STELLINGEN

behorende bij het proefschrift 'Osteoarthritis, a degenerative disease of the articular joints; towards the implementation of functional genomics in OA' (Yolande F. M. Ramos; 26 mei 2015)

1. The finding that OA patients can be distinguished from healthy persons based on gene expression profiles in blood demonstrates the potential of molecular determinants as new biomarkers (this thesis).

2. The success of identifying genes underlying susceptibility to OA in regions associated with OA in genome wide association analyses depends on integration of multi-level molecular determinants (genetics, epigenetics, trancriptomics; this thesis).

3. The application of serum cartilage oligomeric matrix protein (COMP) as biochemical marker for OA could be enhanced by taking into account the inherited capacity of patients to perform phagocytosis (this thesis).

4. To get from bench to bed, it is essential to have the availability of a tailored collection of diseased and healthy tissues and cells (this thesis).

5. The genetic variant in a family with severe early onset OA emphasizes that increased bone mineral density can be causal to OA which should be taken into account for emerging opinions suggesting that OA treatment should involve increasing bone density (this thesis; Reginster *et al.* Ann Rheum Dis 2013;72:179-86).

6. 'Unified forces give power': Despite the heterogeneity of OA extensive collaboration among different cohorts has resulted in a number of OA susceptibility loci with genome wide significance together explaining about 13% of its heritability (this thesis; Evangelou *et al.* Ann Rheum Dis 2011;70:349–355; Evangelou *et al.* Ann Rheum Dis. 2014;73:2130-6).

7. The fact that OA is now generally recognized to be a 'whole joint disease' emphasizes the need for development of sophisticated *in vitro* co-culture model systems to study effects of mutations and/or effectiveness of drugs and biologicals (this thesis; Alexander *et al.* Exp Biol Med 2014;239:1080-95).

8. The use of destabilization of the medial meniscus (DMM) as an OA mouse model does not enhance our understanding of the pathophysiology of common age-related OA in humans (Little *et al*, Nat Rev Rheumatol 2013;9:485-97; Fang *et al*, Nat Rev Rheumatol 2014;10:413-21).

9. The identified epigenetic clock that apparently does not have association to the transcriptome demonstrates the large gap between our knowledge and our understanding of the functioning of the human genome (Horvath Genome Biol 2013;14:R115).

10. The biggest challenge for 'Big Data' in the 21st century is to translate acquired data to applied knowledge and personalized medicine.

11. He who asks a question is a fool for five minutes; he who does not ask a question remains a fool forever (Chinese proverb).