

Chapter 53

Epidermal and Epidermal–Dermal Adhesion

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REFERENCES

1. Getsios S, Huen AC, Green KJ: Working out the strength and flexibility of desmosomes. *Nat Rev Mol Cell Biol* **5**:271, 2004
2. Calkins CC, Setzer SV: Spotting desmosomes: The first 100 years. *J Invest Dermatol* **127**:E2, 2007
3. Staehelin LA: Structure and function of intercellular junctions. *Int Rev Cytol* **39**:191, 1974
4. Gorbsky G, Steinberg MS: Isolation of the intercellular glycoproteins of desmosomes. *J Cell Biol* **90**:243, 1981
5. Staehelin LA, Hull BE: Junctions between living cells. *Sci Am* **238**:140, 1978
6. Ihrie RA et al: Perp is a p63-regulated gene essential for epithelial integrity. *Cell* **120**:843, 2005
7. Lechler T, Fuchs E: Desmoplakin: An unexpected regulator of microtubule organization in the epidermis. *J Cell Biol* **176**:147, 2007
8. Groot KR et al: Kazrin, a novel periplakin-interacting protein associated with desmosomes and the keratinocyte plasma membrane. *J Cell Biol* **166**:653, 2004
9. Jonca N et al: Corneodesmosin, a component of epidermal corneocyte desmosomes, displays homophilic adhesive properties. *J Biol Chem* **277**:5024, 2002
10. North AJ et al: Molecular map of the desmosomal plaque. *J Cell Sci* **112**:4325, 1999
11. Koch PJ et al: Complexity and expression patterns of the desmosomal cadherins. *Proc Natl Acad Sci USA* **89**:353, 1992
12. Arnemann J et al: Stratification-related expression of isoforms of the desmosomal cadherins in human epidermis. *J Cell Sci* **104**:741, 1993
13. Wu H, Stanley JR, Cotsarelis G: Desmoglein isotype expression in the hair follicle and its cysts correlates with type of keratinization and degree of differentiation. *J Invest Dermatol* **120**:1052, 2003
14. Mahoney MG et al: Delineation of diversified desmoglein distribution in stratified squamous epithelium: Implications in diseases. *Exp Dermatol* **15**:101, 2006
15. Wang LH et al: Immunohistochemical distribution pattern of desmocollin 3, desmocollin 1 and desmoglein 1,2 in the pemphigus of oral mucosa and skin. *Oral Med Pathol* **5**:87, 2000
16. Chen YJ et al: DSG3 is overexpressed in head neck cancer and is a potential molecular target for inhibition of oncogenesis. *Oncogene* **26**:467, 2006
17. Schafer S, Koch PJ, Franke WW: Identification of the ubiquitous human desmoglein, Dsg2, and the expression catalogue of a subfamily of desmosomal cadherins. *Exp Cell Res* **211**:391, 1994
18. Whittock NV, Bower C: Genetic evidence for a novel human desmosomal cadherin, desmoglein 4. *J Invest Dermatol* **120**:523, 2003
19. Bazzi H et al: Desmoglein 4 is expressed in highly differentiated keratinocytes and trichocytes in human epidermis and hair follicle. *Differentiation* **74**:129, 2006
20. King IA et al: The desmocollins of human foreskin epidermis: Identification and chromosomal assignment of a third gene and expression patterns of the three isoforms. *J Invest Dermatol* **105**:314, 1995
21. Khan K et al: Desmocollin switching in colorectal cancer. *Br J Cancer* **95**:1367, 2006
22. Posthaus H, Dubois CM, Muller E: Novel insights into cadherin processing by subtilisin-like convertases. *FEBS Lett* **536**:203, 2003
23. Shapiro L et al: Structural basis of cell-cell adhesion by cadherins. *Nature* **374**:327, 1995
24. Nagar B et al: Structural basis of calcium-induced E-cadherin rigidification and dimerization. *Nature* **380**:360, 1996
25. Boggon TJ et al: C-cadherin ectodomain structure and implications for cell adhesion mechanisms. *Science* **296**:1308, 2002
26. Al-Amoudi A et al: The molecular architecture of cadherins in native epidermal desmosomes. *Nature* **450**:832, 2007

