

PROPOSITIONS BELONGING TO THE THESIS

HIP OSTEOARTHRITIS: GENETICS, EPIDEMIOLOGICAL RISK FACTORS AND BURDEN OF THE DISEASE

1. Advances in the understanding of hip osteoarthritis (OA) will benefit from a standardized definition using joint space width as a quantitative measure, as was the case for osteoporosis and Bone Mineral Density (BMD) (this thesis).
2. The high incidence of osteoporotic fractures in subjects with atrophic type of hip OA and lumbar disc degeneration, argues against the generalization about an inverse relationship between OA and osteoporosis (this thesis).
3. Next to pain assessment, walking disability and functional limitations in activities of daily life are adequate proxies to evaluate the severity and prognosis of hip and knee OA, and need to be prioritized in the treatment of OA (this thesis).
4. Candidate genes near DNA variants associated with joint space width and endochondral bone formation are implicated in development of hip OA (this thesis).
5. The use of endophenotypes, such as joint space width for hip OA, offers not only the possibility of finding new genetic variants associated with a complex disease, but also help to understand previous genetic findings and epidemiological associations (this thesis).
6. Finding more genetic variants explaining the heritability of OA will require an in depth study of endophenotypes and risk factors for each particular joint affected (this thesis).
7. While genetic susceptibility to OA may differ between genders, genetic and epidemiological studies will benefit from sex-stratified studies of OA to find more causal genetic variants and to understand sex differences in risk factors for OA (John Loughlin, Stratification Analysis of an Osteoarthritis Genome Screen. *Am J Hum Genet.* 1999; 65(6): 1798).
8. "Genes containing common variants with modest effects on complex traits may also contain rare variants with larger effects" (Terry A. Manolio, Finding the missing heritability of complex diseases. *Nature* 2009; 8; 461(7265): 747–753).
9. Variations in bone geometry are a risk factor for age at onset of OA, as is the case for subjects with severe dysplasia where OA develops several years earlier than for subjects without dysplasia (Wiberg G, Studies on dysplastic acetabula and congenital subluxation of the hip joint. With special reference to the complication of osteo-arthritis. *Acta Chir Scand.* 1939;58(Suppl):5-135).
10. About the possible association between BMD-SNPs and OA, It is plausible that the BMD-associated SNPs do not only cause difference in BMD, but that they also stimulate or not the development of osteophytes" (LM Yerges-Armstrong Association Analysis of BMD-associated SNPs with Knee Osteoarthritis. *J Bone Miner Res.* 2014; 29(6):1373-9).
11. "The voyage of discovery lies not in seeking new horizons, but in seeing with new eyes" (Marcel Proust 'In Search of Lost Time' (1871–1922)).