CHAPTER I
INTRODUCTION

1.1 RATIONALE

Amelogenesis Imperfecta (AI) is a hereditary condition that affects the enamel of both primary and permanent dentitions in widely varying phenotypes with the absence of other systemic manifestations (Witkop, 1988; Aldred and Crawford, 1995; Pavlic et al., 2007). AI can be classified into hypoplastic, hypocalcified, and hypomaturation forms, based on the appearance of the affected enamel. The classification of Witkop, which is widely used, distinguishes 14 subtypes of AI by using phenotype as the primary mode of classification and inheritance pattern (autosomal dominant (AD), autosomal recessive (AR), X-linked) as the secondary criterion for diagnosis (Witkop, 1988).

Genetic factors have been implicated in AI. Mutations in several genes, such as the amelogenin gene (*AMEL*) (Greene et al., 2002; Kim et al.,2004; Kida et al.,2007), the enamelin gene (*ENAM*) (Rajpar et al., 2001; Hart et al., 2003a; Hart et al., 2003b; Ozdemir et al., 2005a; Gutierrez et al., 2007; Pavlic et al., 2007, Kang et al., 2009), the kallikrein4 gene (*KLK4*) (Hart et al., 2004), the matrix metalloproteinase 20 gene (*MMP20*) (Ozdemir et al., 2005b) and the family with sequence similarity 83 member H gene (*FAM83H*) (Ozdemir et al., 2005b; Kim et al., 2008; Hart et al., 2009; Hyun et al., 2009), have been reported to be associated with different types of AI.

During enamel formation, approximately 1-5% of total enamel proteins are enamelin, which is suggested to play an important role in the initiation of enamel mineralization and regulation of crystal growth (Rajpar et al., 2001; Hart et al., 2003b; Masuya et al., 2005). Enamelin is expressed in the secretory stage and its expression disappears early in the maturation stage of amelogenesis (Hu et al., 1997). *ENAM* is a strong candidate gene, associated with both localized and generalized hypoplastic AI, with many previously reported mutations (Table 2.1).

The association between hypoplastic AI and *ENAM* mutations has been studied in different populations, such as Turkish (Ozdemir et al., 2005a), Iranian (Kim et al., 2005a) and Japanese (Kida et al., 2002) families. Therefore, I hypothesize that AI in the patients with AI, hypoplastic type in my research may be the result of *ENAM* mutations as well. Identification of genes responsible for amelogenesis imperfecta has contributed to a better understanding of the disease pathogenesis.

1.2 OBJECTIVE

To find *ENAM* mutations in patients with hypoplastic amelogenesis imperfecta.

1.3 HYPOTHESIS

H_o: *ENAM* mutations are associated with hypoplastic amelogenesis imperfecta in patients with AI in this study.

H_1: *ENAM* mutations are not associated with hypoplastic amelogenesis imperfecta in patients with AI in this study.