COENZYME A SYNTHESIS IN ISOLATED RAT HEART MITOCHONDRIA. Arun G. Tahiliani, Constance Q. Mahar and James R. Neely. Department of Physiology, Milton S. Hershey Medical Center, Hershey, PA 17033.

Isolated cardiac mitochondria incubated with 4'-phosphopantetheine (4'PP) synthesized coenzyme A (CoA). Under the conditions used, synthesis was dependent on the presence of added ATP in the incubation medium. Increasing the pH of the buffer from 7.4 to 8.5 increased the rate of synthesis. When the mitochondria were separated from the incubation mixture by centrifugation, the amount of CoA appearing in the supernatent increased with time while that in the mitochondrial pellet remained constant. Although this suggests that the synthesis of CoA may be external, the following results suggest that CoA may be synthesized in the matrix. First, neither carboxyatractyloside (10μM) nor FCCP (100nM) when used alone inhibited synthesis of CoA, but a combination of the two significantly inhibited the synthesis. This inhibition was not due to lack of ATP in the incubation medium and the inhibition could be overcome by incubating the mitochondria with DOC (0.01%). Second, isolated mitochondria take up CoA (medium concentration 25μM - 200μM) against a higher matrix concentration. Thus, it is conceivable that the transport system can also work in the opposite direction, i.e., cause an efflux of newly synthesized CoA from the mitochondria. The data suggest that cardiac mitochondria are capable of synthesizing CoA internally from 4'-PP and that there is a transport system for CoA in the mitochondria. (Supported by Grant # HL 13028.)

RELEASE OF ATP METABOLITES, AS A CRITICAL FACTOR FOR REOXYGENATION-INDUCED RECOVERY OF CARDIAC CONTRACTILE FORCE AFTER HYPOXIA. S. Takeo, K. Tanonaka and *N. Makino. Department of Physiology and Pharmacology, Faculty of Pharmaceutical Sciences, Fukuyama University, Fukuyama, Japan, and *Department of Internal Medicine, Institute of Bioregulation, Kyushu University, Beppu, Japan.

The present study was designed to elucidate critical factors responsible for reoxygenation-induced recovery of cardiac contractile force after hypoxia. For this purpose, the rabbit heart was perfused for 20 min under hypoxic conditions, followed by 45 min-reoxygenation, and relationships between the recovery of cardiac contractile force and hemodynamic parameters, or several biochemical parameters were examined. Reoxygenation-induced recovery of cardiac contractile force after 20 min-hypoxia was correlated with a rise in resting tension and an increase in perfusion pressure of the heart at 20 min-hypoxia. The recovery was also correlated with ATP and creatine phosphate contents of the reoxygenated heart, and a release of ATP metabolites from the perfused heart. The release of ATP metabolites during hypoxia was related to the rise in resting tension of the hypoxic heart. Furthermore, the release of ATP metabolites during hypoxia and reoxygenation was related to the decrease in ATP contents of the reoxygenated heart. The results suggest that the release of ATP metabolites from the perfused heart is a critical factor for reoxygenation-induced recovery of cardiac contractile force after hypoxia.

DUAL REGULATION OF HEART ADENYLATE CYCLASE BY HORMONES AND CALCIUM IONS. V.A.Tkachuk, M.P.Panchenko, E.E.Illarionova. Cardiology Research Center of the USSR, Academy of Medical Sciences, Moscow, USSR.

Hormonal receptors regulate the adenylate cyclase (AC) via the coupling of AC catalytic component (C) with the GTP-binding stimulatory (Ns) or inhibitory (Ni) proteins. We have found that glucagon (G) can either activate (Ka of 30 nM) or inhibit (Ki of 40 nM) AC from rabbit heart plasma membranes in a GTP-dependent manner. G attenuated activation of AC by catecholamines and inhibited AC activity in membranes after ß-adrenoceptor desensitization. Inhibitory action of G was abolished by selective inactivation of Ni. These data indicate that the heart AC can be coupled with G receptor via both Ns and Ni. Ca^{2+} inhibited AC with Ki of 50 μM. Mg^{2+} stimulated AC (Ka of 1,5 mM) and competitevely blocked Ca^{2+}-dependent AC inhibition. Ca^{2+}/Mg^{2+} AC regulation was identical in membranes and in preparations of C free of Ns, Ni and calmodulin (CaM). In the presence of CaM (0,05-10 μM) Ca^{2+} was an AC activator with Ka of 1 μM. Trifluoperazine (1-10 μM), troponin I (10 μM) and high Mg^{2+}/Ca^{2+} ratio prevented this activation. CaM-dependent activity of AC was directly proportional to the concentration of Ns•C complex. We suggest that in myocardium Ca^{2+} and CaM activate GTP-sensitive hormone-dependent AC, and the inhibitory action of Ca^{2+} is due to Ca^{2+}/Mg^{2+}-competition for specific regulatory site located on C.