

Distribution and Dynamics of Quasispecies Related
with Bovine Viral Diarrhea Virus Infection

Abstract of Doctoral Thesis

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Bovine viral diarrhoea virus (BVDV) can be classified into cytopathogenic (CP) and noncytopathogenic (NCP) biotypes based on morphological changes in virus-infected cultured cells. NCP BVDV can be further classified as either the exaltation of Newcastle disease virus phenomenon positive (END⁺), which suppresses antiviral activity in cultured cells, or negative (END⁻), which induces antiviral activity. These biologically distinct viruses may be present as quasispecies within the same isolate, suggesting that the distribution of these viruses might influence the clinical condition of an infected host. However, whether a causal link exists between quasispecies distribution and clinical condition is unclear because the distribution and dynamics of field strains and strains from infected animals have not been researched. This study examined the distribution of END⁺ and END⁻ viruses in field isolates and their presence and dynamics in persistently infected (PI) cattle.

Because the geographical regions examined in the previous study were limited to Hokkaido Prefecture, in the present study, 39 BVDV field strains were isolated from another prefecture to determine whether END⁺ and END⁻ viruses coexist in the field. END⁻ virus predominated in 32 of the field isolates (82%) from other prefectures, in contrast with Hokkaido Prefecture, in which END⁺ virus predominated in 52% of field isolates. These results suggest that the distribution of quasispecies varies geographically. To rule out the possibility that virus passage during isolation may influence the distribution of quasi-species in field isolates, the supernatants of four field isolates of known passage number were analyzed. The results demonstrated that several passages do not significantly influence virus composition, supporting data indicating that END⁺ and END⁻ viruses are widely distributed in the field.

Next, direct detection of END⁺ and END⁻ viruses in PI cattle was attempted. END⁺ and END⁻ viruses were detected in varying proportions in

the blood of 26 PI cows. Then, blood samples were regularly collected from three breeding PI animals and the sera were tested. The results showed that the virus composition changes during persistent infection and that END⁻ virus eventually predominate in long-surviving PI cows.

This study revealed that END⁺ and END⁻ viruses are widely distributed and coexist in the field isolates. These viruses are also harbored by PI animals, and their proportions change over time. These data suggest that a relationship exists between the duration of persistent infection and the content of END⁻ virus. From these results, it can be inferred that the co-existence of BVDV quasispecies and changes in their proportions during persistent infection affect the clinical condition during BVDV infection, such as the onset of fatal mucosal disease (MD). A more thorough understanding of the distribution of quasispecies in persistent infection and MD may clarify the mechanism of disease status on BVDV infection.