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Evaluation of Laminin-5γ as Prognostic Marker in Oral Squamous Cell Carcinoma

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ABSTRACT

Oral Squamous Cell Carcinoma (OSCC) is the most prevalent malignant neoplasm. Despite the ready accessibility of the oral cavity to direct examination, these malignancies are often still not detected until it is very late and as a result, the survival rate for oral cancer has remained essentially unchanged over the past decades. This study was conducted to evaluate laminin-5 γ2 expression in various grades of OSCC and to determine whether this protein can be used as a marker for aggressiveness of oral cancer. Laminin-5 has been shown to be highly expressed in several types of squamous and other epithelial tumors including cutaneous, oesophageal, laryngeal, tracheal, cervical and colon carcinomas. In these tumors, Laminin-5 often is noted to accumulate at the interface of the tumor with the surrounding stroma so Laminin-5 expression has been shown to correlate well with tumor invasiveness and poor patient prognosis.

Key words: Laminin-5, OSCC, invasion, expression, ECM

INTRODUCTION

Oral cancer is estimated to present more than 400,000 new cases worldwide, establishing it as the sixth most common worldwide[1]. Squamous Cell Carcinoma (SCC) is the most common malignant tumor of the oral cavity and one of the 10th most common causes of death[2]. OSCC accounts for approximately 3% of all malignancies and more than 90% of cancers of the oral cavity and oropharynx[3,4]. Metastatic spread of cancer continues to be the greatest challenge to cancer cure. At the core of the process lie the changing adhesive preferences of the tumor cells which determine their interactions with other cells and with the extracellular matrices mainly in attachment and degradation processes[5]. This study was conducted to evaluate laminin-5 γ2 expression in various grades of OSCC and to determine whether this protein can be used as a marker for aggressiveness of oral cancer.

THE EXTRACELLULAR MATRIX

The extracellular matrix (ECM) is the non-cellular component present within all tissues and organs and provides not only essential physical scaffolding for the cellular

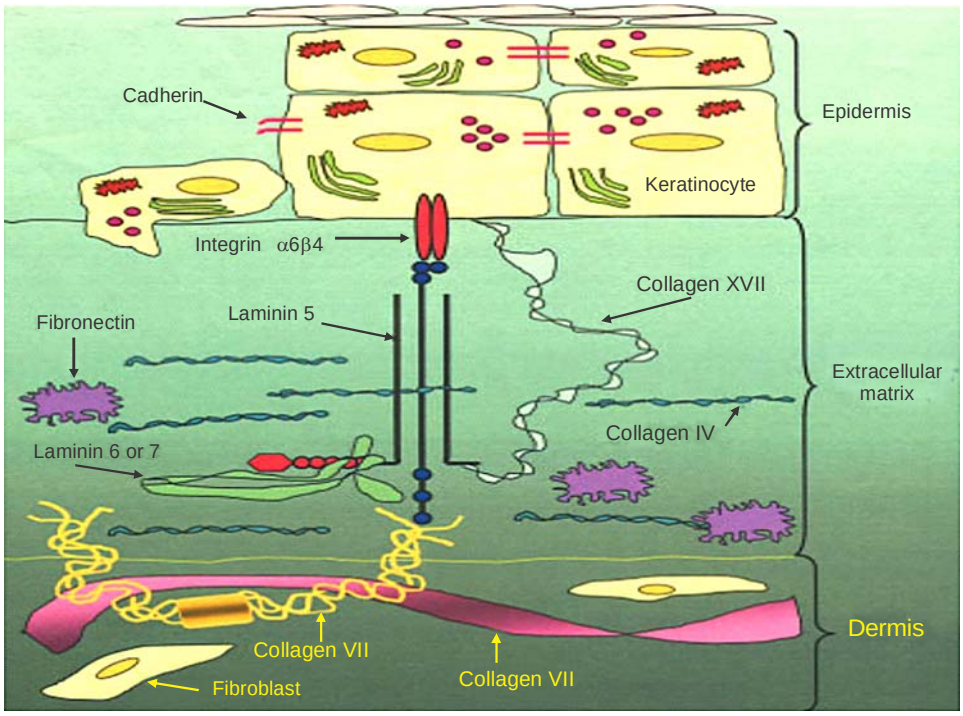

Fig. 1: The ECM of the oral epithelium. Hypothetical interactions of the ECM components with cell surface receptors of the epidermis and anchoring molecules of the dermis. The major ECM molecules are labeled[13]

constituents but also initiates crucial biochemical and biomechanical cues that are required for tissue morphogenesis, differentiation and homeostasis. The importance of the ECM is vividly illustrated by the wide range of syndromes which can be anything from minor to severe that arise from genetic abnormalities in ECM proteins[6]. The ECM of most epithelial layers is typically composed of laminin, collagen, fibronectin and glycosaminoglycans derived from keratinocytes and stromal cells or from the cooperative interactions between these two cell populations (Fig. 1). Once viewed only as an architectural support for epithelial cells, the ECM is now recognized as a major component in regulating cell activity. ECM molecules have been shown to be important in proper tissue development, adult tissue maintenance, wound healing and oncogenesis[7].

