BACKGROUND PAPER

ASPECTS OF CORONAVIRUS EVOLUTION

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The word "evolution" usually evokes thoughts of events which occurred in the distant past, but it is self-evidently an ongoing process. The application of intense selective pressure, for example by the wide-spread use of vaccination, and also the transport of infected animals over large distances may have contributed to what may be considered "short-term" evolution. Papers relevant to putative coronavirus evolution in both recent and distant time-scales are presented in this volume.

A major contribution to our understanding of the evolution of this genus was the demonstration, both *in vitro* and *in vivo*, of high frequency recombination between strains of murine hepatitis virus (MHV) (1,3,5). Recombination has been shown to occur at many positions throughout the genome and may be related to the propensity of the replicase to fall off its template and then to continue RNA replication on the homologous or heterologous template (copy choice mechanism) during a mixed infection. A more unexpected finding has been the discovery that the HE glycoprotein possessed by some coronaviruses has homology with the HEF 1 subunit of the influenza virus C glycoprotein (4; chapter 2, this volume). This implies that at some time a coronavirus and an influenza virus (or their respective progenitors) have undergone non-homologous recombination.

Given the experimental evidence for recombination of MHV strains and the revelation regarding the HE glycoprotein it will not be surprising to find that some coronavirus isolates from the field are, in fact, recombinants. Indeed sequencing of the S and M genes of infectious bronchitis virus (IBV) strains has provided circumstantial evidence for this having occurred (2; Cavanagh *et al.*, this chapter).

Another observation which may be related to the tendency of the replicase to fall off its template is the highly variable length of the S protein among strains of MHV (7; papers in this chapter). MHV strains with different passage histories both *in vitro* and *in vivo* can differ by as many as 150 amino acids in the length of the S1 subunit. Moreover, such variants which have been selected with monoclonal antibodies differ in neurovirulence from the parental population.

An example of the economic consequences of a coronavirus "evolutionary" event, which may have occurred in the recent past, is that of the emergence of porcine respiratory coronavirus (PRCV) (chapter 9, this volume). First isolated in 1984, in Western Europe (6), this virus is closely related to porcine transmissible gastroenteritis virus (TGEV). Unlike the latter, however, the primary replication site is not the gut but the respiratory tract.

It is to be hoped that in the near future it will be made clear to what extent possession of HE affects host cell range and pathogenicity. Further elucidation of the functional domains of the S protein will help to explain the differences in neurovirulence exhibited by monoclonal antibody selected variants. The elucidation of the molecular basis for the different tissue tropisms of TGEV and PRCV is eagerly awaited. Also required is further evidence for recombination among IBV strains since, if confirmed, this factor must be taken into account when attempting to clarify the epizootiology of this widespread, economically important virus. One thing is clear that, through one mechanism or another, an important feature of the coronaviruses is the inconstant nature of the genome.

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