Title

The Basement Membrane Zone in Asthma: The Supracellular Anchoring Network.

Journal

Current Respiratory Medicine Reviews, 9(4)

ISSN

1573-398X

Authors

Evans, Michael J

Miller, Lisa A

Hyde, Dallas M

Publication Date

2013-08-01

DOI

10.2174/1573398x09666131121231852

Peer reviewed

HHS Public Access

Author manuscript

Curr Respir Med Rev. Author manuscript; available in PMC 2022 May 02.

Published in final edited form as:

Curr Respir Med Rev. 2013 August ; 9(4): 268–273. doi:10.2174/1573398x09666131121231852.

The Basement Membrane Zone in Asthma: The Supracellular Anchoring Network

Michael J Evans, **Lisa A Miller**, **Dallas M Hyde**

California National Primate Research Center; and Center for Comparative Respiratory Biology and Medicine; University of California, Davis, CA 95616

Abstract

Thickening of the basement membrane zone (BMZ) is a characteristic feature of airway remodeling in the lungs of asthmatics. However the significance of a thickened BMZ in the pathology of the asthmatic airway is not known. In this review we show that the columnar epithelium is linked to the reticular BMZ through the supracellular anchoring network. We discuss the evidence that changes in the width of the BMZ in control airways are part of a supracellular anchoring mechanism for increasing the strength of attachment between the airway epithelium and the extracellular matrix (ECM). We then review the effects of asthma on this anchoring mechanism. We conclude that both thickening of the BMZ and sloughing of columnar epithelium (creola bodies) in asthma represent abnormalities in the supracellular anchoring network attaching the airway epithelium to the ECM. Future research directed toward studying the regulation and development of the supracellular anchoring network may help better understand sloughing of columnar epithelium and the significance of reticular BMZ thickening in the asthmatic airway.

Keywords

basement membrane zone; supra cellular anchoring network; airway epithelium; asthma

INTRODUCTION

Thickening of the BMZ is a characteristic feature of airway remodeling in the lungs of asthmatics (1). Thickening of the reticular BMZ has been reported in the upper and lower respiratory tract in asthmatics (2) and in experimental models of asthma (3). Increases in the thickness of the BMZ are correlated with other remodeling changes in the airway such as increases in smooth muscle, submucosal glands and inner wall area (4–6). This information indicates that thickening of the BMZ is a general characteristic that occurs throughout the airways and is an intrinsic part of the asthma phenotype. However, the amount of BMZ thickening is not correlated with the severity of the disease (7, 8).

CORRESPONDING AUTHOR: Michael J Evans, PhD, California National Primate Research Center, One Shields Avenue, University of California, Davis, CA 95616. Telephone: (530) 754-7540, Fax: (530) 752-7690, mevans@ucdavis.edu.

CONFLICT OF INTEREST

There is no conflict of interest for any of the authors.

Currently the significance of a thickened reticular BMZ in the pathology of the asthmatic airway is not known. A thickened reticular BMZ in asthma is thought to be due to an imbalance in expression of growth factors due to tissue damage caused by chronic inflammation and/or cell sloughing (9, 10).. However a recent review concerning the airway epithelium in asthma suggested that thickening of the reticular BMZ may not to be the result of chronic inflammation and tissue damage but other factors (11). This concept was based on studies showing the presence of reticular BMZ thickening in children younger than 3 with persistent wheezing before the diagnosis of asthma. Thickening occurs early in the disease and is present in symptomatic children 1 year and older (6, 12, 13). This concept has also been mentioned in a review stressing the importance of the epithelium in asthma (14). However in a recent review of remodeling in childhood asthma it was pointed out that thickening of the reticular BMZ in wheezing children is not a specific requirement for asthma, since not all of these children went on to develop asthma (15). The authors suggested that the thickened BMZ may not be directly related to the asthma but to something else.

In previous reviews we discussed development of the BMZ, the role of the BMZ in regulating growth factor trafficking, and the effects of asthma on these processes (16, 17). In this review we discuss the evidence that changes in the width of the BMZ in control airways are part of a supracellular anchoring mechanism for increasing the strength of attachment between the airway epithelium and the extracellular matrix (ECM). We then discuss the effects of asthma on this anchoring mechanism. We conclude that both thickening of the BMZ and sloughing of columnar epithelium in asthma represent abnormalities in the supracellular anchoring network attaching the airway epithelium to the ECM.

BACKGROUND

Characteristics of the Supracellular Anchoring Network in the Conducting Airways

The supracellular anchoring network is the means by which the airway epithelium is attached to the ECM. In this network columnar cells are attached to basal cells by means of desmosomes. Basal cells are attached to the BMZ with hemidesmosomes. Within basal cells desmosomes are connected to hemidesmosomes by intermediate filaments (cytokeratin 5 & 14) (Fig 1). The BMZ is the first extracellular element in the anchoring network. It has three anatomical zones, the lamina lucida, lamina densa and lamina reticularis (Table I). Each of these zones plays a role in the supracellular anchoring net work. The lucida BMZ is the area between the epithelial cells and the densa BMZ. This zone contains various epithelial integrins including the integrin α6β4 of hemidesmosomes that attach basal cells to the densa BMZ. The densa BMZ is a thin sheet of connective tissue made up of non-fibrillar type IV collagen, laminins, entactin/nidogen and heparan sulfate proteoglycan. It is commonly referred to as the basal lamina, basement membrane or true basement membrane. Laminin 5 (laminin 332) is an essential molecule in the densa BMZ. It links the basal cells with extracellular elements of the anchoring network by binding with the α6β4 integrin in the lucida BMZ and collagen VII anchoring fibrils in the reticular BMZ (18) (Fig 2). The reticular BMZ is the region of the BMZ that is visible in standard light microscope preparation and becomes thickened in asthma. It is commonly referred to as the reticular

basement membrane. It consists of collagen types I, III, V, VI and VII collagen and three BMZ specific proteoglycans (perlecan, collagen XVIII and bamacan) (19). Collagen types I, III and V form heterogeneous fibers that account for the thickness of the reticular BMZ (20). Type VII collagen is part of the anchoring fiber complex between the densa BMZ and the reticular BMZ (21). The collagen VII anchoring fibers bind to laminin 332 molecules in the densa BMZ (18) and then intertwine and bind to collagen I fibers in the reticular BMZ (21). In this interconnected sequence (desmosomes, hemidesmosomes, laminin 332, collagen VII and reticular BMZ) the reticular BMZ is last and acts as the foundation of the anchoring network attaching the epithelium to the ECM. The reticular BMZ is attached to the underlying ECM by oxytalan fibers of the elastic fiber system (22, 23) (Fig 1).

