## NICOLE J. DE NISCO, PH.D.

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## EDUCATION

- August 2013Ph.D. in Molecular Biology, Massachusetts Institute of Technology, Department<br/>of Biology, Cambridge, MA.<br/>Thesis Advisor: Dr. Graham C. Walker<br/>Dissertation: Global analysis of the transcriptional regulation of Sinorhizobium<br/>meliloti cell cycle progression and study of cell cycle regulation during symbiosis<br/>with Medicago sativa
- May 2007Bachelor of Science in Biology with a minor in Biomedical Engineering,<br/>Massachusetts Institute of Technology, Cambridge, MA.

# **RESEARCH POSITIONS**

October 2018 – Present: Assistant Professor, Department of Biological Sciences, University of Texas at Dallas

Research Focus: Molecular basis of clinically-relevant microbial pathogenesis and host response during recurrent urinary tract infection through an ongoing clinical collaboration with the Department of Urology at UT Southwestern Medical Center. Current research directions include: (1) Characterizing the host inflammatory response during RUTI and elucidating its role in recurrence (2) Deciphering the virulence mechanisms of clinically-relevant RUTI pathogens (3) Understanding the impact of the urinary microbiome on UTI recurrence through metagenomics.

January 2014 – September 2018: Postdoctoral Fellow, Howard Hughes Medical Institute, UT Southwestern Medical Center (2017-2018); Department of Molecular Biology, UT Southwestern Medical Center (2014-2017). Advisor: Dr. Kim Orth

Research Focus: (1) Manipulation of host signaling pathways by *Vibrio parahaemolyticus* Type III Secretion System 1 (T3SS1) effectors, (2) Mechanism of autophagosome-lysosome fusion inhibition and MAPK activation by T3SS1 effector VopQ, and (3) Etiology, pathology, and virulence mechanisms defining recurrent urinary tract infections in postmenopausal women.

June 2008 - August 2013: Graduate Research Assistant, Massachusetts Institute of Technology, Department of Biology. Advisor: Dr. Graham C. Walker Research Focus: (1) Efficient synchronization of *Sinorhizobium meliloti* through activation of the stringent response by nutrient deprivation, (2) Global analysis of the transcriptional regulation of *S. meliloti* cell cycle progression, (3) Study of the role cell cycle regulation in *S. meliloti* bacteroid differentiation during symbiosis with *Medicago sativa*.

January 2004 - August 2007: Undergraduate Research Assistant, Massachusetts Institute of Technology, Department of Chemistry. Advisor: Dr. Cathy L. Drennan

Research Focus: Structural and biophysical analysis of the mechanism of action of the *Lactobacillus leichmannii* monomeric ribonucleotide reductase RTPR.

## **HONORS AND AWARDS**

2018	Rising STARs Award, University of Texas System Board of Regents
2016	UT STEMS Teaching Fellowship, University of Texas Southwestern Medical Center and University of Texas at Dallas
2011	The Gene Brown-Merck Award for Excellence in Teaching, Department of Biology, Massachusetts Institute of Technology
2007	The Merck Prize for outstanding research and academic performance in biophysical or bioinformatics science, Department of Biology, Massachusetts Institute of Technology
2006	Carl P. and Marie G. Dennett Memorial Scholar, Massachusetts Institute of Technology. Awarded a full year of tuition based on academic merit, quality of character, leadership and general future promise.
2004-2006	The Eleanor and Anthony DeFrancis Scholarship, National Italian American Foundation. Awarded \$10,000/year for undergraduate tuition based on academic merit with required yearly reapplication. Awarded for 3 consecutive years.

# PUBLICATIONS

**De Nisco NJ**, Rivera-Cancel G, Orth K. (2018) The biochemistry of sensing: Enteric pathogens regulate type III secretion in response to environmental and host cues. *mBio* 9: e02122-17

Chimalapati S, de Souza Santos M, Servage K, **De Nisco NJ**, Dalia AB, Orth K. (2018) Natural Transformation in *Vibrio parahaemolyticus:* a Rapid Method to Create Genetic Deletions. *J Bacteriol* **200:** e00032-18

**De Nisco NJ**, Kanchwala M, Li P, Xing C, Orth K. (2017) Cytotoxic Vibrio T3SS1 Rewires Host Gene Expression to Subvert Cell Death Signaling and Activate Cell Survival Networks. *Science Signaling* **10(479):** eaal4501.