27. Amagai M et al: The extracellular domain of pemphigus vulgaris antigen (desmoglein 3) mediates weak homophilic adhesion. *J Invest Dermatol* **102**:402, 1994
28. Chitaev NA, Troyanovsky SM: Direct Ca²⁺-dependent heterophilic interaction between desmosomal cadherins, desmoglein and desmocollin, contributes to cell-cell adhesion. *J Cell Biol* **138**:193, 1997
29. Marcozzi C et al: Coexpression of both types of desmosomal cadherin and plakoglobin confers strong intercellular adhesion. *J Cell Sci* **111**:495, 1998
30. Hatzfeld M et al: The function of plakophilin 1 in desmosome assembly and actin filament organization. *J Cell Biol* **149**:209, 2000
31. Bonn e S et al: Defining desmosomal plakophilin-3 interactions. *J Cell Biol* **161**:403, 2003
32. Den ZN et al: Desmocollin 3 is required for pre-implantation development of the mouse embryo. *J Cell Sci* **119**:482, 2006
33. Koch PJ et al: Identification of desmoglein, a constitutive desmosomal glycoprotein, as a member of the cadherin family of cell adhesion molecules. *Eur J Cell Biol* **53**:1, 1990
34. Amagai M et al: Toxin in bullous impetigo and staphylococcal scalded-skin syndrome targets desmoglein 1. *Nature Med* **6**:1275, 2000
35. Descargues P, Deraison C., Bonnart C et al: Spink5-deficient mice mimic Netherton syndrome through degradation of desmoglein 1 by epidermal protease hyperactivity. *Nat Genet* **37**:56, 2004
36. Hanakawa Y et al: Molecular mechanisms of blister formation in bullous impetigo and staphylococcal scalded skin syndrome. *J Clin Invest* **110**:53, 2002
37. Sekiguchi M et al: Dominant autoimmune epitopes recognized by pemphigus antibodies map to the N-terminal adhesive region of desmogleins. *J Immunol* **167**:5439, 2001
38. Li N et al: The role of intramolecular epitope spreading in the pathogenesis of endemic pemphigus foliaceus (fogo selvagem). *J Exp Med* **197**:1501, 2003
39. Ishii K et al: Isolation of pathogenic monoclonal anti-desmoglein 1 human antibodies by phage display of pemphigus foliaceus autoantibodies. *J Invest Dermatol* **128**:939, 2008
40. Rickman L et al: N-terminal deletion in a desmosomal cadherin causes the autosomal dominant skin disease striate palmoplantar keratoderma. *Hum Mol Genet* **8**:971, 1999
41. Keren H et al: Diffuse nonepidermolytic palmoplantar keratoderma caused by a recurrent nonsense mutation in *DSG1*. *Arch Dermatol* **141**:628, 2005
42. Milingou M et al: Focal palmoplantar keratoderma caused by an autosomal dominant inherited mutation in the desmoglein 1 gene. *Dermatology* **212**:117, 2006
43. Pilichou K et al: Mutations in desmoglein-2 gene are associated with arrhythmogenic right ventricular cardiomyopathy. *Circulation* **113**:1171, 2006
44. Futei Y et al: Use of domain-swapped molecules for conformational epitope mapping of desmoglein 3 in pemphigus vulgaris. *J Invest Dermatol* **115**:829, 2000
45. Payne AS et al: Genetic and functional characterization of human pemphigus vulgaris monoclonal autoantibodies isolated by phage display. *J Clin Invest* **115**:888, 2005
46. Koch PJ et al: Targeted disruption of the pemphigus vulgaris antigen (desmoglein 3) gene in mice causes loss of keratinocyte cell adhesion with a phenotype similar to pemphigus vulgaris. *J Cell Biol* **137**:1091, 1997
47. Sharma P, Mao X, Payne AS: Beyond steric hindrance: The role of adhesion signaling pathways in the pathogenesis of pemphigus. *J Dermatol Sci* **48**:1, 2007
48. Schaffer JV et al: Mutations in the desmoglein 4 gene underlie localized autosomal recessive hypotrichosis with monilethrix hairs and congenital scalp erosions. *J Invest Dermatol* **126**:1286, 2006
