I. INTRODUCTION

1.1 Background

Colorectal cancer (CRC) is one of the deadliest cancers which is categorized as the top three causes of cancer-related death in the world (Sieminska & Baron, 2020). In 2020, the incidence of CRC reached 1.93 million cases, with 0.94 million deaths, which is approximately 10% of the global cancer incidence and 9.4% of all cancer-related deaths respectively (American Cancer Society, 2020; Xi & Xu, 2021). In Indonesia itself, CRC prevalence reached 946,088 cases in 2015-2020. Based on gender, males and females in Indonesia are 11.9% and 5.8% at risk of contracting CRC respectively. This means that 1 out of every 9 males is at risk of being diagnosed with CRC during their lifetime (Globocan, 2020). Although so, there is still a lot to be explored to be able to fully understand the mechanism of CRC, which includes the determination of its prognosis, prevention, early diagnostics, treatments and monitoring (Krzyszczyk et al., 2018).

A cancer patient's journey can generally be divided into four main stages: pre-diagnostic, diagnostic, treatment, and post-treatment. In pre-diagnostic stage, patients commonly seek and explain their symptoms to a primary care provider (PCP). Afterwards, the PCP would do diagnostic tests and provide a verdict on what the patient is experiencing. Alongside with the verdict, first-line treatments such as chemotherapy treatment are also given, if the diagnosis result is positive for cancer. As cancer disease shows no symptoms in most cases until it reaches the latter stages, early diagnostics are essential to improve the prognosis and survival rate of the patients (Maravic et al., 2020).

There are two main aspects that are essential in conducting early diagnostics: tumor profile and host immune response. These factors are what would be taken into consideration to provide a personalized treatment for the cancer patients. There are several approaches in tumor profiling, where the tumor is identified based on the genomics, epigenomics, transcriptomics, and proteomics aspects. In the genomic aspect, cancer-related genes such as the KRAS and BRAF genes would be observed for any abnormalities to determine the tumor profile. In the epigenomic aspect, DNA methylations are observed to detect occurrence of epigenetic alterations in the tumor cells. The transcriptomic aspect inspects more on the consensus molecular subtypes and categorizes them based on their subtypes. Lastly, one of the most commonly used approaches in tumor profiling is the proteomic approach which utilizes carcinoembryonic antigen (CEA), a biomarker that is used to determine prognosis in CRC patients. CEA is found to be increased as the tumor progresses in the patient, which causes CEA to be able to determine cancerous activity in its host. As a result, CEA is also commonly used for cancer progression monitoring as well. However, its non-specificity causes it to have lower accuracy in determining cancer progressions, as it could also be elevated due to malignancy or other inflammation sources. Aside from that, its sensitivity in detecting recurrent CRC is considerably low, which requires it to be paired with another diagnostic method. Therefore, another approach is required to obtain a more potential biomarker, particularly on the host immune response (Martins et al., 2019).

The other aspect is seen through the host immune response which is tightly related to the microenvironment created by the interaction between immune and tumor cells. There

are two main aspects of the host immune response: pro-tumorigenic and anti-tumorigenic. Increasing the understanding of the tumor microenvironment enables novel findings on immune-based biomarkers and target agents for diagnostics and targeted therapy. One of the emerging diagnostic methods which have high potential to be utilized as a cancer biomarker is the myeloid-derived suppressor cells (MDSC) (Angell et al., 2016). MDSC are cells that act to suppress the immune system, which allows tumors to develop, expand through angiogenesis, and form metastasis (Sieminska & Baran, 2020). Past research has found that the MDSC level positively correlates with malignancy and patient survival rate, such as in patients with thyroid, lung, and breast cancer (Angell et al., 2016; Ma et al., 2019; Yang, Guo, et al., 2020). Therefore, the potential of MDSC as a novel CRC biomarker will be further studied in this research utilizing the flow cytometry method.

1.2 Objective

There are three main objectives in this study:

1. Compare MDSC level of CRC patients towards the healthy population,
2. Compare trend of M-MDSC towards PMN-MDSC level in CRC patients,
3. Compare the trend of M-MDSC and PMN-MDSC towards CEA in D0, D14, and 100%.

The main hypothesis for the study is that the MDSC level may be used as a novel biomarker for CRC. From the main hypothesis, three supporting hypotheses can be withdrawn:

1. MDSC level will be different between CRC patients to the healthy population,
2. Trend of PMN-MDSC will be more distinguishable compared to M-MDSC in CRC patients,
3. The trend exhibited by MDSC will be more distinguishable compared to CEA.

1.3 Research Scope of Work

The scope of work for this experiment includes the processing of blood samples, flow cytometry, and its analysis.