일반논문발표 초록

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Strain Differences in Mitochondrial Respiration: Effects on Dose responses to Oligomycin in Diabetes-prone and Normal rats

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The BHE/Cdb rat is a specific strain of rat that mimics the human who develops non-insulin dependent diabetes mellitus (NIDDM). One of the challenges in working with this rat stock has been the detection the genetic error. Recent studies have shown that the BHE/Cdb rat strain have a mitochondrial genomic mutation in the region that encodes subunit 6 of F_0ATPase. The mutation changes the amino acid sequence of that portion of the subunit that forms the proton channel. The inferred amino acid substitution in F_0 moiety could have an effect on the functional characteristics. In addition, The F_0 portion is embedded in the inner mitochondrial membrane, its degree of movement is likely affected by the fluidity of that membrane. Thus the strain differences with respect to the mobility of subunit 6 of the F_1F_0ATPase likely could explain the characteristics of the BHE/Cdb rat.

The functional assessment of F_1F_0ATPase from BHE/Cdb and SD rats was studied. The responsiveness of hepatic mitochondria isolated from NIDDM-prone BHE/Cdb and normal Sprague Dawley (SD) rats to oligomycin, a specific inhibitor of tightly coupled respiration, was performed. Dose response curves of state 3 and state 4 respiration, respiratory control (RC) ratio and ADP:O ratio to oligomycin levels (0 to 0.10 *ug*/mg of mitochondrial protein) were generated. Mitochondria from BHE/Cdb rats were more sensitive to oligomycin addition than mitochondria from SD rats.

The different extent of inhibition by oligomycin on mitochondrial respiration is directly influenced by the structural configuration. Marked differences in inhibitory effect of oligomycin on mitochondrial ATPase are found with various phospholipids in inner mitochondrial membrane. It was thus speculated that the quantitative and qualitative composition of the phospholipids present in the membrane might regulate the extent of inhibition by oligomycin. Since molecular mobility is essential to ATPase function, a small change in protein structure potentiated by the relative rigidity of the surrounding lipid could explain the strain differences in functional characteristics.◎