ANTIGENIC ANALYSIS OF HFRS VIRUSES WITH MONOCLONAL ANTIBODIES AND PREPARATION OF ANTIGENIC VARIANTS AND TEMPERATURE-SENSITIVE MUTANTS

Yoshihiro NAKAMURA

Department of Veterinary Public Health
Faculty of Veterinary Medicine
Hokkaido University,
Sapporo 060, Japan

Monoclonal antibodies (MAbs) were prepared against HFRS virus strain SR–11, which was isolated from laboratory rat. The indirect immunofluorescent antibody (IFA) technique, neutralization test (NT) and hemagglutination-inhibition (HI) test were selected for examination of antigenic variants.

In addition, to examine the relationship between antigenic variants and persistent infection *in vivo*, MAbs were utilized to characterize variants that appeared during persistent infection in rats. Furthermore, temperature-sensitive mutants were obtained for the marker in the genetic study.

The results were summarized as follows;

1. Antigenic relationships among 5 strains of HFRS viruses isolated from different rodent species were examined with 12 MAbs against strain SR–11 and one against strain H–76–118. Antigenic analysis by cross-IFA demonstrated that HFRS viruses may be divided into four host-dependent serotypes.
2. Thirteen MAbs were classified into 6 groups based on the reactions in IFA, NT and HI tests, and cross reactivities against strain SR–11 and strain H–76–118. Four MAbs had both NT and HI activities, which suggested that some HA and NT sites were closely located and/or overlapped each other.
3. MAbs were classified into two groups based on the IFA staining pattern of the HFRS virus-infected cells: (i) antibodies which showed a fine granular pattern in the cytoplasm by IFA, probably reacting with virus glycoproteins and (ii) antibodies which showed a large, patchy granular pattern in the cytoplasm, and had no or little HI and NT activities, probably reacting with virus nucleocapsid proteins.
4. Virus clone E10 was isolated from a persistently infected rat with strain SR–11 and was not completely neutralized by MAb 3F11 against the virus envelope protein. It was supposed that clone E10 was an antigenic variant selected during persistent infection in rats.
5. In order to obtain the genetic marker of HFRS virus, four temperature-sensitive mutants, which included three from strain SR–11 and one from strain H–76–118, were isolated. Their sensitivities to non-permissive temperature, however, were not high enough for further study.