Relationship of BMZ Width to the Height of the Columnar Epithelium and the Supracellular Anchoring Network

The width of the reticular BMZ was first shown to be related to the height of the columnar epithelium by Tsartsali et al (24). In a study of humans that included 43 infants 10 children and 18 adults, without respiratory disease or asthma, they found that increases in the height of the columnar epithelium were closely related to similar increases in the width of the reticular BMZ ($r = 0.65$). They speculated that as a taller epithelium developed, thickening of the reticular BMZ was necessary in order to anchor the epithelium to the ECM. Studies of the supracellular anchoring network in the lung support this concept. In the conducting airways the height of the columnar epithelium is variable. In large airways the height of the columnar epithelium is much taller than in the smaller airways (25). Changes in epithelial height can be studied in developing airways where the height of the epithelium increases as the airway grows in circumference (Fig 3). Previous studies in developing airways of the rat found that an increase in height of the epithelium is accompanied by an increase in elements of the supracellular anchoring network (26). In this period of growth there was an increase in basal cells that resulted in increased desmosome attachment with columnar cells and hemidesmosome attachment between basal cells and the densa BMZ (Figs 4 & 5). In a more recent paper of developing airways in the rhesus monkey, collagen VII anchoring fibers and the reticular BMZ were studied. During the growth of the airway there was an increase in the amount of collagen VII anchoring fibers within the reticular BMZ (27). There was also increase in the width of the reticular BMZ (20). Both the increase in width of collagen VII and the width of the reticular BMZ were closely related to the increasing height of the adjacent epithelium (Fig 6). These studies of the supracellular anchoring network in developing airways, demonstrate that the amount of anchoring (desmosomes, hemidesmosomes, collagen VII and reticular BMZ) is closely related to the height of the adjacent columnar epithelium. This relationship indicates that in the control airways the width of the reticular BMZ is a reflection of the amount of anchoring in the supracellular network necessary to support the adjacent columnar epithelium. Thus a tall epithelium in the proximal bronchi would have a thicker reticular BMZ than a shorter epithelium in the distal bronchi, supporting the conclusions of Tsartsali et al (24).

THE SUPRACELLULAR ANCHORING NETWORK IN ASTHMA

Sloughing of Columnar Epithelium

Two characteristics of the asthma phenotype feature elements of the supracellular anchoring network (1) sloughing of columnar epithelium and (2) thickening of the reticular BMZ. Sloughing of airway epithelium is a pathology associated with desmosome adhesion between columnar cells and basal cells within the supracellular anchoring network (28). In the asthmatic airway the sloughed patches of epithelium are termed creola bodies (29). Formation of creola bodies occurs when the desmosome attachments between columnar and basal cells are broken. The cause of epithelial sloughing is thought to be an influx of inflammatory cells (30). An influx of inflammatory cells is common to a number of lung diseases, but the production of creola bodies is unique to the asthmatic airway (29). Creola bodies are made up of columnar airway cells connected to each other with desmosomes and appear as palisades of sloughed cells not as single cells. This characteristic suggests that changes within the supracellular anchoring system of the asthmatic airway epithelium resulted in a weaker attachment between basal cells and columnar cells than between adjacent columnar cells.

In human allergic asthmatic airways several changes of the supracellular anchoring network have been reported. Shahana et al (31) and Shebani et al (32) in detailed studies using electron microscopy showed that desmosome attachments between columnar cells and basal cells were significantly smaller in allergic asthmatic airways than controls. Shahana et al (31) also found that the densa BMZ was significantly wider in allergic asthmatic airways. These authors concluded that reduced desmosomes contact may be an important factor associated with epithelial shedding in asthma. In a study concerning laminin in the densa BMZ, Amin et al (33) found that laminin 332 molecules are assembled in an uncoordinated manner in allergic asthmatic airways. The authors concluded that this may be an important feature since laminin 332 is a nucleation point in the densa BMZ for attachment with the α6β4 integrin of hemidesmosomes (Fig 2). Laminin 332 is also a nucleation point for collagen VII anchoring fibrils in the reticular BMZ (18). Atypical formation of laminin 332 molecules in allergic asthmatic airways could limit the number of attachment sites linking α6β4 integrins of hemidesmosomes and collagen VII anchoring fibrils in the reticular BMZ. In support of this concept incomplete formation of laminin 332 during lung development was associated with abnormal development of hemidesmosomes in tracheal epithelium (34) and in a primate model of allergic asthma, there was reduction in collagen VII anchoring fibrils in the reticular BMZ (27).

Abnormal assembly and/or deposition of laminin 332 could be a primary lesion in the supracellular anchoring network causing reduced hemidesmosome formation followed by reduced desmosome contact between basal and columnar cells resulting in an increased susceptibility for cell sloughing in the asthmatic airway. Although there are very few studies of the supracellular anchoring network in asthmatic airways (Table II) it seems clear from other studies that laminin 332 plays a pivotal role in connecting the epithelium to the BMZ (18).

Thickening of the Reticular BMZ in Asthma

Thickening of the reticular BMZ is a characteristic feature of airway remodeling in the lungs of asthmatics. In the normal airway the thickening of the reticular BMZ is related to the height of the columnar epithelium (Fig 6). Based on this information, thickening of the reticular BMZ in asthmatic airways implies an increase in the height of the columnar epithelium. However in papers that have reported epithelial height in asthmatic airways, there was not a significant difference between asthmatic and controls (27, 31). In asthmatic airways there is a decrease in elements of the anchoring network (desmosomes, laminin 332 and collagen VII), attaching the columnar epithelium to the reticular BMZ (Table II). A decrease in elements of the anchoring network implies a shorter epithelium or one that is of normal height but fragile and subject to cell sloughing. The formation of creola bodies in asthmatic airways suggests that the latter is probably the case.

During normal development of the airway the reticular BMZ and collagen VII anchoring fibers develop postnatally (17, 27). Both the reticular BMZ and collagen VII anchoring fibers increase in width together, maintaining a constant relationship with the height of the columnar epithelium (Fig 6). However in an animal model of allergic asthma this relationship was not maintained. Compared to controls the amount of collagen VII anchoring fibers was reduced 42. % (27) but the width of the reticular BMZ was increased 43.2% (35, 36). In the large airways collagens I, III and V making up the reticular BMZ are produced by the attenuated fibroblasts / myofibroblasts of the mesenchymal cell population. Collagen VII anchoring fibers are produced by basal cells of the epithelial cell population. This suggests an imbalance exists in the asthmatic airway in collagen VII production by the basal cells and collagen I, III and V production by the attenuated fibroblast / myofibroblast complex that results in thickening of the reticular BMZ.