49. Shimomura Y et al: Mutations in the desmoglein 4 gene are associated with monilethrix-like congenital hypotrichosis. *J Invest Dermatol* **126**:1281, 2006
50. Zlotogorski A et al: An autosomal recessive form of monilethrix is caused by mutations in *DSG4*: Clinical overlap with localized autosomal recessive hypotrichosis. *J Invest Dermatol* **126**:1292, 2006
51. Kljuic A et al: Desmoglein 4 in hair follicle differentiation and epidermal adhesion: Evidence from inherited hypotrichosis and acquired pemphigus vulgaris. *Cell* **113**:249, 2003
52. Lai-Cheong JE, Arita K, McGrath JA: Genetic diseases of junctions. *J Invest Dermatol* **127**:2713, 2007
53. Nagasaka T et al: Defining the pathogenic involvement of desmoglein 4 in pemphigus and staphylococcal scalded skin syndrome. *J Clin Invest* **114**:1484, 2004

54. Heuser A et al: Mutant desmocollin-2 causes arrhythmogenic right ventricular cardiomyopathy. *Am J Hum Genet* **79**:1081, 2010
55. Simpson MA et al: Homozygous mutation of desmocollin-2 in arrhythmogenic right ventricular cardiomyopathy with mild palmoplantar keratoderma and woolly hair. *Cardiology* **113**:28, 2009
56. Ayub M et al: A homozygous nonsense mutation in the human desmocollin-3 (DSC3) gene underlies hereditary hypotrichosis and recurrent skin vesicles. *Am J Hum Genet* **85**:1, 2009
57. Hisamatsu Y et al: The detection of IgG and IgA autoantibodies to desmocollins 1–3 by enzyme-linked immunosorbent assays using baculovirus-expressed proteins, in atypical pemphigus but not in typical pemphigus. *Br J Dermatol* **151**:73, 2004
58. Cowin P et al: Plakoglobin: A protein common to different kinds of intercellular adhering junctions. *Cell* **46**:1063, 1986
59. Korman NJ et al: Demonstration of an adhering-junction molecule (plakoglobin) in the autoantigens of pemphigus foliaceus and pemphigus vulgaris. *N Engl J Med* **321**:631, 1989
60. Peifer M, Berg S, Reynolds AB: A repeating amino acid motif shared by proteins with diverse cellular roles. *Cell* **76**:789, 1994
61. Chitaev NA et al: The binding of plakoglobin to desmosomal cadherins: Patterns of binding sites and topogenic potential. *J Cell Biol* **133**:359, 1996
62. Wahl JK et al: Plakoglobin domains that define its association with the desmosomal cadherins and the classical cadherins: Identification of unique and shared domains. *J Cell Sci* **109**(Pt 5):1143, 1996
63. Witcher LL et al: Desmosomal cadherin binding domains of plakoglobin. *J Biol Chem* **271**:10904, 1996
64. Kowalczyk AP et al: The amino-terminal domain of desmoplakin binds to plakoglobin and clusters desmosomal cadherin-plakoglobin complexes. *J Cell Biol* **139**:773, 1997
65. Williams BO et al: A comparative evaluation of beta-catenin and plakoglobin signaling activity. *Oncogene* **19**:5720, 2000
66. Williamson L et al: Pemphigus vulgaris identifies plakoglobin as key suppressor of c-Myc in the skin. *EMBO J* **25**:3298, 2006
67. Bornslaeger EA et al: Plakophilin 1 interferes with plakoglobin binding to desmoplakin, yet together with plakoglobin promotes clustering of desmosomal plaque complexes at cell-cell borders. *J Cell Sci* **114**:727, 2001
68. Drees F et al: Alpha-catenin is a molecular switch that binds E-cadherin-beta-catenin and regulates actin-filament assembly. *Cell* **123**:903, 2005
69. Yamada S et al: Deconstructing the cadherin-catenin-actin complex. *Cell* **123**:889, 2005
70. McKoy G et al: Identification of a deletion in plakoglobin in arrhythmogenic right ventricular cardiomyopathy with palmoplantar keratoderma and woolly hair (Naxos disease). *Lancet* **355**:2119, 2000
71. Mueller H, Franke WW: Biochemical and immunological characterization of desmoplakins I and II, the major polypeptides of the desmosomal plaque. *J Mol Biol* **163**:647, 1983