- Science Signaling Cover Article, May 2017
- Featured in UT Southwestern Medical Center Press Release, June 2017

**De Nisco NJ**, Orth K, VanHook AM. (2017) *Vibrio* rewires host cells. *Science Signaling* **10(479)**: eaan5621. *Podcast.* 

- Pini F\*, De Nisco NJ\*, Ferri L, Penterman J, Fioravanti A, Brilli M, Mengoni A, Bazzicalupo M, Viollier PH, Walker GC, Biondi EG. (2015) Cell cycle control by the master regulator CtrA in *Sinorhizobium meliloti.* PLOS Genetics 11(5): e1005232. (\*co-first author)
- **De Nisco NJ**, Abo RP, Wu CM, Penterman J, Walker GC. (2014) Global analysis of cell cycle gene expression of the legume symbiont *Sinorhizobium meliloti*. *Proc Natl Acad Sci U S A* 111(9): 3217-24.
  - Featured Research on MIT Bio MicroCenter website, October 2016
- Penterman J, Abo RP, **De Nisco NJ**, Arnold MF, Longhi R, Zanda M, Walker GC. (2014) Host plant peptides elicit a transcriptional response to control the *Sinorhizobium melilot*i cell cycle during symbiosis. *Proc Natl Acad Sci U S A* 111(9): 3561-6.

Pini F, Frage B, Ferri L, De Nisco NJ, Mohapatra S, Taddei L, Fioravanti A, Dewitte F, Galardini M, Brilli M, Villeret V, Bazzicalupo M, Mengoni A, Walker GC, Becker A, Biondi EG. (2013) The DivJ, CbrA and PleC system controls DivK phosphorylation and symbiosis in *Sinorhizobium meliloti*. *Mol Microbiol* 90: 54-71.

Kobayashi H, **De Nisco NJ**, Chien P, Simmons LA, Walker GC. (2009) *Sinorhizobium meliloti* CpdR1 is critical for co-ordinating cell cycle progression and the symbiotic chronic infection. *Mol Microbiol* **73**: 586-600.

- Molecular Microbiology Cover Article, August 2009

### MANUSCRIPTS IN REVISION

**De Nisco, NJ,** Casey AK, Kanchwala M, Coskun F, Xing C, Orth K. (2019) Manipulation of noncanonical Ire1-dependent MAPK signaling by a Vibrio agonist-antagonist effector pair. *In revision.* 

### MANUSCRIPTS IN PREPARATION

**De Nisco NJ\***, Neugent M, Mull J, Chen L, Kuprasertkul I, de Souza Santos M, Palmer K, Zimmern PE, Orth K\*. Direct detection of intracellular bacteria and chronic inflammation in the bladder wall of postmenopausal women with recurrent urinary tract infection. *In preparation.* 

### **RESEARCH FUNDING**

### **GRANTS AWARDED**

- July 2018University of Texas System Board of Regents Rising STARsAward. Recruitment grant from the UT-System covering lab startup<br/>capital expenses.
- August 2014-August 2017 Infectious Diseases Training Program Postdoctoral Fellowship NIAID T32 Ruth L. Kirschstein NRSA 5T32AI070116-08, 5T32AI070116-09, 5T32AI070116-10. UT Southwestern Medical Center institutional training program fellowship with competitive application and renewal process.
- September 2007-June 2010 Biology Training Program Pre-doctoral Grant in the Biological Sciences NIGMS NRSA 5T32GM007287-33, 5T32GM007287-34,

### **GRANTS SUBMITTED**

October 2017

**NIH Pathway to Independence Award (K99/R00).** Submitted October 2017. Title: "Uncovering the pathogens and pathology responsible for UTI recurrence in postmenopausal women."

## **TEACHING POSITIONS**

Fall 2016: Visiting Lecturer, UT-PACT BA/MD Program, University of Texas at Dallas

### BIOL1V00.PA2. The Modern Purge: Disease Eradication in the 21<sup>st</sup> Century

Developed and taught a Readings Course for UT-PACT as part of the UT STEMS Teaching Fellowship Program. I was responsible for the conception and implentation of this course. I curated course material, developed the syllabus, lectured, moderated class discussions and debates, managed the course website, assigned weekly written excercises, graded all coursework, and designed the final project. I developed this public health-focused readings course to introduce students to basic principles of infectious disease and public health on a global scale. Student readings contained a mixture of fiction, non-fiction, primary research articles, and film. Case studies covered diverse pathogens from viruses (e.g. smallpox) to parasitic nematodes (e.g. Guinea Worm). Received high student evaluation scores (Course Experience: 4.93/5, Instructor: 4.97/5, Student Experience 5/5).

July 2012-May 2013: Content Developer, edX (MITx), Massachusetts Institute of Technology

#### 7.00x. Introduction to Biology - The Secret of Life

As part of a team of educators led by Dr. Eric Lander of the Broad Institute, I helped to develop the course architecture and content for MITx/EdX's first online biology course launched in Spring 2013. I was involved in multiple aspects of content development from the inception of the project until the end of the inaugural run of the course. I specifically contributed to learning objective development, module architecture and content, lecture production, lab video design, problem type research, problem set design and testing, and forum moderation.

