Salivary Soluble CD44 As A potential Molecular Marker for Oral cancer

Thesis

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Abstract

One candidate molecular marker for oral cancer is CD44. The present study was carried out on 40 subjects. Levels of salivary sCD44 among patients with: oral cancer, premalignant lesions with & without dysplasia and controls were measured using an ELISA assay. The results of the present study indicate that a level of salivary sCD44 lying within the range of 19.2 to 20.4 ng/ml could indicate malignant transformation. The significant increase in CD44 level in oral cancer patients makes it a potential molecular marker for oral cancer.

Keywords:

Cancer, molecular marker, CD44, premalignant, dysplasia.

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INTRODUCTION

Oral cancers annually strike hundreds of thousands around the globe. Despite treatment advances, the disease's overall five-year survival rate has not improved in the past three decades and remains among the worst of all cancers. One factor behind oral cancer's high mortality is the difficulty of detecting it at its early stages ***(Wong, 2006; Prince et al., 2007)***.

Invasive oral squamous cell carcinoma is often preceded by the presence of clinically identifiable premalignant changes of the oral mucosa. Identification of high-risk oral premalignant lesions and intervention at premalignant stages could constitute one of the keys to reducing the mortality, morbidity and cost of treatment associated with OSCC ***(Neville and Day, 2002)***.

The last three decades have witnessed a rapid advancement and diffusion of technology in health services. Technological innovations have given health service providers the means to diagnose and treat an increasing number of illnesses, including cancer. In this effort, research on biomarkers for cancer detection and risk assessment has taken a center stage in the effort to reduce cancer deaths. For the first time, scientists have the technologies to decipher and understand these biomarkers and to apply them to earlier cancer detection. By identifying people at high risk of developing cancer, it would be possible to develop intervention efforts on prevention rather than treatment. Once fully developed and validated, then the regular clinical use of biomarkers in early detection and risk assessment will

meet nationally recognized health care needs: detection of cancer at its earliest stage ***(Verma et al., 2001).***

One candidate molecular marker for HNSCC is CD44 which is one of the adhesion molecules. CD44 proteins are also released in soluble form (sCD44) via proteases and are detectable in normal circulation. Circulating levels of sCD44 correlate with metastases in some tumors ***(O'Hara and Bradley, 2002).***

Actually, increased levels of sCD44 were not only reported in head & neck cancer, but also it was reported to be increased in colorectal cancer, gastric carcinoma, renal cancer, primary breast cancer and non-Hodgkin's lymphoma (NHL) ***(Harn et al., 1996; Kan et al., 1996; Masson et al.,1999; Niitsu and Iijima, 2002; Mayer et al., 2008).*** These authors came out with the conclusion that sCD44 could be considered as a marker in all these types of cancer.

Technological advances over the past decades have enabled oral fluid to expand its usefulness in the diagnosis of disease, prediction of disease progression, monitoring of therapeutic drug levels and detection of illicit drugs. The easy non-invasive nature of collection and the relationship between oral fluid and plasma levels make oral fluid a valuable clinical tool ***(Choo and Huestis, 2004)***.

Franzmann et al. (2005, 2007) reported correlation between high level of salivary sCD44 and malignant transformation in oral lesions. Consequently, it became a tempting issue for research**.**

بسم الله الرحمن الرحيم

"علم الإنسان ما لم يعلم"

صدق الله العظيم

سورة العلق آية "٥"

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Dedication

To my Family,

My parents,

My husband,

And my sweethearts, Mariam & Mostafa.

CONTENTS

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AIM OF THE STUDY

This study was carried out in order to determine the validity of sCD44 ELISA test on saliva and its effectiveness in detecting oral cancer and possibly early malignant transformations in some premalignant lesions.

REVIEW OF LITERATURE

Head and neck squamous cell carcinoma (HNSCC) accounts for more than 95% of all head and neck malignancies. Unfortunately, the majority of HNSCC patients present with advanced stage disease, requiring multimodality therapy. Even with combinations of intensive chemotherapy, radiotherapy, and surgery, cure rates are only 30% for advanced stage disease. Those cured often face serious morbidities including speech and swallowing problems, disfigurement, and exorbitant healthcare costs ***(Franzmann et al., 2005; Mehrotra and Yadav, 2006).***

Early oral cancers and precancerous lesions are often subtle and asymptomatic. Therefore, it is important for the clinician to maintain a high index of suspicion, especially if risk factors such as tobacco use or alcohol abuse are present. A key factor in the lack of improvement in prognosis over the years is the fact that a significant proportion of oral squamous cell carcinoma (OSCC) are not diagnosed or treated until they reach an advanced stage. This diagnostic delay may be caused by either patients (who may not report unusual oral features) or by health care workers (who may not investigate observed lesions thoroughly) and it is presumed that such delays are longer for asymptomatic lesions. The prognosis for patients with OSCC that is treated early is much better, with 5-year survival rates as high as 80%. In addition, the quality of life improves after early treatment, because cure can be achieved with less