Interaction between tumor cells and ECM components is essential for tumor growth and for the onset of cell spreading and subsequent metastatic activity[8]. Two basic ultrastructures of the ECM have been identified: The interstitial matrix and the Basement Membrane (BM)[9]. BMs are thin sheets of specialized ECM that surround epithelia, endothelia, muscle cells, fat cells, schwann cells and peripheral nerves as well as the entire central nervous system. They play important roles in maintaining tissue integrity and compartmentalization, in filtration and in diverse developmental processes. All BMs contain type IV collagen, nidogen, sulfated proteoglycans and laminin[10]. Immunohistochemical studies of basal membrane components have been shown to be effective in diagnosing and establishing the prognosis of cancer. Basal membrane components are not only an important structural barrier but also act as barrier against neoplastic invasion in SCC, thus avoiding tumor cell dissemination[11].

LAMININ-5

The laminins are heterotrimeric proteins of the ECM that are composed of alpha, beta and gamma subunits, laminin heterotrimers are relatively large proteins (with molecular masses ranging from 400 to 900 kDa) and exist as cross-shaped molecules with two or three short arms and one long arm[12].

Laminins are a family of ECM proteins that constitute the major non-collagenous glycoproteins found in the BM and are involved in multiple important biological activities such as assembly of the BM, cell attachment, migration, growth and differentiation, neurite outgrowth and angiogenesis. In addition, laminins promote the invasive phenotype of cancer. The interaction of cancer cells with laminin is a key event in tumor invasion and metastasis[14]. One of the mechanisms by

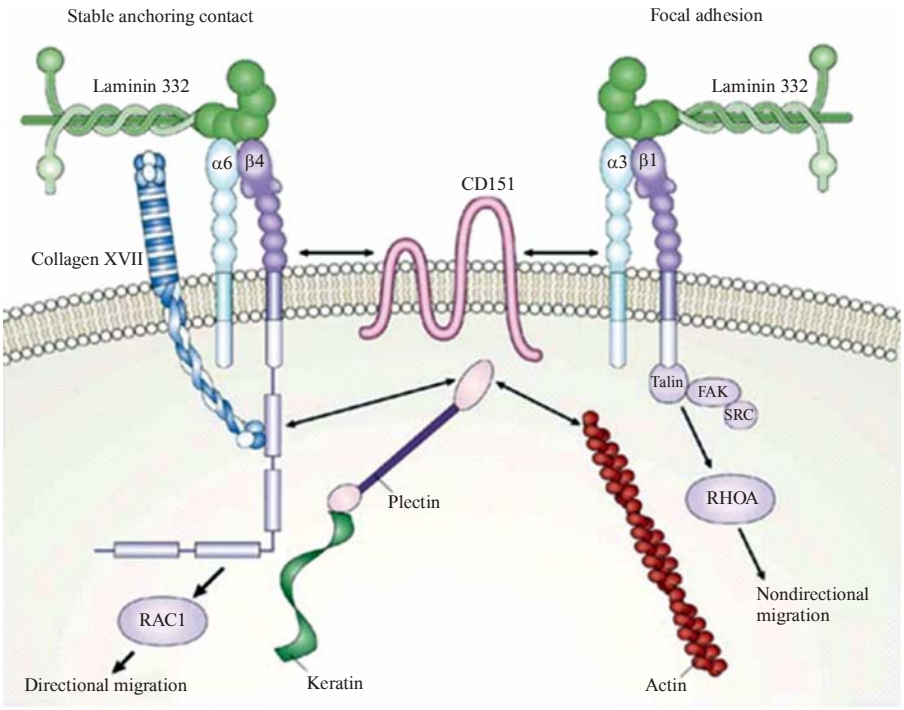

Fig. 2: Laminin 332 (laminin-5) promotes two separate integrin-mediated epithelial adhesion contacts[16]

which laminin contributes to the metastatic spread is induction of proteolytic activity. It has been shown that in certain metastatic cells, but not in normal cells, laminin induces an increase in matrix metalloproteinase-2 (MMP-2) activity. MMP-2 is an extracellular marix-degrading endopeptidase, which has a key role in invasion and metastasis and is frequently correlated with tumor progression[15]. Integrins, dystroglycan and other receptors mediate the binding and interactions of laminins to other matrix macromolecules (Fig. 2), by these interactions, laminins play critical role in maintenance of tissue phenotypes, cell shape, movement and cell differentiation[11].

Several previous studies showed that Laminin-5 is frequently expressed at the invading edges of epithelial tumor. Induction of cancer cell migration by this molecule, especially by its γ2 chain, has been suggested as a possible pathogenetic mechanism[17]. In OSCC, Laminin-5 is diminished in the BM, but shows an increased cytoplasmic accumulation and deposition in the stroma close to budding tumor cells within the invasive front. Thus, Laminin-5 guided carcinoma invasion has been suggested[18]. The remodeling of the Laminin-5 matrix is accompanied by a proteolytic processing of the Laminin-5 γ2 chain, which has been described to be important for promoting carcinoma cell migration[19]. OSCC is one of the most invasive human tumors. Unraveling how laminin influences tumor development and invasion is fundamental in the development of prognostic indicators for OSCC.