Spring 2011: Teaching Assistant, OCW Scholar, Massachusetts Institute of Technology

#### 7.01SC. Fundamentals of Biology

Developed content for the Biochemistry section of the MIT Open Courseware (OCW) Scholar course 7.01SC. Specifically, I curated lecture clips, created quiz questions and practice problems I also filmed a recitation (help session) for covalent bonds, hydrogen bonds section.

### Spring 2010-Fall 2011: Teaching Fellow, Harvard University Extension School

#### BIOS E-155. Medical Microbiology

This popular course offered by the Harvard Extension School introduces students to the microbial species that cause human disease. Topics include bacteria, fungi, viruses, protozoa, antibiotic resistance, and global public health. For three semesters, I led two mandatory weekly sections for undergraduate and graduate students of about 20 students each. For each section, I composed a set of discussion questions, which I used to gauge the student's understanding of the

lecture material and pinpoint topics that needed further review. I also helped to design and grade weekly assignments, midterm and final exams. **Received high student evaluation scores** (average 4.8/5 on overall instructor score)

Fall 2010: Teaching Assistant, Department of Biology, Massachusetts Institute of Technology

#### 7.21 Microbial Physiology

This mixed undergraduate and graduate level course introduces students to the biochemical properties of microorganisms that enable growth in diverse conditions. Topics include genetic and metabolic regulation of enzymes, structure and function of the bacterial cell envelope, protein secretion in pathogensis, quorum sensing and biofilms. As the sole teaching assistant, I led two weekly sections of 20-25 students covering lecture topics, created and graded weekly problem sets, wrote and graded midterm and final exam questions, and assigned course grades. I also helped to develop a new component of the course, the *Microbiology in the News* group presentation project, for which students present a recent microbiology-related news article and explain the science behind the discovery. **Received high student evaluation scores (average 4.9/5 on overall instructor score). Received the Gene Brown-Merck Award for Excellence in Teaching** for my work in this course in Spring 2011.

Spring 2009: Teaching Assistant, Department of Biology, Massachusetts Institute of Technology

### 7.014. Introductory Biology

This introductory biology course fulfills the general core biology requirement for all undergraduates. I led two biweekly sections of about 20-25 students each consisting of primarily non-majors. I graded problem sets and exams and also helped the course administrator develop course materials including problem sets, exams and study guides. **Received high student evaluation cores (average 4.7/5 on overall instructor score).** 

# **MENTORING POSITIONS**

Summer 2015: STARS Summer Research Program Mentor, UT Southwestern Medical Center Supervised and mentored a Dallas area high school student (Catherine Jiang) for a summer in the Orth lab as part of the Science Teacher Access to Resources at Southwestern (STARS) summer research program. I designed Catherine's project, taught her the scientific process, trained her in diverse lab techniques and supervised her work in the lab daily. The progress Catherine made on the project, which is being continued by a graduate student, will earn her junior authorship when it is published.

Fall 2010-Spring 2013: Undergraduate Research Opportunitiies Program (UROP) Mentor,

Massachusetts Institute of Technology

Supervised and mentored an MIT undergraduate (Max Wu) for three years in the Walker lab. I trained Max in diverse laboratory techniques, helped to set his research goals, evaluated his research progress on a monthly basis and supervised his work in the lab for typically 12 hours a week. During his time as my mentee, Max made significant contributions that earned him junior authorship on my 2014 PNAS manuscript. Max was also selected to give an oral presentation on his research at the MIT Undergraduate Research Symposium in 2013.

### Fall 2009-Spring 2013: Graduate Resident Tutor, Massachusetts Institute of Technology Served as a graduate resident tutor (GRT) for the Next House undergraduate dormitory for four

years. I lived in the dormitory and was responsible for supporting and enhancing the residential living and learning environment for a group of 40 undergraduate students. I was a mentor and role model in charge of fostering a supportive, safe and positive living environment for all of my residents. I provided stress-reducing and community-building programming in the form of group activities and study breaks. Importantly, I provided an outlet for stress management and 24 hour access to academic, medical and mental health services. I received extensive training in counseling, conflict management, emergency response and mental health.

