I. INTRODUCTION

1.1 Background

Neutrophils are a type of white blood cells (leukocytes) that can act as the first line of innate immune defense to protect and rapidly kill the invading pathogens from the human body. The primary role of neutrophils is to phagocytize which engulf and kill invading pathogens as well as being effective against extracellular pathogens (Mortaz et al., 2018). Neutrophils also have an important role in the modulation of the immune system in response to inflammation. As a component of the innate immune system, neutrophils are able to rapidly respond to the infections by preventing the spread of infections until the adaptive immune response involves particular specific immune cells and antibodies to kill the invading pathogens (Malech et al., 2014).

Moreover, the activation of neutrophils contribute significantly to enhance the immune system's response to against microbial infections by several mechanisms including, reactive oxygen species (ROS) production, phagocytosis, degranulation, chemotaxis, releasing granules, and neutrophil extracellular traps (NETs) formation (Mayadas et al., 2014). Thus, the activation of neutrophils is important for host defense against microbial infections and various inflammatory diseases (Németh et al., 2020). Additionally, activated neutrophils can adapt to a variety of signals by creating a number of cytokines and other inflammatory substances that regulate and influence inflammation as well as the immune system (Fang et al., 2015).

DA-22 is a pseudonym of the real drug name due to its confidentiality and the most common drug for atypical glandular cells (AGC) kinase inhibitors, which potentially inhibits Rho kinase (ROCK) and anti-protein kinase B (AKT). AKT and other AGC kinases are dysregulated in cancer cells due to high activation of receptor tyrosine kinase (RTKs), genetic modification of several key kinases, increase the growth and progression of cancer (Hirai et al., 2010). Furthermore, the importance of this project is to further investigate the ability of DA-22 towards human neutrophil activation and immune response enhancement of the rapid innate immune system in order to represent a crucial area of science and pharmaceutical advancement with wide-ranging benefits for society.

1.2 Research Objectives

The effects of DA-22 on human neutrophil activation are still under investigation due to there is no previous study that investigates this drug on neutrophil experiment. Beforehand, our lab has done drug screening for each drug to be investigated and the results showed that DA-22 tends to have a stimulating effect in human neutrophils. Thus, the objective of this research is to investigate the

ability of DA-22 mechanisms towards human neutrophil activation and their immune response enhancement.

1.3 Scope of Research

This research will focus on the immune response enhancement of human neutrophils which were examined from isolated blood samples and purified neutrophils that are collected from healthy informed and consent participants within the age range of 20-35 years old. The other process is also followed by an elastase release and superoxide generation test to assess degranulation and respiratory burst in neutrophils and will be continued by luminescence-luminol assay to further investigate the ROS production. Another experiment will also be performed, including NETs and CD marker detection. NETs will be done to assess the formation of NETs in human neutrophils and CD marker detection will be done to evaluate the release of granules in the surface of neutrophils.

1.4 Hypothesis

This research is hypothesized that DA-22 is effective to enhance human immune response which can activate the neutrophil functions.