LOCALIZATION OF THE GENE FOR GLUTATHIONE S-TRANSFERASE P ON RAT CHROMOSOME 1 AT BAND q43

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An intron fragment of a rat glutathione S-transferase P (GST-P) genomic clone was used to assign the chromosomal localization of the GST-P gene. In situ hybridization analysis with the genomic DNA indicated that the GST-P gene was localized on band q43 of rat chromosome 1.

Key words: Rat glutathione S-transferase P gene — In situ hybridization — Rat chromosome 1

The placental type of glutathione S-transferase of the rat (GST-P) is a new enzyme marker of preneoplasia in chemical hepatocarcinogenesis.1-4 Although the GST-P enzyme is detected very little in normal liver cells, it is induced at a very high frequency (almost 100%) and is constitutively expressed in hyperplastic nodules and in hepatocellular carcinomas caused by carcinogen treatments.5 The mechanism of activation of the GST-P gene during chemical hepatocarcinogenesis is not known, but Northern blot analysis of RNA from rat hepatocellular carcinomas suggested that the expression of GST-P in carcinoma cells is regulated mainly at the transcriptional level.5 In this study, we have used the in situ hybridization technique to examine the chromosomal localization of the GST-P structural gene, and have shown that this gene is localized on rat chromosome 1 at band q43.
Fig. 1. Diagram showing the distribution of labeled sites with GST-P probe in 58 rat metaphases. A high concentration of grains can be seen in the long arm of chromosome 1.

Fig. 2. Hybridization of $^3$H-labeled GST-P probe to the chromosomes of a rat metaphase, followed by Q-band staining. A silver grain is seen on 1q43 (arrow).
and transmitted visible light (for identification of silver grains). Grain analysis was done on 58 metaphases and the results were plotted on an idiogram established by Levan.8 In situ hybridization of the 3H-labeled rat GST-P probe, the 0.6 kb Smal fragment in the fifth intron, resulted in specific labeling of rat chromosome 1 (Fig. 1). Of 58 cells examined, 24 cells (41%) had silver grains on the long arm of chromosome 1. An example of grain localization is shown in Fig. 2. A total of 27 grains were found on the long arm of chromosome 1, and 14 (52%) were clustered on the portion 1q43→q51, with most grains at lq43 (Fig. 3). Therefore, we concluded that the GST-P gene is located on rat chromosome 1 at band q43.

The isozyme pattern of rat glutathione S-transferase shows tissue-specific differences and comprises homo- or heterodimers of the four kinds of subunits, suggesting that each subunit is coded by different genes. The human glutathione S-transferase isozyme 3 (GST3) gene has recently been mapped to human chromosome 11, and its homologous mouse gene, Gsta, was mapped on mouse chromosome 9.9 However, the rat GST-P gene is different from the GST3 and Gsta genes. In the present study, we assigned GST-P gene to rat chromosome 1, on which ten genes including two oncogenes, HRAS1 and YES1, are located (M. C. Yoshida, unpublished data). The GST-P locus is an additional member of this syntenic (linkage) group, although the gene order is not known. Knowledge of the location of the GST-P gene on rat chromosome 1 provides a basis for further studies to clarify the mechanism of activation of the GST-P gene in chemical hepatocarcinogenesis.

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Fig. 3. Distribution of silver grains on rat chromosome 1.

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