

BIBLIOGRAFÍA

1. Carter MJ, Lobo AJ, Travis SP. Guidelines for the management of inflammatory bowel disease in adults. *Gut* 2004;53:V1-V16.
2. Podolsky DK. Inflammatory bowel disease. *N Engl J Med* 2002;347:417-29.
3. Shanahan F. Crohn's disease. *Lancet* 2002;359:62-9.
4. Farrell RJ, Peppercorn MA. Ulcerative colitis. *Lancet* 2002;359:331-40.
5. Brullet E, Bonfill X, Urrutia G, Ruiz O, V, Cueto M, Clofent J, Martinez Salmeron JF, Riera J, Obrador A. Epidemiological study on the incidence of inflammatory bowel disease in 4 Spanish areas. *Med Clin (Barc)* 1998;110:651-6.
6. Sands BE. From symptom to diagnosis: clinical distinctions among various forms of intestinal inflammation. *Gastroenterology* 2004;126:1518-32.
7. Egan LJ, Sandborn WJ. Advances in the treatment of Crohn's disease. *Gastroenterology* 2004;126:1574-81.
8. Hanauer SB. Medical therapy for ulcerative colitis 2004. *Gastroenterology* 2004;126:1582-92.
9. Larson DW, Pemberton JH. Current concepts and controversies in surgery for IBD. *Gastroenterology* 2004;126:1611-9.
10. Ahmad T, Tamboli CP, Jewell D, Colombel JF. Clinical relevance of advances in genetics and pharmacogenetics of IBD. *Gastroenterology* 2004;126:1533-49.
11. 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, Thomas G. Association of NOD2 leucine-rich repeat variants with susceptibility to Crohn's disease. *Nature* 2001;411:599-603.
12. Ogura Y, Bonen DK, Inohara N, Nicolae DL, Chen FF, Ramos R, Britton H, Moran T, Karaliuskas R, Duerr RH, Achkar JP, Brant SR, Bayless TM, Kirschner BS, Hanauer SB, Nunez G, Cho JH. A frameshift mutation in NOD2 associated with susceptibility to Crohn's disease. *Nature* 2001;411:603-6.
13. Ahmad T, Armuzzi A, Bunce M, Mulcahy-Hawes K, Marshall SE, Orchard TR, Crawshaw J, Large O, de Silva A, Cook JT, Barnardo M, Cullen S, Welsh KI, Jewell DP. The molecular classification of the clinical manifestations of Crohn's disease. *Gastroenterology* 2002;122:854-66.
14. Cuthbert AP, Fisher SA, Mirza MM, King K, Hampe J, Croucher PJ, Mascheretti S, Sanderson J, Forbes A, Mansfield J, Schreiber S, Lewis CM, Mathew CG. The contribution of NOD2 gene mutations to the risk and site of disease in inflammatory bowel disease. *Gastroenterology* 2002;122:867-74.
15. Lesage S, Zouali H, Cezard JP, Colombel JF, Belaiche J, Almer S, Tysk C, O'Morain C, Gassull M, Binder V, Finkel Y, Modigliani R, Gower-Rousseau C, Macry J, Merlin F, Chamaillard M, Jannot AS, Thomas G, Hugot JP; EPWG-IBD Group; EPIIMAD Group; GETAID Group. CARD15/NOD2 mutational analysis and genotype-phenotype correlation in 612 patients with inflammatory bowel disease. *Am J Hum Genet* 2002;70:845-57.
16. Loftus EV Jr. Clinical epidemiology of inflammatory bowel disease: Incidence, prevalence, and environmental influences. *Gastroenterology* 2004;126:1504-17.
17. Evans JM, McMahon AD, Murray FE, McDevitt DG, MacDonald TM. Non-steroidal anti-inflammatory drugs are associated with emergency admission to hospital for colitis due to inflammatory bowel disease. *Gut* 1997;40:619-22.
18. Andersson RE, Olaison G, Tysk C, Ekbom A. Appendectomy and protection against ulcerative colitis. *N Engl J Med* 2001;344:808-14.

19. Cosnes J, Beaugerie L, Carbonnel F, Gendre JP. Smoking cessation and the course of Crohn's disease: an intervention study. *Gastroenterology* 2001;120:1093-9.
20. Lindberg E, Tysk C, Andersson K, Jarnerot G. Smoking and inflammatory bowel disease. A case control study. *Gut* 1988;29:352-7.
21. Blumberg RS, Strober W. Prospects for research in inflammatory bowel disease. *JAMA* 2001;285:643-7.
22. Rath HC, Schultz M, Freitag R, Dieleman LA, Li F, Linde HJ, Scholmerich J, Sartor RB. Different subsets of enteric bacteria induce and perpetuate experimental colitis in rats and mice. *Infect Immun* 2001;69:2277-85.
23. Darfeuille-Michaud A, Neut C, Barnich N, Lederman E, Di Martino P, Desreumaux P, Gambiez L, Joly B, Cortot A, Colombel JF. Presence of adherent Escherichia coli strains in ileal mucosa of patients with Crohn's disease. *Gastroenterology* 1998;115:1405-13.
24. Swidsinski A, Ladhoff A, Pernthaler A, Swidsinski S, Loening-Baucke V, Ortner M, Weber J, Hoffmann U, Schreiber S, Dietel M, Lochs H. Mucosal flora in inflammatory bowel disease. *Gastroenterology* 2002;122:44-54.
25. Mashimo H, Wu DC, Podolsky DK, Fishman MC. Impaired defense of intestinal mucosa in mice lacking intestinal trefoil factor. *Science* 1996;274:262-5.
