

6 Literaturverzeichnis

1. Gitter AH, Bendfeldt K, Schulzke JD, and Fromm M (2000) Leaks in the epithelial barrier caused by spontaneous and TNF-alpha-induced single-cell apoptosis. *Faseb J* 14(12): 1749-53
2. Gitter AH, Wullstein F, Fromm M, and Schulzke JD (2001) Epithelial barrier defects in ulcerative colitis: characterization and quantification by electrophysiological imaging. *Gastroenterology* 121(6): 1320-8
3. Madara JL (1990) Maintenance of the macromolecular barrier at cell extrusion sites in intestinal epithelium: physiological rearrangement of tight junctions. *J Membr Biol* 116(2): 177-84
4. Baron DA and Miller DH (1990) Extrusion of colonic epithelial cells in vitro. *J Electron Microsc Tech* 16(1): 15-24
5. Staehelin LA (1973) Further observations on the fine structure of freeze-cleaved tight junctions. *J Cell Sci* 13(3): 763-86
6. Balda MS, Whitney JA, Flores C, Gonzalez S, Cereijido M, and Matter K (1996) Functional dissociation of paracellular permeability and transepithelial electrical resistance and disruption of the apical-basolateral intramembrane diffusion barrier by expression of a mutant tight junction membrane protein. *J Cell Biol* 134(4): 1031-49
7. Bamforth SD, Kniessl U, Wolburg H, Engelhardt B, and Risau W (1999) A dominant mutant of occludin disrupts tight junction structure and function. *J Cell Sci* 112 (Pt 12): 1879-88
8. Saitou M, Fujimoto K, Doi Y, Itoh M, Fujimoto T, Furuse M, Takano H, Noda T, and Tsukita S (1998) Occludin-deficient embryonic stem cells can differentiate into polarized epithelial cells bearing tight junctions. *J Cell Biol* 141(2): 397-408
9. Schneeberger EE and Lynch RD (2004) The tight junction: a multifunctional complex. *Am J Physiol Cell Physiol* 286(6): C1213-28
10. Rahner C, Mitic LL, and Anderson JM (2001) Heterogeneity in expression and subcellular localization of claudins 2, 3, 4, and 5 in the rat liver, pancreas, and gut. *Gastroenterology* 120(2): 411-22
11. Simon DB, Lu Y, Choate KA, Velazquez H, Al-Sabban E, Praga M, Casari G, Bettinelli A, Colussi G, Rodriguez-Soriano J, McCredie D, Milford D, Sanjad S, and Lifton RP (1999) Paracellin-1, a renal tight junction protein required for paracellular Mg²⁺ resorption. *Science* 285(5424): 103-6
12. Morita K, Sasaki H, Fujimoto K, Furuse M, and Tsukita S (1999) Claudin-11/OSP-based tight junctions of myelin sheaths in brain and Sertoli cells in testis. *J Cell Biol* 145(3): 579-88
13. Furuse M, Sasaki H, and Tsukita S (1999) Manner of interaction of heterogeneous claudin species within and between tight junction strands. *J Cell Biol* 147(4): 891-903

14. Furuse M, Hata M, Furuse K, Yoshida Y, Haratake A, Sugitani Y, Noda T, Kubo A, and Tsukita S (2002) Claudin-based tight junctions are crucial for the mammalian epidermal barrier: a lesson from claudin-1-deficient mice. *J Cell Biol* 156(6): 1099-111
15. Van Itallie C, Rahner C, and Anderson JM (2001) Regulated expression of claudin-4 decreases paracellular conductance through a selective decrease in sodium permeability. *J Clin Invest* 107(10): 1319-27
