I. Introduction

The SARS-CoV-2 worlwide pandemic is still ongoing with the confirmed case of 240 million patients by the end of 2021. The virus is responsible for driving a medical condition SARS with a fever, anosmia, hyposmia, difficulty in breathing, throat infection, and severe chest pain. While SARS-CoV-2 infection is considered to have a low mortality rate of only 2 to 4 %, however the issue that caused the outbreak to occur is that the viral agent responsible for the disease has a very high transmission rate (Challen et al., 2021). The virus spread mainly through contact with infected people and respiratory droplets/aerosols containing the virus and through the formation of fomites on objects in contact with the virus (WHO, 2020). The consideration that SARS-CoV-2 has high virulence properties and its transmission method allow the virus to have effortless transmission, especially in an area with a crowded population due to the availability of vectors and hosts.

Until May 2022, a considerable period has passed since the first outbreak of the virus in December 2019. However, there is still no clarity as to how long the pandemic will persist nor how it will end. In most cases of infected individuals, while recovery without treatments is possible, the mortality within the disease is often related to pre-existing medical conditions which worsen due to the side effect of the infection. Furthermore, the unavailability of therapeutic agents practical for SARS-CoV-2 infection worsens the situation. Multiple drug repurposing studies had been done to find possible therapeutic agents for SARS-CoV-2, yet most of the findings only worked for tentative treatment and could not eliminate the infection of SARS-CoV-2 (Bolarin et al., 2021).

Vaccination is essentially one of the most significant actions against pathogen infection, which also works against virus. The information is valuable especially under the current situation of the global SARS-CoV-2 pandemic. The concept of vaccination against viral infection refers to introducing a component of the virus whether it is synthesized or isolated from the virus itself that will activate the immune system in order to form immunity period within patient for that particular virus. The components capable of activating the immune responses called the epitopes will be received by either T cell or B cell to allow humoral immune response or cellular immune response (Welsh and Fujinami, 2007). However, a vaccine has a limitation coming from the design and viral components the vaccine is based on; that is, the vaccine will only work efficiently if the virus maintains the same variant and type the vaccine is based on. In addition, a slight mutation in the viral genome and protein may significantly alter the vaccine's effectiveness (Callaway, 2021).

The virus of interest was found to be originating from the coronaviridae family and is expected to have similarities with the SARS-CoV-1, responsible for a similar pandemic in 2003. The comparison of both viruses revealed a significant level of genetic similarity, reaching up to 83%, which was also represented in a similar phenotype comparison (Kaur et al., 2021). Furthermore, as both viruses originated from the same family, they maintain the same structure with the presence of Spike protein (S) forming a crown-like structure on the cell surface, Nucleocapsid (N) capsule that interacts with the RNA genome, Envelope (E) forming a structure that enveloped the virus, and Membrane (M) Proteins. However, as many as 380 amino acid substitutions were able to be identified within the comparison of the novel and late coronaviridae virus.

Multiple studies had successfully identified the main difference between the novel virus with the previous generation of coronavirus consisting of their RBD, and cleavage sites. Both of the said differences are located on the spike protein which is responsible to make a contact with the ACE2 receptor, thus becoming the first component of the virus that will make direct contact with outside stimuli or target cells and mediate the entry of the virus. Therefore, any slight change within its genome may affect the translation process, possibly resulting in different peptide chain formations leading to different amino acid sequences. The difference in the encoded peptide chain will lead to the formation of different protein structures that will compromise the spike protein's ability to bind and enter the corresponding cells it interacts with. Moreover, it has been identified that the changes occur as a random mutation due to deletions or insertion in the S region (Walls, 2020; Zhou et al., 2020). The compromised binding capability of the S protein leads to the possibility of changes in infectivity, affecting antibodies, binding affinity, and strength, and even changes/addition in target hosts for infection (Andersen et al., 2020). Moreover, multiple mutations concerning the SARS-CoV-2 virus had occurred, creating multiple subtypes of the virus throughout the pandemic. Comparative studies from the newly emerging variants were able to identify alarming differences whereas several new variants were found to be able to avoid the humoral immune response (Syed et al., 2022). With the decrease of humoral immune response effectivity against recent SARS-CoV-2 variants, the other pathway of adaptive immunity becomes an essential consideration to control the spread of the infection.

A type of vaccine that makes a suitable candidate with the capability to evoke both immune system mechanisms is the multi-epitope vaccine. The epitopes identified from the virus genome become the essential building block of the multiepitope vaccine in which interaction with their respective receptors for either T or B cell epitopes will trigger the activation of multiple immune responses at once which will increase the chances of viral elimination from the patient (Naz et al.,

2020). While multiple vaccines of said type had been studied and are in wait for clinical trials, however, vaccine designs based on Indonesian isolates are still considered rare.

In the first semester of 2022, the trend of COVID-19 cases in Indonesia was recorded to be increasing significantly in February affected by the peak wave of the new variant Omicron spread and gradually decreasing until May (Mediatama, 2022; Ritchie et al., 2022). While the current situation has improved significantly in Indonesia, the risk of further mutation and the outbreak of possible new variants persists. In such a situation, a vaccine design that is designated for the Indonesian population based on the isolates of local variants will provide benefits as a preemptive action against the virus.

The goal of the project was to make a vaccine design that can be used against SARS-CoV-2 within regional limitation in Indonesia. The design utilizes the consensus sequence retrieved from the isolates followed by epitope prediction in which the potential epitopes were further tested for their immunogenicity, allergenicity, their safety characteristics, and homology with human proteomes. The remaining candidates were then used as the building blocks for the vaccine design.