26. Schmitz H, Barmeyer C, Fromm M, Runkel N, Foss HD, Bentzel CJ, Riecken EO, Schulzke JD. Altered tight junction structure contributes to the impaired epithelial barrier function in ulcerative colitis. *Gastroenterology* 1999;116:301-9.
27. Fiocchi C. Inflammatory bowel disease: etiology and pathogenesis. *Gastroenterology* 1998;115:182-205.
28. Fuss IJ, Neurath M, Boirivant M, Klein JS, de la Motte C, Strong SA, Fiocchi C, Strober W. Disparate CD4+ lamina propria (LP) lymphokine secretion profiles in inflammatory bowel disease. Crohn's disease LP cells manifest increased secretion of IFN-gamma, whereas ulcerative colitis LP cells manifest increased secretion of IL-5. *J Immunol* 1996;157:1261-70.
29. Sans M, Panes J, Ardite E, Elizalde JI, Arce Y, Elena M, Palacin A, Fernandez-Checa JC, Anderson DC, Lobb R, Pique JM. VCAM-1 and ICAM-1 mediate leukocyte-endothelial cell adhesion in rat experimental colitis. *Gastroenterology* 1999;116:874-83.
30. Koizumi M, King N, Lobb R, Benjamin C, Podolsky DK. Expression of vascular adhesion molecules in inflammatory bowel disease. *Gastroenterology* 1992;103:840-7.
31. Von Andrian UH, Mackay CR. T-cell function and migration. Two sides of the same coin. *N Engl J Med* 2000;343:1020-34.
32. Panés J, Granger DN. Leukocyte-endothelial cell interactions: molecular mechanisms and implications in gastrointestinal disease. *Gastroenterology* 1998;114:1066-90.
33. Tedder TF, Steeber DA, Chen A, Engel P. The selectins: vascular adhesion molecules. *FASEB J* 1995;9:866-73.
34. Geng JG, Bevilacqua MP, Moore KL, McIntyre TM, Prescott SM, Kim JM, Bliss GA, Zimmerman GA, McEver RP. Rapid neutrophil adhesion to activated endothelium mediated by GMP-140. *Nature* 1990;343:757-60.
35. Sanders WE, Wilson RW, Ballantyne CM, Beaudet AL. Molecular cloning and analysis of in vivo expression of murine P-selectin. *Blood* 1992;80:795-800.

36. Weller A, Isenmann S, Vestweber D. Cloning of the mouse endothelial selectins. Expression of both E- and P-selectin is inducible by tumor necrosis factor alpha. *J Biol Chem* 1992;267:15176-83.
37. Issekutz AC, Lopes N. Endotoxin activation of endothelium for polymorphonuclear leucocyte transendothelial migration and modulation by interferon-gamma. *Immunology* 1993;79:600-7.
38. Eppihimer MJ, Wolitzky B, Anderson DC, Labow MA, Granger DN. Heterogeneity of expression of E- and P-selectins in vivo. *Circ Res* 1996;79:560-9.
39. Bevilacqua MP, Pober JS, Mendrick DL, Cotran RS, Gimbrone MJ. Identification of an inducible endothelial-leukocyte adhesion molecule. *Proc Natl Acad Sci USA* 1987;84:9238-42.
40. Jutila MA, Rorr L, Berg EL, Butcher EC. Function and regulation of the neutrophil MEL-14 antigen in vivo: Comparison with LFA-1 and MAC-1. *J Immunol* 1989;143:3318-24.
41. Kishimoto TK, Jutila MA, Berg EL, Butcher EC. Neutrophil Mac-1 and MEL-14 adhesion proteins inversely regulated by chemotactic factors. *Science* 1989; 245:1238-41.
42. Kishimoto TK, Jutila MA, Butcher EC. Identification of a human peripheral lymph node homing receptor: a rapidly down-regulated adhesion molecule. *Proc Natl Acad Sci USA* 1990;87:2244-48.
43. Foxall C, Watson SR, Dowbenko D, Fennie C, Lasky LA, Kiso M, Hasegawa A, Asa D, Brandley BK. The three members of the selectin receptor family recognize a common carbohydrate epitope, the sialyl Lewis(x) oligosaccharide. *J Cell Biol* 1992;117:895-902.
44. Lasky LA, Singer MS, Dowbenko D, Imai Y, Henzel WJ, Grimley C, Fennie C, Gillett N, Watson SR, Rosen SD. An endothelial ligand for L-selectin is a novel mucin-like molecule. *Cell* 1992;69:927-38.
45. Sako D, Chang XJ, Barone KM, Vachino G, White HM, Shaw G, Veldman GM, Bean KM, Ahern TJ, Furie B, et al. Expression cloning of a functional glycoprotein ligand for P-selectin. *Cell* 1993;75:1179-86.
46. Moore KL, Stults NL, Diaz S, Smith DF, Cummings RD, Varki A, McEver RP. Identification of a specific glycoprotein ligand for P-selectin (CD62) on myeloid cells. *J Cell Biol* 1992;118:445-56.
47. Ohmori K, Takada A, Yoneda T, Buma Y, Hirashima K, Tsuysaka K, Hasegawa A, Kannagi R. Differentiation-dependent expression of sialyl stage-specific embryonic antigen-1 and I-antigens on human lymphoid cells and its implications for carbohydrate-mediated adhesion to vascular endothelium. *Blood* 1993;81:101-11.
48. Marlin SD, Springer TA. Purified intercellular adhesion molecule-1 (ICAM-1) is a ligand for lymphocyte function-associated antigen (LFA-1). *Cell* 1987;51:813-9.
49. Bell RG, Issekutz T. Expression of a protective intestinal immune response can be inhibited at three distinct sites by treatment with anti-alpha 4 integrin. *J Immunol* 1993;151:4790-802.