16. Wen H, Watry DD, Marcondes MC, and Fox HS (2004) Selective decrease in paracellular conductance of tight junctions: role of the first extracellular domain of claudin-5. *Mol Cell Biol* 24(19): 8408-17
17. Furuse M, Furuse K, Sasaki H, and Tsukita S (2001) Conversion of zonulae occludentes from tight to leaky strand type by introducing claudin-2 into Madin-Darby canine kidney I cells. *J Cell Biol* 153(2): 263-72
18. Amasheh S, Meiri N, Gitter AH, Schoneberg T, Mankertz J, Schulzke JD, and Fromm M (2002) Claudin-2 expression induces cation-selective channels in tight junctions of epithelial cells. *J Cell Sci* 115(Pt 24): 4969-76
19. Matter K and Balda MS (1999) Occludin and the functions of tight junctions. *Int Rev Cytol* 186: 117-46
20. Crohn BB, Ginzburg, L., Oppenheimer, G.D. (1932) Regional ileitis; pathological and clinical entity. *JAMA* (99): 1323-1329
21. Kirsner JB (2001) Historical origins of current IBD concepts. *World J Gastroenterol* 7(2): 175-84
22. Crohn BB (1967) Granulomatous diseases of the small and large bowel. A historical survey. *Gastroenterology* 52(5): 767-72
23. Moschowitz E, Wilensky, A.O. (1923) Nonspecific granulomata of the intestine. *Am J Med* 166: 48-66
24. Greenstein AJ, Janowitz HD, and Sachar DB (1976) The extra-intestinal complications of Crohn's disease and ulcerative colitis: a study of 700 patients. *Medicine (Baltimore)* 55(5): 401-12
25. Timmer A, Breuer-Katschinski B, and Goebell H (1999) Time trends in the incidence and disease location of Crohn's disease 1980-1995: a prospective analysis in an urban population in Germany. *Inflamm Bowel Dis* 5(2): 79-84
26. Loffler A and Glados M (1993) [Data on the epidemiology of Crohn disease in the city of Cologne]. *Med Klin (Munich)* 88(9): 516-9
27. Steinhardt HJ, Loeschke K, Kasper H, Holtermuller KH, and Schafer H (1985) European Cooperative Crohn's Disease Study (ECCDS): clinical features and natural history. *Digestion* 31(2-3): 97-108
28. Podolsky DK (2002) Inflammatory bowel disease. *N Engl J Med* 347(6): 417-29
29. Tysk C, Lindberg E, Jarnerot G, and Floderus-Myrhed B (1988) Ulcerative colitis and Crohn's disease in an unselected population of monozygotic and dizygotic twins. A study of heritability and the influence of smoking. *Gut* 29(7): 990-6

30. Orholm M, Munkholm P, Langholz E, Nielsen OH, Sorensen IA, and Binder V (1991) Familial occurrence of inflammatory bowel disease. *N Engl J Med* 324(2): 84-8
31. Hugot JP, Chamaillard M, Zouali H, Lesage S, Cezard JP, Belaiche J, Almer S, Tysk C, O'Morain CA, Gassull M, Binder V, Finkel Y, Cortot A, Modigliani R, Laurent-Puig P, Gower-Rousseau C, Macry J, Colombel JF, Sahbatou M, and Thomas G (2001) Association of NOD2 leucine-rich repeat variants with susceptibility to Crohn's disease. *Nature* 411(6837): 599-603
32. Hoffmann JC, Kroesen, A.J., Klump, B. (2004) Chronisch entzündliche Darmerkrankungen, Thieme, Stuttgart
33. Rath HC, Schultz M, Freitag R, Dieleman LA, Li F, Linde HJ, Scholmerich J, and Sartor RB (2001) Different subsets of enteric bacteria induce and perpetuate experimental colitis in rats and mice. *Infect Immun* 69(4): 2277-85
