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1. Main Research Topics Bone is an important organ to support our body, and continually subject to mechanical forces. During walking, running and other exercises, daily forces change with time, and responding bone structures also do so. Metabolic activities of bone causing its structural changes result from activities of bone cells, for example, osteoblasts on the bone surface and osteocytes within calcified bone matrix. Osteoblasts and osteocytes sense the outer forces, and respond to those as sending biochemical signals. That is why researchers think that these bone cells are essential players in the mechanism of the structural changes of bone. My study aims to answer to the questions, “how osteoblasts and osteocytes sense the outer forces?”, and “how these cells respond to these forces”, focusing on subcellular elements, especially, biomolecules and their complexes. ① Analysis of mechanical properties of focal adhesions in osteoblasts Osteoblasts play pivotal roles to new bone, where cells attach to the bone surface, and the extracellular forces from bone are input at attachment molecular complexes named as focal adhesions. Focal adhesions have structures which respond to the extracellular forces, supposedly with changes in their mechanical properties. These changes are closely related to cellular force-sensing, but are unclear in detail. Thus, mechanical properties of focal adhesions were analyzed using cultured osteoblast cells derived from mice. By utilizing atomic force microscopy for molecular-level mechanical measurement, tensile-tests were performed for pre-formed focal adhesions on the cell surface. As a result, tensile stiffness of these molecular complexes was revealed to increase on the second timescale after the force application. ② Analysis of biochemical responses of focal adhesion-mediated osteocytes Osteocytes regulate the activities of other bone cells (other osteocytes, osteoblasts, osteoclasts and so on). Osteocytes also have focal adhesions, and application of the excessive outer forces to them is suggested to cause programmed death named as apoptosis. Other previous studies suggest that apoptosis is important to reform the bone structures, but the relationship between magnitude of applied force and osteocyte death had been unclear. In current experiments, using a magnetic tweezer, mechanical forces were applied to magnetic beads targeting focal adhesions of osteocytes isolated from the bone of mice. As a result, cells underwent apoptosis in the case of larger magnitude, while apoptosis did not occur in the case of smaller magnitude. Moreover, such apoptosis of osteocytes is revealed to need intracellular production of nitric oxide, a kind of small signaling molecule.		
2. Keywords bone cells, focal adhesions, biomolecules, molecular complexes, strength of materials, mechanical measurements		
3. Remarks and Websites My study is located in an interdisciplinary field between mechanical engineering (especially, material mechanics) and molecular and cell biology. In the future, I would like to expand the research subjects to various intracellular elements and their mutually interacting behaviors. researchmap: https://researchmap.jp/nakao-nobuhiko Laboratory: https://www.st.nagasaki-u.ac.jp/laboratories/nakao/		