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Editorial

Preface to the BONE special issue on skeletal genomics

1. "Bone-Omics"

The field of skeletal genetics has undergone a transformation as advancing technologies have enabled scientists to search the whole genome, transcriptome, proteome and metabolome to understand the key contributors to disease affecting the skeleton. From zebrafish to mice to humans, collaborative efforts across the translational spectrum have led to the identification of new pathways influencing bone metabolism and have opened up a new frontier for therapeutic targets at a time when the pharmaceutical pipeline for bone active drugs has been drying up. Genome wide association studies in both humans and mice have identified over 1000 genetic loci associated with bone mineral density, bone geometry, bone microarchitecture and bone strength. The availability of extremely large genome wide association study meta-analyses provides invaluable data to conduct Mendelian randomization studies to determine causal pathways influencing the skeleton. More than a dozen bone fragility genes have been characterized for a variety of skeletal dysplasias. The genetic architecture underlying important bone hormones such as vitamin D provides additional insights regarding possible causal pathways between vitamin D, bone and other diseases. The field of proteomics and the skeleton is in a very early stage of maturation but is already beginning to identify new biomarkers and drug targets. This special genomics issue of *Bone* includes outstanding papers on many of these topics, written in a way to both educate readers and review where the field of skeletal genomics stands today.

The explosion of new "omic" data and resources has created several dilemmas for the scientific community. First, keeping up with the field has become a full time job. Second the vast amounts of data challenge the field to optimally integrate these data for scientific discovery. One of the goals of this special genomics issue of *Bone* is to provide an overview of some of the more important aspects of skeletal genetics so that scientists can better use developing resources. To better consume the growing array of findings from genetic studies, the skeletal genomics community is working towards making resources available for others to use. In the field of diabetes, the so-called "Knowledge Portal" idea represents a way to organize human genetic and related data, and present analyses of them to non-experts (http://www.type2diabetesgenetics.org/). A similar undertaking is planned for the field of musculoskeletal disease. This has been motivated by several needs. First, to be able to understand disease biology or develop therapies, this requires experiments coming from model systems that can be validated for their human relevance. Second, in human genetics, experiments of nature in the form of naturally occurring genetic variants open up the possibility of understanding how these variants perturb the function of a gene. Third, testing for association between genetic variants and a collection of phenotypes produces effect sizes (direction, magnitude) and p-values (significance) for each variant (or gene) that can be compiled for the scientific community. Finally genetic association studies of musculoskeletal phenotypes are now mature and widespread but usually conducted by consortia; results are not typically made available to those who might use them to guide their experiments. By connecting all of the accumulating data in the field of skeletal genetics, the hope is that new discoveries can lead to new treatments to optimize skeletal health. We hope this collection of seven papers are helpful to scientists working in the field, and also useful to those who are not working directly in these areas, but who wish to stay current in this vast sea of genomic data. Doing so will improve our science, but more importantly, enable delivery of improved musculoskeletal care in the clinic.

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