34. Darfeuille-Michaud A, Neut C, Barnich N, Lederman E, Di Martino P, Desreumaux P, Gambiez L, Joly B, Cortot A, and Colombel JF (1998) Presence of adherent Escherichia coli strains in ileal mucosa of patients with Crohn's disease. *Gastroenterology* 115(6): 1405-13
35. Swidsinski A, Ladhoff A, Pernthaler A, Swidsinski S, Loening-Baucke V, Ortner M, Weber J, Hoffmann U, Schreiber S, Dietel M, and Lochs H (2002) Mucosal flora in inflammatory bowel disease. *Gastroenterology* 122(1): 44-54
36. Bjarnason I, O'Morain C, Levi AJ, and Peters TJ (1983) Absorption of 51chromium-labeled ethylenediaminetetraacetate in inflammatory bowel disease. *Gastroenterology* 85(2): 318-22
37. Bjarnason I, MacPherson A, and Hollander D (1995) Intestinal permeability: an overview. *Gastroenterology* 108(5): 1566-81
38. Soderholm JD, Olaison G, Lindberg E, Hannestad U, Vindels A, Tysk C, Jarnerot G, and Sjodahl R (1999) Different intestinal permeability patterns in relatives and spouses of patients with Crohn's disease: an inherited defect in mucosal defence? *Gut* 44(1): 96-100
39. Soderholm JD, Peterson KH, Olaison G, Franzen LE, Westrom B, Magnusson KE, and Sjodahl R (1999) Epithelial permeability to proteins in the noninflamed ileum of Crohn's disease? *Gastroenterology* 117(1): 65-72
40. Wyatt J, Vogelsang H, Hubl W, Waldhoer T, and Lochs H (1993) Intestinal permeability and the prediction of relapse in Crohn's disease. *Lancet* 341(8858): 1437-9
41. Schmitz H, Barmeyer C, Fromm M, Runkel N, Foss HD, Bentzel CJ, Riecken EO, and Schulzke JD (1999) Altered tight junction structure contributes to the impaired epithelial barrier function in ulcerative colitis. *Gastroenterology* 116(2): 301-9
42. Claude P (1978) Morphological factors influencing transepithelial permeability: a model for the resistance of the zonula occludens. *J Membr Biol* 39(2-3): 219-32
43. Burgel N, Bojarski C, Mankertz J, Zeitz M, Fromm M, and Schulzke JD (2002) Mechanisms of diarrhea in collagenous colitis. *Gastroenterology* 123(2): 433-43
44. Kucharzik T, Walsh SV, Chen J, Parkos CA, and Nusrat A (2001) Neutrophil transmigration in inflammatory bowel disease is associated with differential expression of epithelial intercellular junction proteins. *Am J Pathol* 159(6): 2001-9

45. MacDonald TT, Hutchings P, Choy MY, Murch S, and Cooke A (1990) Tumour necrosis factor-alpha and interferon-gamma production measured at the single cell level in normal and inflamed human intestine. *Clin Exp Immunol* 81(2): 301-5
46. Guy-Grand D, DiSanto JP, Henchoz P, Malassis-Seris M, and Vassalli P (1998) Small bowel enteropathy: role of intraepithelial lymphocytes and of cytokines (IL-12, IFN-gamma, TNF) in the induction of epithelial cell death and renewal. *Eur J Immunol* 28(2): 730-44
47. Marini M, Bamias G, Rivera-Nieves J, Moskaluk CA, Hoang SB, Ross WG, Pizarro TT, and Cominelli F (2003) TNF-alpha neutralization ameliorates the severity of murine Crohn's-like ileitis by abrogation of intestinal epithelial cell apoptosis. *Proc Natl Acad Sci U S A* 100(14): 8366-71
48. Hagiwara C, Tanaka M, and Kudo H (2002) Increase in colorectal epithelial apoptotic cells in patients with ulcerative colitis ultimately requiring surgery. *J Gastroenterol Hepatol* 17(7): 758-64
