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DNA RESTRICTION FRAGMENT LENGTH POLYMORPHISMS OF
THE GLUTATHIONE S-TRANSFERASE GENE IN
THE LEC/Hkm RAT WITH SPONTANEOUS HEPATITIS

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The LEC rat, which has been established from a closed colony of the Long-Evans rats, is a mutant strain with hereditary hepatitis associated with severe jaundice. A single autosomal recessive gene is responsible for the hepatitis, but the gene is as yet unidentified. To investigate the presence of restriction fragment length polymorphisms (RFLPs) which are correlated with the disease allele, genomic DNAs prepared from 9 inbred strains of rats, including the LEC rat were analyzed by the DNA fingerprinting method using a synthetic oligonucleotide, (CAC)₅, as a probe. Highly polymorphic bands of DNA were observed and individual strains were identified by their patterns. However, bands which correlated with the disease allele could not be detected.

One of the biochemical traits of the LEC rat is an altered expression of glutathione S-transferase (GST), which plays an important role in drug metabolism. The rat liver GSTs are homodimers or heterodimers consisting of subunit families which are designated Ya, Yb and Yc. The characteristic augmentation of Yc-Yc activity and the diminution of Ya-Ya activity have been reported in the LEC rat before the occurrence of jaundice. To investigate whether the altered expression of GSTs was attributable to changes in the regulatory regions of the GST gene, the genomic DNA was analyzed by the Southern blot hybridization technique using cDNA of Yc mRNA and a synthetic oligonucleotide specific to the Yc gene as a probe. Since a high homology of nucleotide sequences between Ya and Yc cDNA has been reported, the Yc-specific oligonucleotide was used for the detection of DNA fragments specified by the Yc gene. When genomic DNAs prepared from 9 inbred strains of rats were digested with restriction endonucleases, several bands which hybridized to cDNA of Yc mRNA and the Yc-specific oligonucleotide were shown. The DNA bands that were detected in individual strains were highly polymorphic, but RFLPs which characterized the disease allele of the LEC rat could not be detected. These results suggested that the Yc gene was a complex structure consisting of multiple exons and introns, and that some DNA fragments which hybridized to the Yc-specific oligonucleotide probe, might be derived from some processed-type pseudogenes.