Chapter 1

Introduction

1.1 Background

Obesity has become a major and rapidly growing public health challenge worldwide, including in Indonesia. Global Obesity Observatory (2024) indicates a continuous increase in the prevalence of overweight and obesity among both adults and younger populations, driven by lifestyle changes, excessive caloric intake, and reduced physical activity. This rising trend is particularly concerning because obesity can be strongly associated with the development of metabolic disorders such as type 2 diabetes mellitus, dyslipidemia, and other metabolic syndrome (Ahmed & Mohammed, 2025). In Indonesia, the burden of diabetes continues to increase, affecting millions of adults with prevalence of 11.3% from total adult populations, and this highlights the urgent need for effective preventive and therapeutic strategies (IDF, 2024). Since obesity-related metabolic dysfunction is closely linked to the expansion and functional alteration of adipose tissue, understanding the biological mechanisms that regulate adipose tissue development and function has become an important area of research.

Understanding the molecular mechanisms and regulatory factors that may influence adipocytes is essential for identifying potential therapeutic targets. Whereas adipose tissue itself plays a central role in maintaining metabolic homeostasis and its dysfunction can further contribute to developments of obesity, and diseases such as type 2 diabetes mellitus, and cardiovascular diseases (An et al., 2023).

Recent studies have demonstrated the participation of E4BP4 gives an effect in the regulation of adipocytes, a browning process that emerges as a response to cAMP signaling *in vitro* (So et al., 2022). However, the effects of sustained E4BP4 overexpression during adipocyte differentiation remain insufficient. To further investigate this limitation, an *in vivo* experimental approach is necessary to investigate the role of E4BP4 within the physiological environment of adipose tissue. *In*

vivo studies allow the evaluation of adipocyte differentiation and thermogenic regulation under systemic influences such as hormonal signaling, metabolic state, and environmental factors, which cannot be fully replicated in isolated cell culture systems. Therefore, conducting this study *in vivo* provides a more comprehensive understanding of how E4BP4 overexpression influences adipocyte differentiation and phenotype across different adipocyte subtypes. Investigation of the influences from overexpressed E4BP4 for white adipocyte and its differentiation processes can contribute to a deeper understanding of transcriptional control in adipose tissue biology and give a closer insight into adipocyte transcriptional regulation for further development of therapeutic strategies for obesity and other related metabolic disorders.

1.2 Objective

To investigate the effects of E4BP4 overexpression on the differentiation of SVF-derived adipocytes using a doxycycline-inducible lentiviral expression system.

1.3 Research Questions

1. Can E4BP4 be successfully overexpressed using a doxycycline-inducible lentiviral system?
2. Does E4BP4 overexpression influence the morphological characteristics of differentiating SVF-derived adipocytes?
3. Does lentiviral-mediated E4BP4 overexpression alter E4BP4 expression at the mRNA and protein levels in SVF-derived adipocytes?

1.4 Hypothesis

E4BP4 overexpression influences the differentiation of SVF-derived adipocytes and may alter adipocyte morphology and phenotype.