49. Singleton JW, Hanauer SB, Gitnick GL, Peppercorn MA, Robinson MG, Wruble LD, and Krawitt EL (1993) Mesalamine capsules for the treatment of active Crohn's disease: results of a 16-week trial. Pentasa Crohn's Disease Study Group. *Gastroenterology* 104(5): 1293-301
50. Malchow H, Ewe K, Brandes JW, Goebell H, Ehms H, Sommer H, and Jesdinsky H (1984) European Cooperative Crohn's Disease Study (ECCDS): results of drug treatment. *Gastroenterology* 86(2): 249-66
51. Papi C, Luchetti R, Gili L, Montanti S, Koch M, and Capurso L (2000) Budesonide in the treatment of Crohn's disease: a meta-analysis. *Aliment Pharmacol Ther* 14(11): 1419-28
52. Ewe K, Press AG, Singe CC, Stufler M, Ueberschaer B, Hommel G, and Meyer zum Buschenfelde KH (1993) Azathioprine combined with prednisolone or monotherapy with prednisolone in active Crohn's disease. *Gastroenterology* 105(2): 367-72
53. Schreiber S, Campieri M, Colombel JF, van Deventer SJ, Feagan B, Fedorak R, Forbes A, Gassull M, Gendre JP, van Hogezand RA, Lofberg R, Modigliani R, Pallone F, Petritsch W, Prantera C, Rampton D, Seibold F, Vatn M, Zeitz M, and Rutgeerts P (2001) Use of anti-tumour necrosis factor agents in inflammatory bowel disease. European guidelines for 2001-2003. *Int J Colorectal Dis* 16(1): 1-11; discussion 12-3
54. Stack WA, Mann SD, Roy AJ, Heath P, Sopwith M, Freeman J, Holmes G, Long R, Forbes A, and Kamm MA (1997) Randomised controlled trial of CDP571 antibody to tumour necrosis factor-alpha in Crohn's disease. *Lancet* 349(9051): 521-4
55. Targan SR, Hanauer SB, van Deventer SJ, Mayer L, Present DH, Braakman T, DeWoody KL, Schaible TF, and Rutgeerts PJ (1997) A short-term study of chimeric monoclonal antibody cA2 to tumor necrosis factor alpha for Crohn's disease. Crohn's Disease cA2 Study Group. *N Engl J Med* 337(15): 1029-35
56. Hanauer SB, Feagan BG, Lichtenstein GR, Mayer LF, Schreiber S, Colombel JF, Rachmilewitz D, Wolf DC, Olson A, Bao W, and Rutgeerts P (2002) Maintenance infliximab for Crohn's disease: the ACCENT I randomised trial. *Lancet* 359(9317): 1541-9
57. Lugering A, Schmidt M, Lugering N, Pauels HG, Domschke W, and Kucharzik T (2001) Infliximab induces apoptosis in monocytes from patients with chronic active Crohn's disease by using a caspase-dependent pathway. *Gastroenterology* 121(5): 1145-57

58. ten Hove T, van Montfrans C, Peppelenbosch MP, and van Deventer SJ (2002) Infliximab treatment induces apoptosis of lamina propria T lymphocytes in Crohn's disease. *Gut* 50(2): 206-11
59. Van den Brande JM, Braat H, van den Brink GR, Versteeg HH, Bauer CA, Hoedemaeker I, van Montfrans C, Hommes DW, Peppelenbosch MP, and van Deventer SJ (2003) Infliximab but not etanercept induces apoptosis in lamina propria T-lymphocytes from patients with Crohn's disease. *Gastroenterology* 124(7): 1774-85
60. Suenaert P, Bulteel V, Lemmens L, Noman M, Geypens B, Van Assche G, Geboes K, Ceuppens JL, and Rutgeerts P (2002) Anti-tumor necrosis factor treatment restores the gut barrier in Crohn's disease. *Am J Gastroenterol* 97(8): 2000-4
61. Ussing HH, Zerahn, K. (1951) Active transport of sodium as the source of electric current in the short-circuited isolated frog skin. *Acta phys Scandinav* 23: 110-127
