

INCREASED SUSCEPTIBILITY OF AGING KIDNEY TO ISCHEMIC INJURY: IDENTIFICATION OF MOLECULAR PATHWAYS USING MICROARRAY

G Chen, EA Bridenbaugh, DC Zawieja, AR Parrish (P)

College of Medicine, Texas A&M University System Health Science Center, College Station, Texas 77843-1114

Aging is associated with an increased incidence and severity of acute renal failure; however, the molecular mechanisms underlying the increased susceptibility remain undefined. These experiments were designed to investigate the influence of age on the response of the kidney to ischemia. Renal slices were prepared from young (5 month), aged ad libitum (24 month) and aged caloric restricted (24 month) male Fischer 344 rats and subjected to ischemic stress (anoxia, 100% N₂) for 0-60 min. As assessed by ATP content and LDH leakage, slices from aged ad libitum rats were more susceptible to injury than young counterparts. Importantly, caloric restriction attenuated this increased susceptibility to injury. In an attempt to identify molecular pathway underlying this response, microarray analysis was performed on tissue harvested from the same animals used for the functional analysis. RNA was isolated and the corresponding cDNA was hybridized to CodeLink™ Rat Whole Genome Bioarray slides. Subsequent gene expression analysis was performed using GeneSpring software. Using a 3-fold difference as a cut-off and a Welch ANOVA (Benjamini and Hochberg False Discovery Rate of 0.05), we identified 78 genes whose pattern of expression suggested that caloric restriction attenuated a change induced by aging. The expression of twenty-eight genes was reduced during aging but rescued by caloric restriction including the alpha1 subunit of the Na⁺K⁺-ATPase. The expression of 50 genes was increased during aging but attenuated by caloric restriction. We found significant similarities between this list of 50 genes and the Gene Ontology lists related to host pathogen interaction and defense immunity protein activity. In summary, we have identified several changes that may be associated with the increased susceptibility of aging kidney to ischemic insult.