CHAPTER I. INTRODUCTION

Chronic Myeloid Leukemia is a form of leukemia resulting from a genetic mutation that takes place in early, immature versions of myeloid cells, which form red blood cells, platelets, and most types of white blood cells. (Eden & Coviello, 2023) In all leukemia cases, 15% were CML, and it usually occurs in older patients. In the United States and European Union, the median age of CML patients is 60-67. However, it is different in Asia, where the median age of CML patients is shown to be 36-55. On the other hand, Indonesia's age median for CML sits at 34-35 (Rajabto et al., 2022). It is currently not yet understood why the discrepancy exists in this region. However, the fact remains that CML can occur more frequently in Asian countries, and it is important to be able to diagnose the disease sooner.

The drug that is used for treating CML is called a TKI. It blocks the activity of tyrosine kinases and disrupts the signaling pathways of cancer cells, effectively slowing or stopping the growth. The T315i mutation is the most common drug-resistant mutation of CML, with a mutation rate of 15%. This mutation is resistant to most TKIs currently used, including all of the first and second generations of TKIs. (Mu et al., 2024)

Currently, the preferred way of detecting and monitoring CML is by performing a PCR test. That is because it is sensitive, quick, and accessible. PCR tests can detect even small amounts of the BCR-ABL1 gene. It can be performed in a short amount of time and on peripheral blood samples. Different types of PCR tests are used for this, such as qPCR, RT-PCR, and Digital PCR.

This project that I participated in was aimed at finding a more efficient method that detect the BCR-ABL1 T315I mutation. The current method at KALGen Innolab was only able to produce a consistent result in samples that show mutation around amino acid positions 253 and 255. The method struggled to detect mutations at higher amino acid positions, such as at position 315. The trial was the main objective in trying to improve the method for detecting BCR-ABL T315I mutation by optimizing the PCR test. Previously, the test only used standard PCR that targets the M-bcr; instead, the use of nested PCR was tested, where the target region would be reduced specifically aiming for the region where the T315I mutation occurs. The prediction was that by implementing nested PCR into the procedure and adjusting the annealing temperatures of the new primers that would be used, would allow the detection for T315i mutation and this implementation does not hinder its ability to detect other mutations.