62. Gitter AH, Schulzke JD, Sorgenfrei D, and Fromm M (1997) Ussing chamber for high-frequency transmural impedance analysis of epithelial tissues. *J Biochem Biophys Methods* 35(2): 81-8
63. Stockmann M, Gitter AH, Sorgenfrei D, Fromm M, and Schulzke JD (1999) Low edge damage container insert that adjusts intestinal forceps biopsies into Ussing chamber systems. *Pflugers Arch* 438(1): 107-12
64. Barmeyer C (2002) Diarrhoe und Malabsorption bei Colitis ulcerosa und zugrunde liegende Mechanismen in den Modellen der Interleukin-2-defizienten Maus und der Zytokin-exponierten Kolonmucosa der Ratte, Shaker Verlag, Berlin
65. Fromm M, Schulzke JD, and Hegel U (1985) Epithelial and subepithelial contributions to transmural electrical resistance of intact rat jejunum, *in vitro*. *Pflugers Arch* 405(4): 400-2
66. Darzynkiewicz Z, Li X, and Gong J (1994) Assays of cell viability: discrimination of cells dying by apoptosis. *Methods Cell Biol* 41: 15-38
67. Bojarski C, Gitter AH, Bendfeldt K, Mankertz J, Schmitz H, Wagner S, Fromm M, and Schulzke JD (2001) Permeability of human HT-29/B6 colonic epithelium as a function of apoptosis. *J Physiol* 535(Pt 2): 541-52
68. Anderson JM, Stevenson BR, Jesaitis LA, Goodenough DA, and Mooseker MS (1988) Characterization of ZO-1, a protein component of the tight junction from mouse liver and Madin-Darby canine kidney cells. *J Cell Biol* 106(4): 1141-9
69. Stevenson BR, Siliciano JD, Mooseker MS, and Goodenough DA (1986) Identification of ZO-1: a high molecular weight polypeptide associated with the tight junction (zonula occludens) in a variety of epithelia. *J Cell Biol* 103(3): 755-66
70. Bentzel CJ, Hainau B, Ho S, Hui SW, Edelman A, Anagnostopoulos T, and Benedetti EL (1980) Cytoplasmic regulation of tight-junction permeability: effect of plant cytokinins. *Am J Physiol* 239(3): C75-89
71. Schulzke JD, Fromm M, von Hippel C, Sandforth F, Menge H, Bentzel CJ, and Riecken EO (1990) Adaptation of epithelial ion transport in the short bowel syndrome. *Digestion* 46 Suppl 2: 467-71
72. Best WR, Becktel JM, and Singleton JW (1979) Rederived values of the eight coefficients of the Crohn's Disease Activity Index (CDAI). *Gastroenterology* 77(4 Pt 2): 843-6

73. Claude P and Goodenough DA (1973) Fracture faces of zonulae occludentes from "tight" and "leaky" epithelia. *J Cell Biol* 58(2): 390-400
74. Soderholm JD, Olaison G, Peterson KH, Franzen LE, Lindmark T, Wiren M, Tagesson C, and Sjodahl R (2002) Augmented increase in tight junction permeability by luminal stimuli in the non-inflamed ileum of Crohn's disease. *Gut* 50(3): 307-13
75. van Dullemen HM, van Deventer SJ, Hommes DW, Bijl HA, Jansen J, Tytgat GN, and Woody J (1995) Treatment of Crohn's disease with anti-tumor necrosis factor chimeric monoclonal antibody (cA2). *Gastroenterology* 109(1): 129-35
76. Stockmann M, Fromm M, Schmitz H, Schmidt W, Riecken EO, and Schulzke JD (1998) Duodenal biopsies of HIV-infected patients with diarrhoea exhibit epithelial barrier defects but no active secretion. *Aids* 12(1): 43-51
