DESAIN *IN SILICO* KANDIDAT VAKSIN MULTI-EPITOP UNTUK HUMAN METAPNEUMOVIRUS (HMPV) BERBASIS ALEL HLA INDONESIA

SKRIPSI

Diajukan untuk memenuhi salah satu syarat memperoleh Gelar Sarjana Sains
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HALAMAN PENGESAHAN

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ABSTRAK

Human Metapneumovirus (HMPV) merupakan salah satu patogen penyebab infeksi saluran pernapasan akut (ISPA) yang kerap berko-infeksi dengan patogen berbahaya seperti SARS CoV-2 dan *Streptococcus pneumoniae*. Namun, saat ini belum vaksin HMPV yang telah lulus uji klinis. Oleh karena itu, penelitian ini mengembangkan model vaksin HMPV berbasis multi-epitop secara *in silico* sebagai pendekatan awal yang efisien dari segi waktu, biaya, dan sumber daya. Desain multi-epitop dipilih karena dapat memicu respons imun adaptif yang luas dan spesifik. Tahapan penelitian yang dilakukan meliputi: prediksi epitop sel T berdasarkan protein target HMPV yang diseleksi berdasarkan karakteristik imunogenik, non toksik, dan non-alergenik, perancangan vaksin multi-epitop dengan *linker* dan adjuvan, analisis interaksi dengan reseptor imun (TLR-2 dan TLR-4), serta evaluasi stabilitas, antigenisitas, dan cakupan populasi berdasarkan HLA dominan Indonesia. Vaksin dirancang spesifik untuk populasi Indonesia sehingga epitop yang dipilih bersifat imunogenik, non-toksik, dan non-alergenik, serta mencakup populasi Indonesia dengan afinitas ikatan tinggi terhadap HLA dominan. Kandidat vaksin bersifat stabil, imunogenik, dan berinteraksi kuat terhadap TLR-2 dan TLR-4 yang secara teoritis dapat mengaktivasi sistem imun melalui produksi antibodi, sel B memori, sel T, makrofag, dan sitokin. Vaksin multi-epitop yang dikonstruksi berhasil dioptimasi untuk diekspresikan pada sistem inang *Escherichia coli* dengan vektor pET-30a(+). Adaptasi kodon meningkatkan *Codon Adaptation Index* (CAI) dan menurunkan kandungan GC kedua vaksin, yang menunjukkan potensi tinggi untuk ekspresi protein rekombinan pada galur *E. coli* K12. Meskipun masih berada pada tahap in silico, hasil yang diperoleh menunjukkan potensi untuk dikembangkan secara eksperimental sebagai langkah awal menuju formulasi vaksin yang lebih efektif.

Kata kunci: Desain kloning, Human Leukocyte Antigen (HLA)-Indonesia, Human Metapneumovirus (HMPV), *reverse vaccinology*, simulasi imun, vaksin multi-epitop

ABSTRACT

Human Metapneumovirus (HMPV) is one of the leading causes of Acute Respiratory Tract Infection (ARTI) that usually co-infect with SARS-CoV-2 and Streptococcus pneumoniae. However, currently there is no HMPV Vaccine that passed the clinical test. In consequence, this study aims to develop multi-epitop vaccine model with in silico approach as an efficient effort in terms of time, cost, and resource. Multi-epitope vaccine design is chosen for its ability to induce broad and specific adaptive immune responses. This study involve: prediction of T cell epitope based on the target protein of HMPV that is selected based on its immunogenicity, non-toxicity, and non-allergenicity, constructing multi-epitope vaccine with linker and adjuvant, analysis of interaction between vaccine and immune receptors (TLR-2 and TLR-4), and evaluation of vaccine stability, antigenicity, and population coverage based on dominant HLA in Indonesia. The vaccine is designed specifically for the Indonesian therefore the chosen epitopes are immunogenic, non-toxic, non-allergenic, and cover Indonesian population with high binding affinity towards dominant HLA. The vaccine candidate is predicted to be stable, immunogenic, and has high affinity towards TLR-2 and TLR-4 that theoretically can activate the immune system through the production of antibody, B cell memory, T cell memory, macrophage, and cytokine. Furthermore, the multi-epitope vaccine constructs were successfully optimized for expression in Escherichia coli host cells using the pET-30a(+) vector. Codon optimization increased the Codon Adaptation Index (CAI) and decreased GC content of both vaccine, indicating high potential for recombinant protein expression in E. coli K12. Despite being developed by in silico approach, this vaccine shows a potential to be further developed experimentally as a starting point towards a more effective vaccine formulation.

Keywords: Cloning design, immune simulation, Human Leukocyte Antigen (HLA)-Indonesia, Human Metapneumovirus (HMPV), multi-epitope vaccine, reverse vaccinology

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AFND	:	The Allele Frequency Net Database
ANN	:	*Artificial Neural Network*
APC	:	*Antigen Presenting Cell*
BA	:	*Binding Affinity*
BD-3	:	*Beta Defensin 3*
BLAST	:	Basic Local Aligment Sequence Tool
CAI	:	*Codon Adaptation Index*
CDC	:	Center for Disease Control and Prevention
CDR	:	*Complementary Determining Region*
CTL	:	*Cytotoxic T Lymphocytes*
DNA	:	*Deoxyribonucleic Acid*
EL	:	*Eluted Ligand*
GHE	:	Global Health Estimates
GRAVY	:	*Grand Hydropathicity Index*
HLA	:	*Human Leukocyte Antigen*
HMPV	:	Human Metapneumovirus
HPV	:	Human Papillomavirus
HTL	:	*Helper T Lymphocytes*
IB	:	*Inclusion Bodies*
ICU	:	*Intensive Care Unit*
IEDB	:	Immune Epitope Database & Tools
IFN-γ	:	*Interferon Gamma*
IgG	:	Imunoglobulin G
IgM	:	Imunoglobulin M
IHME	:	Institute foe Health Metrics and Evaluation
IHWs	:	International HLA and Immunogenetics Workshops
IL-2	:	Interleukin 2
IL-4	:	Interleukin 4
IPTG	:	β-*D-1-thiogalactopyranoside*

ISPA	:	Infeksi Saluran Pernapasan Akut
LPS	:	Lipopolisakarida
MHC	:	*Major Histocompatibility Complex*
NCBI	:	National Center for Biotechnology Information
PAMP	:	*Pathogen-Associated Molecular Pattern*
PCR	:	*Polymerase Chain Reaction*
pI	:	*Isoelectric Point*
PI	:	*Protrusion Index*
PRR	:	*Pattern Recognition Receptors*
RBS	:	*Ribosome Binding Site*
RE	:	Retikulum Endoplasma
RNA	:	*Ribonucleic Acid*
RSV	:	Respiratory Syncytial Virus
RT-PCRS	:	*Real Time Polymerase Chain Reaction*
SVM	:	*Support Vector Machine*
Th1	:	*T Helper 1*
Th2	:	*T Helper 2*
TLR	:	*Toll Like Receptor*
WHO	:	*World Health Organization*

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