Pengambangan vaksin DNA tetravalen dengue berbasis gen PrM-E DENV isolat Indonesia : Uji imunogenesitas vaksin dalam menginduksi antibodi netralisasi dan respon anamnestik untuk semua serotipe DENV = Tetravalent DNA vaccine development based on prM-E gene DENV Indonesia strain : Immunogenecity of the candidate DNA vaccine to induce neutralization antibody and anamnestic immune response in mice

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Abstrak

[ABSTRAK
Pendahuluan: Infeksi dengue merupakan salah satu penyakit endemik di daerah tropis dan subtropis yang disebabkan oleh virus dengue (DENV). Hingga saat ini belum ada antiviral yang efektif untuk infeksi dengue. Penyebaran dan sirkulasi serotipe DENV berfariasi di setiap lokasi geografi, hal ini menyulitkan dalam melakukan evaluasi vaksin DENV. Oleh karena itu perlu dikembangkan kandidat vaksin DENV menggunakan strain Indonesia supaya dapat memberikan proteksi maksimal. Pada peneltian ini dikembangkan kandidat vaksin DNA tetravalen DENV berbasis gen prM-E DENV strain Indonesia.
Metode: Konstruksi plasmid rekombinan kandidat vaksi dilakukan dengan cara menyisipkan gen prM-E setiap serotipe DENV ke dalam vektor pUMVC4a. Gen prM-E DENV merupakan strain Indonesia, yang diamplifikasi dari serum pasien yang terinfeksi dengan virus ini. Kemampuan plasmid rekombinan mengekspresikan protein prM-E DENV diuji di sel mamalia. Kemampuan kandidat vaksin menginduksi respon imun humoral dievaluasi secara monovalen dan tetravalen di mencit jenis ddY. Titer IgG anti dengue diperiksa menggunakan teknik ELISA, sedangkan titer antibodi netralisasi di tentukan dengan uji FRNT. Proteksi vaksin terhadap mencit yang diimunisasi dievaluasi dengan melakukan uji tantang menggunakan sel K562 yang diinfeksi DENV-2. Viremi virus di tentukan dengan menggunakan teknik foccus assay.
Hasil: Konstruksi plasmid rekombinan kandidat vaksin DENV-1 dan DENV-3 sudah berhasil dilakukan. Plasmid dapat mengekspresikan protein prM-E DENV di sel mamalia, namun karakteristik dan kinetik protein masih belum dapat diketahui dengan jelas. Keempat kandidat vaksin DNA yang sedang dikembangkan dapat menginduksi respon imun, baik secara monovalen maupun tetravalen. Imunisasi secara tetravalen dapat memberikan proteksi pada mencit yang diuji tantang dengan sel K562 yang diinfeksi dengan DENV-2.;
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ABSTRACT
Introduction: Dengue infections are caused by dengue viruses (DENV) and are endemic in tropical and subtropical regions. At present, there is no effective antiviral treatment for dengue infection. Distribution and circulation of DENV serotypes varies by geographic location, it is difficult to evaluate DENV vaccine. Therefore, it is necessary to develop a vaccine candidate DENV using Indonesian strains in order to provide maximum protection. However, in this study, we constructed a recombinant plasmid-based prM-E gene from the Indonesia strain as a DENV DNA vaccine candidate.
Methode: The recombinant plasmid was prepared by inserting the prM-E gene from each DENV serotypes

into the plasmid backbone pUMVC4a. prM-E gene an Indonesia strain, which was amplified from patient sera infected with DENV. The ability of the recombinant plasmid expressing the prM-E DENV protein tested in mammalian cells. The ability of candidate vaccines induce humoral immune responses were evaluated monovalent and tetravalent in ddY mice. IgG titers of anti-dengue examined using ELISA technique, while neutralizing antibody titers determined with FRNT test. Vaccine protection against the immunized mice was evaluated by conducting challenge test using K562 cells infected by DENV-2. Viremia was determined by using the foccus assay.
Result: Construction of recombinant plasmid vaccine candidate DENV-1 and DENV-3 was successfully performed. Plasmids can express prM-E DENV proteins in mammalian cells, but the characteristics and kinetics of protein still can not clearly known. Fourth DNA vaccine candidate that is being developed to induce an immune response, either monovalent or tetravalent. Tetravalent immunization may provide protection in mice challenged tested with K562 cells infected with DENV-2.;Introduction: Dengue infections are caused by dengue viruses (DENV) and are endemic in tropical and subtropical regions. At present, there is no effective antiviral treatment for dengue infection. Distribution and circulation of DENV serotypes varies by geographic location, it is difficult to evaluate DENV vaccine. Therefore, it is necessary to develop a vaccine candidate DENV using Indonesian strains in order to provide maximum protection. However, in this study, we constructed a recombinant plasmid-based prM-E gene from the Indonesia strain as a DENV DNA vaccine candidate.
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