

## Research/Scholarly /Academic activities.

Understanding the differentiation of salivary cells is a necessary step to enable the restoration of diseased or destroyed parotid salivary tissue in patients. Dr. Darling's research group uses gene expression arrays of differentiating salivary glands to identify networks that cause terminal differentiation. We study the relation between changes of microRNAs and mRNAs during differentiation. This is described at: http://www.youtube.com/watch?v=N1zVH9eGf6M Computer modeling is expected to have the capacity to test the relative importance of specific pathways within the networks, allowing validation by laboratory work. We are also studying the molecular basis for trafficking of secreted proteins within the cell during regulated secretion. We use a novel model for sorting of salivary proteins in which Parotid Secretory Protein (PSP) binds the membrane at phosphatidylinositol bisphosphate. Separately, our laboratory is interested in the role of ZEB and related genes in early development, and the molecular interactions that underlie those roles.

Dr. Darling directs a gateway course on experimental design for the Masters program, and lectures on molecular genetics and molecular pathology in the School of Dentistry, School of Medicine, and School of Nursing. While at ULSD, he has been awarded \$5,451,000 in biomedical research grants as Principal Investigator, in addition to participating in other NIH grants for research or training. He has served UofL on the Executive Committees for the University Center for Genetics and Molecular Medicine (CGeMM), and for the Center for Environmental Genomics and Integrative Biology (CEGIB), including directing a small grants program, and developing core research facilities. Dr. Darling is currently Associate Research Integrity Ombudsman for the UofL Health Sciences Campus.

## **Grants:**

Role: PI

Grant Title: Mathematical Model of Parotid Acinar Differentiation

Funding Agency: NIH, NIDCR Total Direct Costs Funded: \$1,323,347

Role: Mentor for Melissa Metzler (PhD student)

Grant Title: MicroRNAs and Parotid Acinar Cell Differentiation

Funding Agency: NIH, NIDCR Total Direct Costs Funded: \$172,128 Role: PI for Pilot Program Subaward

Grant Title: Center for Environmental Genomics and Integrative Biology

Funding Agency: NIH, NIEHS

Total Direct Costs Funded: ~ \$900,000 for subaward

## Publications:

SG Venkatesh, D Goyal, AL Carenbauer, and **DS Darling**. Parotid secretory protein binds Phosphatidylinositol (3,4)bisphosphate. J. Dental Research, 90(9): 1085 - 1090 (2011) PMCID:PMC3169880.

AP Putzke, AP Ventura, AM Bailey, C Akture, J Opoku-Ansah, M Celiktas, MS Hwang, **DS Darling**, IM Coleman, PS Nelson, HM Nguyen, E Corey, M Tewari, C Morrissey, RL Vessella, and BS Knudsen. Metastatic progression of prostate cancer and E-cadherin. Regulation by Zeb1 and SRC family kinases. Am. J. Pathol., 179(1): 400-10 (2011). PMCID:PMC3123858.

S Ohashi, M Natsuizaka, S Naganuma, S Kagawa, S Kimura, H Itoh, RA Kalman, M Nakagawa, **DS Darling**, D Basu, PA Gimotty, AJ Klein-Szanto, J Diehl, M Herlyn, and H Nakagawa. A NOTCH3-Mediated Squamous Cell Differentiation Program Limits Expansion of EMT-Competent Cells That Express the ZEB Transcription Factors. Cancer Research, 71: 6836 - 6847 (2011). PubMed Central PMCID:

R Hertzano, R Elkon, K Kurima, A Morrisson, SL Chan, M Sallin, A Biedlingmaier, **DS Darling**, AJ Griffith, DJ Eisenman, SE Strome. Cell type-specific transcriptome analysis reveals a major role for Zeb1 and miR-200b in mouse inner ear morphogenesis. PLoS Genetics 7(9):e1002309, (2011). PMCID: PMC3183091.

DS Darling, SG Venkatesh, D Goyal and AL Carenbauer (2012). Phosphatidylinositol Bisphosphate Mediated Sorting of Secretory Granule Cargo; Chapter 3 in "Crosstalk and Integration of Membrane Trafficking Pathways," Dr. Roberto Weigert (Ed.), ISBN: 978-953-51-0515-2, InTech, Available from: http://www. intechopen.com/books/crosstalk-and-integration-of-membrane-trafficking-pathways/ phosphatidylinositol-bisphosphate-mediated-sorting-of-secretory-granule-cargo

E Sanchez-Tillo, Y Liu, O de Barrios, L Siles, L Fanlo, M Cuatrecasas, DS Darling, DC Dean, A Castells, and A Postigo. EMT-activating transcription factors in cancer: beyond EMT and tumor invasiveness. Cell Mol Life Sci, Oct 2012; 69(20): 3429-56 (2012). PMID: 22945800

## **External Professional Activities:**

Member of Faculty Research Advisory Council for UofL Executive VP for Research. Reviewer for International Journals, e.g., EMBO Journal, Nature Gene Therapy,

Grant reviewer: NIH NIDCR ZDE1 MH (14) RFA Special Review Panel, 2012 Grant reviewer: Austrian Science Fund, Cell and Molecular Biology, 2012 Grant reviewer: National Science Foundation, Science and Technology Centers (STC), 2012

Plenary speaker for the Symposium "miRNAs in Salivary Biology" International Association for Dental Research, Annual Meeting, San Diego, CA. 2011