen Identifies a Regulator of DNA Methylation. Submitted.
7. Zhu S, Wurdak H, Wang Y, Galkin A, Tao H, Li J, **Lyssiotis CA**, Yan F, Tuu B, Miraglia L, Walker J, Sun F, Orth A, Harris J, Schultz PG & Wu X. (2009) A Genomic Screen Identifies TYRO3 as a MITF Regulator and Melanoma Oncogene. *Proc. Natl. Acad. Sci.* 106. 17025-17030.
6. Blatt NB, Boitano AE, **Lyssiotis CA**, Oipari AW & Glick GD. (2009) Bz-423 Superoxide Signals B Cell Apoptosis via Mcl-1, Bak, and Bax. *Biochem. Pharmacol.* 78. 966-973.

5. **Lyssiotis CA**, Foreman RK, Staerk J, Garcia M, Mathur D, Markoulaki S, Hanna J, Lairson LL, Charette BD, Bouchez L, Kunick C, Brinker A, Cho CY, Schultz PG & Jaenisch R. (2009) Reprogramming of Murine Fibroblasts to iPS Cells With Chemical Complementation of Klf4. *Proc. Natl. Acad. Sci.* 106. 8912-8917.
 - » PNAS most read articles, June 2009.
 - » Highlighted in *Nature Cell Biology* **11**, 796 (2009).
 - » Highlighted in *Nature Reports Stem Cells*, May (2009).
 - » Highlighted in *Regenerative Medicine* **4**, 371-374 (2009).
 - » Highlighted in *Assay and Drug Development Technologies*, August (2009).
4. Zhu S, Wurdak H, Wang J, **Lyssiotis CA**, Peters EC, Cho CY, Wu X & Schultz PG. (2009) A Small Molecule Primes Embryonic Stem Cells for Differentiation by Targeting NME2. *Cell Stem Cell.* **4**, 416–426.
 - » Highlighted in *Cell Stem Cell* **4**, 373-374 (2009).
 - » Highlighted in *Nature Chemical Biology* **5**, 456-457 (2009).
 - » Highlighted in *Molecular Interventions* **9**, 167 (2009).
3. Blatt NB, Boitano AE, **Lyssiotis CA**, Opipari AW & Glick GD. (2008) Bz-423 Superoxide Signals Apoptosis via Selective Activation of JNK, Bak, and Bax. *Free Radic. Biol. Med.* **45** (9), 1232-42.
2. **Lyssiotis CA**, Walker J, Wu C, Kondo T, Schultz PG & Wu X. (2007) Inhibition of Histone Deacetylase Activity Induces Developmental Plasticity in Oligodendrocyte Precursor Cells. *Proc. Natl. Acad. Sci.* **104**, 14982-14987.
 - » Highlighted in *Cell* **131**, 197-198 (2007).
1. Bednarski JJ, **Lyssiotis CA**, Roush RR, Boitano AE, Glick GD & Opipari AW. (2004) A novel benzodiazepine increases the sensitivity of B Cells to receptor stimulation with synergistic effects on calcium signaling and apoptosis. *J. Biol. Chem.* 279, 29615 – 29621.

REVIEWS

11. **Lyssiotis CA**, Lairson LL, Boitano AE & Schultz PG. (2009) Pharmacological Control of Stem Cell Fate and Developmental Potential: A Comprehensive Review. *Angew. Chem. Int. Ed.* Manuscript in Preparation, invited review.
10. **Lyssiotis CA**, Charette BD & Lairson LL. (2009) Reprogramming Developmental Potential. Lakshmi pathy U, Chesnut JD & Thyagarajan B, eds. In: *Emerging Technology Platforms for Stem Cells*. New York, NY. John Wiley & Sons Press, Inc. 51-85.

TALKS

- “Chemical Methods to Reprogram Developmental Potential.” *Genomics Institute of the Novartis Research Foundation Board Meeting, San Diego, CA – (March 2009).*
- “Reprogramming of murine fibroblasts to iPS cells: Chemical Complementation of Klf4.” *Stem Cells and Regenerative Medicine World Congress, Palm Springs, CA – (January 2009).*
- “Chemical Complementation of Klf4 in a reduced reprogramming cocktail.” *Graduate Student Retreat, San Diego, CA – (September 2008).*

DISTINCTIONS

2010	Human Frontiers Science Foundation Fellowship
2006-2009	National Science Foundation Fellowship
2005	American Chemical Society Outstanding Senior Award
2005	Sidney Find Teaching Prize Nominee
2005	Eli Lilly Chemistry Scholarship

2004 Eli Lilly Research Fellowship
2004 Smeaton Research Fellowship
2003 Lubrizol Chemistry Scholarship
2002 Smeaton Research Fellowship

TEACHING EXPERIENCE

Graduate Student Instructor

Advisor – Professor Peter G. Schultz
Bio-organic Chemistry, *Fall 2007*

Undergraduate Student Instructor

Advisor – Professor Brian P. Coppola
Introductory Organic Chemistry 210 Honors, *Fall 2003*
Advanced Organic Chemistry 216 Honors, *Winter 2004*
Introductory Organic Chemistry 210 Honors, *Fall 2004*
Organic Chemistry 215 Honors, *Winter 2005*

REFERENCES

Lewis C. Cantley
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Harvard Medical School
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Professor, Department of Chemistry
The Scripps Research Institute
And
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Rudolf Jaenisch, M.D.
Professor of Biology
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Benjamin Cravatt, Ph.D.
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