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BASEMENT MEMBRANE: THE SILENT SENTINEL OF ORAL HEALTH

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Abstract

The basement membrane (BM) is a thin layer of intercellular material with a complicated composition that lies between the epithelium and the connective tissue. In general, their sheet-like protein matrices are used to separate epithelial or endothelial cell layers from beneath mesenchymal tissues, serving as a hub to encourage and control interactions between cells, between cells and proteins, as well as providing biophysical support for the tissue above. In the latter case, BM is becoming increasingly well acknowledged as a mediator of growth factor interactions throughout development. Basement membranes are extracellular matrix specializations that play a crucial role in disease development. Certain staining methods can be seen under a light microscope, although routine H&E staining does not reveal a distinct membrane. Despite of basement membrane its importance, there is a lack of easily available literature that provides a comprehensive overview of the state of the art on its composition and pathological guiding techniques such as identifying autoimmune illnesses, evaluating tumour invasion, and distinguishing benign from malignant lesions.

Key words: Autoimmune disease, Carcinogenesis, Basement membrane, Oral health, Collagen and Laminin

INTRODUCTION:

The epithelium lines the cavities and surfaces of all organs, while the mesenchymal cell layer beneath provides signals for epithelial differentiation and proliferation. The loosely packed mesenchymal cells and the tightly packed epithelial cells are separated by a fibrous sheet called the Basement Membrane (BM). These membranes are dense, amorphous materials associated with various cells like muscle, fat, capillary endothelium, epithelium, and Schwann cells. In the cornea, BM is termed Descemet's membrane, and in the placenta, Reichert's membrane. The electron-dense layer, also known as basal lamina, is about 100nm thick and follows the cell surface's contours up to 60 nm from the cell membranes. Initially, the terms BM and basal lamina were used interchangeably, but it is now clear that the basal lamina represents only part of BM. The BM provides structural support, regulates growth agents, and transfers functional information between tissue layers. Defects in BM composition are linked to diseases such as Alport's syndrome, congenital muscular dystrophy (type IA), kidney disease, diabetes mellitus, Alzheimer's disease, multiple sclerosis, and various cancers. This paper highlights the importance of BM composition and function in autoimmune diseases and tumorigenesis, suggesting that differential expression patterns could help predict disease outcomes and develop novel therapeutic strategies [1-3].

Basic Constituents of the Basement Membrane:

The basic structural components of BMs are collagen IV, laminins, perlecan, nidogens, agrin and the heparan sulfate proteoglycans (HSPGs). These fibrous proteins form the intercellular framework. Collagen provides tensile strength producing strong fibers that resist stretching, while elastin passively lengthens when stretched and rebounds when released.

Collagens:
The main component of BM is collagen IV, a large multidomain glycoprotein with a molecular mass of 150–1000 kDa.It has six collagen IV genes that encode a1–a6 chains. At the end of each collagen IV a-chain is a 7Sdomain, a C-terminal lagen IV, and a core collagenous domain. A lattice network of collagen protomers gives BM structural rigidity and creates the lamina densa that EM sees. Three trimeric combinations of collagen IV—a1a1a2, a3a4a5, and a5a5a6—are present, and each one differs in composition depending on the organ and stage of development. With an interrupted triple helical domain, a C-terminal NC1 domain, and an N-terminal non-collagenous domain, collagens XVIII and XV are members of the multiplex in protein family. The multiplex family of proteins includes the collagens XVIII and XV, which have an interrupted triple helical domain, a C-terminal NC1 domain, and an N-terminal non-collagenous domain. After agrin and perlecan, these collagens are among the most prevalent HSPGs in BM. In the lamina densa, the C-terminal domain binds perlecan and laminin. An endostatin fragment found in the NC1 domain could prevent the migration and proliferation of endothelial cells. Collagen XVIII regulates cell adhesion, motility, and angiogenesis through interactions with growth factors and their receptors. The condition was neither improved nor worsened by double deletion of murine collagens XVIII and XV, indicating the absence of compensatory mechanisms [4].
Among the collagenous elements found in different tissue and developmental situations are epithelial collagens XVII an d VII, which are mostly found in the BM lining the mucous membrane of the orifices and the dermal-epidermal junction (DEJ).
With a short N-terminal cytoplasmic domain, an ADAM protease cleavage site, a helical collagenous ectodomain scattered with non-collagenous motifs (NC1-16), and a C-terminal tail that inserts into the lamina densa and binds to laminin-332, collagen XVII is a homotrimer of a1 chains. In the cytoplasmic plaque of the epidermal hemidesmosomes, multiprotein adhesion complexes that bind epithelial cells to the BM, the N-terminal domain interacts with integrin B4, BP230, and pectin. Bone morphogenetic protein (BMP)-1 proteolytically cleaves collagen VII to produce its mature form, which attaches to dermal collagen networks to anchor BM and binds collagen IV as well as the b3 and c2 chains of laminin-332 in the skin.

Laminin: In BM, laminin is the most prevalent non-collagenous protein. Eleven laminin genes (LAMB1 3, LAMC1, 2, and LAMA1–5) encode a, b, and c. The LE modules, which are EGF-like repetitions that serve as spacer elements between domains III and V instead of possessing EGF activity, are what make up these domains. Nidogen-1, which binds to collagen IV, is bound by one of the LE repetitions in domain III of laminin c1 (LEb), joining the supramolecular networks of collagen IV and laminin. Proteolytic cleavage of the N-terminal pro peptide in the LG3 motif initiates this interaction in the a2 chain. The disruption of the actin cytoskeleton linked to these receptors also eliminated laminin assembly, while the G domain's interaction with the cell surface proteins a-dystroglycan and b1 integrin promotes laminin polymerization. Through noncovalent interactions, laminin self-assembles via the N-terminal globular domains. The molecule's long arm is formed by the C-terminal domains I and II of each chain coiling around one another in a helical shape similar to collagens. Laminins can create higher order structures, which are a crucial structural component of BMs, much like collagen IV. For the construction of higher order laminin networks necessary for proper BM function, these LN modules act as a focal interaction.