Desmosome proteins, cytokeratins 5 and 14, hemidesmosome proteins, laminin 332 and collagen Vll are all produced by basal cells. Previous studies have shown there is a close relationship between the growth of the epithelium and development of the supracellular anchoring network in the airways (Figs 3–6). This close relationship suggests that a lesion in one component of the supracellular anchoring network may affect development of the whole network. Thus the thickened reticular BMZ in the asthmatic airway may reflect a decrease in collagen VII and also the rest of the elements of the supracellular anchoring network (laminin 332, hemidesmosomes and desmosomes) rather than being the result of chronic injury or a change in epithelial height (Table 2). Such an interpretation may help explain the developmental data showing the appearance of thickened BMZ in children before the appearance of asthma symptoms.

CONCLUSIONS

In this review we have shown that the columnar epithelium is linked to the reticular BMZ through the supracellular anchoring network. We conclude that both sloughing of columnar epithelium (creola bodies) and thickening of the BMZ in asthmatic airways represent abnormalities in the supracellular anchoring network attaching the columnar epithelium to the ECM. However this conclusion is based on only a few studies of the supracellular anchoring network in asthmatic airways. Future research directed toward studying the

regulation and development of the supracellular anchoring network in the asthmatic airway is needed to advance and further understand epithelial cell sloughing and the significance of reticular BMZ thickening.

ACKNOWLEDGEMENTS:

Thanks to Susan Nishio for preparation of the figures. Also the authors acknowledge the staff at the Respiratory Diseases Unit at California National Primate Research Center and the members of the Comparative Respiratory Biology Group at UC Davis for their collaborative efforts in this research. Supported by grants: P01 ES-11617 NIEHS P01 ES-00628 and NCRR RR000169.

LIST OF ABBREVIATIONS

BMZ	Basement Membrane Zone
ECM	Extracellular Matrix

REFERENCES

1. Bousquet J, Jeffery PK, Busse WW, Johnson M, Vignola AM. Asthma. From bronchoconstriction to airways inflammation and remodeling. Am J Respir Crit Care Med 2000;161(5):1720–1745. [PubMed: 10806180]
2. Jeffery PK. Remodeling in asthma and chronic obstructive lung disease. Am J Respir Crit Care Med 2001;164(10 Pt 2):S28–38. [PubMed: 11734464]
3. Schelegle ES, Gershwin LJ, Miller LA, Fanucchi MV, Van Winkle LS, Gerriets JP, Walby WF, Omlor AM, Buckpitt AR, Tarkington BK, et al. Allergic asthma induced in rhesus monkeys by house dust mite (dermatophagoides farinae). Am J Pathol 2001;158(1):333–341. [PubMed: 11141508]
4. James AL, Maxwell PS, Pearce-Pinto G, Elliot JG, Carroll NG. The relationship of reticular basement membrane thickness to airway wall remodeling in asthma. Am J Respir Crit Care Med 2002;166(12 Pt 1):1590–1595. [PubMed: 12471074]
5. Kasahara K, Shiba K, Ozawa T, Okuda K, Adachi M. Correlation between the bronchial subepithelial layer and whole airway wall thickness in patients with asthma. Thorax 2002;57(3):242–246. [PubMed: 11867829]
6. Cokugras H, Akcakaya N, Seckin, Camcioglu Y, Sarimurat N, Aksoy F. Ultrastructural examination of bronchial biopsy specimens from children with moderate asthma. Thorax 2001;56(1):25–29. [PubMed: 11120900]
7. Chu HW, Halliday JL, Martin RJ, Leung DY, Szefler SJ, Wenzel SE. Collagen deposition in large airways may not differentiate severe asthma from milder forms of the disease. Am J Respir Crit Care Med 1998;158(6):1936–1944. [PubMed: 9847289]
8. Benayoun L, Druilhe A, Dombret MC, Aubier M, Pretolani M. Airway structural alterations selectively associated with severe asthma. Am J Respir Crit Care Med 2003;167(10):1360–1368. [PubMed: 12531777]
9. Davies DE. The role of the epithelium in airway remodeling in asthma. Proc Am Thorac Soc 2009;6(8):678–682. [PubMed: 20008875]
10. Royce SG, Cheng V, Samuel CS, Tang ML. The regulation of fibrosis in airway remodeling in asthma. Molecular and cellular endocrinology 2012;351(2):167–175. [PubMed: 22266540]
11. Lambrecht BN, Hammad H. The airway epithelium in asthma. Nature medicine 2012;18(5):684–692.
12. Payne DN, Rogers AV, Adelroth E, Bandi V, Guntupalli KK, Bush A, Jeffery PK. Early thickening of the reticular basement membrane in children with difficult asthma. Am J Respir Crit Care Med 2003;167(1):78–82. [PubMed: 12502479]