50. Allavena P, Paganin C, Martin-Padura I, Peri G, Gaboli M, Dejana E, Marchisio PC, Mantovani A. Molecules and structures involved in the adhesion of natural killer cells to vascular endothelium. *J Exp Med* 1991;173:439-48.
51. Holzmann B, McIntyre BW, Weissman IL. Identification of a murine Peyer's patch-specific lymphocyte homing receptor as an integrin molecule with an alpha chain homologous to human VLA-4 alpha. *Cell* 1989;56:37-46.
52. Tsuzuki Y, Miura S, Suematsu M, Kurose I, Shigematsu T, Kimura H, Higuchi H, Serizawa H, Yagita H, Okumura K, Ishii H. α_4 integrin plays a critical role in early stages of T lymphocyte migration in Peyer's patches of rats. *Intl Immunol* 1996;8:287-95.

53. Farstad IN, Halstensen TS, Kvale D, Fausa O, Brandtzaeg P. Topographic distribution of homing receptors on B and T cells in human gut-associated lymphoid tissue: relation of L-selectin and integrin alpha 4 beta 7 to naive and memory phenotypes. *Am J Pathol* 1997;150:187-99.
54. Cordell JL, Pulford K, Turley H, Jones M, Micklem K, Doussis IA, Tyler X, Mayne K, Gatter KC, Mason DY. Cellular distribution of human leucocyte adhesion molecule ICAM-3. *J Clin Pathol* 1994;47:143-47.
55. Panés J, Perry MA, Anderson DC, Manning A, Leone B, Cepinskas G, Rosenbloom CL, Miyasaka M, Kvietys PR, Granger DN. Regional differences in constitutive and induced ICAM-1 expression in vivo. *Am J Physiol* 1995;269:H1955-64.
56. Staunton DE, Dustin ML, Springer TA. Functional cloning of ICAM-2, a cell adhesion ligand for LFA-1 homologous to ICAM-1. *Nature* 1989;339:61-4.
57. Elices MJ, Osborn L, Takada Y, Crouse C, Luhowskyj S, Hemler M, Lobb RR. VCAM-1 on activated endothelium interacts with the leukocyte integrin VLA-4 at a site distinct from the VLA-4/fibronectin binding site. *Cell* 1990;60:577-84.
58. Strauch UG, Lifka A, Gossler U, Kilshaw PJ, Clements J, Holzmann B. Distinct binding specificities of integrins alpha 4 beta 7 (LPAM-1), alpha 4 beta 1 (VLA-4), and alpha IEL beta 7. *Int Immunol* 1994;6:263-75.
59. Streeter PR, Berg EL, Rouse BTN, Bargatze RF, Butcher EC. A tissue-specific endothelial cell molecule involved in leukocyte homing. *Nature* 1988;331:41-6.
60. Berg EL, McEvoy LM, Berlin C, Bargatze RF, Butcher EC. L-selectin-mediated lymphocyte rolling on MAdCAM-1. *Nature* 1993;366:695-8.
61. Berlin C, Berg EL, Briskin MJ, Andrew DP, Kilshaw PJ, Holzmann B, Weissman IL, Hamann A, Butcher EC. Alpha 4 beta 7 integrin mediates lymphocyte binding to the mucosal vascular addressin MAdCAM-1. *Cell* 1993;74:185-95.
62. Albelda SM, Oliver PD, Romer LH, Buck CA. EndoCAM: A novel endothelial cell-cell adhesion molecule. *J Cell Biol* 1990;110:1227-37.
63. Wakelin MW, Sanz MJ, Dewar A, Albelda SM, Larkin SW, Boughton-Smith N, Williams TJ, Nourshargh S. An anti-platelet-endothelial cell adhesion molecule-1 antibody inhibits leukocyte extravasation from mesenteric microvessels in vivo by blocking the passage through the basement membrane. *J Exp Med* 1996;184:229-39.
64. Read MA, Neish AS, Luscinskas FW, Palombella VJ, Maniatis T, Collins T. The proteasome pathway is required for cytokine-induced endothelial-leukocyte adhesion molecule expression. *Immunity* 1995;2:493-506.
65. Conner EM, Brand S, Davis JM, Laroux FS, Palombella VJ, Fuseler JW, Kang DY, Wolf RE, Grisham MB. Proteasome inhibition attenuates nitric oxide synthase expression, VCAM-1 transcription and the development of chronic colitis. *J Pharmacol Exp Ther* 1997;282:1615-22.
66. Neurath MF, Pettersson S, Meyer zum Buschenfelde KH, Strober W. Local administration of antisense phosphorothioate oligonucleotides to the p65 subunit of NF-kappa B abrogates established experimental colitis in mice. *Nat Med* 1996;2:998-1004.
67. Schreiber S, Nikolaus S, Hampe J. Activation of nuclear factor kappa B inflammatory bowel disease. *Gut* 1998;42:477-84.
68. Ardite E, Panes J, Miranda M, Salas A, Elizalde JI, Sans M, Arce Y, Bordas JM, Fernandez-Checa JC, Pique JM. Effects of steroid treatment on activation of nuclear factor kappaB in patients with inflammatory bowel disease. *Br J Pharmacol* 1998;124:431-3.

69. Ala A, Dhillon AP, Hodgson HJ. Role of cell adhesion molecules in leukocyte recruitment in the liver and gut. *Int J Exp Pathol* 2003;84:1-16.
70. McCafferty DM, Smith CW, Granger DN, Kubes P. Intestinal inflammation in adhesion molecule-deficient mice: an assessment of P-selectin alone and in combination with ICAM-1 or E-selectin. *J Leukoc Biol* 1999;66:67-74.
