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mulation of NFs in the distal part of the axons and Quv quail lacking NFs may not be affected with the distal axonopathy. Alternatively, because Quv quail died or were euthanatized after a short treatment period, acute neurotoxicity may not have had time to develop.

To investigate the possibility that the absence of the distal axonopathy in Quv quail might be due to the shortness of the treatment period, a lower dose of 2,5-HD (175 mg/kg per day) was

administered for a long term (24 weeks) to normal and Quv quail. Some treated normal quail had central-peripheral distal axonopathy. In contrast, distal axonal degeneration did not appear in any Quv quail. These results indicated that distal axonal degeneration did not occur without NF accumulation. In conclusion, NF accumulation is an essential factor in the development of distal axonopathy in  $\gamma$ -diketone neuropathy.

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#### Studies on latent infection, and immediate early and early protein gene of canine herpesvirus

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Canine herpesvirus (CHV), belonging to the subfamily *Alphaherpesvirinae*, causes a fatal hemorrhagic disease in neonatal pups, and usually subclinical infection in the respiratory and genital tracts in adult dogs. The virus remains latent in convalescent dogs and stress or immunosuppression leads the virus to reactivate. Asymptomatic excretion of the reactivated CHV usually occurs and pose risks for transmission of the virus, causing neonatal mortality in breeding kennels and the spread of CHV infection. It is, therefore, important to clarify the mechanisms of latency and reactivation of the virus.

To provide information on the latency and reactivation of CHV, the virus was inoculated into female adult dogs via different routes. *In situ* hybridization analyses on tissues of the convalescent dogs revealed that the latent CHV harbored in the nuclei of the trigeminal ganglionic neurons and the retropharyngeal lymphocytes. North-

ern blot hybridization and reverse transcription-PCR analyses on the latently infected tissues demonstrated that the latency associated transcript (LAT) of CHV was an approximately 6kb RNA and generated as an antisense transcript to the immediate early (IE) and early (E) genes of the virus. Thus, the CHV LAT was suggested to be involved in the latency and reactivation.

To define the structure of the CHV IE and E proteins, the inverted repeat region and its vicinity linked to the unique long region of the genome were cloned and sequenced. The IE protein was predicted to consist of 1,383 amino acids. The amino acid sequence suggested that CHV IE protein was a homologue of the infected cell protein 4 (ICP4) of herpes simplex virus 1 (HSV-1) which played an important role in viral gene expression as a transactivator. The gene flanking downstream the IE protein gene was transcribed in the E phase and encoded the ICP0

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