Syndecan: Syndecan is a transmembrane HSPG that links the actin cytoskeleton to heparin-binding growth-factor receptors on the cell surface. All four of the Syndecan types (SDC1-4) are type I transmembrane proteins that have a transmembrane domain, a short cytoplasmic tail, and a large GAG-bearing ectodomain. Syndecan could control signal transduction by binding growth factor receptors.

Perlecan:
The scaffold protein perlecan uses its core protein and heparan sulfate modifications to interact with several developmental partner proteins. The molecule particularly controls the bioavailability of extracellular FGF in the extracellular milieu. A perlecan deficiency caused the BM components to decrease and the organs to exhibit mechanical instability.

NIDOGENS: The growth of BMs depends on sulfated glycoproteins called nidogen-1 and -2, also referred to as Entactin. N- and O-linked oligosaccharide chains significantly alter them, and they are made up of three globular-like domains, G1, G2, and G3. Nidogen-2 is also present in various protein matrices in the skeleton and vasculature, and these proteins are widely expressed in BMs throughout the body. It is believed that nidogen-1 plays a role in linking the supramolecular networks of collagen IV and laminin c1 by binding to both of these molecules via their G3 and G2 domains. Animals lacking both genes have more severe abnormalities, whereas null Nid1 mice show normal BMs with just minor eye and vascular impairments. The most common BM HSPG is perlecan, a complex multi-domain protein with five different domains (I–V). It is most known for its HS-mediated and core fibroblast growth factor (FGF) binding capacity, as well as the roles that follow. It is important in controlling numerous signaling pathways[5-7].
Formation of Basement membrane
BM formation begins on embryonic day 4–4.5, when the endoderm differentiates and secretes key components such as laminin and collagen IV, essential for epiblast formation and morphogenesis. The key laminin components include five α, four β, and three γ chains, forming 16 unique isoforms depending on subunit composition. These laminins adopt various

shapes and interact with receptors like integrins, agrin, and nidogen. Early BM assembly stages are critical, as inactivation of specific laminin genes in mice leads to developmental failure. Although laminin, collagens, nidogens, and perlecan play vital roles throughout life, they are necessary during early differentiation. Collagen IV, built from six α chains, forms crucial trimeric units in BM types, with differing distributions across tissues. Proteomic studies identified 61 distinct components, including various laminins, collagens, nidogens, and glycoproteins, maintaining tissue integrity and function. The structure of collagen IV and laminins, adjacent to the retina, revealed complex composition and variability, highlighting BM's significance in maintaining organ integrity. BM formation occurs by a self-assembly process involving cell–matrix interactions. Surface adhesion and inter-component binding of laminins play a crucial role by facilitating assembly of remaining components and binding to other BM molecules and cell surfaces that express specific receptors through their LN domains. The BM is anchored to the cytoskeleton via integrin and dystroglycan receptors, essential for triggering signaling pathways across tissues. In order to regulate cellular processes, specialized receptors like the Lutheran protein bind with laminin-511, and receptor tyrosine kinases interact with growth factors attached to the HSPG chains. The laminin scaffold facilitates assembly of remaining components and connections between integrin, dystroglycan, and collagen IV through HSPG interactions. Perlecan interacts with nidogen, alpha-dystroglycan, and collagen IV, aiding BM stabilization. Deletion of laminin γ-subunit disrupts hair morphogenesis, showing its critical role in dermal–epidermal connections. Collagen VII links anchoring fibrils at the stromal–BM interface, while collagen IV self-assembles into networks that maintain tissue integrity. Proteomic and structural studies reveal that many BMs undergo compositional and mechanical changes with aging, contributing to variations in BM strength and flexibility across different tissues[8-12].

Functions of Basement Membrane:
BMs have an incredibly intricate function in controlling differentiation, development, tissue homeostasis, and the body's reaction to infection, damage, and disease. The BM's significance and specialization in many tissues and organs are highlighted by the variety of these functions and the wide range of illnesses linked to BM malfunction. Cell specification and movement during pre-implantation and peri-implantation development are essential for early embryonic development, and BMs are crucial in controlling these processes structurally as well as in relation to growth factor presentation and activity during cell differentiation. Components of the BM are expressed very early in development, and the earliest BMs are formed around implantation. Their critical importance is underscored by the assertion that life cannot exist without them, and any abnormalities in BMs can lead to significant health challenges. A deeper understanding of the assembly of BMs, their interactions with cells, the signaling cues they provide, and their role in maintaining organ structure and function could pave the way for targeted therapies that address both genetic and acquired BM-related diseases[13,14].