71. Sans M, Salas A, Soriano A, Prats N, Gironella M, Pizcueta P, Elena M, Anderson DC, Pique JM, Panes J. Differential role of selectins in experimental colitis. *Gastroenterology* 2001;120:1162-72.
72. Hamamoto N, Maemura K, Hirata I, Murano M, Sasaki S, Katsu K. Inhibition of dextran sulphate sodium (DSS)-induced colitis in mice by intracolonically administered antibodies against adhesion molecules (endothelial leucocyte adhesion molecule-1 (ELAM-1) or intercellular adhesion molecule-1 (ICAM-1)). *Clin Exp Immunol* 1999;117:462-8.
73. Segui J, Gironella M, Sans M, Granell S, Gil F, Gimeno M, Coronel P, Pique JM, Panes J. Superoxide dismutase ameliorates TNBS-induced colitis by reducing oxidative stress, adhesion molecule expression, and leukocyte recruitment into the inflamed intestine. *J Leukoc Biol* 2004;76:537-44.
74. Salas A, Gironella M, Salas A, Soriano A, Sans M, Iovanna J, Pique JM, Panes J. Nitric oxide supplementation ameliorates dextran sulfate sodium-induced colitis in mice. *Lab Invest* 2002;82:597-607.
75. Kawachi S, Jennings S, Panes J, Cockrell A, Laroux FS, Gray L, Perry M, van der Heyde H, Balish E, Granger DN, Specian RA, Grisham MB. Cytokine and endothelial cell adhesion molecule expression in interleukin-10-deficient mice. *Am J Physiol Gastrointest Liver Physiol* 2000;278:G734-43.
76. Kawachi S, Morise Z, Jennings SR, Conner E, Cockrell A, Laroux FS, Chervenak RP, Wolcott M, van der Heyde H, Gray L, Feng L, Granger DN, Specian RA, Grisham MB. Cytokine and adhesion molecule expression in SCID mice reconstituted with CD4+ T cells. *Inflamm Bowel Dis* 2000;6:171-80.
77. Gironella M, Molla M, Salas A, Soriano A, Sans M, Closa D, Engel P, Salas A, Pique JM, Panes J. The role of P-selectin in experimental colitis as determined by antibody immunoblockade and genetically deficient mice. *J Leukoc Biol* 2002;72:56-64.
78. Picarella D, Hurlbut P, Rottman J, Shi X, Butcher E, Ringler DJ. Monoclonal antibodies specific for beta 7 integrin and mucosal addressin cell adhesion molecule-1 (MAdCAM-1) reduce inflammation in the colon of scid mice reconstituted with CD45RBhigh CD4+ T cells. *J Immunol* 1997;158:2099-106.
79. Podolsky DK, Lobb R, King N, Benjamin CD, Pepinsky B, Sehgal P, deBeaumont M. Attenuation of colitis in the cotton-top tamarin by anti-a 4 integrin monoclonal antibody. *J Clin Invest* 1993;92:372-80.
80. Hesterberg PE, Winsor Hines D, Briskin MJ, Soler Ferran D, Merrill C, Mackay CR, Newman W, Ringler DJ. Rapid resolution of chronic colitis in the cotton-top tamarin with an antibody to a gut-homing integrin a 4B7. *Gastroenterology* 1996;111:1373-80.
81. Wong PY, Yue G, Yin K, Miyasaka M, Lane CL, Manning AM, Anderson DC, Sun FF. Antibodies to intercellular adhesion molecule-1 ameliorate the inflammatory response in acetic acid-induced inflammatory bowel disease. *J Pharmacol Exp Ther* 1995;274:475-80.
82. Binion DG, West GA, Ina K, Ziats NP, Emancipator SN, Fiocchi C. Enhanced leukocyte binding by intestinal microvascular endothelial cells in inflammatory bowel disease. *Gastroenterology* 1997;112:1895-907.

83. Pooley N, Ghosh L, Sharon P. Up-regulation of E-selectin and intercellular adhesion molecule-1 differs between Crohn's disease and ulcerative colitis. *Dig Dis Sci* 1995;40:219-25.
84. Cellier C, Patey N, Fromont-Hankard G, Cervoni JP, Leborgne M, Chaussade S, Barbier JP, Brousse N. In-situ endothelial cell adhesion molecule expression in ulcerative colitis. E-selectin in-situ expression correlates with clinical, endoscopic and histological activity and outcome. *Eur J Gastroenterol Hepatol* 1997;9:1197-203.
85. Nakamura S, Ohtani H, Watanabe Y, Fukushima K, Matsumoto T, Kitano A, Kobayashi K, Nagura H. In situ expression of the cell adhesion molecules in inflammatory bowel disease. Evidence of immunologic activation of vascular endothelial cells. *Lab Invest* 1993;69:77-85.
86. Oshitani N, Campbell A, Bloom S, Kitano A, Kobayashi K, Jewell DP. Adhesion molecule expression on vascular endothelium and nitroblue tetrazolium reducing activity in human colonic mucosa. *Scand J Gastroenterol* 1995;30:915-20.
87. Briskin M, Winsor-Hines D, Shyjan A, Cochran N, Bloom S, Wilson J, McEvoy LM, Butcher EC, Kassam N, Mackay CR, Newman W, Ringler DJ. Human mucosal addressin cell adhesion molecule-1 is preferentially expressed in intestinal tract and associated lymphoid tissue. *Am J Pathol* 1997;151:97-110.
88. Haraldsen G, Kvale D, Lien B, Farstad IN, Brandtzaeg P. Cytokine-regulated expression of E-selectin, intercellular adhesion molecule-1 (ICAM-1), and vascular cell adhesion molecule-1 (VCAM-1) in human microvascular endothelial cells. *J Immunol* 1996;156:2558-65.
