acids 1 to 84, and the region between amino acids 114 to 243 containing acidic amino acid sequences were required for the transactivation. Among the mutants constructed, interestingly, the mutant consisting amino acids 1 to 113 (dlC113) possessed a dominant-negative property. This mutant could inhibit transcription and a cell line stably transformed with this mutant gene showed resistance to PRV infection.

To analyse the reguratory mechanisms of EP0 gene expression, various fragment-chloramphenicol acetyltransferase constructs containing a series of deletions within the upstream region of the EP0 gene were constructed. It was shown that the EP0 gene was transcribed from the region between −170 and +43 relative to the transcription start site of the EP0 gene reported previously, although 5' end of EP0 mRNA was not identified. This region lacked a TATA element and contained an Inr element, the putative binding site for IE protein of PRV (IE180), and three consensus Sp1 binding sites as *cis*-reguratory elements. It was demonstrated that the EP0 gene might be transcribed from the TATA-less promoter, and that transcription from this promoter was activated by IE180. Analysis of deletion mutants of the promoter revealed that Sp1 binding sites were critical for the basal and IE180-mediated transcription.

Results obtained in this study suggest a possible mechanism for the enhancement of PRV replication by EP0 and that a dominant-negative mutant of EP0 may be applicable for the antiviral therapy. The mechanism could be explained as follows; EP0 in the virion is released in the infected cells, and transactivates the IE gene, resulting in enhancement of initiation of PRV infection. After this, IE180 expressed from the IE gene transactivate the early and late genes, leading efficient replication of PRV. The mechanism by which the mutant dlC113 inhibited the viral gene transcription and replication remains unknown, however, these findings are notable from standpoint of an antiviral therapy. If expression of this mutant gene can be controled, it will be very useful for the therapy.

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Antibacterial Activity of Plaunotol, a Cytoprotective Antiulcer Agent, against *Helicobacter pylori*

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Recently, some antiulcer agents have been reported to have antibacterial activity against *Helicobacter pylori*, which is highly associated with gastritis and peptic ulcers. *In vitro* activity of plaunotol, a cytoprotective antiulcer agent, against *H. pylori* was investigated. Plaunotol showed the most potent antibacterial activity against *H. pylori* among the cytoprotective antiulcer agents. Moreover, plaunotol had a strong bactericidal effect against this organism. This bactericidal effect resulted in a rapid reduction of culture turbidity, with an extensive loss of viability. In addition, cell lysis also occurred in gram-positive and some gram-negative bacteria.

The mode of the bactericidal action of plaunotol was investigated using its derivatives. The bactericidal activities of plaunotol and its derivatives were related to the hydrophobicity of these compounds. The effects of plaunotol and its derivatives on liposomal membranes prepared from phosphatidylethanolamine and cardiolipin were also related to their bactericidal activities. Plaunotol led to an increase in permeability of the membrane, as evidenced by measurement of the leakage of 260 nm-absorbing material from *H. pylori*. The molecular motion of the spin label was measured from the electron spin resonance spectrum, by determining the order parameter S, an index of membrane fluidity. Plaunotol increased fluidity in *H. pylori* membrane. These results suggested that the mechanism of the bactericidal effect of plaunotol against *H. pylori* may be the membrane fluidity alteration, with associated increased membrane permeability.

The therapeutic efficacy of plaunotol was evaluated in a nude mouse gastritis model. Plaunotol significantly decreased the number of *H. pylori* in the stomach of nude mice. In addition, this compound enhanced the therapeutic activity of amoxycillin or clarithromycin in the infection model. Thus, the activity of plaunotol against *H. pylori is* expected to provide some clinical benefits to treatment with this antiulcer drug for gastroduodenal disease.

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Host defense mechanisms and pathogenesis of *Babesia* infection, and analysis of piroplasm surface antigen.

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Babesia is a tick-borne intra-erythrocytic protozoa which causes a disease in mammals generally called piroplasmosis. The disease is characterized by fever, anemia, icterus, hepato- and splenomegaly.

The present study was designed to investigate, 1) the immune response in mice experimentally inoculated with *Babesia microti*, 2) the pathogenesis and immune response in horses experimentally inoculated with *B. caballi*, and 3) the identification of the B cell epitope of a 30 kDa *B. equi* merozoite surface antigen to develop sensitive and reliable serodiagnostic method. The results obtained in this study are summarized as follows.

1. $CD4^+$ T cells and interferon-gamma (IFN-γ) were observed to be involved in protection against infection with *B. microti*. Specific $CD4^+$ T cells were generated *in vitro* from BALB/c mice recovered from infection and their protective activity was tested *in vivo*. The cells produced varying amounts of IFN-γ *in vitro* in response to parasite antigens. In passive transfer experiments, three out of eleven T cell clones tested exerted protective activity in the early phase of infection. Although the protection was partial and short-lived, the results provided direct evidence that $CD4^+$ T cells play crucial role in