Editorial

Introduction: Epigenomics and Prevalent Skeletal Disorders

A common definition of epigenetics refers to the mechanisms that modify gene expression in a stable manner without changing DNA sequence. They include the methylation of cytosines, noncoding RNAs, and chromatin modifications. Epigenetic mechanisms are also understood as mediators of the interaction between environmental factors and the genetic background. Thus, epigenetics is likely to play an important role in the pathogenesis of the so called complex disorders, which result from the interaction of acquired and hereditary factors. Osteoporosis and osteoarthritis are the most prevalent complex disorders of the skeleton. Osteoporosis is characterized by a decrease in bone mass that results from an imbalance between the activity of the bone forming osteoblasts and the bone resorbing osteoclasts. On the other hand, cartilage degeneration is the hallmark of osteoarthritis. Secondary changes in the adjacent bone also contribute to the disease. These disorders represent an important burden in men and women over 50 years of age. This thematic issue includes a number of reviews about the role of epigenetic mechanisms in the biology of bone and cartilage cells and in the pathogenesis of osteoarthritis and osteoporosis. The reviews focus particularly on DNA methylation and microRNAs.

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Genetic and environmental factors determine the peak bone mass attained by the third decade of life, which is, in turn, a critical factor determining the risk of osteoporosis later in life. In line with this, in the first paper Wood *et al.* review the role of developmental factors in osteoporosis, and specifically the influence of the intrauterine environment. Then, Papaioannou focuses on the role of microRNAs in the development of the skeleton.

Mesenchymal stem cells are the common progenitors of adipocytes, muscle cells, chondrocytes and osteoblasts. Therefore, an adequate pool of mesenchymal stem cells is critical to maintain the pool of skeletal forming cells. Pérez-Campo *et al.* review how epigenetic mechanisms modulate the proliferation and differentiation of these important cells. In the next article, Reppe *et al.* focus on the involvement of epigenetic mechanisms, and particularly DNA methylation, in the regulation of the activity of differentiated bone cells.

Several microRNAs appear to be involved in the homeostasis of cartilage. Therefore, they are likely important in the pathogenesis of osteoarthritis. This subject is reviewed by Li *et al.*

Several studies in the last decade have shown that aging is associated with changes in the level of DNA methylation. In fact, with aging there is a trend for a decrease in cytosine methylation. However this phenomenon is not uniform throughout the genome. The role of the changes in DNA methylation in age-related disorders is reviewed by Sierra *et al.* In the next paper, den Hollander and Meulenbelt focus on the specific role of changes in DNA methylation in the pathogenesis of osteoarthritis.

Then, I provide a brief overview of the current evidence about the involvement of epigenetic mechanisms in osteoporosis. Also, a framework to critically appraise studies of epigenetic epidemiology is proposed. The differences between genetic and epigenetic studies are highlighted.

Finally, Nakasa *et al.* address the potential role of manipulating microRNA signals to enhance bone formation. They specifically consider the therapeutic tool when bone regeneration is needed.

Overall, this thematic issue provides an update of the role of epigenetic mechanisms in skeletal biology and pathophysiology. New data in this emerging field are deepening our understanding the pathophysiology of complex disorders and in future years may lead to the discovery of new therapeutic targets for prevalent skeletal diseases.

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