89. Sandborn WJ, Faubion WA. Biologics in inflammatory bowel disease: how much progress have we made? *Gut* 2004;53:1366-73.
90. Sandborn WJ, Targan SR. Biologic therapy of inflammatory bowel disease. *Gastroenterology* 2002;122:1592-608.
91. Lim WC, Hanauer SB. Emerging biologic therapies in inflammatory bowel disease. *Rev Gastroenterol Disord* 2004;4:66-85.
92. Rutgeerts P, Van Deventer S, Schreiber S. Review article: the expanding role of biological agents in the treatment of inflammatory bowel disease - focus on selective adhesion molecule inhibition. *Aliment Pharmacol Ther* 2003;17:1435-50.
93. Rutgeerts P, Van Assche G, Vermeire S. Optimizing anti-TNF treatment in inflammatory bowel disease. *Gastroenterology* 2004;126:1593-610.
94. Panes J, Peñalva M, Pique JM. New therapeutic targets in inflammatory bowel disease (IBD): cell adhesion molecules. *Inmunología* 2003;22:1-12.
95. Ulbrich H, Eriksson EE, Lindblom L. Leukocyte and endothelial cell adhesion molecules as targets for therapeutic interventions in inflammatory disease. *Trends Pharmacol Sci* 2003;24:640-7.
96. Van Assche G, Rutgeerts P. Antiadhesion molecule therapy in inflammatory bowel disease. *Inflamm Bowel Dis* 2002;8:291-300.
97. Panes J, Perry M, Granger DN. Leukocyte-endothelial cell adhesion: avenues for therapeutic intervention. *Br J Pharmacol* 1999;126:537-50.
98. Pierce JW, Read MA, Ding H, Luscinskas FW, Collins T. Salicylates inhibit I kappa B-alpha phosphorylation, endothelial-leukocyte adhesion molecule expression, and neutrophil transmigration. *J Immunol* 1996;156:3961-9.
99. Lee CH, Chen HH, Hoke G, Jong JS, White L, Kang YH. Antisense gene suppression against human ICAM-1, ELAM-1, and VCAM-1 in cultured human umbilical vein endothelial cells. *Shock* 1995;4:1-10.

100. Bennett CF, Kornbrust D, Henry S, Stecker K, Howard R, Cooper S, Dutson S, Hall W, Jacoby HI. An ICAM-1 antisense oligonucleotide prevents and reverses dextran sulfate sodium-induced colitis in mice. *J Pharmacol Exp Ther* 1997;280:988-1000.
101. Yacyshyn BR, Bowen-Yacyshyn MB, Jewell L, Tami JA, Bennett CF, Kisner DL, Shanahan WR Jr. A placebo-controlled trial of ICAM-1 antisense oligonucleotide in the treatment of Crohn's disease. *Gastroenterology* 1998;114:1133-42.
102. Schreiber S, Nikolaus S, Malchow H, Kruis W, Lochs H, Raedler A, Hahn EG, Krummenerl T, Steinmann G; German ICAM-1 Study Group. Absence of efficacy of subcutaneous antisense ICAM-1 treatment of chronic active Crohn's disease. *Gastroenterology* 2001;120:1339-46.
103. Yacyshyn BR, Chey WY, Goff J, Salzberg B, Baerg R, Buchman AL, Tami J, Yu R, Gibiansky E, Shanahan WR; ISIS 2302-CS9 Investigators. Double blind, placebo controlled trial of the remission inducing and steroid sparing properties of an ICAM-1 antisense oligodeoxynucleotide, alicaforseen (ISIS 2302), in active steroid dependent Crohn's disease. *Gut* 2002;51:30-6.
104. Yacyshyn BR, Barish C, Goff J, Dalke D, Gaspari M, Yu R, Tami J, Dorr FA, Sewell KL. Dose ranging pharmacokinetic trial of high-dose alicaforseen (intercellular adhesion molecule-1 antisense oligodeoxynucleotide) (ISIS 2302) in active Crohn's disease. *Aliment Pharmacol Ther* 2002;16:1761-70.
105. van Deventer SJ, Tami JA, Wedel MK. A randomised, controlled, double blind, escalating dose study of alicaforseen enema in active ulcerative colitis. *Gut* 2004;53:1646-51.
106. Miner P, Wedel M, Bane B, Bradley J. An enema formulation of alicaforseen, an antisense inhibitor of intercellular adhesion molecule-1, in the treatment of chronic, unremitting pouchitis. *Aliment Pharmacol Ther* 2004;19:281-6.
107. Wallace JL, Higa A, McKnight GW, MacIntyre DE. Prevention and reversal of experimental colitis by a monoclonal antibody which inhibits leukocyte adherence. *Inflammation* 1992;16:343-54.
108. Palmen MJ, Dijkstra CD, van der Ende MB, Pena AS, van Rees EP. Anti-CD11b/CD18 antibodies reduce inflammation in acute colitis in rats. *Clin Exp Immunol* 1995;101:351-6.
109. Gordon FH, Lai CW, Hamilton MI, Allison MC, Srivastava ED, Fouweather MG, Donoghue S, Greenlees C, Subhani J, Amlot PL, Pounder RE. A randomized placebo-controlled trial of a humanized monoclonal antibody to alpha4 integrin in active Crohn's disease. *Gastroenterology* 2001;121:268-74.
110. Ghosh S, Goldin E, Gordon FH, Malchow HA, Rask-Madsen J, Rutgeerts P, Vyhalek P, Zadorova Z, Palmer T, Donoghue S; Natalizumab Pan-European Study Group. Natalizumab for active Crohn's disease. *N Engl J Med* 2003;348:24-32.