Basement Membrane Pathology:
The importance of the basement membrane (BM) in the development of disease is evident from numerous inherited disorders caused by mutations in BM components. Defects in BM components especially the Lmγ1 chain lead to embryonic lethality or severe developmental abnormalities. Non-lethal mutations in BM genes, such as laminins, collagen IV, and perlecan, are noted. Laminin mutations cause congenital muscular dystrophies such as MDC1A and limb-girdle types linked to the LAMA2 gene, resulting in severe muscle weakness and peripheral nerve defects. Junctional Epidermolysis bullosa, resulting from LAMB3, LAMC2, or LAMA3 mutations, manifests as lethal skin blistering due to BM disruption.
Pierson syndrome, resulting from LAMB2 mutations, features proteinuria and ocular defects, indicating BM's role in kidney filtration. Mutations in COL4A3, COL4A4, or COL4A5 cause Alport syndrome, characterized by nephritis, proteinuria, ocular anomalies, and hearing loss. COL4A5 mutations, being X-linked, often lead to more severe manifestations. Defects in COL18A1 are associated with Knobloch syndrome, featuring ocular and cerebrovascular abnormalities, while COL6A1 mutations cause muscular dystrophy and joint laxity. Collagen XVII mutations affect hemidesmosomes, leading to epidermolysis bullosa. Overall, these genetic defects highlight BM's critical role in maintaining tissue integrity and organ function across multiple systems [15]. Table.1 shows various stains ,components of basement membrane and interpretation.

Table.1 Various Stains used for Basement Membrane Identification (Light microscope)

Stain	Component stained	Colour
H&E	Collagen/proteins	Pink
PAS	Glycoproteins/glycolipids	Magenta pink
Silver stains	Reticulin/type IV collagen	Black
Fluorescent PAS–Acriflavine	Glycoproteins	Golden yellow
Masson's trichrome	Collagen differentiation	Blue- green
IHC	Type IV collagen, laminin, proteoglycans	Green

Autoimmune Diseases and Basement Membrane:
In the skin, the epidermis is separated from the dermis by a basement membrane (BM) composed of laminin-511, laminin-332, collagen IV a1a1a2a5a5a6, nidogen-1 and -2, and perlecan. This structure anchors to the dermis via a hemidesmosome, which connects the intermediate filament (Keratin 5/14) of basal keratinocytes to the BM.

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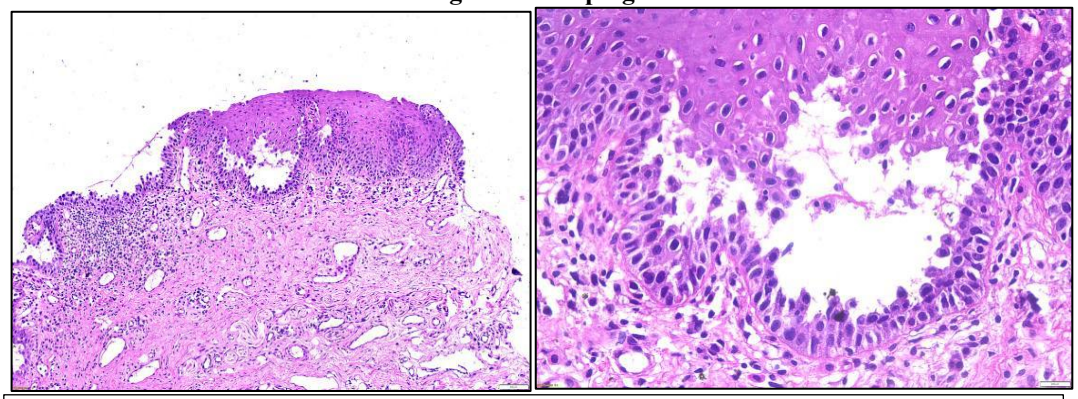
Hemidesmosomes connect through pectin and BPAGe1, associated with transmembrane proteins integrin a6b4 and collagen XVII. Laminin-332 serves as a crucial link between keratinocytes and the BM, interacting with laminins, collagen XVII, and integrin a6b4, collagen VII, nidogen, and fibulin. The connection with nidogen is vital for linking the laminin network to the collagen IV network, and the association with collagen VII is key in establishing links to the dermis. Histopathological examination of Autoimmune diseases reveals intraepidermal cleavage and the lesions are divided into suprabasal and basal subtypes shown Table.2 and Figures1 to 4

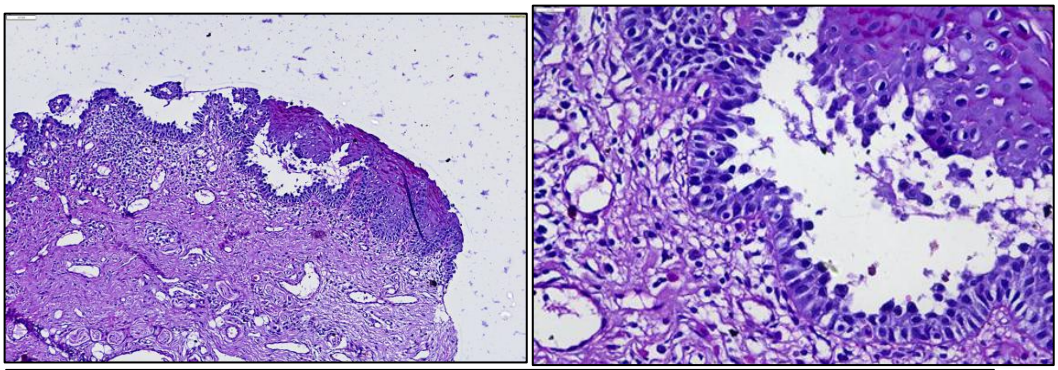
Table .2 Represents the basement membrane split into various Autoimmune conditions with H& E and PAS STAINS

