## A New Influenza B Live Vaccine Generated by Modification of the Haemagglutinin Cleavage Site

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Both influenza A and B viruses give rise to yearly epidemics in humans accompanied with high mortality and morbidity. As an alternative approach for an influenza A live vaccine, we generated previously by reverse genetics elastase-dependent haemagglutinin cleavage site mutants of the laboratory strain A/WSN/33 (H1N1) and of a highly-pathogenic mouse-adapted influenza A strain (H7N7) which were highly attenuated and immunogenic in mice. In the present study, we applied this approach to obtain an influenza B live vaccine. Therefore, we replaced the arginine at the haemagglutinin cleavage site of the strain B/Lee/40 with alanine resulting in an elastase motif. This mutant was strictly elastase-dependent and replicated in cell culture to the same titer as the wild-type. In contrast to the wild-type which is pathogenic for mice, the cleavage site mutant was fully attenuated and not detectable in the lung. After one intranasal immunization, the mice survived the lethal challenge with wild-type virus without weight loss or other signs of disease; no challenge virus could be detected in mouse lungs. These observations demonstrate that a mutated haemagglutinin dependent on elastase cleavage can serve as an attenuating component of a live vaccine against influenza A or B viruses.

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