Chapter 1

Introduction

1.1. Background

Allergy or allergic disease is an abnormal reaction (over-reactivity) of the immune system to otherwise harmless substances that may come from the environment, food, medication, and insect bites; these antigenic substances are commonly known as allergens. The prevalence of allergies, including their severity and complexity, is increasing worldwide (Pawankar, 2014). Most allergic reactions are mediated by an antibody called immunoglobulin type E (IgE), produced when the body is exposed to an allergen. The production of IgE is mediated by type 2 helper T-lymphocytes (Th2) cells (Dimitrov, Flower & Doytchinova, 2013). The first exposure to an allergen is usually asymptomatic. However, upon further exposure, the allergen will bring together two IgE receptors present on the surface of mast cells or basophils, triggering a signaling cascade that will induce the production of inflammatory chemicals such as histamine, leukotrienes, and prostaglandins, causing allergic reactions (Renz et al., 2018).

Food allergy is one of the major types of allergic reactions that should be considered a threat to the health of susceptible individuals. Over the years, food allergy prevalence has increased (Savage & Johns, 2015). As an example, the consumption of seafood allergy has been increasing in the last 40 years worldwide (Turner et al., 2011), followed by an increase in the incidence of the allergy at the same time. According to Savage & Johns (2015), about 4% of the population in the United States is reported to have food allergies, with peanut, milk, and shellfish being the most common causative agents, while in Asian countries are accounted for two-thirds of global seafood consumption has a higher prevalence in seafood allergy where it can reach 7.7% of cases in some countries, including Indonesia. According to Garna et al. (2017), a skin prick test experiment on 63 people revealed that 47.71% of the group had shellfish allergies.

Shellfish sensitization can be caused by a protein allergen called tropomyosin, which is classified as a major allergen in various shellfish species (Faber et al., 2017). Tropomyosin was first discovered in brown shrimp, called Pen a 1 (*Penaeus aztecus*) by Hoffman et al. (1981), and it was found to be a heat-stable IgE-binding allergen. Tropomyosin is a heat-resistant allergen that can withstand high temperatures, food processing techniques such as ultrasound and gamma irradiation, and gastric digestion (Leung et al., 2012). Besides shellfish, this allergenic protein is also present in crustaceans, mollusks, abalones, and even in insects such as mites and cockroaches. Humans also possess tropomyosin in their muscle and nonmuscle cells, but they only have 55% sequence homology with the tropomyosin from invertebrates (Faber et al., 2017). IgE-binding B-cell and probable T-cell epitopes have been identified in tropomyosin, especially in shellfish allergy (Faber et al., 2017).

Different therapeutic modalities are available to treat allergies, and still, there are new ones currently under development. One is the epitope-based allergy vaccine, which can be designed using an immunoinformatics approach. This strategy not only saves development time and costs but can also improve the treatment's specificity and efficacy (Parvizpour, Pourseif, Razmara, Rafi & Omidi, 2020). Thus, designing epitope-based allergy vaccines to target tropomyosin Pen a 1 is a rational strategy to develop a treatment modality that can provide immune system tolerance to this important allergen as well as observing the mechanism of inducing Th2 switch into Th1, resulting in generation of IgG instead of IgE by a mechanism called antibody class switching (Aalberse, 2011), a process where B cells change the class of the antibody they produce by recombination of the immunoglobulin (Ig) genes that lead to activation of different constant region genes of the antibody.

1.2. Objective

This study aims to design a multi-epitope vaccine from T cell and B cell epitopes using an immunoinformatics approach from Pen a 1 allergen derived from *Penaeus aztecus* as the representative of shellfish that are presented by HLA Class I and HLA Class II in the Indonesian population.

1.3. Hypothesis

The analysis of T-cell and B-cell epitopes derived from tropomyosin Pen a 1 allergen in the Indonesian population will reveal specific HLA allele-associated antigenic regions, providing valuable insights into the immunogenicity and potential sensitization patterns of tropomyosin Pen a 1 allergen in this population.