I. INTRODUCTION

1.1 Background

Skeletal muscle is considered to be the most abundant tissue in the human body, providing for a wide range of physiological traits (Biolo et al., 2014). This muscle tissue contains almost 75% of the body's protein and is essential for physical mobility, posture, and important functions. Skeletal muscle also regulates interorgan interaction for both protein and energy metabolism throughout the body, a lesser-known but crucial role (Shiozu et al., 2015). Therefore, protein and energy availability throughout our body is reduced as skeletal muscle is lost. Muscle loss is linked to impaired wound healing, a lower resting metabolic rate, physical impairment, a lower quality of life, and increased health-care expenses (Argilés et al., 2016). One of the factors that contributes to the degeneration of muscle tissue is age. Aging can cause muscle mass loss due to both the shrinking of muscle fibers (atrophy) and the removal of fibers entirely. Sarcopenia is the medical term for this condition (Larsson et al., 2019).

Sarcopenia is defined as a decrease in skeletal muscle mass with age (Marty et al., 2017). Although sarcopenia is typically associated with the older age group, it can also be associated with conditions that are not limited to the aged, such as disuse, malnutrition, and cachexia. It can be found in younger persons, such as those suffering from inflammatory illnesses such as osteopenia (Santilli et al., 2014). The prevalence of sarcopenia in patients aged 60 and above is estimated to be between 5% to 13%, and 11% to 50% in patients aged 80 and above, respectively, while the global prevalence of sarcopenia in adults over the age of 60 is estimated to be 10% (Aedeljan et al., 2020; von Haehling et al., 2010; Shafiee et al., 2017). Furthermore, sarcopenia prevalence ranges from 4.6% to 43% in communities and from 23% to 68% in clinical settings in Europe and the United States. Sarcopenia was recently discovered to be prevalent in Taiwan, ranging from 6.7% to 10% in communities and up to 50% in clinical settings (Chang et al., 2021). A study conducted by Bayraktar et al., (2020) found that patients with sarcopenia had an in-hospital death rate of 28.6%, while patients without sarcopenia had an in-hospital mortality rate of 11%. In addition, conservative projections based on sarcopenia prevalence and World Health Organization (WHO) population data show that sarcopenia currently affects more than 50 million individuals and will impact more than 200 million people over the next 40 years (Wang & Bai, 2012).

With the high prevalence of sarcopenia, it is indeed important to understand the underlying pathophysiology of the disease to improve sarcopenia treatment. Nowadays, the ongoing treatment for sarcopenia itself includes therapy in nutrition as well as daily exercise (Chen et al., 2020). A combination of dietary therapy and a thorough exercise program involving resistance training is more

successful in treating sarcopenia than a single intervention alone (Kakehi et al., 2022). However, these therapies are very limited to the person's mobility and not consistent with different patients who are diagnosed with sarcopenia. Therefore, there is a need for an emergent study regarding which molecular pathway can be targeted to provide an effective and efficient treatment for each individual with sarcopenia indication.

Since sarcopenia corresponds to muscle mechanism, mitochondria activities would be one of the factors that may contribute to the degeneration of muscle. Mitochondria perform critical functions in maintaining cellular homeostasis and skeletal muscle health; hence mitochondrial injury can result in a variety of pathological alterations. Mitochondrial malfunction can cause skeletal muscle atrophy, and the molecular process underlying this is complex (Chen et al., 2023). Recently, a study conducted by Chen et al., (2019) has found that the homeostasis of mitochondria indeed has a correlation with the Rrm2b gene. However, this study was purely conducted on kidney tissue and there has been no comprehensive study regarding the effect of the Rrm2b gene on mitochondrial homeostasis in skeletal muscle tissue. The Rrm2b gene itself is an enzyme that helps to catalyze dNTPs in nucleus and mitochondria (Fassulo & Endres, 2015). This gene was deemed noteworthy because when there is a loss of function of the Rrm2b gene, there is an increased progression of muscle fiber loss in the tissue, similar to a sarcopenic tissue (Chen et al., 2022). Therefore, this study aims to uncover the molecular effects as well as physical functions of the Rrm2b gene in skeletal muscle tissue by knocking out the Rrm2b gene in the skeletal muscle tissue of mice and to find out which mechanisms of the Rrm2b gene should be targeted to help treat sarcopenic patients.

1.2 Research Scope

The scope of this study are:

1. Tissue collection from 2 groups of mice model, the Rrm2b gene knockout mice and normal mice that act as a control
2. Comparison study of molecular analysis of both nucleic and protein molecules between the 3-month and 5-month knockout Rrm2b mice and control mice
3. Comparison study of physical functions analysis using Immunohistochemistry (IHC) of the knockout Rrm2b mice skeletal muscle tissue with the control mice

1.3 Research Question

In accordance with the background and objectives mentioned above, here are the research questions:

1. Does the loss of the Rrm2b gene generate a significant difference of molecular mechanisms in the comparison between Rrm2b skeletal muscle knockout mice and control (F/F) mice?
2. Does the loss of the Rrm2b gene generate a significant difference of physiological characteristics in the comparison between Rrm2b skeletal muscle knockout mice and control (F/F) mice?
3. Does the age of the mice result in a different outcome of molecular mechanisms and physical characteristics when there is a knockout of the Rrm2b in skeletal muscle mice tissue?

1.4 Hypothesis

From the research questions mentioned above, here are the hypotheses constructed:

1. H0: A clear significant difference is found in the comparison between Rrm2b skeletal muscle knockout mice with control (F/F) mice in molecular mechanisms

   H1: No clear significant difference is found in the comparison between Rrm2b skeletal muscle knockout mice with control (F/F) mice in molecular mechanisms
2. H0: A clear significant difference is found in the comparison between Rrm2b skeletal muscle knockout mice with control (F/F) mice in physiological characteristics

   H1: No clear significant difference is found in the comparison between Rrm2b skeletal muscle knockout mice with control (F/F) mice in physiological characteristics
3. H0: Age does have a direct effect in the changes of molecular mechanisms and physical characteristics observed in both control and Rrm2b skeletal muscle knockout mice

   H1: Age does not have a direct effect in the changes of molecular mechanisms and physical characteristics observed in both control and Rrm2b skeletal muscle knockout mice