JOINT-ON-A-CHIP - Capturing essential physiological aspects of interacting cartilage and bone tissue to unravel underlying biological mechanisms of OA risk genes

Margo Tuerlings[1,2], Yolande Ramos[2], Hossein Eslami Amirabadi[1], René van Donkelaar[3], Keita Ito[3], Ingrid Meulenbelt[2], Jaap den Toonder[1]

[1]Dept. Department of Mechanical Engineering, Eindhoven University of Technology [2]Dept. Molecular Epidemiology, Leiden University Medical Center [3]Department of Biomedical Engineering, Eindhoven University of Technology.

Osteoarthritis (OA) is a joint disease in which progressive and irreversible degeneration of the articular cartilage and structural changes in the subchondral bone arise. Despite increasing prevalence, there is no proven therapy to prevent or slow down OA, leading to both social and economic burden to society. Heritability is considered to play a considerable role in the pathophysiology of OA. Studying the underlying effects of identified OA risk variants on joint tissue homeostasis will contribute to enhanced understanding of disease aetiology and identification of effective therapeutic targets. However, suitable human *in-vitro* model systems, preferably representing the interacting joint tissues bone and cartilage, are currently not available. Therefore, we will build on a NanoNext pilot project to optimize a joint-on-a-chip model system in which primary chondrocytes and osteocytes can be co-cultured. The developed microfluidic device will be optimized at the TU/e. It contains an electrospun matrix consisting of two layers: a microfiber layer to provide structural support to culture osteocytes, and a nanofiber layer to separate the osteogenic from the chondrogenic compartment. Chondrocytes can be seeded at high concentration in a well-like structure. Media will be refreshed via microfluidic channels. At the boundary, a gradient of osteogenic and chondrogenic medium will be created resulting in a functionally relevant interphase. As a proof of concept, the joint-on-chip model system will be used at the LUMC to study the role of *WWP2* (WW domain-containing protein 2), identified as OA-susceptibility gene, in the maintenance of joint homeostasis. *WWP2* is involved in SOX-9 dependent regulation of chondrogenesis. Gene expression will be modified using lentiviral particles and matrix deposition in the joint-on-a-chip will be evaluated. Development of these state-of-the-art human disease models will allow translation of compelling OA risk genes towards development of novel therapeutic options.