BIOGRAPHICAL SKETCH

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NAME: Arin B. Aurora, Ph.D.

eRA COMMONS USER NAME (credential, e.g., agency login): AAUROR

POSITION TITLE: Assistant Professor, Research, Children's Medical Center Research Institute (CRI), University of Texas Southwestern Medical Center

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Cornell University, Ithaca, NY	B.S.	05/1998	Biology
University of California San Francisco, CA	Ph.D.	05/2004	Immunology
Northwestern University, Chicago, IL	Fellow	08/2007	Cell and Molecular Biology
University of Texas Southwestern Medical Center, Dallas, TX	Fellow	01/2014	Cell and Molecular Biology

A. Personal Statement

During my Postdoctoral Fellowship training, I acquired a strong background studying angiogenesis and cardiac repair using numerous mouse models. Now I have applied my knowledge and experience to exclusively focus on the biology of melanoma metastasis and, as a result, have generated several projects likely to uncover previously unknown aspects of cancer biology. The primary interest of my work is to identify barriers to cancer cell metastasis and to understand how metastasizing tumor cells successfully overcome them. Metastasis of solid tumors is a very inefficient process and it is not known why. As a new faculty member and co-investigator working closely with Dr. Sean Morrison, I am specifically interested in the metabolic plasticity that successfully metastasizing melanoma cells acquire. Recent work in the Morrison lab, which has been corroborated by independently published studies, discovered that distant metastasis is limited by oxidative stress. To advance these studies, I have found evidence that metastasizing melanoma cells use a number of metabolic pathways and mechanisms to survive oxidative stress. My emerging work focuses on exploring and defining these novel mechanisms of melanoma metastasis. In addition to working with members of the Morrison laboratory, I collaborate closely with Dr. Tim Johnson and Dr. Travis Vandergriff to assimilate relevant clinical information into the interpretation of our data. I also work closely with Dr. Ralph DeBerardinis and with Dr. Doug Spitz who are experts in the assessment of metabolism in mice and in assessing oxidative stress respectively.

B. Positions and Honors

Positions and Employment

2004 – 2007 Postdoctoral Fellow (with Dr. Olga V. Volpert), Northwestern University Feinberg School of Medicine
2007 – 2014 Postdoctoral Fellow (with Dr. Eric N. Olson), UT Southwestern Medical Center
2014 – present Assistant Professor, Research Track, Children's Research Institute, UT Southwestern Medical Center

Professional Memberships

2011 – 2014 American Heart Association
2016 – present American Association for Cancer Research

Honors and Awards

1996	Howard Hughes Undergraduate Research Fellow
2001	University of California San Francisco Graduate Student Research Award
2003	American Association for Cancer Research -Takeda Scholar-in-Training Award
2005	European School of Haematology Marie Curie Actions Scholarship
2005	Robert H. Lurie Cancer Center Katten Muchin Rosenman Scholarship
2006 – 2009	American Cancer Society Postdoctoral Fellowship
2014	American Heart Association Beginning Grant-in-Aid

C. Contribution to Science

1. Cell intrinsic and extrinsic mechanisms regulating angiogenesis: During my PhD thesis research, I used a model of chronic airway inflammation to study how the immune system acts extrinsically upon the vasculature to promote angiogenesis. Previously, the innate immune system, and in particular macrophages, were shown to regulate angiogenesis in a number of settings, including cancer. Using genetic models, I showed that angiogenesis could be driven by the adaptive immune response. Specifically, a T-cell dependent antibody response was required to recruit and activate inflammatory cells that secreted growth factors necessary for vessel growth and integrity. Then as a post-doctoral fellow in Olga Volpert's lab at Northwestern University Feinberg School of Medicine, I focused on the endothelial cell intrinsic mechanisms that activate or repress post-natal angiogenesis. I showed that NFkB is a central mediator of endothelial cell survival or death and that its activity as a transcriptional activator or repressor can be dictated by epigenetic modulation through HDACs. Clinically, these findings were relevant because we could demonstrate that two angiogenic inhibitors being developed for therapeutic use, Pigment Epithelial Derived Factor (PEDF) and Thrombospondin-1 (TSP1), functioned through this pathway to induce endothelial apoptosis and block angiogenesis in vivo. The addition of low doses of histone deactlase inhibitors enhanced PEDF and TSP1 activity, suggesting a combination of HDAC inhibitors and angiogenesis inhibitors could be used to effectively block angiogenesis.
   a. Aurora A.B., Baluk P., Zhang D., Sidhu S.S., Dolganov G.M., Basbaum C., McDonald D.M., Killeen N. 2005. Immune-Complex-Dependent Remodeling of the Airway Vasculature in Response to a Chronic Bacterial Infection. **Journal of Immunology** 175:6319-26. PMID 16272283
   b. Nelius T., Filleur S., Yemelyanov A., Budunova I., Shroff E., Mirochnik Y., Aurora A.B., Veliceasa D. and Volpert O.V. 2007. Androgen receptor targets NFkappaB and TSP1 to suppress prostate tumor growth in vivo. **International Journal of Cancer** 121:999-1008. PMC2810747
   c. Mirochnik Y., Aurora A.B., Schulze-Hoepfner F.T., Deabes A., Shifrin V., Beckmann R., Polsky C., Volpert O.V. 2009. Short pigment epithelial-derived factor-derived peptide inhibits angiogenesis and tumor growth. **Clinical Cancer Research** 15:1655-63. PMC2854536
   d. Aurora A.B., Biyashev D., Mirochnik Y., Zaichuk T., Renault M.A., Losordo D., and Volpert O.V. 2010. NF- B balances vascular regression and angiogenesis via chromatin remodeling and NFAT displacement. **Blood** 116:475-84. PMC2913457

