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

Houtman, E.

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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*