111. Rutgeerts P, Colombel J, Enns R, et al. Subanalyses from a phase 3 study on the evaluation of natalizumab in active Crohn's disease therapy-1 (ENACT-1). *Gut* 2003;52:A239.
112. Sandborn WJ, Colombel JF, Enns R, Feagan B, Hanauer SB, Lawrence I, Panaccione R, Sanders M, Schreiber S, Targan SR, Van Deventer SJ, Rutgeerts P. *Gut* 2004;53:A69.
113. Gordon FH, Hamilton MI, Donoghue S, Greenlees C, Palmer T, Rowley-Jones D, Dhillon AP, Amlot PL, Pounder RE. A pilot study of treatment of active ulcerative colitis with natalizumab, a humanized monoclonal antibody to alpha-4 integrin. *Aliment Pharmacol Ther* 2002;16:699-705.
114. Sandborn WJ, Yednock TA. Novel approaches to treating inflammatory bowel disease: targeting alpha-4 integrin. *Am J Gastroenterol* 2003;98:2372-82.

115. Feagan BG, Greenberg G, Wild G, McDonald JWD, Fedorak R, Pare P, Kishimoto K, Gutierrez-Ramos JC ,Krop J. Efficacy and safety of a humanized $\alpha_4\beta_7$ antibody in active Crohn's disease (CD). *Gastroenterology* 2003;124:A25-6.
116. Feagan BG, Greenberg G, Wild G, McDonald J, Fedorak R, Pare P, Kishimoto K, Gutierrez-Ramos JC ,Krop J, Vanderwoort M. A randomized controlled trial of a humanized $\alpha_4\beta_7$ in ulcerative colitis. *Gastroenterology* 2003;125:606.
117. Podolsky DK. Mucosal immunity and inflammation. V. Innate mechanisms of mucosal defense and repair: the best offense is a good defense. *Am J Physiol* 1999;277:G495-9.
118. Taupin D, Podolsky DK. Trefoil factors: initiators of mucosal healing. *Nat Rev Mol Cell Biol* 2003;4:721-32.
119. Wong WM, Poulsom R, Wright NA. Trefoil peptides. *Gut* 1999;44:890-5.
120. Thim L. Trefoil peptides: from structure to function. *Cell Mol Life Sci* 1997;53:888-903.
121. Gajhede M, Petersen TN, Henriksen A, Petersen JF, Dauter Z, Wilson KS, Thim L. Pancreatic spasmolytic polypeptide: first three-dimensional structure of a member of the mammalian trefoil family of peptides. *Structure* 1993;1:253-62.
122. Rio MC, Chenard MP, Wolf C, Marcellin L, Tomasetto C, Lathe R, Bellocq JP, Champon P. Induction of pS2 and hSP genes as markers of mucosal ulceration of the digestive tract. *Gastroenterology* 1991;100:375-9.
123. Wright NA, Poulsom R, Stamp G, Van Noorden S, Sarraf C, Elia G, Ahnen D, Jeffery R, Longcroft J, Pike C, et al. Trefoil peptide gene expression in gastrointestinal epithelial cells in inflammatory bowel disease. *Gastroenterology* 1993;104:12-20.
124. Khulusi S, Hanby AM, Marrero JM, Patel P, Mendall MA, Badve S, Poulsom R, Elia G, Wright NA, Northfield TC. Expression of trefoil peptides pS2 and human spasmolytic polypeptide in gastric metaplasia at the margin of duodenal ulcers. *Gut* 1995;37:205-9.
125. Luqmani YA, Ryall G, Shousha S, Coombes RC. An immunohistochemical survey of pS2 expression in human epithelial cancers. *Int J Cancer* 1992;50:302-4.
126. Uchino H, Kataoka H, Itoh H, Sekiya R, Onitsuka T, Koono M. Roles of intestinal trefoil factor (ITF) in human colorectal cancer: ITF suppresses the growth of colorectal carcinoma cells. *Hum Cell* 1999;12:181-8.
127. Katoh M. Trefoil factors and human gastric cancer (review). *Int J Mol Med* 2003;12:3-9.
128. Vestergaard EM, Brynskov J, Ejskjaer K, Clausen JT, Thim L, Nexo E, Poulsen SS. Immunoassays of human trefoil factors 1 and 2: measured on serum from patients with inflammatory bowel disease. *Scand J Clin Lab Invest* 2004;64:146-56.
129. Tran CP, Cook GA, Yeomans ND, Thim L, Giraud AS. Trefoil peptide TFF2 (spasmolytic polypeptide) potently accelerates healing and reduces inflammation in a rat model of colitis. *Gut* 1999;44:636-42.
130. Kornbluth A. Is there still a role for cyclosporine in the treatment of inflammatory bowel disease? Pro argument. *Inflamm Bowel Dis* 2003;9:194-7.
131. Fellermann K, Luhmann D, Stange EF. Is there still a role for cyclosporine in the treatment of inflammatory bowel disease? Con argument. *Inflamm Bowel Dis* 2003;9:198-201.
132. Edwards FC, Truelove SC. The course and prognosis of ulcerative colitis. *Gut* 1963;41:299-315.

133. Langholz E, Munkholm P, Davidsen M, Binder V. Course of ulcerative colitis: analysis of changes in disease activity over years. *Gastroenterology* 1994;107:3-11.
134. Modigliani R. Medical management of fulminant colitis. *Inflamm Bowel Dis* 2002;8:129-34.
135. Duncley P, Jewell D. Management of acute severe colitis. *Best Pract Res Clin Gastroenterol* 2003;17:89-103.
136. Arts J, D'Haens G, Zeegers M, Van Assche G, Hiele M, D'Hoore A, Penninckx F, Vermeire S, Rutgeerts P. Long-term outcome of treatment with intravenous cyclosporin in patients with severe ulcerative colitis. *Inflamm Bowel Dis* 2004;10:73-8.
