

**Significance of sequence variation in the P1 and 3A
genes of foot-and-mouth-disease virus isolates from
southern Africa.**

By

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degree M.Sc (Agric) Microbiology.

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I declare that the dissertation, which I hereby submit for the degree M.Sc (Agric) Microbiology at the University of Pretoria, is my own work and has not previously been submitted by me for a degree at another university."

Heath.
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11/06/2001
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LIST OF CONFERENCES AND SYMPOSIUMS AT WHICH THE WORK WAS PRESENTED.

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Abstract

- Title:** Significance of sequence variation in the P1 and 3A genes of foot-and-mouth disease virus isolates from southern Africa.
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Foot-and-mouth disease (FMD) virus is a highly contagious pathogen responsible for one of the most economically devastating diseases in cloven-hoofed animals. The disease threatens the economies of southern African countries that are dependent on agricultural export of animal origin. The majority of outbreaks in southern Africa are caused by the 3 SAT serotypes. The geographical distribution of these serotypes is largely restricted to sub-Saharan Africa with SAT 1 and 2 accounting for more than 80% of the outbreaks in domestic livestock. Due to this, research on the third of the SAT types has been somewhat neglected. The lack of genetic information with regards to the structural-protein coding region of the SAT type 3 viruses limits the determination of the level of correlation between the genetic characteristics of prevalent isolates and strains currently being used in vaccine production. In order to broaden the understanding of the genetic characteristics of the SAT 3 serotype, the structural-protein-coding region of the FMDV KNP/10/90/3 isolate was determined and compared to representative isolates of six FMDV serotypes. Nucleotide and amino acid sequence analyses showed the genetic makeup and protein organisation of KNP/10/90/3 to be typical of FMDV. As would be expected the isolate shared a high level of sequence homology with Bec/1/65/3 and was more closely related to the other SAT serotypes than to European FMD viruses. Data indicate that intratypic variation for the P1 region of the SAT type viruses is significantly higher compared to that of serotypes A, O and C.

In addition to the four structural proteins (P1 precursor), the FMD genome encodes multiple mature polypeptides and intermediate cleavage products. The mature polypeptides include the 3A protein. This 153 amino acid protein, as well as its precursor (3AB), has been shown to be involved in viral RNA replication and death of infected cells. Changes in 3A have been associated with altered host range in the hepatoviruses, rhinoviruses, and enteroviruses. Recently a direct correlation was shown to exist between a 10 amino acid deletion within the 3A protein FMDV and attenuation of the virus in cattle. Although the 3A coding region has been shown to be highly conserved among several European FMD virus isolates, nothing is known about the sequence characteristics of the 3A of the SAT type viruses. In light of this, the nucleotide sequences of the 3A non-structural-coding sequence of several African FMD virus isolates were determined and comparatively analysed. We compared this region of the genome among different SAT serotypes and with that of European, South American and Asian isolates in order to assess the extent of genetic variation within the 3A coding region of naturally occurring viruses in sub-Saharan Africa. Our results indicated that the 3A region of the SAT isolates differed markedly from that of the European isolates but were closely related within the serogroup. The percentage site conserved in all isolates examined was calculated to be 47.4% at nucleotide sequence level and 50.3% at amino acid level. The different SAT serotypes were indistinguishable within the phylogenetic arrangement.