Pestivirus diversity

A meeting was held at the Forte Crest Hotel, Glasgow on 10th August 1993 to discuss the topic of antigenic diversity in pestiviruses, to consider whether such diversity had any practical significance in terms of control, and the plan steps to correlate and collate the considerable body of data already existing on this subject in various laboratories around the world. The meeting was chaired by Prof. Marian Horzinek, and sponsored by SmithKline Beecham (represented by Dr. N. Zygraich).

It was agreed that antigenic diversity exists among the pestivirus genus, and that this could not be readily defined in conventional terms of serotypes. *Hog cholera virus* strains appear to form a tight antigenic cluster and can be adequately defined for practical purposes by the binding of species-specific monoclonals to the dominant epitope on the gp55. This is important for regulatory authorities seeking to verify their hog cholera-free status in the face of endemic infection with other pestiviruses, which sometimes spread from ruminants into pigs. The group would not address further the definition of HCV.

The terms *bovine viral diarrhoea virus* (BVDV) and *border disease virus* (BDV) are used rather loosely. They could refer to virtually identical viruses isolated respectively from cattle and sheep, or to widely divergent viruses isolated from a single species. The definition of virus species on the basis of host broke down further when non-HCV pestiviruses isolated from pigs were labelled BVDV or BDV. No satisfactory nomenclature exists for pestiviruses isolated from ruminants other than cattle of sheep.

There is good evidence accumulating from a number of research teams that ruminant pestiviruses tend to cluster in 2–3 distinct groups. This is supported by three strands of evidence – polyclonal neutralisation tests, murine monoclonal binding studies, and genetic sequence data. The fact that the three approaches give broadly similar results confounds to some extent the suggestion that murine antibodies may not detect meaningful epitopes in terms of immunity in ruminants. It is hoped that an ad hoc group of pestivirus workers can make progress by sharing data and exchanging reagents with the aim of reaching a consensus view. In particular there is no certainty that pestivirus strains circulating in one country of continent are the same as those elsewhere, although it is commonly assumed that they are so.

The question of antigenic diversity is important practically, most particularly as it raises the spectre of naturally occurring vaccine escape variants. There is evidence from USA that such variants do arise in vaccinated cattle. Nevertheless a view is widely held that single strain vaccines provide reasonable protection in most cases. Pestiviruses present a challenge for the vaccinologist because of the need to prevent fetal infection in pregnant dams exposed to infection. Only by protecting the fetus can the establishment of persistently-infected offspring be prevented and the main cycle of infection broken.

Following the main meeting a smaller group assembled of those who felt they could contribute to the proposed exchanges of materials. It was agreed that two main approaches would be adopted in parallel for the definition of antigenic types among ruminant pestiviruses:

1. The differentiation of strains by the binding of monoclonal antibodies. These would be mainly, but not exclusively, directed towards the gp53. Because of difficulties in international exchange of viruses, it was agreed that the general approach would be for each collaborating laboratory to test their own strains, and for those with suitable monoclonals to make them available (as hybridoma supernatants) to the other partners. A standardised immunoperoxidase-based test procedure will be recommended, to minimise variations due to fixation or other technical variables. Some virus exchanges could be arranged on a individual basis.
2. The establishment of a panel of polyclonal ruminant sera, available in reasonable large quantities, which would provide useful discrimination between viruses in neutralisation tests. Preliminary screening of candidate sera would be carried out at the Bovine Pathology Lab in Lyon. Sera would then be shared among the participants for testing against their own strains. If a full range of suitable sera cannot be assembled from existing stocks, some of the participating laboratories should raise new sera. For practical reasons, sera would normally be collected approximately one month after intranasal inoculation of a virus strains into a calf or sheep, although it was noted that neutralising responses of animals tend to narrow to greater strains specificity if sera are harvested later. Again a standardised neutralisation test procedure should be adopted.
3. A further approach would be to compare nucleotide sequences, particularly in the 5′ non-coding region of the viral genome. This phase of the study would probably follow on after the main antigenic studies were complete. It could be useful to look at sequence data for strains selected as divergent or similar on the basis of the antigen characterisation in 1. and 2.

It is proposed that the data from 1. and 2. above are collated by Dr. Steven Edwards. He will also endeavour to co-ordinate the exchanges of materials. A next meeting on pestivirus diversity will be announced in this column. Interested workers in this field are asked to contact Dr. Steven Edwards, Central Veterinary Laboratory, Virology Department, New Haw, Woodham Lane, Addlestone, Surrey KT15 3NB, U.K.

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