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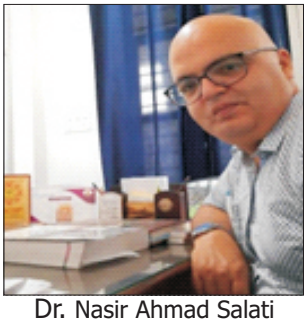
Role of Extracellular Matrix in Progression of Oral Malignancies



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Introduction:

Treatment failure in head and neck cancers can be attributed to multiple factors that are difficult to predict. Additionally, the prognosis often remains uncertain. Extracellular matrix plays a vital role in spread and progression of tumors.

Extracellular Matrix:

The extracellular matrix or ECM is a complex network composed of ground substance, collagen, elastin and various cellular components. More than 300 proteins are present in the ECM in different proportions. These are collagens, proteoglycans, elastin, reticulin and cell-binding glycoproteins. The ground substance is largely viscoelastic, composed mainly of proteoglycans and glycoproteins. Collagen is the most abundant protein in the ECM, known to provide mechanical strength to the tissues. It also maintains structural integrity and helps in resisting tumor cell infiltration. The extracellular matrix (ECM) influences tumor behavior and cellular function in metastatic lesions.

Regulators of tumor progression:

Both positive and negative regulators of cancer development are present in extracellular matrix and stroma. The ability to evade apoptosis, neo-angiogenesis, deregulation of the energy metabolism, resistance to immune detection influence tumor progression. If proper control mechanisms get deactivated, invasion and metastasis is seen. Tumor associated macrophages, CD8+T cells, NK cells, and Cancer Associated fibroblasts (CAFs) increase, as the lesion transforms in malignancy. Different studies indicate the role of tumor-infiltrating lymphocytes (TILs) as a prognostic marker of OSCC. Tumor associated macrophages (TAMs) play an important role in progression of oral cancers, and thus affects prognosis. The tumor associated macrophages also produce VEGF and help in tumor development via neo-vascularization. Mast cells help in the development of primary tumor by the production of many pro-angiogenic factors, such as VEGF, FGF, TGF, TNF-α, tryptase and heparin. These angiogenic factors lead to ECM degradation, angiogenesis, progression and growth of oral squamos cell carcinoma.

Changes in ECM during Tumor Progression:

During tumor progression, reorganization of collagen fibers occurs, which initially prevents the invasion of tumor cells. However, as the tumor advances, stromal changes facilitate the movement of tumor cells within the matrix, leading to metastasis. Solid tumors, such as oral squamous cell carcinoma (OSCC), consist of tumor islands and a modified extracellular matrix (ECM). Matrix metalloproteinases (MMPs) are secreted by cancer-associated fibroblasts and inflammatory cells. As a result, structural components of the ECM are modified and degraded. This degradation increases invasion and progression of the tumor occurs. Throughout tumor progression, the ECM undergoes numerous morphological and architectural alterations.The term 'Tumor Microenvironment' is preferred if the changes in extracellular matrix are defined

Role of Special stains & IHC:

Special stains, including PAS, Masson's Trichrome (MT), and Mucicarmine, are used to study changes in the lamina propria, ECM, and other tissues of the maxillofacial region. Various biomarkers are used to analyze the changes in epithelial islands and ECM. The changes in extracellular matrix are indicative of early invasive changes.

Conclusion:

Treatment failure in head and neck cancers can be attributed to multiple factors that are difficult to predict. Additionally, the prognosis often remains uncertain. Early detection of these lesions continues to be a diagnostic challenge for most clinicians, and idea tools for lesion detection are currently unavailable. Difficulties in evaluating and diagnosing malignant disorders of the oral cavity primarily arise from the lack of standardized criteria for histological grading. Special

stains and IHC are employed to assess qualitative and quantitative differences in various tissues, thereby helping to evaluate the lesion's prognostic potential and risk of recurrence

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