

Feature article: *Prdm16*: a novel gene important for craniofacial development

In the USA, a baby is born with a facial cleft every hour everyday of the year! Such birth defects result from both gene mutations and environmental insults. PRDM16 is a transcription factor originally described as being aberrantly activated in specific types of leukaemias, and more recently as a master regulator of brown adipose tissue differentiation. In a study published on page 387 of this issue of *Experimental Biology and Medicine*, investigators have now shown that this transcription co-factor plays a critical role in development of the embryonic palate. Mice lacking the gene for *Prdm16* exhibit numerous defects including a complete cleft of the secondary palate and a shortened mandible. In a study led by Dr Dennis Warner and his co-investigators at the University of Louisville Birth Defects Center, chromatin immunoprecipitation followed by array analysis was used to identify genes regulated by *Prdm16* in cells isolated from the secondary palate of mouse embryos. This approach revealed the developmental processes regulated by this protein that are important for palate development. 'Identifying the cellular and molecular processes regulated by PRDM16 is an important step toward elucidating the underlying mechanisms important for normal embryonic development of the head and face,' said Dr Warner. Over 100 genes, whose promoters were

bound by PRDM16, were identified. These genes were found to be linked to such diverse processes as chromatin remodeling and muscle and bone development. Dr Michele Pisano, a co-investigator on this study, added that 'little is known of the factors governing differentiation of embryonic palate mesenchymal cells into bone or muscle. Our study suggests that *Prdm16* may be critical for these processes.' Demonstration that loss of *Prdm16* expression led to a significant decrease in the expression of osteopontin, a marker for bone formation, and an increase in the expression of *Myf-4*, a marker for muscle development, support Dr Pisano's contention.

Dr Steven R Goodman, Editor-in-Chief of *Experimental Biology and Medicine*, said 'This important study by Warner and colleagues demonstrates that the transcription co-factor *Prdm16* plays an important role in the normal development of the embryonic palate. They further demonstrate genes essential to muscle and bone development which are regulated by *Prdm16* in cells isolated from the secondary palate of mouse embryos. This study should be of great significance in our understanding of birth defects leading to facial clefts.'

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