UNIVERSITI TEKNOLOGI MARA

DETECTION OF POLYMORPHISMS IN EXON 2 OF HUMAN GLUCOCORTICOID RECEPTOR GENE (NR3C1) USING POLYMERASE CHAIN REACTION (PCR)

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ABSTRACT

There are three documented polymorphisms in exon 2 of Human Glucocorticoid Receptor gene (NR3C1). These include ER22/23EK, N363S and *Bcl*I. ER22/23EK induces glucocorticoid resistance while N363S and *Bcl*I cause hypersensitivity towards glucocorticoids. A probable novel SNP (C40814T) has been detected in a sample where it produces a synonymous mutation with no change in the amino acid. AS-PCR can be done in the future to screen larger group of samples to validate the presence of this SNP.

CHAPTER 1

INTRODUCTION

1.1 Background of study

Cortisol is a major hormone of glucocorticoids, which is released in the human body due to prolonged physical or physiological stress triggered by infections, operation and surgery. Its release is regulated by centrally by the hypothalamic-pituitary adrenal (HPA) axis and peripherally by enzymatic regulations. When an individual is exposed to long-term stress, the body will send signals to the hypothalamus to secrete corticotropin releasing hormone (CRH), which will then further stimulates the pituitary gland to secrete more adrenocorticotropic hormone (ACTH). This hormone will eventually stimulate the adrenal cortex of the adrenal glands to secrete more cortisol and stimulates sympathetic nervous system to increase heart rate, glucose and blood pressure (Maddock & Pariante, 2001). On the other hand, epinephrine and norepinephrine will be released from the adrenal medulla when the body is subjected to short-term stress.

Peripherally, there are two key enzymes involved in the regulation of cortisol in the blood. 11β-dehydrogenase 1 is important for the conversion of cortisone to cortisol. It is highly activated in the subcutaneous adipose tissue of an obese person, and causes him/her to have high serum cortisol level. While 11β-dehydrogenase 2 inactivates the cortisol conversion into cortisone.