13. Pohunek P, Warner JO, Turzikova J, Kudrmann J, Roche WR. Markers of eosinophilic inflammation and tissue re-modelling in children before clinically diagnosed bronchial asthma. Pediatr Allergy Immunol 2005;16(1):43–51. [PubMed: 15693911]
14. Holgate ST. The airway epithelium is central to the pathogenesis of asthma. Allergol Int 2008;57(1):1–10. [PubMed: 18209502]
15. Malmstrom K, Pelkonen AS, Makela MJ. Remodeling, inflammation and airway responsiveness in early childhood asthma. Curr Opin Allergy Clin Immunol 2013;13(2):203–210. [PubMed: 23339936]
16. Evans MJ, Fanucchi MV, Plopper CG. The basement membrane in asthma. Curr Respir Med Rev 2006;2:331 – 337.
17. Evans MJ, Fanucchi MV, Plopper CG, Hyde DM. Postnatal development of the lamina reticularis in primate airways. Anat Rec (Hoboken) 2010;293(6):947–954. [PubMed: 20503389]
18. Schneider H, Muhle C, Pacho F. Biological function of laminin-5 and pathogenic impact of its deficiency. European journal of cell biology 2007;86(11–12):701–717. [PubMed: 17000025]
19. Merker HJ. Morphology of the basement membrane. Microscopy research and technique 1994;28(2):95–124. [PubMed: 8054667]
20. Evans MJ, Fanucchi MV, Van Winkle LS, Baker GL, Murphy AE, Nishio SJ, Sannes PL, Plopper CG. Fibroblast growth factor-2 during postnatal development of the tracheal basement membrane zone. Am J Physiol Lung Cell Mol Physiol 2002;283(6):L1263–1270. [PubMed: 12388330]
21. Villone D, Fritsch A, Koch M, Bruckner-Tuderman L, Hansen U, Bruckner P. Supramolecular interactions in the dermo-epidermal junction zone: Anchoring fibril-collagen vii tightly binds to banded collagen fibrils. J Biol Chem 2008;283(36):24506–24513. [PubMed: 18599485]
22. Bock P, Stockinger L. Light and electron microscopic identification of elastic, elaunin and oxytalan fibers in human tracheal and bronchial mucosa. Anatomy and embryology 1984;170(2):145–153. [PubMed: 6517349]
23. Mauad T, Xavier AC, Saldiva PH, Dolhnikoff M. Elastosis and fragmentation of fibers of the elastic system in fatal asthma. Am J Respir Crit Care Med 1999;160(3):968–975. [PubMed: 10471626]
24. Tsartsali L, Hislop AA, McKay K, James AL, Elliot J, Zhu J, Rosenthal M, Payne DN, Jeffery PK, Bush A, et al. Development of the bronchial epithelial reticular basement membrane: Relationship to epithelial height and age. Thorax 2011.
25. Evans MJ, Moller PC. Biology of airway basal cells. Exp Lung Res 1991;17(3):513–531. [PubMed: 1860451]
26. Evans MJ, Plopper CG. The role of basal cells in adhesion of columnar epithelium to airway basement membrane. The American review of respiratory disease 1988;138(2):481–483. [PubMed: 3143289]
27. Evans MJ, Fanucchi MV, Miller LA, Carlson MA, Nishio SJ, Hyde DM. Reduction of collagen vii anchoring fibrils in the airway basement membrane zone of infant rhesus monkeys exposed to house dust mite. Am J Physiol Lung Cell Mol Physiol 2010;298(4):L543–547. [PubMed: 20139177]
28. Montefort S, Roberts JA, Beasley R, Holgate ST, Roche WR. The site of disruption of the bronchial epithelium in asthmatic and non-asthmatic subjects. Thorax 1992;47(7):499–503. [PubMed: 1412091]
29. Laucirica R, Ostrowski ML. Cytology of nonneoplastic occupational and environmental diseases of the lung and pleura. Archives of pathology & laboratory medicine 2007;131(11):1700–1708. [PubMed: 17979490]
30. Yoshihara S, Yamada Y, Abe T, Linden A, Arisaka O. Association of epithelial damage and signs of neutrophil mobilization in the airways during acute exacerbations of paediatric asthma. Clinical and experimental immunology 2006;144(2):212–216. [PubMed: 16634793]
31. Shahana S, Bjornsson E, Ludviksdottir D, Janson C, Nettelbladt O, Venge P, Roomans GM. Ultrastructure of bronchial biopsies from patients with allergic and non-allergic asthma. Respir Med 2005;99(4):429–443. [PubMed: 15763449]
32. Shebani E, Shahana S, Janson C, Roomans GM. Attachment of columnar airway epithelial cells in asthma. Tissue Cell 2005;37(2):145–152. [PubMed: 15748741]

33. Amin K, Janson C, Seveus L, Miyazaki K, Virtanen I, Venge P. Uncoordinated production of laminin-5 chains in airways epithelium of allergic asthmatics. Respir Res 2005;6:110. [PubMed: 16179086]

34. Nguyen NM, Pulkkinen L, Schlueter JA, Meneguzzi G, Uitto J, Senior RM. Lung development in laminin gamma2 deficiency: Abnormal tracheal hemidesmosomes with normal branching morphogenesis and epithelial differentiation. Respir Res 2006;7:28. [PubMed: 16483354]

35. Evans MJ, Fanucchi MV, Baker GL, Van Winkle LS, Pantle LM, Nishio SJ, Schelegle ES, Gershwin LJ, Miller LA, Hyde DM, et al. The remodelled tracheal basement membrane zone of infant rhesus monkeys after 6 months of recovery. Clin Exp Allergy 2004;34(7):1131–1136. [PubMed: 15248862]

36. Evans MJ, Van Winkle LS, Fanucchi MV, Baker GL, Murphy AE, Nishio SJ, Schelegle ES, Gershwin LJ, Sannes PL, Plopper CG. Fibroblast growth factor-2 in remodeling of the developing basement membrane zone in the trachea of infant rhesus monkeys sensitized and challenged with allergen. Lab Invest 2002;82(12):1747–1754. [PubMed: 12480924]

37. Borradori L, Sonnenberg A. Structure and function of hemidesmosomes: More than simple adhesion complexes. J Invest Dermatol 1999;112(4):411–418. [PubMed: 10201522]

38. Evans MJ, Cox RA, Burke AS, Moller PC. Differentiation of anchoring junctions in tracheal basal cells in the growing rat. Am J Respir Cell Mol Biol 1992;6(2):153–157. [PubMed: 1540378]

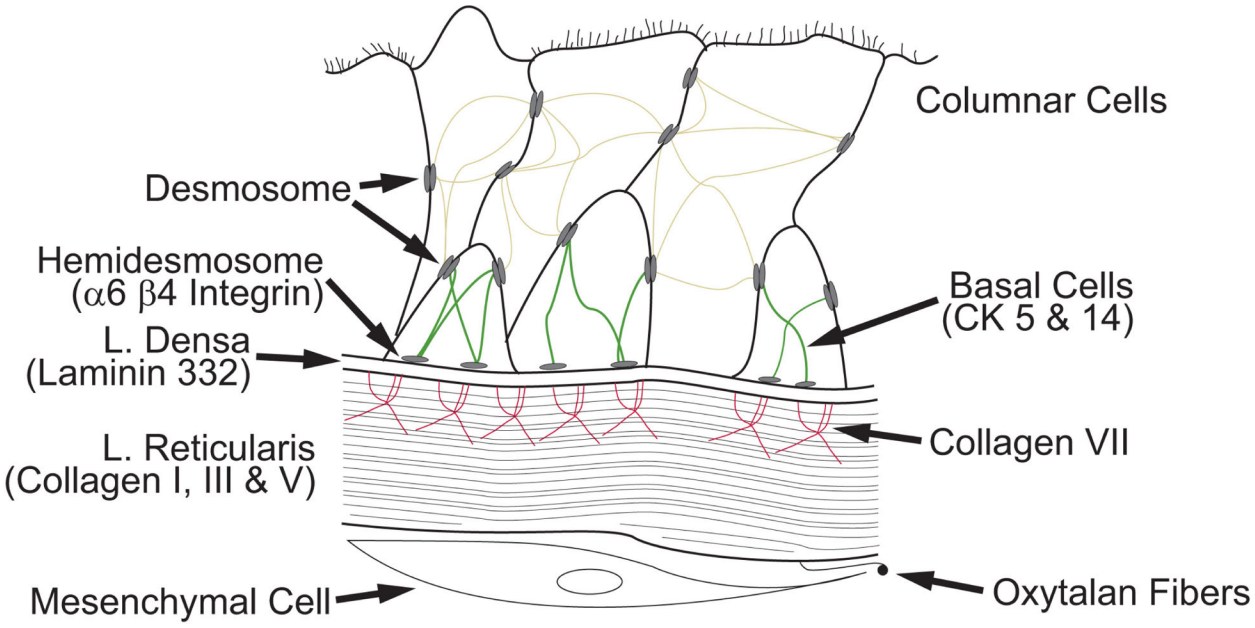

Figure 1.

