The FASEB Journal / Volume 36, Issue S1

Anatomy | Free Access

Using Mouse Metatarsal and Pisiform Ossification to Identify Genes Underlying Growth Plate Formation

Philip L. Reno, Kelsey M. Kjosness, Sungdae Park, Daved Fared, Mallory B. Stubblebine, Meghan T. Fitzwater, Douglas B. Menke

First published: 13 May 2022
https://doi.org/10.1096/fasebj.2022.36.S1.R2231

PCOM Full Text

Funding provided by NSF grants IOS-1656315 & BCS-1638812.

Abstract

Variation in growth rate underlies, in large part, the great diversity in mammalian skeletal shape. Longitudinal growth occurs at growth plates, which amplify and maintain the process of chondrocyte differentiation throughout ontogeny. Experiments using genetic inactivation in the mouse model have expanded knowledge of growth plate physiology; yet, little is known about how growth plate location and behavior are patterned to produce the normal diversity in skeletal shapes. Fortunately, substantial anatomical variation exists within the mammalian skeleton that can be used to identify the mechanisms underlying growth plate formation. Third metatarsals (MT3) form only a single growth plate located at the distal end, and the pisiform (in non-human mammals) forms an active growth plate unlike the other carpals. In both cases, growth plate containing tissues can be paired with those undergoing generalized endochondral ossification which can control for the effects of age, systemic growth factors, and biomechanical environment. We performed global transcriptome sequencing (RNA-seq) on 4- and 9-day old mouse samples comparing either the distal and proximal MT3s or the pisiform and other carpals to identify growth plate-specific differentially expressed genes (DEGs). Gene ontology (GO) analysis revealed DEGs from the MT3 are disproportionately associated with anatomical structure morphogenesis,

developmental growth, and limb development, in addition to the Fzd8-Ror2-Wnt5a pathway. Significant GO terms for the pisiform-carpal comparison include skeletal system development, cartilage development, anatomical structure morphogenesis, and abnormalities of the carpal bones. We identified a limited set of DEGs shared by both the MT3 and Pisiform-Carpal datasets, including *Wnt5a*. Using immunohistochemistry, we observed Wnt5a expression in both the distal and proximal MT3 but identified that intense expression in the bone collar is unique to the distal end adjacent to the growth plate. This conforms with previously identified roles for Wnt5a in regulating osteogenesis and cell polarity within the growth plate and validates this approach for identifying growth plate specific chondrogenic and osteogenic factors.

This is the full abstract presented at the Experimental Biology meeting and is only available in HTML format. There are no additional versions or additional content available for this abstract.