

Memorial Lectures

3ML1A March 29, 13 : 20–14 : 20, Room A

Cardiac mechanoenergetics and calcium handling proteins

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The key framework of myocardial oxygen consumption per beat (VO_2)-systolic pressure-volume area (PVA)-equivalent maximal elastance (eE_{max}) can give us a better understanding for the biology and mechanisms of normal and various failing rat heart models in terms of mechanical work and energetics. Takaki et al. found that left ventricular (LV) curved end-systolic pressure-volume relation (ESPVR) and curved end-diastolic pressure-volume relation (EDPVR) in rat hearts. The slope of VO_2 -PVA relation (oxygen cost of PVA) indicates a ratio of chemomechanical energy transduction. The VO_2 intercept indicates the summation of oxygen consumption for Ca^{2+} handling in excitation-contraction (E-C) coupling and for basal metabolism. Oxygen cost of eE_{max} indicates changes in oxygen consumption for Ca^{2+} handling in E-C coupling per unit changes in LV contractility. Ca^{2+} handling is regulated by cardiac sarcoplasmic reticulum Ca^{2+} -ATPase (SERCA2a), PLB, NCX etc. SERCA 2a is responsible for most of the Ca^{2+} removal during diastole and a larger Ca^{2+} handling energy consumer in E-C coupling. Recently, Takaki et al. established SERCA2 a transgenic (TG) Wistar rats. Long-term SERCA2a overexpression enhanced or maintained LV mechanics, improved contractile efficiency under higher energy expenditure for Ca^{2+} handling and improved Ca^{2+} tolerance, but did not change O_2 cost of LV contractility for Ca^{2+} in normal hearts. In the isoproterenol-induced failing heart model with down-regulated levels of SERCA2a, long-term SERCA2a overexpression improved LV mechanics and O_2 cost of LV contractility and maintained up-regulation of TFAM for genes of mitochondrial enzymes producing ATP. Long-term overexpression of SERCA2a will be beneficial in the isoproterenol-induced failing heart model with down-regulated SERCA2a levels.

Key word : calcium handling, myocardial oxygen consumption per beat (VO_2), SERCA2a, pressure-volume area (PVA)

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Retina as an “analogue-to-digital” converter

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When fully dark-adapted, a rod photoreceptor respond to one photon with a small hyperpolarization, which can evoke spikes in retinal ganglion cells. Interestingly, information processing in the retina is performed mainly by graded potential changes without spikes. Retinal synapses and circuits are specialized and fine-tuned to minimize noise, to amplify signals, to extract features, to adapt environment, and to convert signals to spike trains. Both photoreceptors and bipolar cells (BCs) have synaptic ribbons. Glutamate is continuously released from rods in the dark. Light-evoked hyperpolarization in rods reduces glutamate release, and deactivation of mGluR6 depolarizes ON-type BCs by opening of TRPM1 cation channels. To secure the synaptic transmission, glutamate must be rapidly removed from the synaptic cleft. Rod terminals are equipped with high-density glutamate transporters, and have a capacity to take-up all the released glutamate by themselves. In goldfish Mb1 BCs, L-type Ca^{2+} channels are clustered close to synaptic ribbons. Upon depolarization, immediate and transient glutamate release occurs underneath each ribbon, whereas sustained release occurs away from ribbons by diffused Ca^{2+} . Glutamate release from Mb1 BCs is regulated by two kinds of GABAergic inputs from amacrine cells. Strong depolarization of single BCs can drive local reciprocal inhibition, whereas weak depolarization of electrically-coupled multiple BCs can drive global lateral inhibition. Each inhibition is independently activated through distinct pathways, and both contribute to efficient signal transmission to postsynaptic neurons.