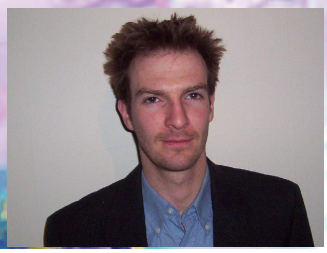
JSPS Core-to-Core Program
The First International Workshop on
Advanced Bone and Joint Science (ABJS)

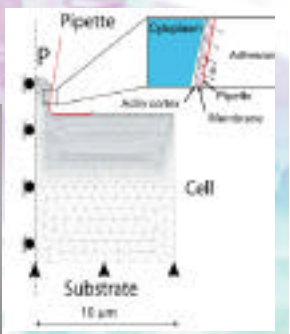
独立行政法人日本学術振興会　先端研究拠点事業　ABJS

東京医科歯科大学･難治疾患研究所・東京大学・ハーバード大学・トロント大学･ウィーン分子病理学研究所共同事業

ABJS国際セミナー（第４回）先端拠点・21世紀COE共催　05年3月1日（火）

骨と関節の先端的疾患分子医科学





How Do Osteoblasts Sense Mechanical Strain?

A Combined Micromanipulation and Finite-Element Modeling Study

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We investigated the nature and magnitude of the mechanical stimuli to which osteoblasts respond using both microindentation and micropipette aspiration. First, we microindented cells with an atomic force microscope and used the increase in intracellular calcium concentrations as a read-out for detection of the mechanical stimulus and identified two pathways for the response to mechanical stimulation. One, consequent upon contact, depended on activation of mechanosensitive ion channels; the second, following stress relaxation, required an intact microtubular cytoskeleton. The cellular responses could be modulated by selectively disrupting cytoskeletal components thought to be involved in the transduction of mechanical stimuli. The F- actin cytoskeleton was not required for responses to mechanical stress, whereas microtubules and vimentin networks were. This technique provided an estimate of the cellular strain magnitude needed to elicit intracellular calcium responses (~2.5%). To get a second estimate of this strain magnitude, we used aspiration of cells into micropipettes combined with patch-clamp electrophysiology, video-microscopy and finite element modeling to determine the magnitude of membrane strain and tension needed to open mechanosensitive channels. To achieve this, we aspirated part of the cell membrane into a micropipette and simultaneously recorded the evolution of membrane extensions into the micropipette, applied pressure, and membrane currents. Non-selective mechanosensitive cation channels with a conductance of 15 pS were observed in primary osteoblasts. Aspiration into the micropipette was simulated using finite element models incorporating the cytoplasm, the actin cortex, the plasma membrane, cellular stiffening in response to strain, and adhesion between the membrane and the micropipette. Using this model, we examine the relative importance of the different cellular components in resisting suction into the pipette and estimate the membrane strains and tensions needed to open mechanosensitive channels. Radial membrane strains of 800% and tensions of 5 10 $^{-4}$ N.m^{-1} were needed to open 50% of mechanosensitive channels. Due to the discrepancy in strain magnitudes needed to elicit mechanical responses in the two techniques, we concluded that mechanosensitive channels detect membrane tensions rather than membrane strain. Finally, using a combination of experimental and modeling techniques, we compare the strain magnitudes exerted in these two techniques with those exerted by other commonly used mechanical stimulation techniques and those exerted on osteoblasts and osteocytes in bone.

第12回　ＣＯＥ海外研究者招聘セミナー

2005年　3月 1日　(火)１６:００　-

会場：東京医科歯科大学難治疾患研究所
第2ゼミナール室

共催：東京医科歯科大学21世紀COEプログラム
「歯と骨の分子破壊と再構築のフロンティア」

問い合わせ：東京医科歯科大学難治疾患研究所
03−5280−8052

骨・軟骨疾患の先端的分子病態生理学研究の国際的拠点形成

http://www.tmd.ac.jp/mri/mph/abj.html