77. Bu P, Keshavarzian A, Stone DD, Liu J, Le PT, Fisher S, and Qiao L (2001) Apoptosis: one of the mechanisms that maintains unresponsiveness of the intestinal mucosal immune system. *J Immunol* 166(10): 6399-403
78. Boirivant M, Marini M, Di Felice G, Pronio AM, Montesani C, Tersigni R, and Strober W (1999) Lamina propria T cells in Crohn's disease and other gastrointestinal inflammation show defective CD2 pathway-induced apoptosis. *Gastroenterology* 116(3): 557-65
79. Ina K, Itoh J, Fukushima K, Kusugami K, Yamaguchi T, Kyokane K, Imada A, Binion DG, Musso A, West GA, Dobrea GM, McCormick TS, Lapetina EG, Levine AD, Ottaway CA, and Fiocchi C (1999) Resistance of Crohn's disease T cells to multiple apoptotic signals is associated with a Bcl-2/Bax mucosal imbalance. *J Immunol* 163(2): 1081-90
80. Di Sabatino A, Ciccioppo R, Cinque B, Millimaggi D, Morera R, Ricevuti L, Cifone MG, and Corazza GR (2004) Defective mucosal T cell death is sustainably reverted by infliximab in a caspase dependent pathway in Crohn's disease. *Gut* 53(1): 70-7
81. Sartor RB (1997) Review article: Role of the enteric microflora in the pathogenesis of intestinal inflammation and arthritis. *Aliment Pharmacol Ther* 11 Suppl 3: 17-22; discussion 22-3
82. D'Haens G, Van Deventer S, Van Hogezand R, Chalmers D, Kothe C, Baert F, Braakman T, Schaible T, Geboes K, and Rutgeerts P (1999) Endoscopic and histological healing with infliximab anti-tumor necrosis factor antibodies in Crohn's disease: A European multicenter trial. *Gastroenterology* 116(5): 1029-34
83. Rucklidge GJ, Milne G, McGaw BA, Milne E, and Robins SP (1992) Turnover rates of different collagen types measured by isotope ratio mass spectrometry. *Biochim Biophys Acta* 1156(1): 57-61
84. Tsukita S, Furuse M, and Itoh M (2001) Multifunctional strands in tight junctions. *Nat Rev Mol Cell Biol* 2(4): 285-93
85. Furuse M, Sasaki H, Fujimoto K, and Tsukita S (1998) A single gene product, claudin-1 or -2, reconstitutes tight junction strands and recruits occludin in fibroblasts. *J Cell Biol* 143(2): 391-401
86. Inai T, Kobayashi J, and Shibata Y (1999) Claudin-1 contributes to the epithelial barrier function in MDCK cells. *Eur J Cell Biol* 78(12): 849-55
87. Sonoda N, Furuse M, Sasaki H, Yonemura S, Katahira J, Horiguchi Y, and Tsukita S (1999) Clostridium perfringens enterotoxin fragment removes specific claudins from tight

- junction strands: Evidence for direct involvement of claudins in tight junction barrier. *J Cell Biol* 147(1): 195-204
88. Fujita K, Katahira J, Horiguchi Y, Sonoda N, Furuse M, and Tsukita S (2000) Clostridium perfringens enterotoxin binds to the second extracellular loop of claudin-3, a tight junction integral membrane protein. *FEBS Lett* 476(3): 258-61
89. Marin ML, Geller SA, Greenstein AJ, Marin RH, Gordon RE, and Aufses AH, Jr. (1983) Ultrastructural pathology of Crohn's disease: correlated transmission electron microscopy, scanning electron microscopy, and freeze fracture studies. *Am J Gastroenterol* 78(6): 355-64
90. Marin ML, Greenstein AJ, Geller SA, Gordon RE, and Aufses AH, Jr. (1983) A freeze fracture study of Crohn's disease of the terminal ileum: changes in epithelial tight junction organization. *Am J Gastroenterol* 78(9): 537-47