homologue of HSV-1 (CICP0), consisting of 333 amino acids. The deduced amino acid sequence contained RING finger and acidic transcriptional activation domain, suggesting that CICP0 functions as a transcriptional regulatory factor.

Alphaherpesviruses remain latent in host cells as genomes after the primary infection and escape host immune responses. Further investigations on the mechanisms of latency and reactivation of CHV would provide information on strategies to control herpesvirus infections.

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Basic study of the application of high-magnetic field MRI to rats and mice as small laboratory animals

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MRI of small laboratory animals such as rats and mice required for a high-magnetic field and a strong gradient-magnetic field to visualize the detailed structures in their tissues and organs since they must be imaged by small voxels with strong signals and high S/N ratios. In the present study, MRI using an Oxford 7.05 T superconducting magnet (higher than those for usual MRI, 0.2–2.0 T) was, therefore, applied to the visualization of copper-induced hepatitis and hepatocellular carcinoma (HCC) in Long-Evans Cinnamon (LEC) rats, as well as the topographical structure of mouse brain. Before MR imaging of LEC rat liver, the effects of an excess amount of paramagnetic ions in tissue and the high magnetic field on not only the chemical shift of liver protons but also their T1 and T2 relaxation times were first examined to adjust an MRI machine to the suitable condition, since an excess amount of paramagnetic ions (40–50 times higher than those of normal rats) was present in the liver of LEC rat. Then, MRI using a gradient coil of 0.3 mT/cm was carried out under 7.05 T to image the livers of rats showing acute and chronic hepatitis, and HCC. In the case of mouse brain, MRI using the extremely strong gradient coil (3.5 mT/cm) was carried out under 7.05 T to visualize its topographical structure.

When the effects of paramagnetic ions under the high magnetic field on the chemical shift of protons in the liver containing a high amount of paramagnetic ions were examined by magnetic resonance spectroscopy (MRS), it was found that (1) MR signal was mainly arisen from water protons, and (2) the chemical shift position of the protons was not different from that of Wistar rat, suggesting that the width and strength of pulse to excite the protons in the liver of normal Wistar rat was applicable to MR imaging of the LEC rat liver. MRS was also employed to measure the

T1 and T2 relaxation times of LEC rat livers in the pre-, acute- and chronic-hepatic phases, and showed that the shortening of both times due to an excess amount of paramagnetic irons were observed in the liver of acute phase. The theoretical calculation of the MR signal intensities using the measured T1 and T2 relaxation times indicated that their imaging might be possible under the condition of TR/TE=2,000ms/20ms that the parameter-weighted index of proton density was largest. In fact, the clear-cut MR image showing hepatitis as hyperintense regions in the livers of the acute-phase was obtained under this condition. The further application of this high-magnetic field MRI to the livers of 50– and 116–week-old rats showed hyperintense regions around the hepatic veins in 50–week-old rat and those throughout the hepatic lobe in 116–week-old rat. These hyperintense regions might be assumed as HCC in LEC rats.

Finally, MRI combining a Bruker 7.05 T superconducting magnet and the extremely strong gradient coil (3.5 mT/cm) was carried out to visualize the topographical structure of mouse brain. Imaging condition was TR/TE=3,000ms/10.4ms, which was more favorable for imaging than TR/TE=2,000ms/20ms since the contribution of proton-density weighting to MRI signal intensity under this condition was greater than that under the TR/TE=2,000ms/20ms. As expected, the resolution of MRI was comparable to that of the histological sections. The white matter was distinguished from the gray matter in some regions of the brain. Coronal sections of the brain also showed that the hippocampal CA1–CA3 regions were distinguishable from the other regions. These results suggested that the high-magnetic field MRI might be a useful tool for studying diseases in animal models like rats and mice.

Alterations in levels of hepatic microsomal cytochrome P450 isozymes following intracerebroventricular injection of bacterial lipopolysaccharide in rats

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To investigate the effect of central inflammation due to bacterial infection such as meningitis on the activities of hepatic cytochromes P450 (CYPs), rats were injected intracerebroventricularly (icv) with 0.1 μg of bacterial lipopolysaccharide (LPS). The LPS icv injection significantly decreased the total P450 contents (by 30% of the levels of control rats treated with saline icv), the contents of CYP1A (48%), 2B (54%), 2C11 (37%) and 3A (40%) and related drug metabolizing activities, 7–ethoxycoumarin O-deethylation (ECOD ; 36%), imipramine N-demethylation (IMND ; 41%) and erythromycin N-demethylation (ERND ; 33%) in liver microsomes 24 hrs after the treatment. In contrast, intraperitoneal (ip) injection of LPS at the same dose as icv (0.1 μg) did not significantly affect the hepatic microsomal contents of total P450 or the content of each individual CYP isozyme and its activity. CYP2D protein and the activity of imipramine 2–hydroxylase (IMOH) were not significantly decreased by LPS injection regardless of the route of administration. The inhibitory effects of 0.1 μg icv-LPS on total P450 contents were almost equal to those of 10 μg ip-LPS. As low as 0.01 μg of icv-LPS significantly decreased