The supracellular anchoring network attaches the columnar epithelium to the BMZ. Columnar cells are attached by desmosomes to basal cells which are attached to the densa BMZ by hemidesmosomes. The densa BMZ is attached to the reticularis BMZ by collagen VII anchoring fibers. The reticularis BMZ is attached to the ECM by oxytalin fibers of the elastic fiber system. (Modified from Evans et al. 2010 (17, 27)).

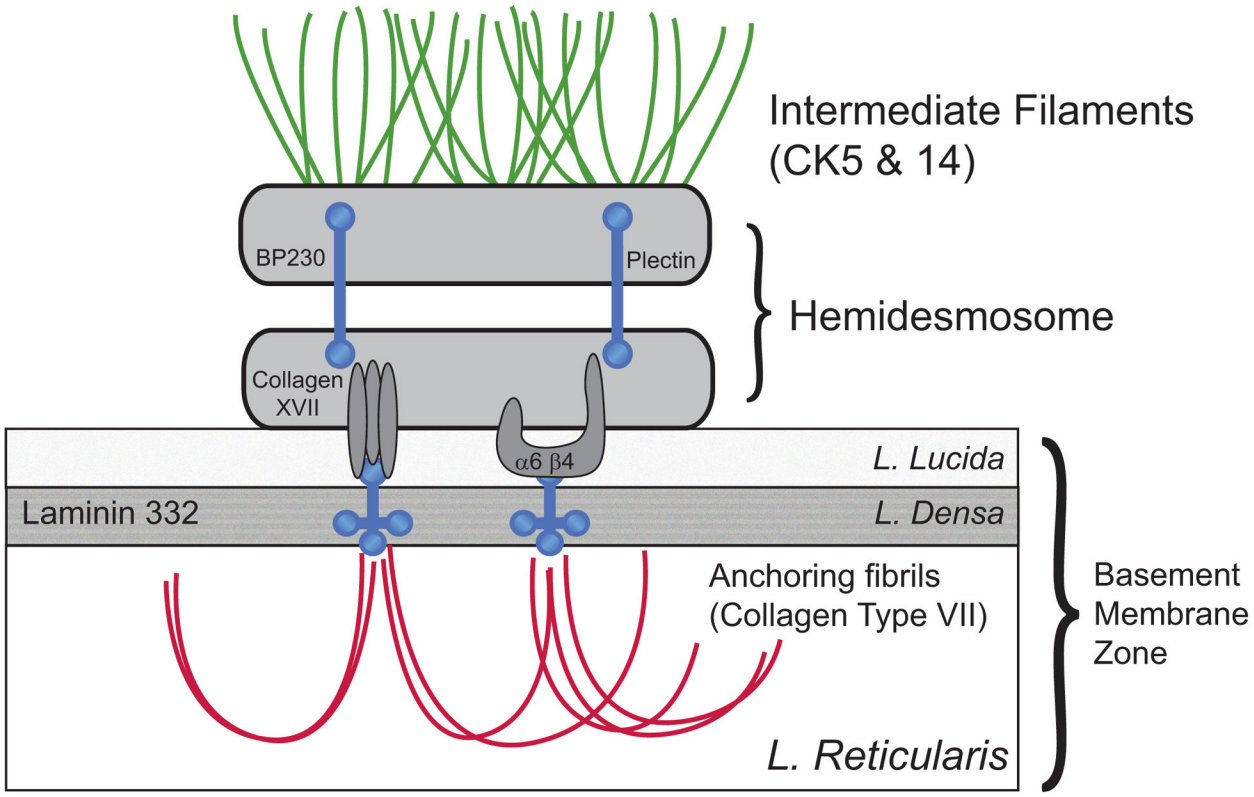

Figure 2.

Illustration of the molecular interactions of the hemidesmosome α6β4 integrin with the BMZ. The alpha α6β4 integrin in the lucida BMZ binds with laminin332 in the densa BMZ. Collagen VII anchoring fibers in the reticular BMZ bind with the opposite end of the laminin 332 molecule and then with collagen I in the reticular BMS. (Modified from Borradori and Sonnenberg, 1999 (37)) .

