

Robert M. Greene, Ph.D.

Professor and Chair

Department of Molecular, Cellular & Craniofacial Biology
School of Dentistry

Director

Birth Defects Center

Associate

Department of Pediatrics

Distinguished University Scholar



Warner DR, Mukhopadhyay P, Brock G, Webb C, Pisano MM, **Greene RM**. MicroRNA expression profiling of the developing upper lip in mice. *Development, Growth & Differentiation* 56:434-447 (2014). Journal cover-featured research publication

Jin J-Z, Warner DR, Lu Q, Pisano MM, Greene RM Ding J. TGF β /Notch signalling mediates murine palatal epithelial specification and fusion. *Development* 243:1536-1543, (2014).

Greene RM and Kirschner RE. Molecular Strategies in the Study and Repair of Palatal Defects. In: *Stem Cell Biology and Tissue Engineering in Dental Sciences*, (editors: A. Vishwakarma, P. Sharpe, S. Shi, X Wang, M Ramalingam), Elsevier Press (in press), (2015).

Greene RM, Pisano MP, Warner D. Genetic and Epigenetic Perspectives of Orofacial Clefting. In: *Comprehensive Cleft Care*, 2nd edition. edit. Losee JE, Kirschner RE., McGraw-Hill (in press), (2015).

Seelan RS, Brock G, Appana SN, Mukhopadhyay P, Warner DR, Pisano MM & **Greene RM**. Methylated microRNA genes of the developing murine palate. *miRNA* (accepted for publication) (2015).

External Professional Activities (2013-2014):

- Editorial Board, *Orthodontics and Craniofacial Research*
- Editorial Board, Associate Editor, *Birth Defects Research, Part A: Clinical and Molecular Teratology*
- Editorial Board, *Progress in Orthodontics*
- Editorial Board, *Frontiers in Craniofacial Biology* subsection of *Frontiers in Physiology and Dentistry*
- January 2013 – Invited to contribute a review chapter for: *Comprehensive Cleft Care*, 2nd edition. edit. Losee JE, Kirschner RE., McGraw-Hill; title: *Perspectives in Orofacial Cleft Research: Molecular Mechanisms*.

- February 2013 – Invitation to serve as a grant reviewer on the *Special Emphasis Panel (SEP)* on *Systems Developmental Biology for Understanding Embryonic Development and the Ontogeny of Structural Birth Defects* – Baltimore, Md

- April 2013 – Invited Speaker – NICHD/NIH, 9th Structural Birth Defects Meeting – Bethesda, MD “Epigenetics and Pregnancy Outcomes”

- April 2013 – Invitation to serve as a grant reviewer on the NIH Infectious Disease, Reproductive Health, and Asthma/Pulmonary Conditions (IRAP) study section. – Silver Spring, Md

- May 2013 – Invitation to serve on Program Committee for the 2014 Annual Teratology Society meeting, Bellevue, Washington

- June 2013 – Selected to organize a research symposium on Epigenetics and Birth Defects for the 2014 Annual Teratology Society meeting, Bellevue, Washington

- June 2013 – Invited speaker - Kentucky Chapter of the International Women's Forum “*Risk Factors for Birth Defects: Is the Unborn at Greater Risk in Kentucky?*”

- Aug 2013 – Invitation to serve on the NIDDK DDK-C Subcommittee study section for review of K01 awards

- Feb, 2014 - Invitation to serve as reviewer on DEV1 study section; Baltimore, Md

- Feb, 2014 - Invitation to serve as reviewer on an NIDCR Special Grants Review Committee (DSR) - review of Fellowship (F), Career Award (K) and small grant (R03) applications for the NIDCR - Bethesda MD.

- Invitation to serve as reviewer on study section to review U01 Research Program Cooperative Agreements entitled: *Reference Profiles of Human Extracellular RNA* – RFA-RM-12-011

- Mar 2014 - Invitation to serve as reviewer on an NIDCR Special Emphasis Panel to review DSR member conflict applications. – teleconference.

- July 2014 - Invitation to serve as reviewer of research grants submitted to the Medical Research Council (MRC) in Great Britain

Scholarly Activities:

A quarter of a million babies—3% of all infants born in the US each year—have some mental or physical defect that is evident at birth. Since the causes of nearly all birth defects are largely unknown, research into molecular regulatory mechanisms responsible for normal embryogenesis provides the framework for investigations into the etiology of abnormal embryonic development.

Craniofacial malformations occur with a frequency of 1 in 600 live births annually in the United States. Our previous studies have provided substantial evidence supporting the premise that various cellular signal transduction pathways interact to regulate cell proliferation and cell differentiation in embryonic craniofacial tissue. Such interactions represent the underpinnings of a complex and delicately balanced developmental system where morphogenesis and cellular differentiation of the craniofacial region are mediated by the sequential expression of molecular signals. Our studies dealing with molecular analyses of gene function in the embryo—utilizing the developing craniofacial region—are designed to provide definition and clarification of developmental signaling pathways critical for normal embryogenesis as well as identification of foci for perturbation and attendant fetal abnormalities.

