PAGE MORTON HUNTER DISTINGUISHED SEMINAR SERIES

PERICELLULAR PERLECAN, OSTEOCYTE MECHANOSENSING, AND BONE ADAPTATION

Perlecan, a large linear proteoglycan encoded by the HSPG2 gene, is widely expressed in basement membranes, cartilage matrix, and in the pericellular matrix around osteocytes in the lacunar-canalicular pore system (LCS). Clinically, perlecan deficiency is a risk factor of osteoporosis and skeletal abnormities are manifested in the perlecan-deficient Schwartz-Jampel Syndrome patients. The underlying causes for these skeletal defects are mainly contributed to impaired endochondral ossifications, accelerated mineralization, and brittle bone property. Our work suggests that the defective osteocyte mechanotransduction associated with perlecan deficiency may be another contributing factor. In this talk, I will summarize a series of investigations, in which (1) we identified the linear perlecan molecules as critical structural components of the mechanosensing apparatus (transverse tethers), (2) we developed a multiscale modeling platform to quantify load-induced fluid/solute flows and the resultant shearing and drag forces experienced by the osteocytes, and (3) we experimentally measured the acute intracellular calcium signaling, downstream mechanotransduction pathways, and in vivo bone adaptation in response to mechanical loading and disuse. I will also share some preliminary data on enhancing the skeletal loading responses in aged mice via Piezo1 activation and quantifying the turnover of pericellular matrix using click chemistry.

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Dr. Liyun Wang is a Professor of Mechanical Engineering at University of Delaware, and the Director of Center for Biomechanical Engineering Research. Trained in Mechanical (BS), Electrical (MS), and Biomedical Engineering (PhD) as well as Orthopaedics (Postdoc), Dr. Wang's research focuses biomechanics and mechanobiology. Combining engineering modeling, mechanical testing, animal models, advanced imaging, and cellular and molecular biology, she has studied how mechanical forces impact bone, cartilage, and vascular health in the context of osteoporosis, osteoarthritis, diabetic bone diseases, and cancer bone metastasis.

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Virtual seminar

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