Department of Molecular Physiology

Yoshiki Umazume, *Professor*
Shigeru Takemori, *Associate Professor*
Maki Yamaguchi, *Assistant Professor*

General Summary

Our efforts have been concentrated on clarifying the mechanism of skeletal muscle contraction.

Research Activities

Ion species affect water states in biological tissues

Magnetic resonance imaging (MRI) depicts cross sections of living humans on the basis of differential responses of water protons. To clarify the origin of the differential responses, we chose water molecules in the lattice space of skeletal muscle, where the milieu of the water molecules can be definitely described in relation to the structure of a sarcomere. Skeletal muscle fibers can be viewed as repeated sarcomeres. We observed the effects of ion species on the structure and function of skinned fibers, which lack a cell membrane to act as a diffusion barrier, to enable any artificial intracellular solutions to penetrate deep into the fiber. We found that the I^-, which has the ability to salt out colloids, hydrates the fiber and suppresses maximal contracting force induced by Ca^{2+}. The results indicate that I^- potently induces the effects of general ionic strength, suggesting that the interfilament spacing of skeletal muscle is strongly affected by the state of water in the interfilament space.

Structure and function of the water within the cell revealed with MRI analysis

Our recent experiment with nuclear magnetic resonance of frog skeletal muscle revealed that tissue water is distinctly classified into 4 groups. From this point of view, MRI of skeletal muscle, the prostate (peripheral zone and prostate cancer), brain, and testis were reconsidered. With a 1.5-T MRI system, a single-slice 32-echo imaging pulse sequence was applied, and the obtained T_2 relaxation curves were analyzed with the Matlab software program (Mathworks, Inc., Natick, MA, USA).

We could separate T_2 relaxation curves obtained with MRI into 2 or 3 exponential components in the 4 tissues. Two exponential components in skeletal muscle obtained with MRI analysis coincided well with central 2 of 4 water components in frog skeletal muscle obtained with nuclear magnetic resonance analysis. The similarities between the testis and peripheral zone of the prostate and between brain and prostate cancers would represent histopathological features, probably cellular density.

The advantage of using an accelerometer to analyze the kinetics of athletes

A general method to analyze the kinetics of performing athletes requires a complicated studio setup and an expensive video system. We attempted to overcome these obstacles

through the use of tiny accelerometers placed on the athletes. We found that a combination of accelerometers and a portable digital recorder worked well with field athletes.

Effect of polyethyleneglycol on the myofilament lattice

Polyethyleneglycol narrows the lattice spacing of skinned skeletal muscle sarcomeres. Because the polyethyleneglycol molecule (molecular weight, 3,350) is several nanometers in size, a lattice spacing of 40 nm appears to be large enough for polyethyleneglycol to penetrate. To determine whether polyethyleneglycol penetrates the sarcomere, the specific gravity of myofibril suspensions from rabbit psoas muscle was measured in the presence or absence of polyethyleneglycol. If polyethyleneglycol does not penetrate into the sarcomere, the specific gravity of the supernatant after centrifugation of myofibril suspension is larger than the specific gravity of myofibril suspension. These measurements suggest that polyethyleneglycol diffuses into the sarcomere at half of the external concentration.

Structural change of mutant troponin related to hypertrophic cardiomyopathy

To clarify the molecular mechanism of troponin-related cardiomyopathy, a molecular dynamics study of the structure of troponin mutants related to familial hypertrophic cardiomyopathy was performed. Three different troponin T mutants related to hypertrophic cardiomyopathy — Glu244Asp, Lys247Arg, and Pro82Ser — were studied.

Dynamics was calculated by the use of the Amber software program (version 9). Model structures of troponin mutants were constructed by introducing the mutation to the crystal structure of human cardiac troponin (core region of the TIC complex) obtained from Protein Data Bank (ID number 1J1E). More than 6 trajectories of 1 ns were obtained for wild-type and mutant structures.

The electrostatic interaction between troponin I and troponin T, which linked the alpha helix of troponin T and troponin I in the wild type, was lost in the mutant. Furthermore, when a terminal residue of troponin I was pulled toward an actin molecule, mimicking the intramolecular force on activation, the observed structural changes differed between the mutant and the wild type. This difference would be involved in the development of cardiomyopathy.

Publications

Takemori S, Yamaguchi, M, Kimura, M. Skinning effects on skeletal muscle myowater probed by T_2 relaxation of ^{1}H-NMR. *Biophys J* 2007; **92:** 3610–4.

Noguchi H[1], Takemori S, Kajiwara J[1], Kimura M, Maruyama K[1], Kimura S[1] ([1]Chiba Univ). Chicken breast muscle connectin: passive tension and I-band region primary structure. *J Mol Biol* 2007; **370:** 213–9.

Morimoto S (Yokohama Natl Univ), Takemori S, Initial mechanomyographical signals from twitching fibres of human skeletal muscle. *Acta Physiol* 2007; **191:** 319–27.

Kimura M, Takemori S. Small solutes compress skinned fibers of skeletal muscle: effects of butanols and pentanols (in Japanese). *Tokyo Jikeikai Ikadaigaku Zasshi (Tokyo Jikeikai Med J)* 2007; **122:** 155–64.

Yamaguchi, M. Structure and function of maticatory (superfast) myosin. *J Oral Biosci* 2007; **49:** 216–8.