Current studies—selected specifics outlined briefly below—are designed to identify means by which signal transduction pathways, known to be critical in development of the craniofacial region, regulate gene expression and embryonic development.

Overview of selected laboratory investigatory areas:

- 1 - microRNAs & epigenetic regulation of craniofacial development
- 2 - Transcriptional coactivators and craniofacial & neural tube development.
- 3 - Cigarette smoke-induced adverse developmental outcomes.
- 4 - TGF β /Smad signaling mechanisms in embryonic craniofacial development.

Grants:

Role: Principal Investigator; Co-I: MM Pisano

Title: *Transcriptional Coactivators and Pregnancy Outcomes*

Funding Agency: NIDCR

Direct Costs Funded: \$1,321,165

Role: Principal Investigator; Co-I: MM Pisano

Title: *Molecular Determinants of Developmental Defects – P20*

Funding Agency: NIGMS – (2008-2014)

Direct Costs Funded: \$12,072,292

Role: Principal Investigator; Co-I: MM Pisano

Title: *Transcriptional Coactivators and Pregnancy Outcomes*

Funding Agency: NICHD

Direct Costs Funded: \$1,503,187

Role: (Mentors) MM Pisano and RM Greene

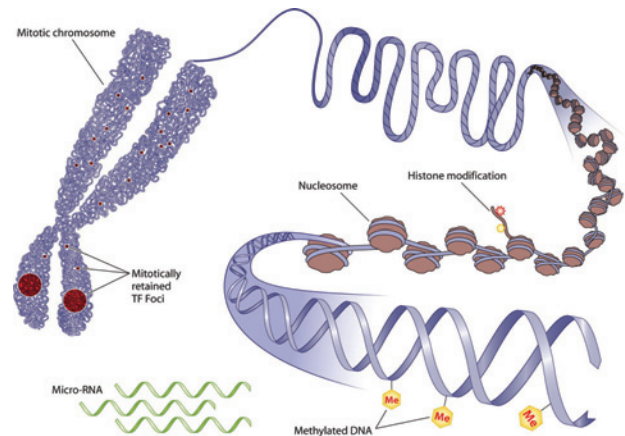
Co-I: (Trainee) Scott Smith

Title: *Epigenetic and Developmental Consequences of Environmental Tobacco Smoke Exposure*

Funding Agency: NIEHS; T32 ES011564

PI: D Hein

Direct Costs Funded: \$48,500



Publications (2013-2014):

Warner D, Wells J, **Greene** RM, Pisano MM. Gene expression changes in the secondary palate and mandible of Prdm16^{-/-} mice. *Cell & Tissue Research* 351: 445-452 (2013).

PMCID: PMC3584240 Awarded the Society for Experimental Biology and Medicine's "Best Clinical, Preclinical and Translational Paper of 2013"

Amos-Kroohs RM, Williams MT, Vorhees CV, Braun AA, Graham DL, Webb CL, Birtles TS, **Greene** RM, Pisano MM. Behavioral phenotype of C57BL/6J mice prenatally and neonatally exposed to cigarette smoke. *Neurotoxicology & Teratology* 35:34-45 (2013). PMCID: PMC3593942

Mukhopadhyay P, Rezzoug F, Kaikaus J, Pisano MM and **Greene** RM. Alcohol modulates expression of DNA methyltransferases and methyl CpG-CpG domain-binding proteins in murine embryonic fibroblasts. *Reprod Tox* 37:40-48 (2013). PMID: 23395981

Brock G, Mukhopadhyay P, Pihur V, Webb C, **Greene** RM, Pisano MM. MmPalateMiRNA, an R Package Compendium Illustrating Analysis of miRNA Microarray Data. Source Code for Biology and Medicine 8(1): <http://www.scfbm.org/content/8/1> - (2013). PMID: 23298515.

Seelan RS, Mukhopadhyay P, Warner DR, Pisano MM, **Greene** RM. Epigenetic regulation of Sox4 during palate development. *Epigenomics* 5:131-146 (2013). PMID: 23566091

Seelan R, Appana SN, Mukhopadhyay P, Warner DR, Brock GN, Pisano MM, **Greene** RM. Developmental profiles of the murine palatal methylome. *Birth Defects Research A* 97:171-186 (2013). PMID: 23554260

Seelan RS, Warner DR, Mukhopadhyay PM, Andres SA, Smolenkova I, Wittliff JL, Pisano MM, **Greene** RM. Epigenetic analysis of laser capture microdissected fetal epithelia. *Analytical Biochem* 442:68-74 (2013) PMID 23911529.

Neal RE, Chen J, Jagadapillai R, Jang H, Abomoelak B, Brock GN, Brock G, **Greene** RM, Pisano MM. Developmental cigarette smoke exposure: hippocampus proteome and metabolome profiles in low birth weight pups. *Toxicology* 317:40-49 (2014) PMID: 24486158

Warner DR, **Greene** RM, Pisano MM. PRDM16 in Development and Disease. *Human Genetics & Embryology* 4:1-4: <http://dx.doi.org/10.4172/2161-0436.1000121> (2014).