72. Green KJ et al: Structure of the human desmoplakins. Implications for function in the desmosomal plaque. *J Biol Chem* **265**:2603, 1990
73. Uzumcu A et al: Loss of desmoplakin isoform I causes early onset cardiomyopathy and heart failure in a Naxos-like syndrome. *J Med Genet* **43**:e05, 2006
74. Green KJ, et al: Comparative structural analysis of desmoplakin, bullous pemphigoid antigen and plectin: members of a new gene family involved in organization of intermediate filaments. *Int J Biol Macromol* **14**:145, 1992
75. Stappenbeck TS, Green KJ: The desmoplakin carboxyl terminus coaligns with and specifically disrupts intermediate filament networks when expressed in cultured cells. *J Cell Biol* **116**:1197, 1992
76. Gallicano GI et al: Desmoplakin is required early in development for assembly of desmosomes and cytoskeletal linkage. *J Cell Biol* **143**:2009, 1998
77. Armstrong DK et al: Haploinsufficiency of desmoplakin causes a striate subtype of palmoplantar keratoderma. *Hum Mol Genet* **8**:143, 1999
78. Carvajal-Huerta L: Epidermolytic palmoplantar keratoderma with woolly hair and dilated cardiomyopathy. *J Amer Acad Dermatol* **39**:418, 1998
79. Jonkman MF et al: Loss of desmoplakin tail causes lethal acantholytic epidermolysis bullosa. *Am J Hum Genet* **77**:653, 2005
80. Wolf A et al: Plakophilin 1 stimulates translation by promoting eIF4A1 activity. *J Cell Biol* **188**:463, 2010

81. McGrath JA et al: Mutations in the plakophilin 1 gene result in ectodermal dysplasia/skin fragility syndrome. *Nat Genet* **17**:240, 1997
82. van Tintelen JP et al: Plakophilin-2 mutations are the major determinant of familial arrhythmogenic right ventricular dysplasia/cardiomyopathy. *Circulation* **113**:1650, 2006
83. Sevilla LM et al: Mice deficient in involucrin, envoplakin, and periplakin have a defective epidermal barrier. *J Cell Biol* **179**:1599, 2007
84. Levy-Nissenbaum E et al: Hypotrichosis simplex of the scalp is associated with nonsense mutations in CDSN encoding corneodesmosin. *Nat Genet* **34**:151, 2003
85. Yurchenco PD, Amenta PS, Patton BL: Basement membrane assembly, stability and activities observed through a developmental lens. *Matrix Biol* **22**:521, 2004
86. Keene DR et al: Immunodissection of the connective tissue matrix in human skin. *Microsc Res Tech* **38**:394, 1997
87. Eady RA et al: Ultrastructural clues to genetic disorders of skin: The dermal-epidermal junction. *J Invest Dermatol* **103**:13S, 1994
88. Goldberg M, Escaig-Haye F: Is the lamina lucida of the basement membrane a fixation artifact? *Eur J Cell Biol* **42**:365, 1986
89. Palade GE, Farquhar MG: A special fibril of the dermis. *J Cell Biol* **27**:215, 1966
90. Keene DR et al: Collagen VII forms an extended network of anchoring fibrils. *J Cell Biol* **104**:611, 1987
91. Shimizu H et al: Most anchoring fibrils in human skin originate and terminate in the lamina densa. *Lab Invest* **76**:753, 1997
92. Ramirez F, Sakai LY: Biogenesis and function of fibrillin assemblies. *Cell Tissue Res* **339**:71, 2010
93. van Agtmael T, Bruckner-Tuderman L: Basement membranes and human disease. *Cell Tissue Res* **339**:167, 2010
94. Myllyharju J, Kivirikko KI: Collagens, modifying enzymes and their mutations in humans, flies and worms. *Trends in Genet.* **20**:33, 2004
95. Khoshnoodi J et al: Mechanism of chain selection in the assembly of collagen IV: A prominent role for the alpha2 chain. *J Biol Chem* **281**:6058, 2006
96. Fleischmajer R et al: There is temporal and spatial expression of alpha1 (IV), alpha2 (IV), alpha5 (IV), alpha6 (IV) collagen chains and beta1 integrins during the development of the basal lamina in an in vitro skin model. *J Invest Dermatol* **109**:527, 1997
