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## **Aged human osteochondral explants as biomimetic osteoarthritis model: towards a druggable target in osteoarthritis**

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**“Aged human osteochondral explants as biomimetic osteoarthritis model: towards a druggable target in osteoarthritis” - Evelyn Houtman**

1. To allow effective development of personalized treatment options, it is important to set up OA models with different relevant perturbations and abandon the ‘One model fits all treatment development’ vision (**This thesis**)
2. To allow pre-clinical investigation, appropriate disease models reflecting the human aged diseased milieu are required (**This thesis**)
3. The observation that treatment with the anti-deiodinase iopanoic acid reduced detrimental mechanical-induced changes implies that reduced metabolic activity of chondrocytes is beneficial for cartilage integrity (**This thesis**)
4. Genome-wide expression analysis after mechanical stress elucidated that pathways such as insulin growth factor binding proteins are important stepping stones to explore in combating chondrocyte inability to repair (**This thesis**)
5. Treatment of patients with vitamin K inhibitors, such as Warfarin, should be reconsidered as vitamin K deficiency leads to increased OA risk (**This thesis; Boer et al. Ann Rheum Dis. 2021;80(5): 598–604; Ballal et al. Ann Rheum Dis. 2021;80(5): 605–609**)
6. As shown by gene expression patterns in chondrocytes, MMP13 might be a specific marker for mechanical stress induced damage and not a good readout to determine OA progression (**This thesis; Coutinho et al. Ann Rheum Dis. 2019 Feb;78(2):270-277; Li et al. Arthritis Res Ther. 2017;19(1):248.**)
7. One of the major hurdles that needs to be overcome in OA is the inability to completely recapitulate the multifactorial osteoarthritis disease milieu in a complete aged human joint environment (**Cope et al Osteoarthritis Cartilage. 2019 Feb; 27(2): 230–239**)
8. To speed up development of disease modifying OA drugs (DMOADs), pre-clinical development should also focus on the development and improvement of slow releasing drug delivery systems in the joint of for example targeted carriers or drug loaded hydrogels (**Gao et al. Trends in Pharmacological Sciences; 2022, Vol. 43, No. 3**)
9. The use of animals in OA research is overrated since they frequently do not take age related changes of cartilage into account and as such are not a good representation of human OA pathophysiology (**Samvelyan et al. Calcified Tissue International (2021) 109:243–256; Esdaille et al. Regen. Eng. Transl. Med. (2022) 8:284–297**)
10. More journals should have free-style submission to reduce publication time for researchers - *Due to the variability of rules regarding structure and figure requirements among different journals is frequently a loss of time while rejection is sometimes received within a few hours*
11. “Shoot for the moon. Even if you miss, you’ll land among the stars.”- **Norman Vincent Peale** *In science nothing goes according to plan, but if you aim big you might not find what you expected but there might be (positive) unexpected findings*