SUPRABASALAR SPLIT	Pemphigus Vulgaris [FIGURE.1] Pemphigus Vegetans Darier's Diseases
BASAL SPLIT	Erythema Multiforme [FIGURE.2] Toxic Epidermal Necrolysis (TEN) Lichen Planus [FIGURE.3] Lupus Erythematous Epidermolysis Bullosa Simplex
SEPARATION AT DERMOEPIDERMAL JUNCTION	1. SPLIT AT LAMINA LUCIDA Bullous Pemphigoid -[FIGURE.4] Cicatricial Pemphigoid Epidermolysis Bullosa Junctional
	2.SPLIT BELOW BASAL LAMINA (SUBLAMINA DENSA) Epidermolysis Bullosa Acquisita Epidermolysis Bullosa Dystrophica Bullous SLE

Figure 1. Pemphigus



H&E STAIN- low & high magnification shows BM preserved; subepithelial split is seen.



PAS Stain - low & high magnification shows BM preserved; subepithelial split is

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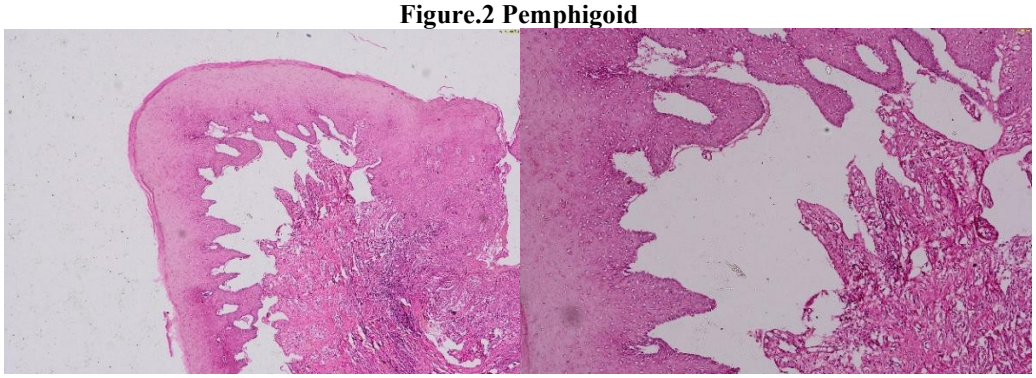
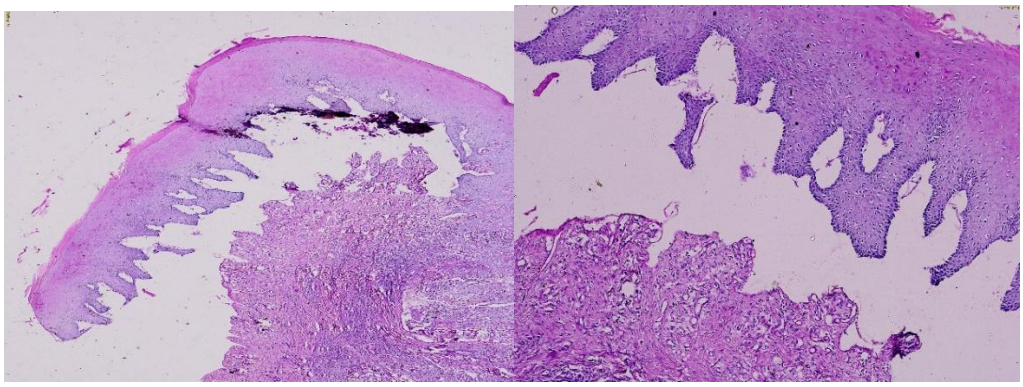
Figure.2 Pemphigoid