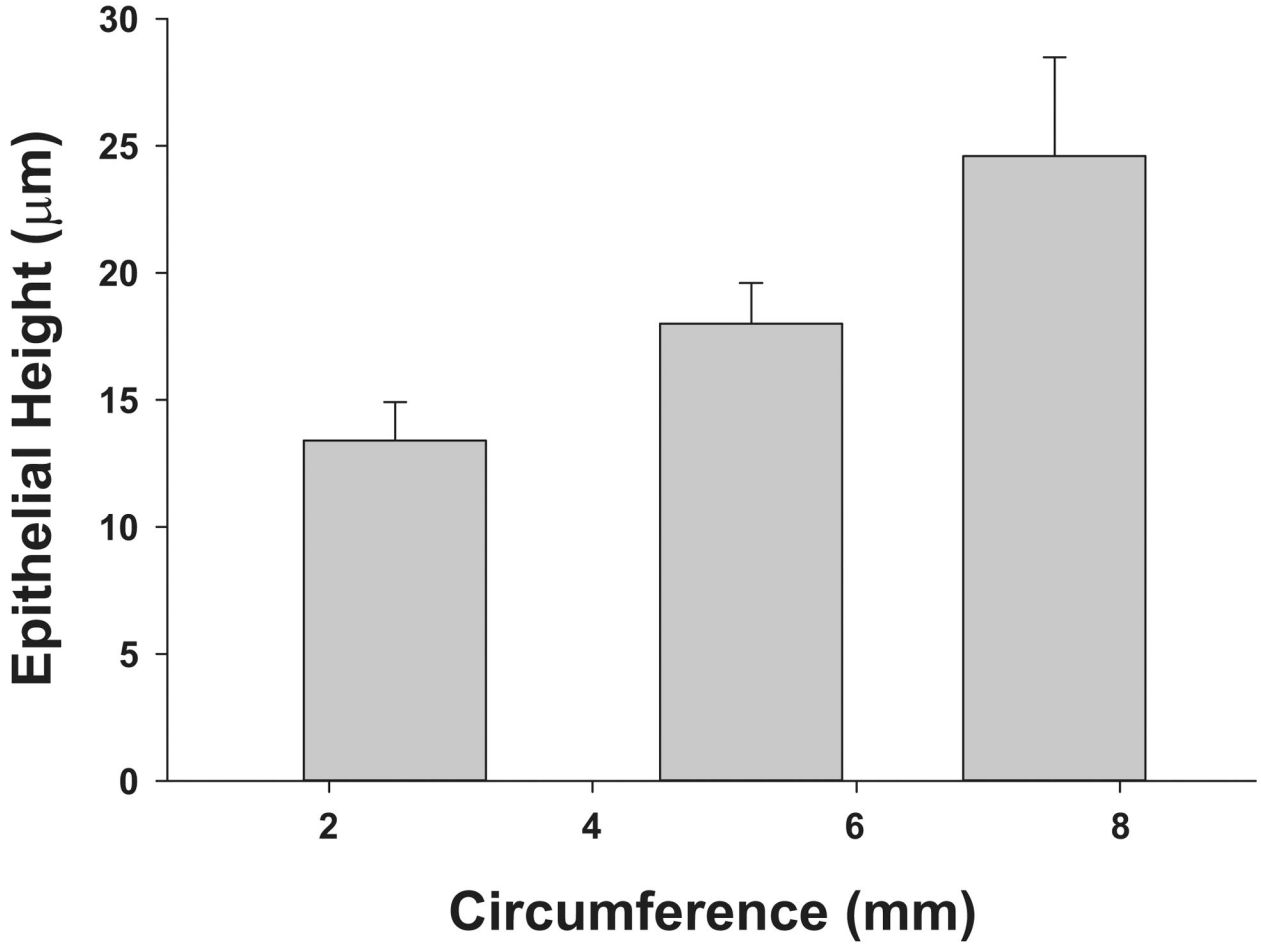

Figure 3.
Illustration of the close relationship between the increasing circumference of the airway and the increasing height of the columnar epithelium in the growing rat trachea at 3, 30 and 90 days of age (38).

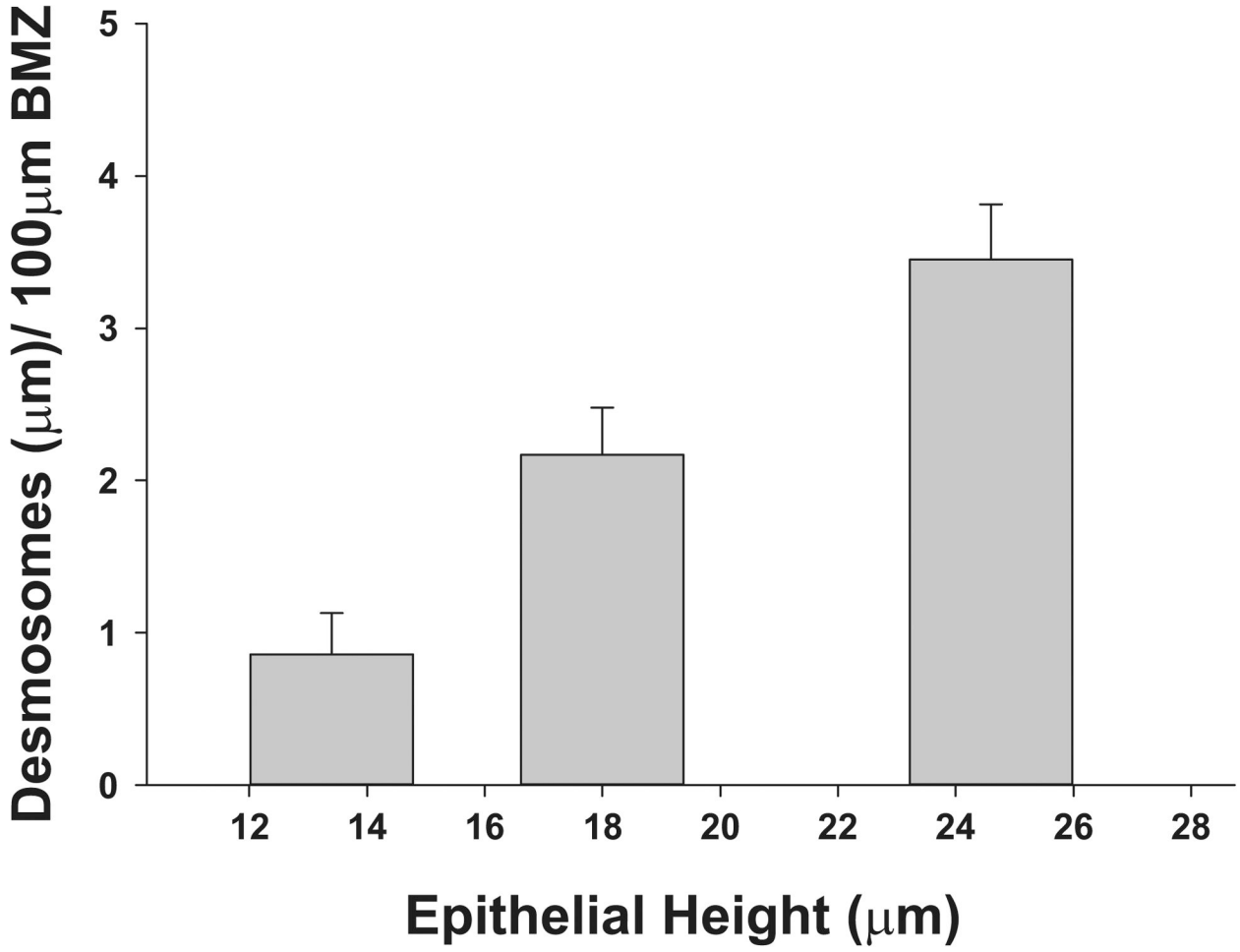

Figure 4.

Illustration of the close relationship between the increasing height of the columnar epithelium and the increasing amount of desmosome attachment with basal cells in the growing rat trachea at 3, 30 and 90days of age (38).

