Publiekssamenvattingen gehonoreerde projecten 'Humane Meetmodellen 3: Next steps in model development

Oimpact: Osteogenesis Imperfecta organ-on-chip Models for Pre-Clinical Testing
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Osteogenesis imperfecta (OI) is characterized by decreased bone mass, increased porosity, and disorganized collagen fibrils, primarily affecting bone formation by osteoblasts. All OI patients suffer from fractures, which can lead to limb deformity and bowing. Current treatments focus on increasing bone mass by inhibiting bone resorption, resulting in low bone turnover and consequently impaired bone strength. Understanding the fracture healing process in OI is crucial for developing effective treatments to prevent fractures and improve fracture healing. Our proposed solution involves creating an in vitro bone disease and fracture model using bone explant tissue from OI patients. Recently, we designed and characterized a broken-bone-on-chip (BBoC) model that includes mechanical actuation modules. This BBoC model can easily be adjusted to the bone microenvironment of OI, comprising the affected bone matrix and all bone cells involved. The model further allowed implementation of a synthetic cell-instructive biomaterial around the bone explants (as bone-lining biomaterials), to mimic healthy bone-lining periosteum tissue, that is highly involved in bone turnover, healing, and stabilization, but has very limited natural resources. Using this model, we will investigate fracture healing and normal bone turnover in OI. This comprehensive BBoC model enables testing novel compounds, which is crucial for advancing OI treatment research. By accurately reflecting the disease's complexity and incorporating patient-derived tissue, this model holds promise for identifying potential treatments for OI, aimed at either preventing fractures or improving fracture healing. The BBoC model, encompassing a bone defect, all cells and relevant (biomimetic) matrices in bone tissue, is physiologically relevant for investigating treatments targeting all aspects of bone remodelling. This model will also be extremely suitable for studying other metabolic bone diseases, such as osteoporosis.