97. Gould DB et al: Role of COL4A1 in small-vessel disease and hemorrhagic stroke. *N Engl J Med* **354**:1489, 2006
98. Firtina Z et al: Abnormal expression of collagen IV in lens activates unfolded protein response resulting in cataract. *J Biol Chem* **284**:35872, 2009
99. Durbecq M: Laminins. *Cell Tissue Res* **339**:259, 2010
100. Aumailley M, et al: A simplified laminin nomenclature. *Matrix Biol* **24**:326, 2005
101. Korpos E et al: Role of the extracellular matrix in lymphocyte migration. *Cell Tissue Res* **339**:47, 2010
102. Bader BL et al: Compound genetic ablation of nidogen 1 and 2 causes basement membrane defects and perinatal lethality in mice. *Mol Cell Biol* **25**:6846, 2005
103. Iozzo RV, Zoeller JJ, Nyström A: Basement membrane proteoglycans: modulators par excellence of cancer growth and angiogenesis. *Mol Cells* **27**:503, 2009
104. Schäfer L, Schäfer RM: Proteoglycans: From structural compounds to signaling molecules. *Cell Tissue Res* **339**:237, 2010
105. Xian X, Gopal S, Couchman J: Syndecans as receptors and organizers of the extracellular matrix. *Cell Tissue Res* **339**:31, 2010
106. Timpl R: Fibulins: A versatile family of extracellular matrix proteins. *Nat Rev Mol Cell Biol* **4**:479, 2003
107. Koster J, Borradori L, Sonnenberg A: Biology of the hemidesmosomes. In: *Handbook of Experimental Pharmacology*, Vol. 165, edited by J Behrens, WJ Nelson. Berlin, Springer 2004, p. 243
108. Sitaru C: Bullous pemphigoid: A prototypical antibody-mediated organ-specific autoimmune disease. *J Invest Dermatol* **129**:822, 2009
109. Groves RW et al: A homozygous nonsense mutation within the dystonin gene coding for the coiled-coil domain of the epithelial isoform of BPAG1 underlies a new subtype of autosomal recessive epidermolysis bullosa simplex. *J Invest Dermatol* 2010 [E-publication]
110. Franzke C-W, Bruckner P, Bruckner-Tuderman L: Collagenous transmembrane proteins – recent insights into biology and pathology. *J Biol Chem* **280**:4005, 2005
111. Franzke CW, Bruckner-Tuderman L, Blobel CP: Shedding of collagen XVII/BP180 in skin depends on both ADAM10 and ADAM9. *J Biol Chem* **284**:23386, 2009
112. Has C, Bruckner-Tuderman L: Molecular and diagnostic aspects of genetic skin fragility. *J Dermatol Science* **44**:129, 2006

113. Nishie W et al: Humanization of autoantigen. *Nat Med* **13**:378, 2007
114. Asaka T et al: Type XVII collagen is a key player in tooth enamel formation. *Am J Pathol* **174**:91, 2009
115. Natsuga K et al: Plectin expression patterns determine two distinct subtypes of epidermolysis bullosa simplex. *Hum Mutat* **31**:308, 2010
116. Sterk LM et al: The tetraspan molecule CD151, a novel constituent of hemidesmosomes, associates with the integrin $\alpha 6 \beta 4$ and may regulate the spatial organization of hemidesmosomes. *J Cell Biol* **149**:969, 2000
117. Karamatic Crew V et al: CD151, the first member of the tetraspanin (TM4) superfamily detected on erythrocytes, is essential for the correct assembly of human basement membranes in kidney and skin. *Blood* **104**:2217, 2004
118. Zhang F et al: Distinct ligand binding sites in integrin $\alpha 3 \beta 1$ regulate matrix adhesion and cell-cell contact. *J Cell Biol* **163**:177, 2003
119. Siegel DH et al: Loss of kindlin-1, a human homolog of the *Caenorhabditis elegans* actin-extracellular-matrix linker protein UNC-112, causes Kindler syndrome. *Am J Hum Genet* **73**:174, 2003
120. Jobard F et al: Identification of mutations in a new gene encoding a FERM family protein with a pleckstrin homology domain in Kindler syndrome. *Hum Mol Genet* **12**:925-935, 2003
121. Meves A et al: The Kindlin protein family: New members to the club of focal adhesion proteins. *Trends Cell Biol.* **19**:504, 2009