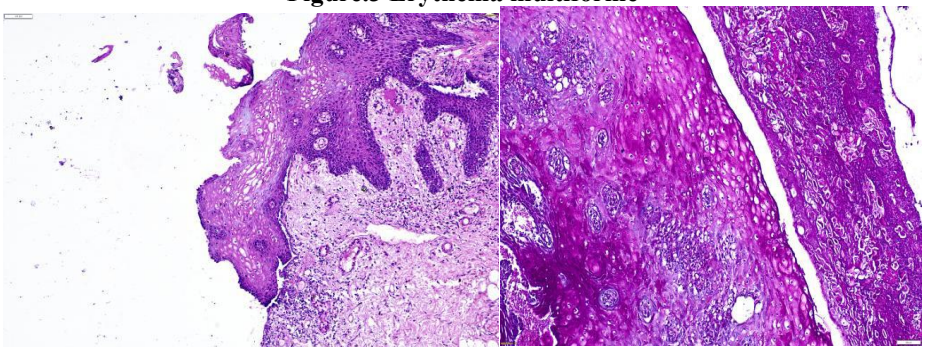


H&E stain - low & high magnification shows subepidermal split at or below BM

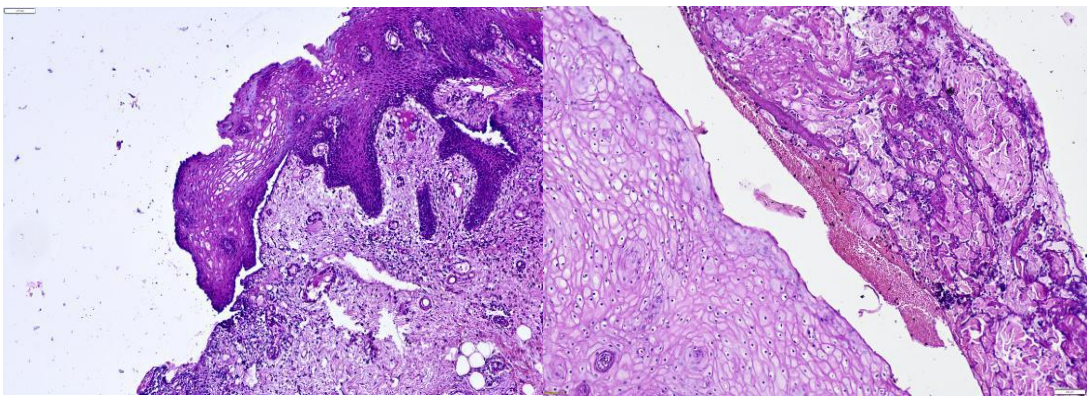


PAS stain low & high magnification shows subepidermal split at or below BM

Figure.3 Erythema multiforme



H&E stain BM damage secondary to cytotoxic T-cell attack



PAS stain BM damage secondary to cytotoxic T-cell attack

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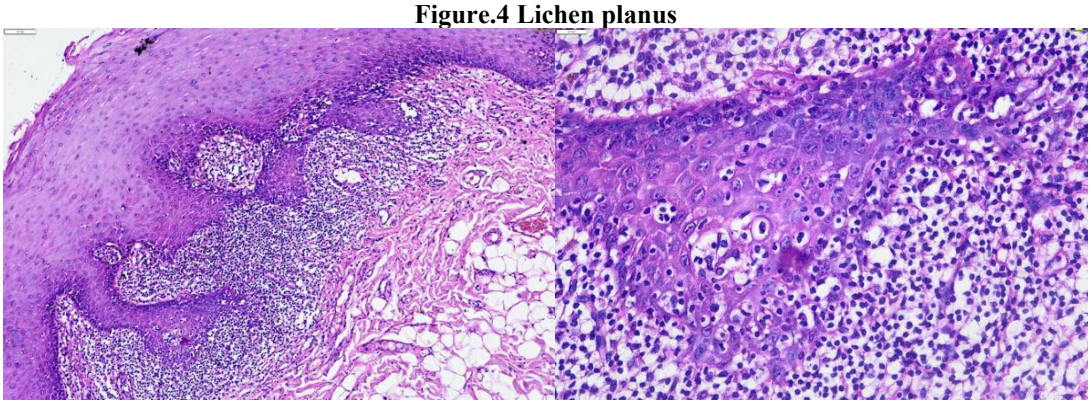
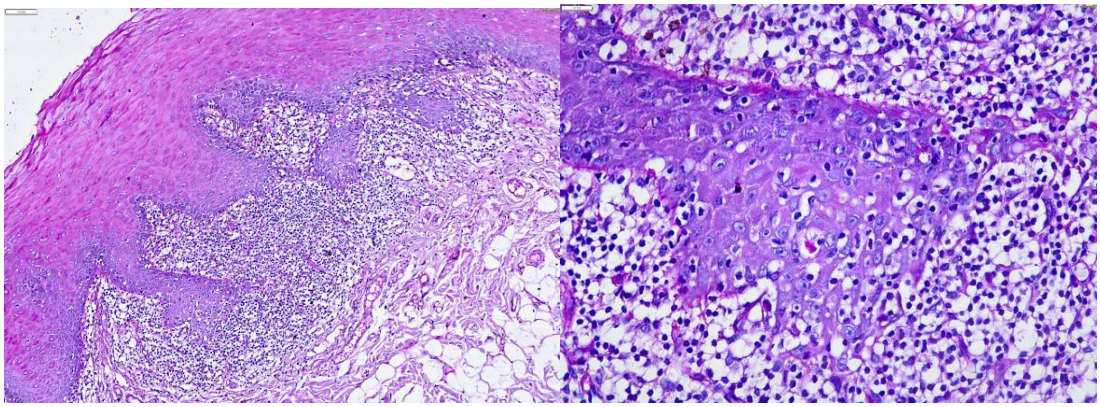
Figure.4 Lichen planus



H&E BM shows thickening and disruption; dense band-like inflammatory cell



PAS BM shows thickening and disruption; dense band-like inflammatory cell

Pemphigus:

Autoantibodies in pemphigus target desmoglein, primarily desmoglein 1 (Dsg1) and desmoglein 3 (Dsg3), which disrupts the keratinocyte adhesion. These autoantibodies bind to specific calcium-sensitive epitopes, with their pathogenic effects established through co-immunoprecipitation of plakoglobin and the identification of Dsg1 and Dsg3 as desmosomal components. Desmoglein has become a focal point for diagnostic enzyme-linked immunosorbent assays (ELISA), which monitor disease activity based on autoantibody levels. Research indicates the IgG4 subclass predominates in PF, and transfer experiments show that antibodies alone can induce disease symptoms without Fc-mediated effects, highlighting how these antibodies disrupt cell adhesion capability. The neonatal form of PV often arises from maternal Dsg3 antibodies, illustrating variable effects based on the newborn's Dsg distribution.

A phenomenon termed desmoglein compensation explains blister localization: in PV, certain patterns of antibodies correspond with distinct disease manifestations, affected by the expression levels of Dsg1 and Dsg3. This model posits that when one desmoglein is inhibited, the other can compensate, preventing injury in certain epidermal layers. The alterations in desmoglein expression and antibody specificity elucidate the pathophysiology of blistering disorders [17,18].

