

BONE PROGRAM

Osteoporosis Epidemiology and Genetics groups

Professor John Eisman (j.eisman@garvan.org.au) Ph: (02) 9295 8242

Associate Professor Tuan Nguyen (t.nguyen@garvan.org.au) (02) 9295 8277

Associate Professor Jackie Center (j.center@garvan.org.au) (02) 9295 8271

Fracture due to osteoporosis is a consequence of accumulated disturbances in skeletal homeostasis, resulting in reduced bone strength and deteriorated bone quality. Identification of early and modifiable risk factors for fracture should lead to prevention, or reduction of fracture among postmenopausal women and older men. We are interested in identifying risk factors that contribute to osteoporotic fractures in men and women. Specific risk factors considered are: genetic factors, physical inactivity, lifestyle factors, dietary habits, medication, fall-related factors and hormonal factors. We are also interested in studying the determinants of progressive change in bone mineral density in the large Dubbo cohort of older men and women.

A second line of investigation relates to the genetics of osteoporosis. Bone is a complex structure, which can be defined by parameters such as bone mass, bone size, and bone structure. These parameters are collectively referred to as 'bone phenotypes'. Bone phenotypes are largely regulated by genetic factors. However, it is not known which specific genes are involved in the genetic regulation or their mode of inheritance.

Project 1: Epidemiology of Osteoporotic fractures

There are a number of possible assignments that are particularly suitable for graduates from various disciplines such as clinical medicine, public health, and epidemiology or biostatistics. Students with backgrounds in medical science and computer science are also welcome.

- a) Study of the distribution and determinants of osteoporosis and fractures
- b) Study of the determinants of adverse outcomes, including repeat fracturing and premature death
- c) Development of case-finding models for identifying high-risk individuals
- d) Development of probabilistic models, especially the Bayesian Belief Network model, for predicting fracture risk
- e) Longitudinal analysis of long-term bone loss
- f) Roles of biochemical markers of bone turnover in the prediction of fractures
- g) Predictive value of quantitative ultrasound measurements in the prediction of fractures

Project 1: Genetics of Osteoporosis

We are conducting a familial study into the genetics of bone phenotypes, by using the extended pedigree design. The study involved some 95 families, in which there are 5 large families with more than 400 individuals.

- a) Study of heritability of bone mineral density, bone turnover, and bone strength
- b) Complex pleiotropic segregation analysis of bone phenotypes
- c) Candidate gene association studies
- d) Genome-wide screening for osteoporosis genes
- e) Gene-environmental interaction studies
- f) Modelling the impact of genotypic effects on fracture risk in the general population