CONCLUSION

Laminin-5 (recently laminin-332) is a BM glycoprotein that plays an important part in cell migration and mobility and in tumor progression and invasion in SCC. Laminin-5 interacts with integrin α6β4 and epidermal growth factor receptor, thereby activating phosphatidylinositol-3-kinase (pI3K). PI3K regulates several cell processes such as proliferation, growth and apoptosis and its activation has been directly associated with tumor invasion. Laminin-5 therefore promotes tumor invasion in SCC through activation of pI3K and is associated with more advanced TNM stages and worse prognosis.

Laminin-5 could be used as a useful marker of OSCC as a strong positive correlation existed between laminin-5 expression and the degree of differentiation of OSCC. This study provides an evidence for the valuable use of laminin-5 as a marker to evaluate tumor histologic differentiation and aggressiveness.

REFERENCES

1. Thomas, J.K., C.C. Bruce, A. Amit, K.C. Steven and M.W. Christopher, 2011. Cancer prevention in population at high risk of development of oral cancer: Clinical trials with black raspberries. Berries Cancer Prev., 14: 259-260.

2. Farnaz, F., D. Zahra, P. Atessa, M. Nooshin and S. Shiva, 2009. Oral squamous cell carcinoma with an unusual clinical manifestation: A case report. Cases J., 2: 1-4.
3. Kademani, D., 2007. Oral cancer. Mayo Clin. Proc., 82: 878-887.
4. Neville, B., D.D. Damm, C.M. Allen and J. Bouquot, 2009. Squamous Cell Carcinoma. In: Oral and Maxillofacial Pathology. 3rd Edn., Dolan J. St Louis: Saunders; 10: 409-422.
5. Chambers, A.F. and L.M. Matrisian, 1997. Changing views of the role of matrix metalloproteinases in metastasis. J. Nat. Cancer Inst., 89: 1260-1270.
6. Jarvelainen, H., A. Sainio, M. Koulu, T.N. Wight and R. Penttinen, 2009. Extracellular matrix molecules: Potential targets in pharmacotherapy. Pharmacol. Rev., 61: 198-223.
7. Albelda, S.M. and C.A. Buck, 1990. Integrins and other cell adhesion molecules. FASEB J., 4: 2868-2880.
8. Fenyvesi, A., 2003. The prognostic significance of type IV collagen expression in colorectal carcinomas. Arch. Oncol., 11: 65-70.
9. Bosman, F.T. and I. Stamenkovic, 2003. Functional structure and composition of ECM. J. Pathol., 200: 423-428.
10. Colognato, H. and P.D. Yurchenco, 2000. Form and function: The laminin family of heterotrimers. Dev. Dyn., 218: 213-234.
11. Shinohara, M., S. Nakamura, T. Harada, M. Shimada and M. Oka, 1996. Mode of tumor invasion in oral squamous cell carcinoma: Improved grading based on immuno histochemical examination of extracellular matrices. Head Neck., 18: 153-159.
12. Aumailley, M., L. Bruckner-Tuderman, W.G. Carter, R. Deutzmann and D. Edgar *et al*., 2005. A simplified laminin nomenclature. Matrix Biol., 24: 326-332.
13. Erica, F., 2005. Oral cancer screening and diagnosis. Indian J. Dermatol. Venereol. Leprol., 71: 161-165.
14. Pupa, S.M., S. Menard, S. Forti and E. Tagliabue, 2002. New insights into the role of extracellular matrix during tumor onset and progression. J. Cell Physiol., 192: 259-267.
15. Nabeshima, K., T. Inoue, Y. Shimao and T. Sameshima, 2002. Matrix metalloproteinases in tumor invasion: Role for cell migration. Pathol. Int., 52: 255-264.
16. Hood, J.D. and D.A. Cheresh, 2002. Role of integrins in cell invasion and migration. Nat. Rev. Cancer, 2: 91-100.
17. Katayama, M. and K. Sekiguchi, 2004. Laminin-5 in epithelial tumor invasion. J. Mol. Histol., 35: 277-286.
18. Haas, K.M., A. Berndt, K.J. Stiller, P. Hyckel and H. Kosmehl, 2001. A comparative quantitative analysis of laminin-5 in the basement membrane of normal, hyperplastic and malignant oral mucosa by confocal immunofluorescence imaging. J. Histochem. Cytochem., 49: 1261-1268.
19. Koshikawa, N., T. Minegishi, A. Sharabi, Q. Vito and S. Motoharu, 2005. Membrane-type matrix metalloproteinase-1 (MT1-MMP) is a processing enzyme for human laminin gamma 2 chain. J. Biol. Chem., 280: 88-93.