

COSTAS A LYSSIOTIS

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EDUCATION

- The Scripps Research Institute**, La Jolla, CA March 2010
Ph.D. Chemical Biology | *Insight into the Reprogramming of Cell Fate with Small Molecules*
National Science Foundation Fellow
- University of Michigan**, Ann Arbor, MI December 2004
B.S. Chemistry and Biochemistry
Graduated with distinction and highest honors in Chemistry

RESEARCH EXPERIENCE

- Damon Runyon Post-Doctoral Fellowship*, Advisor – Professor Lewis C. Cantley 2010 – current
The focus of my research in the Cantley lab is aimed at understanding the underlying differences in metabolism between cancer cells and normal cells. In particular, I am interested in exploring underappreciated transcriptional control mechanisms that are regulated by cellular nutrient levels. Specifically, I am studying the nuclear role of the proliferative isoform of pyruvate kinase (PK-M2) in pancreatic cancer cells and the immune system. Future efforts will extend this experimental strategy to other glycolytic enzymes with purported nuclear roles.
- Human Frontiers Science Program Short-term Fellowship*, Advisor – Professor Douglas Hanahan 2010
My research focused on analyzing the expression of pyruvate kinase isoenzyme expression in two mouse models of *de novo* pancreatic cancer. Specifically, we found that PK-M2 was translocated to the nucleus in (i) a subset of lymphocytes within the tumor mass of pancreatic ductal adenocarcinomas and (ii) a majority of the tumor cells in liver metastases. The biological mechanisms by which this process occurs and its relevance to cancer are being evaluated during my post-doctoral fellowship in the Cantley lab.
- Graduate Thesis Research*, Advisor – Professor Peter G. Schultz 2005-2010
My research focused on the identification and characterization of chemicals that reprogram cell fate [8, 9]. In particular, we found that histone deacetylation (HDAC) is responsible for maintaining the lineage identity of oligodendrocyte precursor cells, where pharmacological inhibition of HDAC activity reverts precursor cells back to the multipotent stem state [2]. We also developed a small molecule screening platform to identify chemical complements for the reprogramming factors that induce pluripotency in somatic cells. Implementation of this strategy led to the identification of compounds that replace the reprogramming factors Klf4 and Sox2 [5, 8-9]. Subsequent efforts with these compounds have furthered our understanding of the mechanisms at play during epigenome overhaul.
- Undergraduate Thesis Research*, Advisor – Professor Gary D. Glick 2002-2005
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

11. Gao D, Inuzuka H, Tan MM, Fukushima H, Locasale JW, Liu P, Wan L, Zhai B, Chin YR, Shaik S, **Lyssiotis CA**, Gygi SP, Toker A, Cantley LC, Asara JM, Harper JW & Wei W. (2011) mTOR Drives its Own Activation via SCF ^{β -TRCP}-dependent Degradation of the mTOR Inhibitor DEPTOR. *Molecular Cell*. 44, 290–303.
10. Locasale JW, Grassian AR, Melman T, **Lyssiotis CA**, Mattiani K, Bass AJ, Heffron G, Metallo CM, Muranen T, Sharfi H, Sasaki A, Anastasiou D, Mullarky E, Vokes NI, Sasaki M, Beroukhim R, Stephanopoulos G, Ligon AH, Meyerson M, Richardson AL, Chin L, Wagner G, Asara JM, Brugge JS, Cantley LC & Vander Heiden MG. (2011) Phosphoglycerate Dehydrogenase Diverts Glycolytic Flux and Contributes to Oncogenesis. *Nat. Genet.* 43, 869–874.
 - » Highlighted in *Nature Reviews Cancer* 11, 621 (2011).
 - » Highlighted in *Nature Biotechnology* 29, 809 (2011).
 - » Highlighted in *Cell Metabolism* 14, 285-6 (2011).
 - » Highlighted in *Science Business Exchange* 4, 30 (2011).
 - » Highlighted in *Pigment Cell Melanoma Research* (2011).
9. Sadanandam A, Futakuchi M, **Lyssiotis CA**, Gibb WJ & Singh RK. (2011) A Mouse Model that Mimics the Osteolytic Microenvironment of Human Breast Cancer Bone Metastasis is Used to Predict a Therapeutic Agent that Targets the Tumor-Bone Interface. *BMC Cancer*. 11, 304–317.
 - » BMC Cancer top-10 articles, August 2011.
8. *Staerk J, ***Lyssiotis CA**, Foreman RK, Bollong M, Zhu S, Garcia M, Bouchez L, Lairson LL, Charette BD, Brinker A, Cho CY, Jaenisch R & Schultz PG. (2011) Inhibition of c-Src kinase activity functionally substitutes for Sox2 during the direct reprogramming of murine fibroblasts to iPS cells. *Angew. Chem. Int. Ed.* 50, 5734–5736. [*shared authorship]
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. *PNAS*. 106, 17025–17030.
6. Blatt NB, Boitano AE, **Lyssiotis CA**, Opipari AW & Glick GD. (2009) Bz-423 Superoxide Signals B Cell Apoptosis via Mcl-1, Bak, and Bax. *Biochemical Pharmacology*. 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. *PNAS*. 106, 8912–8917. [*shared authorship]
 - » 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 Radical Biology and Medicine*. 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. *PNAS*. 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. *Journal of Biological Chemistry*. 279, 29615–29621.

REVIEWS

13. **Lyssiotis CA[#]**, Lairson LL, Boitano AE, Wurdak H, Zhu S & Schultz PG[#]. (2011) Chemical Control of Stem Cell Fate and Developmental Potential. *Angewandte Chemie International Edition*. 50, 200–242. [[#]corresponding author]
12. **Lyssiotis CA[#]**, Charette BD & Lairson LL. (2009) Reprogramming Developmental Potential. Lakshmi U, Chesnut JD & Thyagarajan B, eds. In: *Emerging Technology Platforms for Stem Cells*. New York, NY. John Wiley & Sons Press, Inc. 51–85. [[#]corresponding author]

FELLOWSHIPS AND DISTINCTIONS

- 2010-current Damon Runyon Post-doctoral Fellowship
Reversing the Warburg Effect in Basal-like Breast Cancer: A Unique Point for Therapeutic Intervention
Prof. Lewis Cantley | Harvard Medical School
- 2010 Human Frontiers Science Foundation Short Term Fellowship (June 1st – August 31st)
Analysis of the Role of Pyruvate Kinase Isoform Expression in Pancreatic Cancer
Prof. Doug Hanahan | École Polytechnique Fédérale de Lausanne
- 2006-2009 National Science Foundation Pre-doctoral Fellowship
Probing Signal Transduction Pathways in Stem Cells with Small Molecules
Prof. Peter Schultz | The Scripps Research Institute
- 2005 American Chemical Society Outstanding Senior Award
- 2005 Sidney Fine Teaching Prize Nominee

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.” *The Scripps Research Institute Retreat, San Diego, CA – (September 2008).*

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

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