122. Has C et al: Kindlin-1 is required for RhoGTPase-mediated lamellipodia formation in keratinocytes. *Am J Pathol* **175**:1442, 2009
123. Nonaka S et al: The extracellular domain of BPAG2 has a loop structure in the carboxy terminal flexible tail in vivo. *J Invest Dermatol* **115**:889, 2000
124. Bruckner-Tuderman L et al: Biology of anchoring fibrils: Lessons from dystrophic epidermolysis bullosa. *Matrix Biol* **18**:43, 1999
125. Ryan MC et al: Targeted disruption of the LAMA3 gene in mice reveals abnormalities in survival and late stage differentiation of epithelial cells. *J Cell Biol* **145**:1309, 1999
126. Ramirez F, Dietz HC: Extracellular microfibrils in vertebrate development and disease processes. *J Biol Chem* **284**:14677, 2009
127. Rattenholl A et al: Proteinases of the bone morphogenetic protein-1 family convert procollagen VII to mature anchoring fibril collagen. *J Biol Chem* **277**:26372, 2002
128. Raghunath M et al: Cross-linking of the dermo-epidermal junction of skin regenerating from keratinocyte autografts. Anchoring fibrils are a target for tissue transglutaminase. *J Clin Invest* **98**:1174, 1996
129. Villone D et al: Supramolecular interactions in the dermo-epidermal junction zone: Collagen VII in anchoring fibrils tightly bind to fibrillar collagen I. *J Biol Chem* **283**:24506, 2008
130. Sitaru AG et al: T cells are required for the production of blister-inducing autoantibodies in experimental epidermolysis bullosa acquisita. *J Immunol* **184**:1596, 2010
131. Kern JS et al: 42 novel COL7A1 mutations and the role of a frequent SNP in the MMP1 promoter in modulation of disease severity in a large European dystrophic epidermolysis bullosa cohort. *Br J Dermatol* **161**:1089, 2009
132. Heinonen S et al: Targeted inactivation of the type VII collagen gene (Col7a1) in mice results in severe blistering phenotype: A model for recessive dystrophic epidermolysis bullosa. *J Cell Sci* **112**:3641, 1999
133. Fritsch A et al: A hypomorphic mouse model for dystrophic epidermolysis bullosa reveals disease mechanisms and responds to fibroblast therapy. *J Clin Invest* **118**:1669, 2008
134. Kern JS et al: Mechanisms of fibroblast cell therapy for dystrophic epidermolysis bullosa: High stability of collagen VII favors long-term skin integrity. *Mol Ther* **17**:1605, 2009
135. Tolar J et al: Amelioration of epidermolysis bullosa by transfer of wild-type bone marrow cells. *Blood* **113**:1167, 2009
136. Remington J et al: Injection of recombinant human type VII collagen corrects the disease phenotype in a murine model of dystrophic epidermolysis bullosa. *Mol Ther* **17**:26, 2009
137. Wagner JE et al: Bone marrow transplantation for recessive dystrophic epidermolysis bullosa. *New Engl J Med* **363**:629, 2010
138. Fleischmajer R et al: Skin fibroblasts are the only source of nidogen during early basal lamina formation in vitro. *J Invest Dermatol* **105**:597, 1995
139. Marinkovich MP et al: Cellular origin of the dermal-epidermal basement membrane. *Dev Dyn* **197**:255, 1993
140. Marionnet C et al: Interactions between fibroblasts and keratinocytes in morphogenesis of dermal epidermal junction in a model of reconstructed skin. *J Invest Dermatol* **126**:971, 2006

141. El Ghalbzouri A et al: Basement membrane reconstruction in human skin equivalents is regulated by fibroblasts and/or exogenously activated keratinocytes. *J Invest Dermatol* **124**:79, 2005
142. Fritsch A et al: Conditional collagen VII inactivation allows analysis of anchoring fibril stability and function in vivo and reveals a major role of fibroblasts in collagen VII expression. *J Invest Dermatol* **129**:S81, 2009