□외국 연수 연구발표□

Microarray Analysis of Altered Gene Expression in Kidneys of Spontaneously Hypertensive Rats

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Spontaneously hypertensive rat (SHR) is used as an animal model of essential hypertension in humans. As with human essential hypertension, a polygenic etiology has been considered as the mechanism of hypertension in SHR. We used DNA microarray analysis to explore differentially expressed genes in kidneys between SHR and Wistar-Kyoto (WKY) rat. Among 8,799 known genes and expressed sequence tag (EST) clusters of Affymetrix Rat Genome U34A arrays, we identified 74 transcripts with statistically significant difference in mean expression levels between two groups.

Of these genes and ESTs with changed expression, 43 were up-regulated and 31 were down-regulated in SHR. Those genes with known function were grouped into functional categories including several groups related to lipid and glucose metabolism, insulin resistance, signal transduction and intracellular trafficking, antioxidant and anti-inflammatory defense, drug metabolism, regulation of gene transcription. Real time RT-PCR results independently confirmed the microarray results for four down-regulated genes (glutamylcysteine gamma synthetase light chain, GCGS; glutathione S-transferase, GST; heme oxygenase 3, HO3; phosphatidylinositol 3-kinase p85 alpha subunit, PI3K) and one up-regulated gene (stearoyl-CoA desaturase 2). These findings suggest that beside dysregulation of lipid and glucose metabolism, defect in insulin signal transduction pathway (down-regulated PI3K), oxidative stress and tissue injury caused by defective antioxidant protection (down-regulated GCGS, GST and HO3) and anti-inflammatory defense could be involved in the pathogenesis of hypertension in SHR.