Pemphigoid:

BP180 is a 180 kDa transmembrane glycoprotein with an immunodominant NC16A domain, which induces IgG autoantibody responses. Disease activity correlates with serum IgG levels against this domain. In vitro studies show that BP180-specific antibodies reduce BP180 expression and trigger signaling pathways that lead to keratinocyte detachment and blister formation. BP230, a 230 kDa intracellular hemidesmosomal protein, also acts as a target antigen. Both BP180 and BP230 autoantibodies trigger complement activation, IgG and IgE responses, and protease-mediated tissue injury, leading to subepidermal blistering characteristic of bullous pemphigoid in figure.2[19,20].

Epidermolysis bullosa

Defects in genetic conditions known as epidermolysis bullosa (EB) highlight the importance of basement membrane (BM) protein interactions in preserving epidermal integrity. It is typically present from birth and is characterized by bullous lesions or blisters that can develop spontaneously or as a result of minor trauma. Different EB manifestations are caused by more than 1000 mutations in 13 genes related to structural proteins in

the skin. EB simplex, junctional EB, recessive dystrophic EB, and dominant dystrophic EB are the four main subtypes of EB. Skin cleavage occurs at the dermal–epidermal interface and higher dermis in junctional and dystrophic forms of EB, respectively, and skin fragility varies depending on the molecular abnormalities [21].

ORAL CARCINOGENESIS AND BASEMENT MEMBRANE

Cancer is characterized by dysregulation of the basement membrane (BM), and in breast, prostate, and colon cancers, overexpression of laminin is associated with cell hyperproliferation. While mutations in genes encoding cellular components are known drivers of malignancy, ECM protein gene mutations are not typically viewed as oncogenic. However, laminins play a prominent role in oncogenesis, influencing transformed phenotypes, metastasis, and cancer aggressiveness. Changes in laminin expression, epigenetic and post-transcriptional regulation of laminin chains, and limited proteolysis within the tumor microenvironment (TME) are crucial in malignant transformation. Laminin and perlecan promote angiogenesis, supplying oxygen to proliferating tumor cells.[22] Oral cancer, predominantly oral squamous cell carcinoma (OSCC), constitutes a significant portion of global cancer cases. It commonly affects the lips, tongue, palate, and pharynx. Understanding molecular mechanisms underlying OSCC progression is vital for early detection and better outcomes. When laminin antibodies are used in immunohistochemical investigation of OSCC samples, well-differentiated cases exhibit linear staining at the epithelial–stromal boundary, but poorly-differentiated cases have strong cytoplasmic expression in tumor cells. Recent research demonstrates how laminins (LMs) interact with tumor cells, stromal components, and the TME to play a complex role in oral carcinogenesis. One of the most researched LMs in oral cancer is LM-332, which is found in OSCC but absent from dysplastic tissue [22,23]. The presence of the LM-γ2 chain in tumor-budding areas encircled by myofibroblasts suggests that it contributes to OSCC invasion and poor prognosis. Thus, LM-332 or its γ2 chain may be used as early prognostic and diagnostic indicators. Complex regulation is revealed by in vitro investigations, as LM-332 binding to α3β1 integrin increases adhesion mediated by E-cadherin and decreases motility in weakly invasive. In contrast, LM-γ2 silencing inhibits the creation of LM-332, which increases migration and tumorigenicity. This is associated by decreased α3β1 integrin and poor adherence of E-cadherin, which are indicators of the epithelial–mesenchymal transition (EMT). In OSCC cells, EMT activation by the Snail transcription factor is accompanied with downregulation of LM-332, although LM-γ2 levels are unaltered, indicating selective regulation. Tumor invasion is closely linked to elevated LM-γ2 expression. Long non-coding RNAs (lncRNAs) CASC9 and BBOX1 are involved in the regulation of LM-γ2; they sponge miR-545-3p and miR-3940-3p, preventing LAMC2 from being downregulated and raising the levels of LM-γ2 protein. Constant LAMC2 expression sustains LM-γ2 deposition, improving cell motility, even in the face of EMT-induced decrease in heterotrimeric LM-332. Other LM chains may also be regulated by snail, suggesting that several LMs work in concert to promote OSCC invasion and EMT.Monomeric LM-γ2 affects OSCC motility and proliferation by activating the EGFR/ERK pathway, either indirectly through integrins or directly via LM-γ2 proteolytic fragments interacting with EGFR. A positive feedback loop between EGFR and LM-γ2 expression has been identified in OSCC, promoting tumor progression. Additionally, LM-γ2–enriched extracellular vesicles secreted by OSCC cells stimulate lymphangiogenesis, facilitating lymphatic dissemination. Other LM chains also contribute to OSCC progression. Amplification of LAMA3 and increased LM-β3 expression correlate with enhanced invasiveness and metastasis. The LM-β3 chain may promote formation of specialized ECM-degrading structures, aiding invasion, though it signaling pathways remain unclear. LM-111-derived peptide AG73 enhances OSCC migration and invasion through syndecan-1 and β1 integrin signaling, which upregulate MMP-9 secretion—a key enzyme in ECM degradation, angiogenesis, and migration [24-29]. To influence OSCC motility and proliferation, monomeric LM-γ2 either directly interacts with EGFR through LM-γ2 proteolytic fragments or indirectly through integrins to activate the EGFR/ERK pathway. In OSCC, a positive feedback loop between EGFR and LM-γ2 expression has been found, which accelerates the growth of the tumor. Furthermore, OSCC cells release LM-γ2-enriched extracellular vesicles that promote lymphangiogenesis and aid in lymphatic diffusion. The evolution of OSCC is likewise influenced by other LM chains. greater LM-β3 expression and LAMA3 amplification are associated with greater metastasis and invasiveness. Although its signaling routes are still unknown, the LM-β3 chain may facilitate invasion by encouraging the creation of specific ECM-degrading structures. Through syndecan-1 and β1 integrin signaling, which increase MMP-9 secretion—a crucial enzyme in ECM destruction, angiogenesis, and migration—LM-111-derived peptide AG73 promotes OSCC migration and invasion[30]. The C16 peptide from LM-γ1 cleavage also increases OSCC invasiveness by triggering ERK1/2, Src kinase, and β1 integrin, which controls invadopodia activity and ECM degradation. Additionally, OSCC invasiveness is modulated by the LAMA4 and LAMA5 genes[31]. EMT effectors, such as Snail, affect tumor cell motility by upregulating LAMA4 and downregulating LAMA5. Direct Snail binding to the LAMA4 promoter is confirmed by chromatin immunoprecipitation investigations, which supports the progression of EMT. Several BM components, such as laminin and type IV collagen, are released by both stromal and tumor cells in highly metastatic instances, while only stromal cells do so in less aggressive tumors, according to recent proteomic investigations of metastatic tumors. This shows that primary tumor cells actively change the composition of the BM via modifying signaling and ultrastructure in order to promote metastasis. All of these results demonstrate how important laminin isoforms—particularly LM-332 and LM-γ2—are to the onset and spread of OSCC. Through intricate signaling involving integrins, EGFR, and lncRNA–miRNA regulation, laminin changes impact tumor–stroma interactions, EMT induction, and invasive behavior. Gaining knowledge of these biological pathways can help identify treatment targets and diagnostic biomarkers for oral cancer [32-37].

