oxidase activity (Barrett & Dawson, 1975), and Gutman et al. (1971) have proposed a role for the ubiquinone redox status in the regulation of the activity of succinate dehydrogenase.


Regulation in vivo of Phosphorylase b in Skeletal Muscle of Phosphorylase Kinase-Deficient Mice

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The rate of muscle glycogen degradation is controlled by the activity of glycogen phosphorylase, which provides 90% or more of the glycosyl residues for glycogenolysis (Wilson et al., 1967). The two best-understood mechanisms involve phosphorylation of the inactive b form of the enzyme to the active a form by phosphorylase kinase: (i) Hormonal control mediated by cyclic AMP formation and phosphorylase kinase phosphorylation; (ii) neural control mediated by Ca++ activation of either phosphorylated or dephosphorylated phosphorylase kinase.

A third mechanism has been extensively studied in vitro, but is not well understood in vivo. This involves non-covalent activation of phosphorylase b by AMP or IMP. Activation by these nucleotides was shown by Cori et al. (1938), and numerous allosteric interactions with substrates and inhibitors have subsequently been described, e.g. by Griffiths et al. (1976). AMP has been regarded as the more physiologically significant, since its activation constant (about 50 μM) is much lower than that of IMP (about 2 mM). Little experimental evidence has been produced on this question, however.

The ICR/1An strain of mice almost entirely lacks phosphorylase kinase in its skeletal muscle and provides a useful model in which to study phosphorylase activation by mechanism (iii) in the absence of mechanisms (i) and (ii). Mice that lack muscle phosphorylase kinase are nevertheless able to degrade glycogen during muscle activity (Lyon & Porter, 1963; Danforth & Lyon, 1964), and it has been generally assumed that they do so by AMP activation of phosphorylase b. It has also been suggested that the balance between AMP and ATP may be a primary determinant of the rate and direction of metabolic sequences in general (Ramaiah et al., 1964; Atkinson, 1965, 1966) and that the sequences in these sequences are controlled by the energy charge, defined as ([ATP] + [ADP])/([AMP] + [ADP] + [ATP]).

Studies were done on muscle extracts from the hind leg of mice in which the purine nucleotide (AMP, IMP, ADP, ATP) concentrations were determined as described previously (Rahim et al., 1976). We originally used SAS/4 mice as controls, but more recent studies have included two other control strains, namely C3H and Balb/c (Table I).

The concentrations of ATP, ADP and AMP did not change significantly after muscle activity, whereas that of IMP increased significantly in all strains. The concentration of IMP in ICR/1An mouse quadriceps muscle rose 2.3-fold after swimming, whereas

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