



## Research 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:

- microRNAs & epigenetic regulation of craniofacial development
- Transcriptional coactivators and craniofacial & neural tube development.
- Transcriptional coactivators and folate-mediated development.
- Cigarette smoke-induced intrauterine growth retardation & adverse developmental outcomes.
- TGF $\beta$ /Smad signaling mechanisms in embryonic craniofacial development.

## Grants Funded:

NIH (NICHD) Research Grant, **RM Greene** – PI; MM Pisano – Co-I; (R01–HD053509) “Transcriptional Coactivators and Pregnancy Outcomes”

NIH Research Grant, **RM Greene** – PI; (R01–DE018215) “Nutritional Epigenetics and Orofacial Development”

NCCR Center for Biomedical Research Excellence, **RM Greene** – PI – (P20-RR/DE17702) “Molecular Determinants of Developmental Defects”

Kosair Charities – Birth Defects Center Postdoctoral Fellowship, **RM Greene** – PI

## Peer Reviewed Publications:

Horn K, Warner DR, Pisano MM, **Greene RM**. PRDM16/MEL1 expression in the developing mouse embryo. *Acta Histochem* 113:150-155 (2011). PMID: PMC2891916

Warner DR, Mukhopadhyay P, Brock G, Pihur V, Pisano MM, **Greene RM**. TGF $\beta$ s and Wnt-3a interact to induce unique gene expression profiles in murine embryonic palate mesenchymal cells. *J Reprod Toxicol* 31:128-133 2011. PMID: PMC3138487

Seelan RS, Pisano MM, **Greene RM**, Casanova MF & Parthasarathy. Differential methylation of the gene encoding myo-Inositol synthase (*Isyna1*) in rat tissues. *Epigenomics* 3:111-124 (2011). PMID: PMC3154894

**Greene RM** and MM Pisano, guest editors, *Epigenetic Processes in Development, Birth Defects Research A: Clinical and Molecular Teratology*, (edit. DM Juriloff), Wiley-Blackwell, Hoboken, NJ (2011).

**Greene RM** and MM Pisano, Issue Overview: *Epigenetic Processes in Development, Birth Defects Research A: Clinical and Molecular Teratology*, (edit. DM Juriloff), Wiley-Blackwell, Hoboken, NJ, 91:649-651 (2011). PMID: 21630422

Mukhopadhyay P, Brock G, Appana S, Webb C, **Greene RM**, Pisano MM. miRNA gene expression signatures in the developing neural tube. *Birth Defects Research A - Special Issue: Epigenetics & Development* 91:744-762 (2011).

Warner D, Webb, CL, **Greene RM**, Pisano MM. Altered signal transduction in *folr1*<sup>-/-</sup> mouse embryo fibroblasts. *Cell Biology International* 35:1253-1259 (2011). PMID: 21649587

Rezzoug V, Bhattacharjee V, Seelan, RS, **Greene RM**, Pisano MM. Chemokine-mediated migration of mesencephalic neural crest cells. *Cytokine* 56:760-768 (2011). PMID: PMC3221884

Seelan RS, Mukhopadhyay P, Pisano MM, **Greene RM**. Developmental Epigenetics of the Murine Secondary Palate. *ILAR Journal*, special issue “Epigenetics – From Mice to Men.” 53:236-248 (2012).

Mukhopadhyay P, Singh S, **Greene RM**, Pisano MM. Strain-specific modifier genes governing craniofacial phenotypes. *Birth Defects Res A*. 94:162-175 (2012). PMID: PMC3302963

Warner D, Mukhopadhyay P, Webb CL, **Greene RM**, Pisano MM. Chromatin Immunoprecipitation-promoter microarray identification of genes regulated by PRDM16 in murine embryonic palate mesenchymal cells – *Exper. Biol. & Medicine* 237:387-394 (2012). PMID: 22522345

Warner D, Wells J, **Greene RM**, Pisano MM. Gene expression changes in the secondary palate and mandible of *Prdm16*<sup>-/-</sup> mice. *Cell & Tissue Research* 351: 445-452 (2013). PMID:23149718

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* Jan 8;8(1):1. [Epub ahead of print] (2013). PMID: 23298515.

## Robert M. Greene, Ph.D.

### Professor and Chair

Department of Molecular, Cellular & Craniofacial Biology  
School of Dentistry

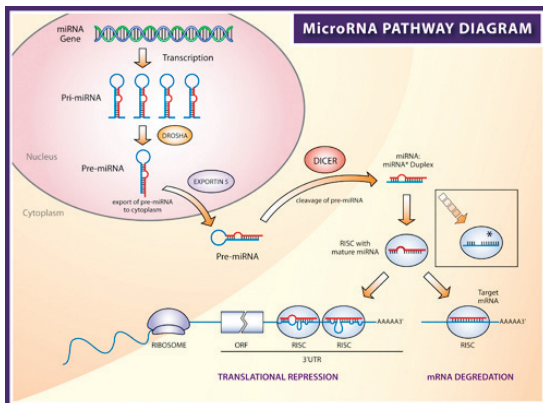
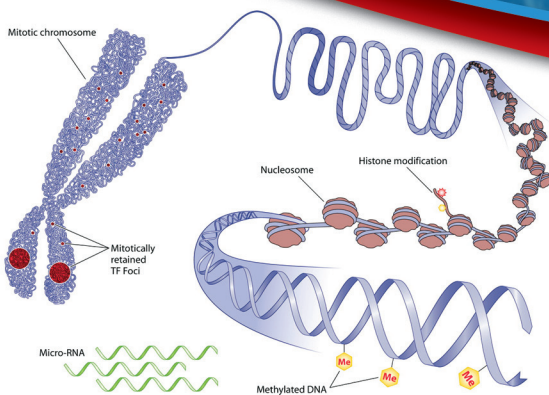
### Director

Birth Defects Center

### Associate

Department of Pediatrics

### Distinguished University Scholar



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). PMID: 23314114

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

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

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* (accepted for publication) (2013).

**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), (2013).

### External Professional Activities:

- 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
- Expert Witness – Schiller Osbourn, Barnes & Maloney, 2010-2011
- Member, Board of Directors, Spina Bifida Association of Kentucky, Inc.
- Scientific Consultant - Genetics & IVF Institute, Inc., Fairfax, VA
- Invited Speaker – 7th KY Innovation Entrepreneurship Conference & 16th KY EPSCOR Joint Conference – Louisville, Ky
- Invited Reviewer – NIDCR - U01 Competitive Revision of The FaceBase Consortium: Functional Genomics of Craniofacial Development and Disease (RFA-DE-09-003) in response to PAR-11-144 Competitive Revision Applications for NIDCR-funded Cooperative Agreements.
- Invited Speaker - Louisville Rotary Club – “Risk Factors for Birth Defects”
- Invitation to serve on the Developmental Biology Subcommittee (CHHD-C) at EKS-NICHD to review P01 applications.
- Invited Reviewer – NIDCR - ZDE1 MH 13 Special Emphasis Panel - “Competitive Revision Applications for NIDCR-funded Cooperative Agreements - U01 revision applications dealing with the creation of mouse models of craniofacial disorders.