CHAPTER 1

Introduction

1.1 Historical background

Oral squamous cell carcinoma (OSCC) is the most common cancer found in the oral cavity. Approximately 90% of cancer cases found in the oral cavity and the oropharynx are squamous cell carcinoma.[1] A number of studies have shown an aggressive behavior of OSCC due to the low five-year survival rate for OSCC patients as most patients die shortly if OSCC is detected in the late stage.[2,3]

A disintegrin and metalloproteinases, or ADAMs, are transmembrane proteins. In several physiologic processes of human cells and tissues, ADAMs play an essential role in proteolysis and cell adhesion; however, they are also shown to be involved with several pathologic conditions, especially in the pathogenesis of cancer and cancer metastasis. Due to their previously-reported involvement with several cancers, several ADAM proteins are proposed to be biomarkers and used as therapeutic targets for various types of cancer, such as breast, prostate and bladder cancers.[4] ADAM9, a member belonging to the ADAM family, has been previously demonstrated to be associated with many cancer types, such as prostate cancer, pancreatic cancer, breast cancer, lung cancer and renal cell carcinoma. Nevertheless, only a few studies that determined the genomic aberration of *ADAM9* and showed ADAM9 mRNA overexpression in OSCC and in oral cancer cell lines have so far been reported in the scientific literature database[5-7] and the findings from these studies are still inconclusive. Moreover, none of these studies has studied ADAM9 protein expression in OSCC and in oral cancer cell lines. Consequently, due to limited and unclear knowledge about the role of ADAM9 in the pathogenesis of OSCC, I want to examine ADAM9 protein expression in OSCC in this study by an immunohistochemical

technique and to further extend an investigation into ADAM9 protein expression in different oral cancer cell lines *in vitro* by immunoblotting and flow cytometry. I wish that new knowledge gained from this research project will be beneficial for better understanding into the role of ADAM9 in the pathogenesis of OSCC and may be clinically applied for future uses of ADAM9 as a diagnostic or a prognostic marker and/or as a new therapeutic target for OSCC.

1.2 Objectives

1.2.1 To determine ADAM9 protein expression by immunohistochemistry using a specific antibody for ADAM9 in formalin-fixed and paraffin-embedded tissue sections of OSCC and normal oral tissues.

1.2.2 To compare ADAM9 protein expression between OSCC and oral tissues.

1.2.3 To find a correlation between ADAM9 protein expression and the histologic grading of OSCC.

1.2.4 To determine ADAM9 protein expression *in vitro* by investigating its expression in OSCC cell lines and normal oral epithelial cells by immunoblotting and flow cytometry.