2006 IOF+ANZBMS Combined Meeting

Combined Meeting of the
3rd IOF Asia-Pacific Regional Conference on Osteoporosis *and the*
16th Annual Meeting of the ANZ Bone & Mineral Society
~ 22-26 October 2006, Port Douglas, Australia ~
www.anzbms.org.au/asm/asm2006

Invited Plenary Abstract
P10

Genetics of osteoporosis – how to get the answers?

Matthew A. Brown
Centre for Immunology and Cancer Research, University of Queensland, Princess Alexandra Hospital, Brisbane, Australia.

To make progress in identifying genes causing osteoporosis, we need to determine what we are actually trying to find, and then pick the best of the available methods to achieve that goal.

Step 1 in this process is clearly to determine what are our goals and subsequently would be the best phenotypes to study. If we are trying to identify genes useful for prediction of those that fracture, then fracture itself would be the appropriate trait to study. If, however, we wish to understand the biology underlying how genes lead to fracture risk, then we will have a far greater chance of success if we study phenotypes closer to the site of action; otherwise noise from other covariates will make the task impossible. The phenotypes we study also need to be able to be measured in large populations robustly, non-invasively, and cheaply measurable, be highly heritable, and be correlated with fracture.

Step 2 is to choose the best available method to identify the genes determining the selected phenotype. The recent record in osteoporosis genetics shows that the following approaches are under-productive given the effort and cost involved: linkage studies in families in the absence of a clear major gene effect, candidate gene studies, and QTL-mouse mapping. These approaches have had some successes, but are not suited to providing a whole genome view of the genetics of osteoporosis. Whilst they will play niche roles, other high-throughput hypothesis-free approaches such as genomewide association studies and mouse mutagenesis offer the best chance of future success. Both these approaches have impressive track records in common diseases, which suggest that applied intelligently in osteoporosis they should be very productive.

Having robustly identified genes by these methods, the challenges will be to determine their role in bone disease, and their contribution to fracture risk in individuals and populations. Simple then! Off we go.