137. Stein RB, Hanauer SB. Medical therapy for inflammatory bowel disease. *Gastroenterol Clin North Am* 1999;28:297-321.
138. Rafiee P, Johnson CP, Li MS, Ogawa H, Heidemann J, Fisher PJ, Lamirand TH, Otterson MF, Wilson KT, Binion DG. Cyclosporine A enhances leukocyte binding by human intestinal microvascular endothelial cells through inhibition of p38 MAPK and iNOS. Paradoxical proinflammatory effect on the microvascular endothelium. *J Biol Chem* 2002;277:35605-15.
139. Umana A, Gomez A, Duran MM, Porras L. Lymphocyte subtypes and adhesion molecules in actinic prurigo: observations with cyclosporin A. *Int J Dermatol* 2002;41:139-45.
140. Asako H, Kubes P, Baethge BA, Wolf RE, Granger DN. Reduction of leukocyte adherence and emigration by cyclosporine and L683,590 (FK506) in postcapillary venules. *Transplantation* 1992;54:686-90.
141. Molossi S, Clausell N, Sett S, Rabinovitch M. ICAM-1 and VCAM-1 expression in accelerated cardiac allograft arteriopathy and myocardial rejection are influenced differently by cyclosporine A and tumour necrosis factor-alpha blockade. *J Pathol* 1995;176:175-82.
142. Strober W, Fuss IJ, Blumberg RS. The immunology of mucosal models of inflammation. *Annu Rev Immunol* 2002;20:495-549.
143. Okayasu I, Hatakeyama S, Yamada M, Ohkusa T, Inagaki Y, Nakaya R. A novel method in the induction of reliable experimental acute and chronic ulcerative colitis in mice. *Gastroenterology* 1990;98:694-702.
144. Kitajima S, Takuma S, Morimoto M. Changes in colonic mucosal permeability in mouse colitis induced with dextran sulfate sodium. *Exp Anim* 1999;48:137-43.
145. Mahler M, Bristol IJ, Leiter EH, Workman AE, Birkenmeier EH, Elson CO, Sundberg JP. Differential susceptibility of inbred mouse strains to dextran sulfate sodium-induced colitis. *Am J Physiol* 1998;274:G544-51.
146. Cooper HS, Murthy SN, Shah RS, Sedergran DJ. Clinicopathologic study of dextran sulfate sodium experimental murine colitis. *Lab Invest* 1993;69:238-49.
147. Kubes P, Jutila M, Payne D. Therapeutic potential of inhibiting leukocyte rolling in ischemia/reperfusion. *J Clin Invest* 1995;95:2510-9.
148. Davenport KL, Steeber DA, Tedder TF, Bochner BS. P- and L-selectin mediate distinct but overlapping functions in endotoxin-induced leukocyte-endothelial interactions in the rat mesenteric microcirculation. *J Immunol* 1997;159:1977-86.
149. Goussov AV, Zhang Z, Anderson DC, Chopp M. P-selectin antibody reduces hemorrhage and infarct volume resulting from MCA occlusion in the rat. *J Neurol Sci* 1998;161:16-22.
150. Carvalho-Tavares J, Fox-Robichaud A, Kubes P. Assessment of the mechanism of juxtagrin activation and adhesion of leukocytes in liver microcirculation. *Am J Physiol* 1999;276:G828-34.

151. Hickey MJ, Kanwar S, McCafferty DM, Granger DN, Eppihimer MJ, Kubes P. Varying roles of E-selectin and P-selectin in different microvascular beds in response to antigen. *J Immunol* 1999;162:1137-43.
152. Elizalde JI, Gomez J, Panes J, Lozano M, Casadevall M, Ramirez J, Pizcueta P, Marco F, Rojas FD, Granger DN, Pique JM. Platelet activation In mice and human Helicobacter pylori infection. *J Clin Inves* 1997;100:996-1005.
153. Tsuzuki Y, Miura S, Kurose I, Suematsu M, Higuchi H, Shigematsu T, Kimura H, Serizawa H, Hokari R, Akiba Y, Yagita H, Okumura K, Tso P, Granger DN, Ishii H. Enhanced lymphocyte interaction in postcapillary venules of Peyer's patches during fat absorption in rats. *Gastroenterology* 1997;112:813-25.
154. Miura S, Tsuzuki Y, Fukumura D, Serizawa H, Suematsu M, Kurose I, Imaeda H, Kimura H, Nagata H, Tsuchiya M, et al. Intravital demonstration of sequential migration process of lymphocyte subpopulations in rat Peyer's patches. *Gastroenterology* 1995;109:1113-23.
155. Panes J, Perez-del-Pulgar S, Casadevall M, Salas A, Pizcueta P, Bosch J, Anderson DC, Granger DN, Pique JM. Impaired mesenteric leukocyte recruitment in experimental portal hypertension in the rat. *Hepatology* 1999;30:445-53.
156. Salas A, Panés J, Elizalde JI, Casadevall M, Anderson DC, Granger DN, Piqué JM. Mechanisms responsible for enhanced inflammatory response to ischemia-reperfusion in diabetes. *Am J Physiol* 1998;275:H1773-81.
157. Salas A, Panes J, Rosenbloom CL, Elizalde JI, Anderson DC, Granger DN, Pique JM. Differential effects of a nitric oxide donor on reperfusion-induced microvascular dysfunction in diabetic and non-diabetic rats. *Diabetologia* 1999;42:1350-58.
