J Musculoskelet Neuronal Interact 2006; 6(1):1-2

Involvement of genetic factors in bone, muscle and nerves

Foreword

Osteoporosis is known to be a genetic disease for more than 20 years. Genetic factors play an important role in determining various osteoporosis-related phenotypes, such as bone mineral density, bone quality, bone turnover, and osteoporotic fractures. Extensive studies have been performed to search for genes predisposing to osteoporosis. However, despite the substantial progress achieved, most of the genes and mutations contributing to the risk for osteoporosis are largely unknown and some results from different studies are inconsistent. In the present JMNI special issue, three papers deal with the search for osteoporosis genes from different perspectives. **Drs. Zmuda, Sheu and Moffett** review the strategies to identify osteoporosis susceptibility genes, including genome-wide linkage analyses and candidate gene association studies[1]. For each application, limitations and strengths are discussed and examples are given. The authors also emphasize the importance of studying inbred animal strains and addressing potential genetic interaction and environmental exposures for dissecting the genetic factors for osteoporosis. **Drs. Uitterlinden, van Meurs, Rivadeneira and Pols** depict and compare the genome-wide linkage, genome-wide association, and candidate gene association analysis in gene identification of osteoporosis[2]. They summarize the main reasons for the controversial results and point out that the best way to identify genetic variants for osteoporosis is candidate gene association analysis followed by replication and meta-analysis. In an extensive review by **Drs. Williams and Spector**, recent advances in the genetics of osteoporosis are summarized, including DNA pooling and gene expression studies[3]. The authors indicate that other bone diseases may shed light on genes of importance in osteoporosis. They propose national and international collaborations to maximize the chances of gene discovery of osteoporosis phenotypes.

The next five articles review the genetic effects on bone, muscle, and neuropeptides from various aspects. **Lei et al.** systematically discuss the potential differential genetic determination of osteoporosis between Asians and Caucasians[4]. Evidences are provided to explain the racial difference in genetic determination of osteoporosis. The review from **Dr. Livshits** covers a wide spectrum of information of current knowledge of biochemical factors involved in bone metabolism and remodeling[5]. It summarizes the molecular genetic studies searching for genes affecting variation of the circulating factors associated with bone metabolism. **Drs. Nguyen and Eisman** review the current development and application of pharmacogenomics in osteoporosis[6]. Key components for future development of the pharmacogenomics of osteoporosis are also discussed. **Drs. Stewart and Rittweger** discuss fundamental topics on molecular and genetic regulation of skeletal muscles in animal models and in humans[7]. Considering the recent new interest of a possible neural control of bone remodeling, **Dr. Lerner** contributes an interesting article discussing the role of genes encoding calcitonin/alpha-calcitonin gene-related peptide (α-CGRP), amylin and calcitonin receptor in bone[8]. Deletions of the genes for ligands in the calcitonin family of peptides and for one of the receptors have revealed unexpected findings, which have significant implication for the understanding of the role of the nervous system in the skeleton.

In summary, this special issue provides a comprehensive review of current understanding of some critical issues relevant for the research of osteoporosis genes. We hope these articles will be useful to provide readers with an insight and instruction in future genetic studies.

References

1. Zmuda JM, Sheu YT, Moffett SP. The search for human osteoporosis genes. J Musculoskelet Neuronal Interact 2006; 6:3-15.
2. Uitterlinden AG, van Meurs JB, Rivadeneira F, Pols H. The role of gene variants in osteoporosis. J Musculoskelet Neuronal Interact 2006; 6:16-26.
3. Williams FM, Spector TD. Recent advances in the genetics of osteoporosis. J Musculoskelet Neuronal Interact 2006; 6:27-35.
4. Lei SF, Chen Y, Xiong DH, Li LM, Deng HW. Differential genetic determination of osteoporosis between Asians and Caucasians. J Musculoskelet Neuronal Interact 2006; 6:36-46.
5. Livshits G. Quantitative genetics of circulating molecules associated with bone metabolism: a review. J Musculoskelet Neuronal Interact 2006; 6:47-61.

6. Nguyen TV, Eisman JA. Pharmacogenomics of osteoporosis: opportunities and challenges. J Musculoskelet Neuronal Interact 2006; 6:62-72.
7. Stewart CE, Rittweger J. Adaptive processes in skeletal muscle: Molecular regulators and genetic influences. J Musculoskelet Neuronal Interact 2006; 6:73-86.
8. Lerner UH. Deletions of genes encoding calcitonin/α-CGRP, amylin and calcitonin receptor have given new and unexpected insights into the function of calcitonin receptors and calcitonin receptor-like receptors in bone. J Musculoskelet Neuronal Interact 2006; 6:87-95.

Lan-Juan Zhao, M.S.[1]
Hong-Wen Deng, Ph.D.[2,3,4]
Guest Editors, JMNI

[1]Osteoporosis Research Center,
Department of Biomedical Sciences,
Creighton University Medical Center, Omaha,
NE 68131, USA
E-mail: lanjuanzhao@creighton.edu

[2]Departments of Orthopedic Surgery and
Basic Medical Science, School of Medicine,
University of Missouri-Kansas City
2411 Holmes Street, Kansas City,
MO 64108, USA
E-mail: dengh@umkc.edu

[3]Laboratory of Molecular and Statistical Genetics,
College of Life Sciences,
Hunan Normal University,
Changsha, Hunan 410081, P.R. China

[4]The Key Laboratory of Biomedical Information
Engineering of Ministry of Education and
Institute of Molecular Genetics,
School of Life Science and Technology
Xi'an Jiaotong University
Xi'an 710049, P.R. China