CONCLUSION

The basement membrane is integral to tissue stability, polarity, and signaling. In oral pathology, BM integrity is a key diagnostic and prognostic marker Understanding BM biology aids in differentiating benign from malignant lesions, assessing tumor invasion, diagnosing autoimmune diseases, and guiding regenerative approaches.

REFERENCE:

1. Engvall E. (1995) Structure and function of basement membranes. Int J Dev Biol. Oct;39(5):781-7. PMID: 8645562.
2. Abrahamson DR, Hudson BG, Stroganova L, Borza DB(2009). Molecular and cellular assembly of the basement membrane. Cell Tissue Res.;339(1):107-24. doi:10.1007/s00441-009-0838-4.
3. Kannan S, Balaram P, Chandran GJ, Pillai MR, Mathew B, Nalinakumari KR, et al. Alterations in expression of basement membrane proteins during tumour.
4. Alport M, Couchman JR, Parks WC, Sage EH(2018.) Basement membrane. In: Aplin JD, editor. Encyclopedia of Reproduction. 2nd ed. Elsevier; p. 388-94.
5. Halfter W, Candiello J, Hu H, Zhang P, Schreiber E, Balasubramani M.(2013) Protein composition and biomechanical properties of in vivo-derived basement membranes. Cell Adh Migr. 7(1):64-71. doi:10.4161/cam.22485.
6. P.D. Yurchenco, P.S. Amenta, B.L. (2004)Patton, Basement membrane assembly, stability and activities observed through a developmental lens, Matrix Biol. 22 521–538.
7. M.J. Randles, M.J. Humphries, R. Lennon. (2017) Proteomic definitions of basement membrane composition in health and disease, Matrix Biol. 57-58 ;12–28.
8. P.D. Yurchenco. (2011). Basement membranes: cell scaffoldings and signaling platforms, Cold Spring Harb.Perspect. Biol. 3.
9. A. Fleger-Weckmann, Y. Ustun, J. Kloepper, R. Paus, W. Bloch, Z.L. Chen, et al. (2016) Deletion of the epidermis derived laminin gamma1 chain leads to defects in the regulation of late hair morphogenesis, Matrix Biol. 56 ;42–56.
10. J. Wegner, K. Loser, G. Apsite, R. Nischt, B. Eckes, T. Krieg, et al., (2016) Laminin alpha5 in the keratinocyte basement membrane is required for epidermal-dermal intercommunication, Matrix Biol. 56 ;24–41.
11. Z. Sun, S.S. Guo, R. Fassler. (2016) Integrin-mediated mechanic transduction, J. Cell Biol. 215 ;445–456.
12. A.J. Engler, S. Sen, H.L. Sweeney, D.E. Discher. (2006) Matrix elasticity directs stem cell lineage specification, Cell 126 ;677–689. J.H. Miner, P.D. Yurchenco, Laminin functions in tissue morphogenesis, Annu. Rev. Cell Dev. Biol. 20 (2004) 255–284.
13. N. Smyth, H.S. Vatansever, P. Murray, M. Meyer, C. Frie, M. Paulsson, et al., (1999) Absence of basement membranes after targeting the LAMC1 gene results in embryonic lethality due to failure of endoderm differentiation, J. Cell Biol. 144 ;151–160.
14. P.D. Yurchenco, B.L. Patton. (2009) Developmental and pathogenic mechanisms of basement membrane assembly, Curr. Pharm. Des. 15 ;1277–1294.
15. J. Khoshnoodi, V. Pedchenko, B.G. Hudson. (2008) Mammalian collagen IV, Microsc. Res. Tech. 71 ;357–370.
16. Kneisel A, Hertl M.(2011) Autoimmune bullous skin diseases. Part 2: diagnosis and therapy. J Dtsch Dermatol Ges.;9(12):927-47. doi:10.1111/j.1610-0387.2011.07859.x.
17. Schmidt E, Kasperkiewicz M, Joly P. (2019) Pemphigus. Lancet.;394(10201):882-94. doi:10.1016/S0140-6736(19)31778-7.
18. Amagai M, Stanley JR.(2012) Desmoglein as a target in skin disease and beyond. J Invest Dermatol.;132(3 Pt 2):776-84. doi:10.1038/jid.2011.390.
19. Rashid KA, Khachemoune A. (2007)Bullous pemphigoid: a review of the literature. Am J Clin Dermatol.;8(6):377-86. doi:10.2165/00128071-200708060-00003.
20. Schmidt E, Zillikens D. Pemphigoid diseases. Lancet. 2013;381(9863):320-32. doi:10.1016/S0140-6736(12)61140-4.
21. Mutalik SS, Inamdar AC, Ajantha GS. (2015)Diagnostic procedures for autoimmune vesiculobullous diseases. J Oral Maxillofac Pathol.;19(2):147-53. doi:10.4103/0973-029X.164529.
22. Rani V, McCullough M, Chandu A.(2013) Assessment of laminin-5 in oral dysplasia and squamous cell carcinoma. J Oral Maxillofac Surg.;71:1873–9.
23. Marangon Junior H, Rocha VN, Leite CF, de Aguiar MCF, Souza PEA, Horta MCR.(2014) Laminin-5 gamma 2 chain expression is associated with intensity of tumor budding and density of stromal myofibroblasts in oral squamous cell carcinoma. J Oral Pathol Med.;43:199–204.
24. Degen M, Natarajan E, Barron P, Widlund HR, Rheinwald JG.(2012) MAPK/ERK dependent translation factor hyperactivation and dysregulated laminin γ2 expression in oral dysplasia and squamous cell carcinoma. Am J Pathol.;180:2462–78.
25. Kuratomi Y, Kumamoto M, Kidera K, Toh S, Masuda M, Nakashima T, et al. (2006).Diffuse expression of laminin gamma2 chain in disseminating and infiltrating cancer cells indicates a highly malignant state in advanced tongue cancer. Oral Oncol.;42:72–5.
26. Yuen HW, Ziober AF, Gopal P, Nasrallah I, Falls EM, Meneguzzi G, et al. (2005)Suppression of laminin-5 expression leads to increased motility, tumori genicity, and invasion. Exp Cell Res.;309:198–210.