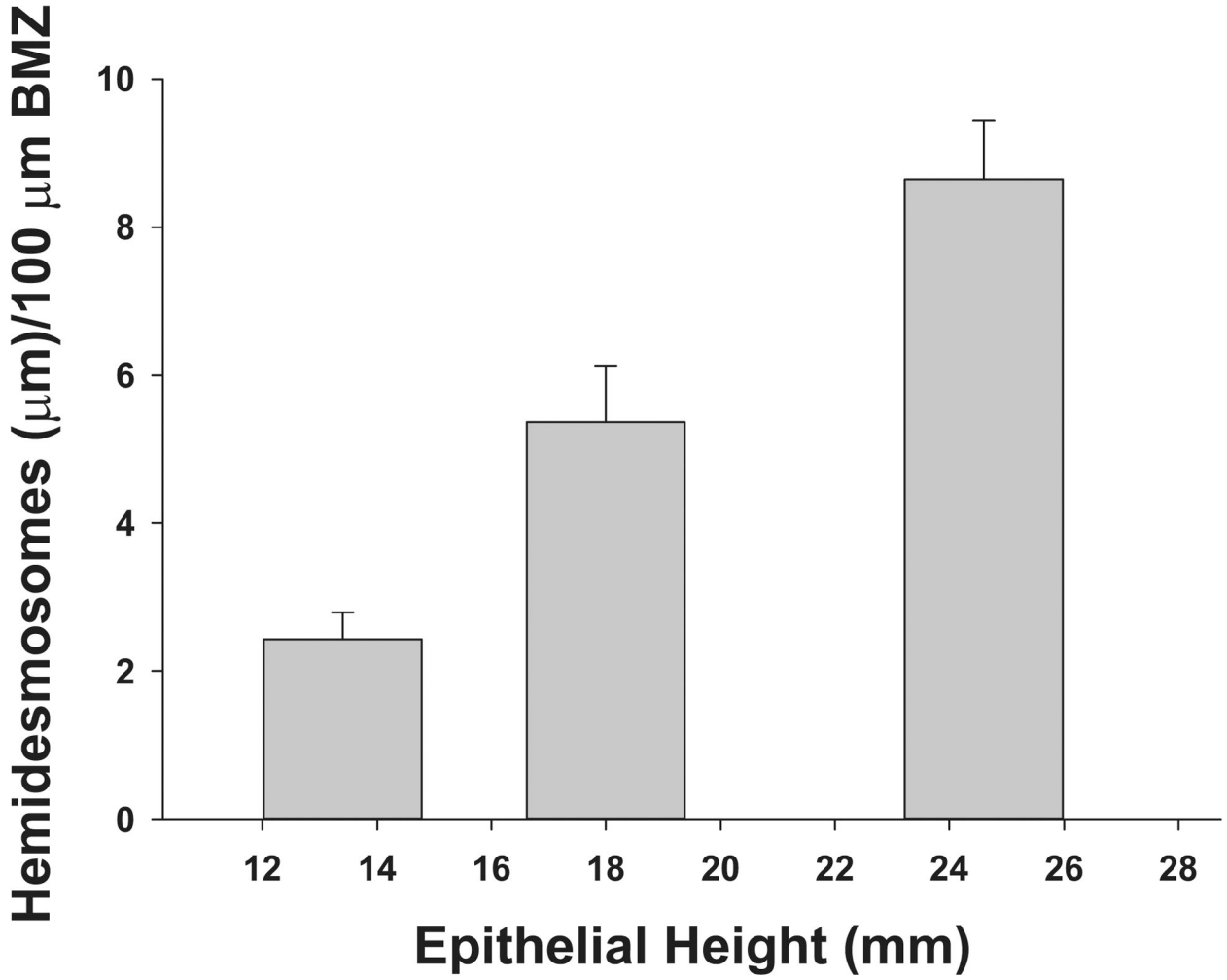

Figure 5.
Illustration of the close relationship between the increasing height of the columnar epithelium and the increasing amount of hemidesmosome attachment with the BMZ in the growing rat trachea at 3, 30 and 90days of age (38).

