GENETICALLY ENGINEERED MICE AS MODELS TO STUDY THE ROLE OF CONNEXIN 43 ON BONES

Baraka S. Williams\textsuperscript{1,3}, Nicolette Bivi\textsuperscript{2}, Racheal Lee\textsuperscript{2}, Yumie Rhee\textsuperscript{2}, Lillian Plotkin\textsuperscript{2} and TeresitaBellido\textsuperscript{2}

\textsuperscript{1}Center for Bioinformatics & Computational Biology, Jackson State University, Jackson, MS 39217, USA
\textsuperscript{2}Department of Anatomy and Cell Biology, Indiana University School of Medicine, Indiana University-Purdue University Indianapolis (IUPUI), Indianapolis, IN 46202, USA
\textsuperscript{3}2009 Summer Intern at IUPUI

Abstract: The validity of mice as an animal model for the study of the pathophysiology and treatment of bone loss has been supported by extensive literature during the past 15 years. Because mice can be genetically manipulated, they are well-suited for studying the role of specific genes in skeletal biology. In this context, transgenic mice are a valuable tool to understand the role of a given gene on the skeleton. The common procedure is to identify mice affected by the genetic manipulation, collect bones for the study and examine the phenotype. To accomplish that goal, we did the following: 1) maintained the mice colonies; 2) genotyped the mice; 3) obtained measurements of bone mineral density (BMD); 4) conducted animal dissection and 5) prepared the samples for the appropriate analysis. The phenotype description was conducted on a mouse model to study Connexin (Cx) 43, a protein essential for the development and function of the bone. A tissue-specific knock out mouse was generated in which Cx43 was removed by using the Cre/LoxP system in osteocalcin-expressing cells: the osteoblasts (ob) and the osteocytes (ocy). From Micro Computerized Technology results of the femur, we observed that the control mice were normal; however, the knockout mice had an increase in bone marrow cavity. We hypothesized that the phenotype observed is increased bone resorption by osteoclast. Sections of distal femurs were stained for the osteoclast-specific enzyme TRAPase (tartrate-resistant acid phosphatase). Osteoclasts were identified as bright red TRAPase positive, multinucleated cells located on the bone surface. We found that osteoclast number and surface were increased in mice lacking Cx43 in osteoblasts and osteocytes. These results suggest that deletion of Cx43 from ob and ocy leads to increase endosteal bone resorption with the consequent increase in bone marrow surface.

Keywords: bone, Connexin 43, genetic manipulation, transgenic, mice

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