## **SCIENTIFIC PRESENTATIONS – INVITED SEMINARS**

- **2018** Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction (SUFU) Winter Meeting. Austin, TX. February 2018. Podium Presentation. Title: "Understanding the pathogens responsible for recurrent urinary tract infections in postmenopausal women."
- 2017 Autophagy Works In Progress Seminar Series, Center for Autophagy Research, University of Texas Southwestern Medical Center. October 2017. Title: "RNA-seq analysis of *Vibrio* T3SS1-orchestrated cell death reveals bacterial effector interplay and cross-talk between host autophagy and MAPK signaling."
- **2017** McDermott Center Works In Progress Seminar Series, McDermott Center for Human Growth and Development, University of Texas Southwestern Medical Center. August 2017. Title: "*V. para* T3SS1 effectors fine-tune host gene expression to subvert cell death signaling and activate cell survival networks."
- **2017** FASEB Science Research Conference on Molecular Pathogenesis. Snowmass CO. July 2017. Title: "*V. para* T3SS1 effectors fine-tune host gene expression to subvert cell death signaling and activate cell survival networks."
- 2015 UT Southwestern Medical Center, Department of Microbiology, Molecular Microbiology Works In Progress Seminar Series. December 2015. Title: "Transcriptome profiling of the host cell death mediated by *Vibrio parahaemolyticus* T3SS1."
- 2012 MIT, Department of Civil and Environmental Engineering, Microbial Systems Seminar Series. November 2012. Title: "Global analysis of cell cycle gene expression of the legume symbiont *Sinorhizobium meliloti.*"

# **SCIENTIFIC PRESENTATIONS – POSTER PRESENTATIONS**

**De Nisco NJ**, Kanchwala M, Xing C, Orth K. November 2017. RNA sequencing analysis of *Vibrio* T3SS1orchestrated cell death reveals a new connection between autophagy and MAPK signaling. Howard Hughes Medical Institute Science Meeting. Chevy Chase, MD.

**De Nisco NJ,** Kanchwala M, Li P, Fernandez J, Xing C, Orth K. July 2017. *V. para* T3SS1 effectors fine-tune host gene expression to subvert cell death signaling and activate cell survival networks. FASEB Science Research Conference on Molecular Pathogenesis, Snowmass CO.

**De Nisco NJ,** Salomon D, Kinch LN, Orth K. July 2015. Elucidating the function of the *Vibrio parahemolyticus* T3SS1 effector VopR. FASEB: Molecular Pathogenesis: Mechanisms of Infectious Disease. Keystone, CO.

**De Nisco NJ,** Salomon D, Li P, Kinch LN, Orth K. December 2104. Elucidating the structure and function of the *Vibrio parahaemolyticus* T3SS1 effector VopR. ASCB/IFCB Meeting. Philadelphia, PA.

**De Nisco NJ**, Penterman J, Walker GC. 2012. Cell cycle regulation in free-living and symbiotic rhizobia. 10<sup>th</sup> UMass Amherst Plant Biology Symposium. Amherst, MA.

**De Nisco NJ**, Pini F, Ferri L, Walker GC, Biondi EG. May 2012. Mechanisms of regulation of CtrA in *Sinorhizobium meliloti* during the free-living cell cycle and symbiosis with *Medicago sativa*. 4<sup>th</sup> ASM Conference on Prokaryotic Cell Biology and Development. Montreal, Quebec.

**De Nisco NJ**, Kobayashi H, Biondi EG, Walker GC. June 2010. Exploring the changes in the *S. meliloti* cell cycle that allow for bacterial differentiation during symbiosis with *M. sativa*. Boston Bacterial Meeting, Cambridge, MA.

**De Nisco NJ**, Kobayashi H, Walker GC. July 2009. Exploring the role of CpdR1 in cell cycle control and symbiosis in *Sinorhizobium meliloti*. 3<sup>rd</sup> ASM Conference on Prokaryotic Development. Cambridge, MA.

**De Nisco NJ**, Kobayashi H, Walker GC. June 2009. Exploring the role of *cpdR1* in cell cylce control and symbiosis in *S. meliloti*. The 16<sup>th</sup> International Congress on Nitrogen Fixation. Big Sky, MT.

## **OUTREACH ACTIVITIES**

**January 2014-present**: **STARS Laboratory Tour Leader**, UT Southwestern Medical Center, Dallas TX. Lead laboratory tours for Dallas area high school students every other month.

## REFERENCES

*Kim Orth, Ph.D.* Howard Hughes Medical Institute Investigator; Professor of Molecular Biology and Biochemistry, Earl A. Forsythe Chair in Biomedical Science, W.W. Caruth, Jr. Biomedical Scholar University of Texas Southwestern Medical Center, Dallas TX Email: <u>Kim.Orth@utsouthwestern.edu</u> Office Phone: 214-648-1685

*Graham C. Walker, Ph.D.* American Cancer Society Professor; Howard Hughes Medical Institute Professor; MacVivar Faculty Fellow Massachusetts Institute of Technology Email: <u>gwalker@mit.edu</u> Office Phone: 617-253-6716

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*Kelli Palmer, Ph.D.* Assistant Professor of Biological Sciences University of Texas at Dallas Email: <u>kelli.palmer@utdallas.edu</u> Office Phone: 972-883-6014

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