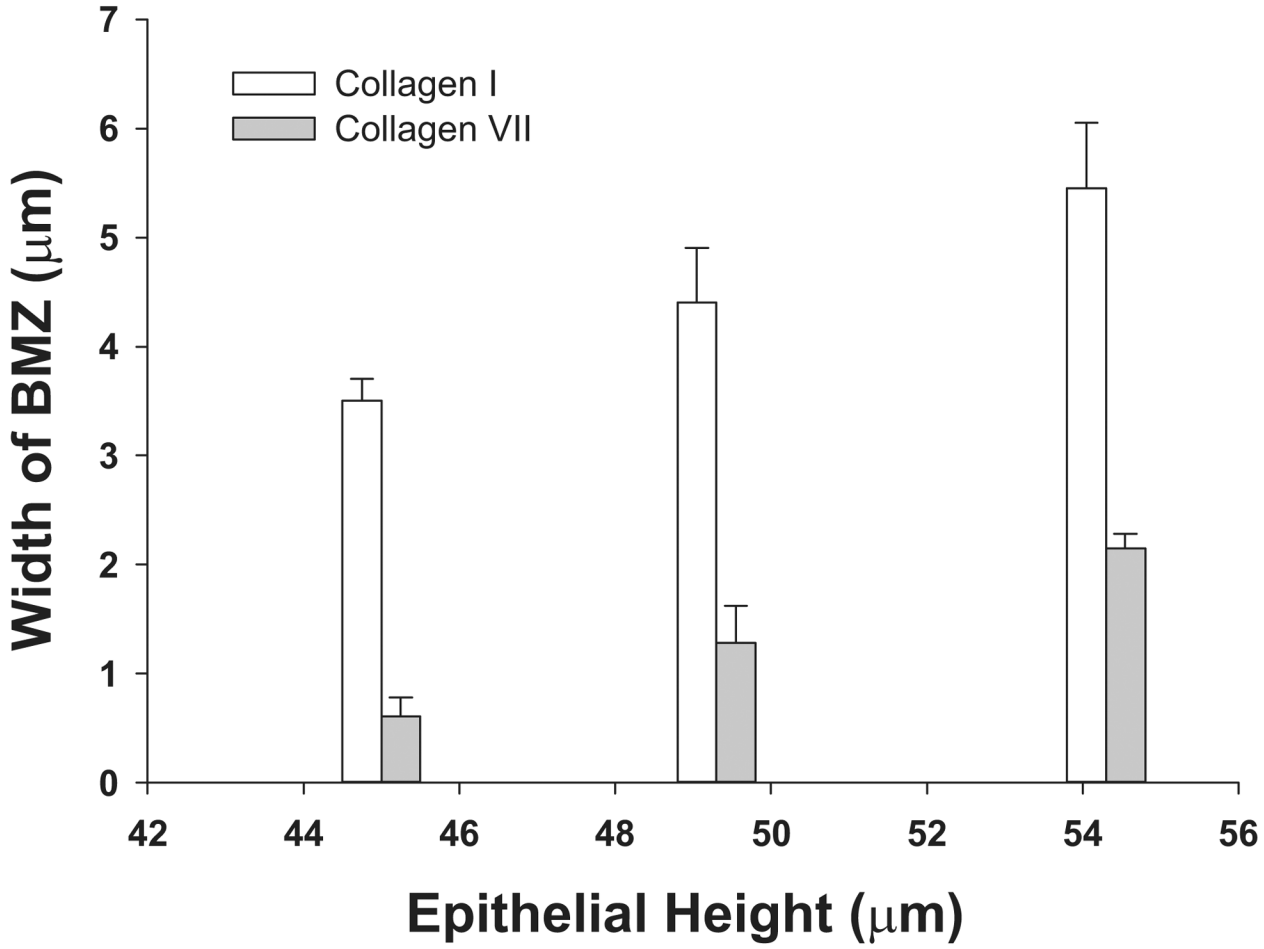

Figure 6.
Illustration of the close relationship between the increasing height of the columnar epithelium, the increasing width of collagen VII fibers and the increasing width of the reticular BMZ (20, 27).

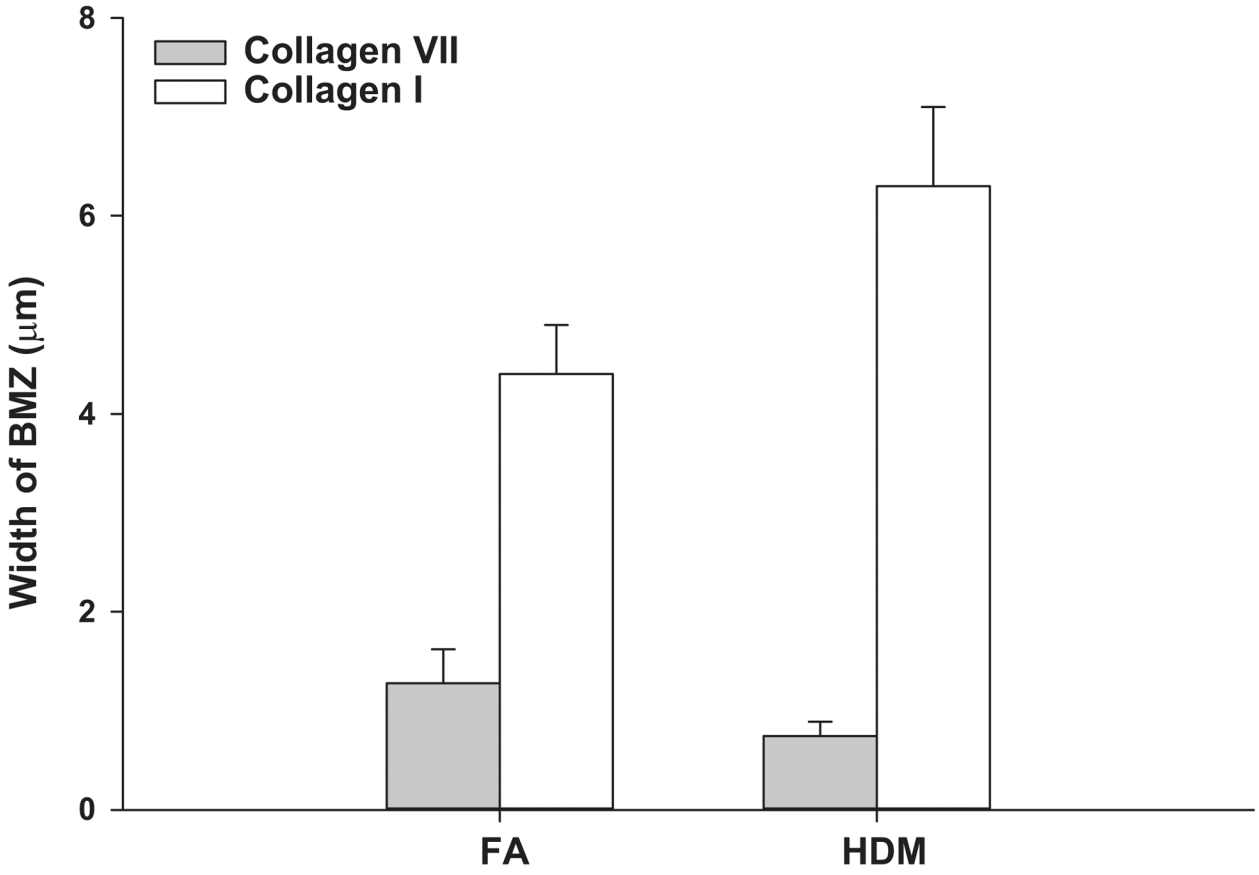

Figure 7.

Changes in the width of the reticular BMZ and the width of collagen VII anchoring fibers in a house dust mite model of asthma compared with filtered air (FA) controls. In the HDM group the reticular BMZ was 43% greater and collagen VII anchoring fibers were 42% less than FA controls (27, 36).

Table I.

Characteristics of the Basement Membrane

Basement membrane (light microscopy)	Basal lamina (electron microscopy)	Basement membrane zone (molecular structure)
Basement membrane	Lamina lucida	**Epithelial interface**
		Collagen (XVII)
		Integrins (α6β4)
	Lamina densa	**Epithlial-mesenchymal interface**
		Collagen (IV)
		Laminin (332)
		Entactin/Nidogen Proteoglycan (Perlecan)
	Lamina reticularis	**Mesenchymal Interface**
		Collagen (I,III, V, VI & VII)
		Proteoglycan (Perlecan, Bamacan, Collagen XVIII)

Table II.

Changes in the Supracellular Anchoring Network in Asthmatic Airways

Anchoring Network Element	Change	Reference
Epithelial height	No change	Shebanbi, et al., 2005
Desmosome contact with columnar cell	Reduced	Shahana, et al., 2005
Hemidesmosome attachment with BMZ	No change	Shahana, et al., 2005
Laminin 332 in densa BMZ	Abnormal assembly	Amin, et al., 2005
Collagen VII in reticular BM|Z	Reduced	Evans, et al., 2010
Width of reticular BMZ	Increased	Evans, et al., 2006