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Development of the head and face is an extraordinarily complex process that requires the precise orchestration of numerous signaling pathways and regulation of the transcription of hundreds, if not thousands, of genes. Not surprisingly, perturbations, either genetic or environmental, can disrupt this fine-tuned process and lead to structural defects, such as clefts of the lip and palate, a common birth defect that can have lifelong consequences. Our research program is singularly focused on unraveling the mechanisms by which clefts of the lip and palate occur with the ultimate goal of prevention or early interventions to ameliorate the morbidity associated with these defects. Over the past two years we have made significant advances in understanding the roles of several key genes, such as Prdm16, in craniofacial development and signaling pathways, such as those regulated by TGFB and Wnts. More recently, we have been actively seeking to identify microRNAs that are important for both lip and palate development. MicroRNAs are small, non-coding RNAs that regulate the expression of messenger RNAs and have emerged as an important level of epigenetic regulation. A comprehensive analysis of this class of epigenetic regulators is an important advance in our understanding of lip and palate development and may lead to development of diagnostic and preventative measures to reduce the incidence of this frequent birth defect.

Publications:

K.H. Horn, **D.R. Warner**, M.M., Pisano, R.M. Greene (2011) Acta Histochemica 113:150-155. "PRDM16 Expression in the Developing Mouse Embryo".

CYTOPLASM

SMAD

TGF61/2/3

TGF6RI TGF6R2

SMAD2/3 SMAD1/5

D.R. Warner, P. Mukhopadhyay, G.N. Brock, V. Pihur, M.M. Pisano, R.M. Greene (2011) Reproductive Toxicology 31:128-133. "TGF β -1 and Wnt-3a Interact to Induce Unique Gene Expression Profiles in Murine Embryonic Palate Mesenchymal Cells".

D.R. Warner, C.L. Webb, R.M. Greene, M.M. Pisano (2011) Cell Biology International 35:1253-1259. "Altered Signal Transduction in Folr1-/- Mouse Embryo Fibroblasts".

D.R. Warner, P. Mukhopadhyay, C.L. Webb, R.M. Greene, M.M. Pisano (2012) Experimental Biology and Medicine 237:387-394. "Chromatin immunoprecipitation-promoter microarray identification of genes regulated by PRDM16 in murine embryonic palate mesenchymal cells".

D.R. Warner, C.L. Webb, R.M. Greene, M.M. Pisano. (2012) Cell and Tissue Research Nov. 13 [Epub ahead of print]. "Gene expression changes in the secondary palate and mandible of Prdm16-/- mice".

R.S. Seelan, P. Mukhopadhyay, **D.R. Warner**, C.L. Webb, M.M. Pisano, R.M. Greene. (2013) Epigenomics 5:131-146 "Epigenetic Regulation of Sox4 During Palate Development".

External Professional Activities:

Judge, DuPont Manual High School Science Fair

Ad hoc manuscript reviewer:

Developmental Dynamics Journal of Cellular Physiology Journal of Cellular Biochemistry International Journal of Developmental Biology In Vitro, Cellular, and Developmental Biology-Animal Orthodontics and Craniofacial Research