27. Takkunen M, Grenman R, Hukkanen M, Korhonen M, García De Herreros A, Virtanen I. (2006) Snail-dependent and -independent epithelial mesenchymal transition in oral squamous carcinoma cells. J Histochem Cytochem.;54:1263–75.
28. Ning B, Guo S, Mei Y.(2021) Long non-coding RNA CASC9 promotes tumor progression in oral squamous cell carcinoma by regulating microRNA 545-3p/laminin subunit gamma 2. Bioengineered.;12:7907–19.
29. Zhao C, Shi W, Chen M. (2022)Long non-coding RNA BBOX1-antisense RNA 1 enhances cell proliferation and migration and suppresses apoptosis in oral squamous cell carcinoma via the miR-3940-3p/laminin subunit gamma 2 axis. Bioengineered.;13:11138–53.
30. Wang SH, Liou GG, Liu SH, Chang JS, Hsiao JR, Yen YC, et al.(2019)Laminin γ2-enriched extracellular vesicles of oral squamous cell carcinoma cells enhance in vitro lymphangiogenesis via integrin α3-dependent uptake by lymphatic endothelial cells. Int J Cancer.;144:2795–810.
31. Ono Y, Nakanishi Y, Gotoh M, Sakamoto M, Hirohashi S.(2002) Epidermal growth factor receptor gene amplification is correlated with laminin-5 γ2 chain expression in oral squamous cell carcinoma cell lines. Cancer Lett.;175:197–204.
32. Siqueira AS, Pinto MP, Cruz MC, Smuczek B, Cruz KS, Barbuto JA, et al.(2016) Laminin-111 peptide C16 regulates invadopodia activity of malignant cells through β1 integrin, Src and ERK 1/2. Oncotarget;7:47904-17.
33. Takkunen M, Ainola M, Vainionpää N, Grenman R, Patarroyo M, García de Herreros A, et al. (2008)Epithelial-mesenchymal transition downregulates laminin alpha5 chain and upregulates laminin alpha4 chain in oral squamous carcinoma cells. Histochem Cell Biol. ;130:509–25.
34. Tanis T, Cincin ZB, Gokcen-Rohlig B, Bireller ES, Ulusan M, Tanyel CR, et al.(2014) The role of components of the extracellular matrix and inflammation on oral squamous cell carcinoma metastasis. Arch Oral Biol. ;59:1155–63.
35. Siqueira AS, Gama-De-Souza LN, Arnaud MVC, Pinheiro JJV, Jaeger RG. (2010) Laminin-derived peptide AG73 regulates migration, invasion, and protease activity of human oral squamous cell carcinoma cells through syndecan-1 and beta1 integrin. Tumour Biol. ;31:46–58.
36. Arakeri G, Brennan PA. Oral cancer: detection of invasion in potentially malignant disorders using histopathological and special stains.(2013) Br J Oral Maxillofac Surg. ;51(6):452-7. doi:10.1016/j.bjoms.2012.10.010.
37. Snijders AM, Schmidt BL, Fridlyand J, Dekker N, Pinkel D, Jordan RCK, et al.(2005) Rare amplicons implicate frequent deregulation of cell fate specification pathways in oral squamous cell carcinoma. Oncogene. ;24:4232–42.