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بعض الوثائق الأصلية تالفة

THE ROLE OF β1 INTEGRINS AND LAMININ IN THE PATHOGENESIS OF ORAL LICHEN PLANUS

Thesis

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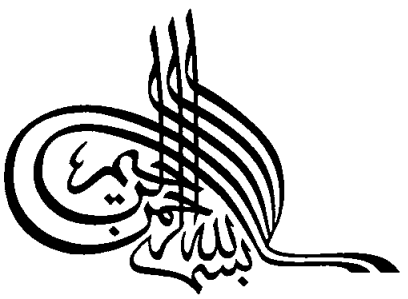

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فينبئكم بما كنتم تعملون

صدق الله العظيم

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INTRODUCTION

Oral lichen planus (OLP) is a common chronic mucocutaneous disease. (Scully and Elkom, 1985). The prevalence of OLP is 1.9% in the general population *(Walton et al., 1994).*

Various forms of OLP appear clinically: reticular, papular, plaque like, atrophic, erosive and bullous lesions that can occur separately or simultaneously. In papular form there is 0.5 to 1mm whitish elevated lesions, or papules while atrophic form describes inflamed areas of the oral mucosa covered by thinned red epithelium. Papular, plaque like, and atrophic forms are very frequently accompanied by reticular lesions, the diagnosis of OLP is often confirmed by identifying an area of reticular pattern which consists of whitish lines (Wickham's striae) that produce either a lace like lesion or annular lesions. Atrophic and erosive forms usually cause symptoms of pain and discomfort. *(Bouquot and Gorlin, 1986;Brown et al., 1993).*

Histophathologically, OLP shows focal hyperkeratosis, irregular acanthosis, basal cell liquefaction degeneration, and a dense bank like infiltrate of T lymphocytes *(Boisnic et al., 1990)* ,changes believed to represent an aberrant cell-mediated immune response directed against basal keratinocytes *(Walsh et al., 1990).*

The majority of cases of lichen planus are idiopathic and the aetiology is not understood, but a cell mediated immune response following antigenic changes in the mucosa is considered to be important. The inflammatory infiltrate is composed of lymphocytes, predominantly T cells (composed of both T_4 and T_8 lymphocytes), but with variable proportions of B cells and natural killer cells, together with macrophages. *(Walsh et al,. 1990).*

Epithelial cells produce the components of the basal lamina, which consists of a mesh work of type IV collagen, the glycoproteins laminin and entactin and proteoglycans, principally heparen sulphate, contact with basal lamina seems to be important for the maintenance of the differentiated characteristics of epithelia. In addition, the basal lamina forms a scaffolding along which cells may migrate during regeneration. Adhesion between the cell and the collagen

meshwork is made possible by laminin which binds both to cell surface receptors and to collagen *(Lackie and More, 1992).*

Cell surface adhesion receptors have been divided into three families: the integrins family ,the immunoglobulin superfamily and the selectins family *(Hynes,1987;Hemler,1988).*

The primary function of the integrin β_1 family is to mediate cell-cell and cell-matrix adhesion interaction and cell migration, also their normal function is critical in the induction and maintenance of cell differentiation *(Hynes, 1992).*

Recent studies indicate that laminin and types IV and VII collagen are significantly increased at the epithelial-mesenchymal junction in LP and thus may bind to β_1 integrins on the surface of infiltrating lymphocytes *(Eversole, 1994).*

It was found that there are an uneven or absent immunostaining for laminin-5, laminin-2 and collogen IV with altered integrin expression in basal keratinocytes in LP *(Giannelli et al. 1996).*

The most frequently described therapy for OLP has been the administration of topical or systemic corticosteroids. The efficacy of corticosteroids for treatment of OLP is mainly attributed to the local anti-inflammatory effect. Some benefit may also result from anti-immunologic properties of suppressing T-cell function *(Pederson and Klausen, 1984).*

Because of the severity and nature of L.P, high doses of corticosteroids are usually needed for prolonged periods for disease control. Because of the frequent occurrence of corticosteroids side effects, inadequate control, or both, supplementation with other drugs often is required **(Silverman et al., 1985).**

Levamisole, the levisomer of tetramisole, was developed in 1966 and put to extensive use worldwide in both humans and domestic animals as an antihelmintic drug. It attracted interest as an effective agent in disease in which cellular immune deficiency was suspected such as chronic and recurrent infections, primary and secondary immune deficiencies, rheumatoid arthritis, and in stabilization of tumor remission in cancer (*Moertel et al., 1990).*

The use of systemic levamisole plus low-dose prednisolone in oral lichen planus showed excellent objective and subjective therapeutic effects, levamisole has been shown to be effective and relatively safe in comparison with high-dose prednisolone, obviously, the role of levamisole in achieving longer term remission and speeding clinical efficacy is positive, this is one of the major advantages of levamisole over prednisolone ***(Shin-Yu et al., 1995, 1998).***