REVIEW

DESMOSOMES IN ORAL DISEASES – A REVIEW

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Abstract:

Desmosomes are the adhesion proteins that function both as an adhesive complex and as a cell surface attachment site for keratin intermediate filaments of the cytoskeleton. Desmosomes are more widely distributed along the lateral membranes. Desmosomes contain two types of transmembrane proteins desmogleins and desmocollins which belong to cadherin family. These desmosomal cadherins are linked to the keratin cytoskeleton via several cytoplasmic proteins such as desmoplakin and plakoglobin. Desmosomes play a critical role in the maintenance of normal tissue architecture. They are frequently mutated and desmosomal adhesion is compromised by antibodies in autoimmune diseases and result in blistering disorders in epithelium. Inherited mutations in genes in desmosomal constituents can also affect the skin and the heart. Desmosomes may have a tumour suppressor function and desmosomal cadherins have the capacity to suppress the invasiveness of cells in culture.

Keywords: Desmoplakin, antibodies, adhesion, pemphigus, autoimmune

INTRODUCTION

The desmosome was first observed in the spinous layer of epidermis by the Italian pathologist Giulio Bizzozero(1846-1901) and it is first named as ‘’nodes of Bizzozero’’. The term desmosomes was later coined by Josef Schaffer in 1920 and it is derived from the Greek words ‘’desmo’’ meaning bond and ‘’soma’’ meaning body (1).

Desmosomes mediate cellular adhesion and are highly organised structures. It is an important structural entity that links epithelial cells to each other and also attaches the keratin intermediate filaments cytoskeleton to the cell surface (2). But they also found in some non-epithelial cells such as myocardial cells in heart. They associated with desmin intermediate filaments and follicular dendritic cells of lymph nodes where they interact with vimentin intermeadiate filaments. Desmosomes provide structural continuity and mechanical strength on entire tissues by linking the intermediate filaments of adjacent cells (3). Other than the main function of providing mechanical integrity to tissues, desmosomes provide dynamic structures that respond with exquisite sensitivity to environmental cues, allowing for tissue remodelling during development, differentiation, wound healing and invasion. And also play an active role in signal cascades initiated by extracellular matrix ligands and growth factors during development and in the adult (4).

In some human diseases, this desmosomal adhesion is disrupted and results in severe consequences for tissue intergrity which causes blistering disorders. This review is focused on the adhesive function of desmosomes and the role of desmosomes in oral diseases.

GENETIC STRUCTURE OF DESMOSOMES

The major constituents of desmosome belong to three gene families. They are cadherin, aemadillo and plakin families. Two types of desmosomal cadherins are present named as Desmogleins (Dsgs) and desmocollins (Dscs) (5). It was found that there are three isoforms of desmocollins (Dsc 1-3) and four isoforms of desmogleins (Dsg 1-4) in humans. All desmosomal cadherin genes are clustered at chromosome 18q12.1. (6). These cadherins typically show homophillic interactions which supports cell-cell adhesion and tissue patterning. And most studies show that both desmocollins and desmogleins are required for strong cell-cell interactions.these proteins function as the intercellular ‘’glue’’(7). Armadillo family of proteins present in desmosomes are plakoglobin and the plakophilins. Plakoglobin is the best characterized armadillo protein in the desmosome(8). Armadillo proteins mediate important signal transduction pathways and it facilitate the tethering of desmoplakin and keratin intermediate filaments to the desmosome and regulate clustering of the desmosomal components (9). Desmoplakin is the most abundant component of the desmosome (10). It acts as the key linker between intermediate filament and the plasma membrane (11). Other members of desmoplakin gene family are BP230, Plectin & IFAP300 (12).

ORAL DISEASES

PEMPHIGUS

Among all the types of pemphigus oral lesions are commonly seen with pemphigus vulgaris and paraneoplastic pemphigus (13).

PEMPHIGUS VULGARIS

It is an autoimmune blistering disease of skin and the mucous membranes due to the production of IgG

autoantibodies against desmoglein 3 which results in separation of keratinocytes from each other and replaced by fluid the blister (14). Patients complain of painful, persistent ulcers and sloughing. It can affect any part of the oral cavity. And most commonly seen first in the buccal mucosa, palatal mucosa and lips (15). Blisters are rupture quickly and are often unnoticed. 50-70% of patients get oral lesions. It is painful and slow to heal. It may spread to larynx and may cause hoarseness of voice. Oral corticosteroids are the drug of choice for treatment.

PARANEOPLASTIC PEMPHIGUS

This is always affects the oral mucosa and it is a rare blistering and ulcerating disease. Oral lesions are very painful and consist of widespread, irregular shallow ulcers at multiple oral sites. It causes hemorrhagic, crushing blisters and erosions. In this auto antibodies are always produced against multiple antigens in the basement membrane zone, desmoglia and intra epithelial plaques, resulting in the disease. This indicates a poor prognosis and it is treated by systemic corticosteroids often combined with other immune suppressive agents. (14)

DARIER'S DISEASE

Darier's disease is an autosomal dominantly inherited genodermatosis caused by mutations in ATP2A2 gene. (16, 17). The defective gene in Darier disease is ATP2A2 found on chromosome 12q23-24.1 (18). The mucous membrane involvement is recognized as white umblicate or cobblestone papules in oral cavity (19).

SQUAMOUS CELL CARCINOMA

The paper entitled "Desmosomal component expression in normal, dysplastic and oral squamous cell carcinoma" by N.Narayana et al. shows that during malignant transformation, cell-cell adhesion is often reorganized with dramatic changes in various junction proteins. The authors showed that the desmomal plaque proteins desmoplakin and plakophilin-1 are downregulated in dyplasias and squamous cell carcinomas as compared to control epithelia. The results identify these proteins as potential markers for neoplastic lesions of the oral cavity (20).

CONCLUSION

In the past decade lot of studies and research has been made to understand the structure , components and the role of desmosomes in autoimmune blistering diseases and also the mutations in the genes encoding a number of desmosomal constituents been identified. Overall these studies have confirmed the importance of desmosomes for cell adhesion and the maintenance of normal tissue architecture. Although these oral diseases are comparatively uncommon conditions, as a dental practitioner they should have high level of awareness of these diseases to recognize and manage them or refer patients when appropriate.

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