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Targeting *Burkholderia pseudomallei* Immunogenic Proteins as Potential Prophylactic Agents Against Melioidosis

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Burkholderia pseudomallei is the etiological agent of melioidosis, a severe invasive disease of humans and animals in subtropical areas and northern Australia. There is an urgent need to develop effective therapeutic molecules against the pathogen for better management of melioidosis. We undertook to survey for all potential *B. pseudomallei* immunogenic proteins in order to dissect the bacterial pathogenesis and evaluate vaccine candidates. In the present study, a *B. pseudomallei clinical isolate* (D286) genomic expression library was constructed and 109 seroreactive clones were identified from the library screened with pooled melioidosis patients' sera. DNA sequence analysis of the seropositive clones revealed 109 putative immunogenic proteins that were annotated and delineated into functional classes of cell envelope components, protein secretion and cell motility, transcription, amino acid transport and metabolism, inorganic ion transport and metabolism, energy production, protein metabolism, nucleic acid metabolism and repair, unknown function hypothetical proteins, and other metabolism and transporter proteins. The complete open reading frame of an immunogenic putative outer membrane protein (Oma) was cloned, expressed and shown to maintain immuno-reactivity with patient sera. Up to 80% of BALB/c mice immunized with recombinant Oma were protected from infectious challenge with 10xLD50 of *B. pseudomallei* D286, compared with non-immunized mouse. Therefore, the utility of Oma as a potential prophylactic agent for melioidosis is proposed. Mouse anti-Oma polyclonal serum confirmed the presence of wild type Oma in *B. pseudomallei* lysate. In addition, protein sequence analysis revealed that Oma is a member of the Omp85 family and is highly conserved among species within the *Burkholderia* genus, suggesting its suitability as a universal vaccine candidate or diagnostic epitope for *Burkholderia* spp. Characterization of the *B. pseudomallei* immunome has shed new light on unraveling the bacterium's pathogenic mechanism and disease severity. These immunogens can be further evaluated as vaccine and serodiagnostic candidates as well as drug targets.

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Derived from Human Alimentary Tract

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Background: It is known that the attenuated polio vaccine viruses derived from oral poliovirus vaccine undergo neurovirulent reversion during repeated replication in the human alimentary tract, and some paralytic cases caused by the revertants have been reported. Furthermore, the revertants are excreted with the feces into the environment, and the viruses have caused new epidemics of poliomyelitis in the world. It is an obstacle for the achievement of polio eradication program.

Objective: In this study, to elucidate the reversion mechanism of polio vaccine virus to the neurovirulent genotype in the human alimentary tract, an accumulation of the reversion of the vaccine viruses passaged in cultivation cells which were derived from the human alimentary tract was analyzed.

Methods: Polio vaccine viruses were passaged three times in Caco-2 cells derived from human colon carcinoma. The reversion of the passaged viruses was analyzed by the ''mutant analysis by PCR and restriction enzyme cleavage (MAPREC)'' method designated to estimate the ratio of revertants in a virus population.

Results: The accumulation of reversion in the vaccine viruses increased rapidly with viruses passaged at a temperature of 37°C compared with those at 34°C. However, it was hardly observed in viruses passaged in HEp-2 cells which were derived from human laryngeal carcinoma at a temperature of 37°C.

Conclusion: A large difference was observed in the frequency of reversion between Caco-2 and HEp-2 cells though both cells were derived from human carcinoma. It is important to elucidate the cellular factors which take part in the reversion frequency of the virus genome. Such research is expected to lead to the elucidation of the reversion mechanism and to the development of a controlling expedient for the neurovirulent reversion of the polio vaccine virus.

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Adaptation of Influenza H5N1 Vaccine Viruses in Vero Cells

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Current egg-based influenza vaccine production technology is labor-intensive and lack of flexibility and its capacity would not be able to meet the demand during influenza pandemics. Therefore, vaccine production using mammalian cell technology is becoming viable and attractive. The current influenza H5N1 vaccine strain (NIBRG-14) could grow efficiently in chicken embroyonated eggs and MDCK cells