2. MicroRNA regulation of angiogenesis and calcium responses to cardiovascular injury: During my postdoctoral fellowship with Eric Olson at UT Southwestern Medical Center, I interrogated how microRNAs (miRs) mediate various aspects of cardiovascular disease including angiogenesis, cardiomyocyte cell cycle arrest, cardiomyocyte cell death, and calcium handling. I developed mouse models to study *miR-126*, *miR-15* family members, and *miR-214* in mammalian development and disease. I showed that *miR-214* was cardioprotective against ischemic injury because it regulated cardiomyocyte calcium signaling and cell death through a number of genes including the sodium calcium exchanger *Ncx1*, *CamKIId*, and *Bim*. I also made significant contributions to studies showing that *miR-126* is necessary for angiogenesis in the heart following ischemic injury and that the *miR-15* family regulates cell cycle genes during post-mitotic arrest of cardiomyocytes in the developing heart. These studies lend support to the development of miR-based therapeutics for use in cardiovascular disease.
   a. Wang S., Aurora A.B., Johnson B.A., Qi X., McAnally J., Hill J.A., Richardson J.A., Bassel-Duby R., Olson E.N. 2008. The endothelial-specific microRNA miR-126 governs vascular integrity and angiogenesis. **Developmental Cell** 15:261-71. PMC2685763

b. Porrello E.R., Johnson B.A., Aurora A.B., Simpson E., Nam Y.J., Matkovich S.J., Dorn G.W. 2nd, van Rooij E., Olson E.N. 2011. MiR-15 family regulates postnatal mitotic arrest of cardiomyocytes. **Circulation Research** 109:670-9. PMC3167208
c. Denby L., Ramdas V., Lu R., Conway B.R., Grant J.S., Dickinson B., Aurora A.B., McClure J.D., Kipgen D., Delles C., van Rooij E., Baker A.H. 2014. MicroRNA-214 Antagonism Protects against Renal Fibrosis. **Journal of the American Society of Nephrology** 25:65-80. PMC3871772
d. Aurora A.B., Mahmoud A.I., Luo X., Johnson B.A., van Rooij E., Matsuzaki S., Humphries K.M., Hill J.A., Sadek H.A. and Olson E.N. 2012. microRNA-214 controls cardiac Ca2+ overload in response to ischemic injury in mice. **Journal of Clinical Investigation** 122:1222-32. PMC3314458

3. Macrophages regulate neonatal heart regeneration: As a senior post-doctoral fellow and Instructor in Eric Olson's lab, I applied my expertise in immune-mediated mechanism of tissue remodeling to the problem of heart repair and regeneration. The adult mammalian heart is one of the least regenerative organs in the body yet the neonatal heart can regenerate completely up until 7 days after birth. I performed a comparative analysis of the immune response to cardiac injury in the neonate and adult and developed models to study the effects of immune-cell depletion on cardiac regeneration. I showed that heart regeneration in the neonate depended on macrophages and that the macrophage response to cardiac injury differed between the adult, where the heart cannot regenerate, and the neonate. The neonatal macrophage population was distinctly polarized from adults and secreted a number of factors that can facilitate angiogenesis crucial to regenerating a damaged tissue. The findings point to the importance of understanding and harnessing the powers of the immune response to injury when developing regenerative therapies for the heart and other tissue.
   a. Aurora A.B., Olson E.N. 2014. Immune Modulation of Stem Cells and Regeneration. **Cell Stem Cell** 15:14-25. PMC4131296
   b. Aurora A.B., Porrello E.R., Tan W., Mahmoud A.I., Hill J.A., Bassel-Duby R., Sadek H.A., and Olson E.N. 2014. Macrophages are required for neonatal heart regeneration. **Journal of Clinical Investigation** 124:1382-92. PMC3938260

Complete List of Published Work in My Bibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/1zSFr5pxBT7QP/bibliography/44271578/public/?sort=date&direction=ascending.

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

(P.I. Morrison, SJ) 12/1/2016-11/30/2019
Cancer Prevention and Research Institute of Texas: Individual Investigator Award
Title: Mechanisms of melanoma metastasis
Number: RP17011
Role: Co-Investigator

Completed Research Support

(P.I. Volpert, OV) 08/01/2006-07/31/2009
American Cancer Society: American Cancer Society Postdoctoral Fellowship
Title: Analysis of the transcriptional network behind the angiogenic switch
Number: PF-06-256-01-CSM
Role: Research Fellow/Trainee

(P.I. Aurora AB & Olson EN) 01/20/2014-02/20/2015
American Heart Association: American Heart Association Beginning Grant-in-Aid
Title: The role of macrophages in neonatal heart regeneration
Number: 14BGIA18780015
Role: Early Stage Investigator

(P.I. Morrison, SJ) 9/1/2011-8/31/2016
Cancer Prevention and Research Institute of Texas: Recruitment of Established Investigators
Title: Stem Cells and Cancer
Number: RP1109
Role: Assistant Professor