158. Eppihimer MJ, Wolitzky B, Anderson DC, Labow MA, Granger DN. Heterogeneity of expression of E- and P-selectins in vivo. *Circ Res* 1996;79:560-9.
159. Komatsu S, Panes J, Russell JM, Anderson DC, Muzykantov VR, Miyasaka M, Granger DN. Effects of chronic arterial hypertension on constitutive and induced intercellular adhesion molecule-1 expression in vivo. *Hypertension* 1997;29:683-9.
160. Altannavach TS, Roubalova K, Kucera P, Andel M. Effect of high glucose concentrations on expression of ELAM-1, VCAM-1 and ICAM-1 in HUVEC with and without cytokine activation. *Physiol Res* 2004;53:77-82.
161. Radder CM, Beekhuizen H, Kanhai HH, Brand A. Effect of maternal anti-HPA-1a antibodies and polyclonal IVIG on the activation status of vascular endothelial cells. *Clin Exp Immunol* 2004;137:216-22.
162. Henninger DD, Panes J, Eppihimer M, Russell J, Gerritsen M, Anderson DC, Granger DN. Cytokine-induced VCAM-1 and ICAM-1 expression in different organs of the mouse. *J Immunol* 1997;158:1825-32.
163. Kindon H, Pothoulakis C, Thim L, Lynch-Devaney K, Podolsky DK. Trefoil peptide protection of intestinal epithelial barrier function: cooperative interaction with mucin glycoprotein. *Gastroenterology* 1995;109:516-23.
164. Dignass A, Lynch-Devaney K, Kindon H, Thim L, Podolsky DK. Trefoil peptides promote epithelial migration through a transforming growth factor beta-independent pathway. *J Clin Invest* 1994;94:376-83.
165. Playford RJ, Marchbank T, Chinery R, Evison R, Pignatelli M, Boulton RA, Thim L, Hanby AM. Human spasmolytic polypeptide is a cytoprotective agent that stimulates cell migration. *Gastroenterology* 1995;108:108-16.

166. Lefebvre O, Chenard MP, Masson R, Linares J, Dierich A, LeMeur M, Wendling C, Tomasetto C, Chambon P, Rio MC. Gastric mucosa abnormalities and tumorigenesis in mice lacking the pS2 trefoil protein. *Science* 1996;274:259-62.
167. Playford RJ, Marchbank T, Goodlad RA, Chinery RA, Poulsom R, Hanby AM. Transgenic mice that overexpress the human trefoil peptide pS2 have an increased resistance to intestinal damage. *Proc Natl Acad Sci USA* 1996;93:2137-42.
168. Van Klinken BJ, Dekker J, Buller HA, Einerhand AW. Mucin gene structure and expression: protection vs. adhesion. *Am J Physiol* 1995;269:G613-27.
169. Cook GA, Familiari M, Thim L, Giraud AS. The trefoil peptides TFF2 and TFF3 are expressed in rat lymphoid tissues and participate in the immune response. *FEBS Lett* 1999;456:155-9.
170. Alon R, Kassner PD, Carr MW, Finger EB, Hemler ME, Springer TA. The integrin VLA-4 supports tethering and rolling in flow on VCAM-1. *J Cell Biol* 1995;128:1243-53.
171. Babyatsky MW, deBeaumont M, Thim L, Podolsky DK. Oral trefoil peptides protect against ethanol- and indomethacin-induced gastric injury in rats. *Gastroenterology* 1996;110:489-97.
172. Poulsen SS, Thulesen J, Christensen L, Nexo E, Thim L. Metabolism of oral trefoil factor 2 (TFF2) and the effect of oral and parenteral TFF2 on gastric and duodenal ulcer healing in the rat. *Gut* 1999;45:516-22.
173. McKenzie C, Thim L, Parsons ME. Topical and intravenous administration of trefoil factors protect the gastric mucosa from ethanol-induced injury in the rat. *Aliment Pharmacol Ther* 2000;14:1033-40.
174. Murthy SN, Cooper HS, Shim H, Shah RS, Ibrahim SA, Sedergran DJ. Treatment of dextran sulfate sodium-induced murine colitis by intracolonic cyclosporin. *Dig Dis Sci* 1993;38:1722-34.
175. Aiko S, Conner EM, Fuseler JA, Grisham MB. Effects of cyclosporine or FK506 in chronic colitis. *J Pharmacol Exp Ther* 1997;280:1075-84.
176. Ekstrom GM. Oxazolone-induced colitis in rats: effects of budesonide, cyclosporin A, and 5-aminosalicylic acid. *Scand J Gastroenterol* 1998;33:174-9.
177. Banic M, Anic B, Brkic T, Ljubicic N, Plesko S, Dohoczky C, Erceg D, Petrovecki M, Stipancic I, Rotkovic I. Effect of cyclosporine in a murine model of experimental colitis. *Dig Dis Sci* 2002;47:1362-8.
178. Cockerill GW, Bert AG, Ryan GR, Gamble JR, Vadas MA, Cockerill PN. Regulation of granulocyte-macrophage colony-stimulating factor and E-selectin expression in endothelial cells by cyclosporin A and the T-cell transcription factor NFAT. *Blood* 1995;86:2689-98.
179. Dogan A, MacDonald TT, Spencer J. Cyclosporin A enhances T cell-mediated induction of E-selectin. *Eur J Immunol* 1993;23:2922-6.
180. Gallego MJ, Zoja C, Morigi M, Micheletti G, Imberti B, Foppolo M, Remuzzi A, Remuzzi G. Cyclosporine enhances leukocyte adhesion to vascular endothelium under physiologic flow conditions. *Am J Kidney Dis* 1996;28:23-31.
181. Rincon J, Parra G, Quiroz Y, Benatui L, Rodriguez-Iturbe B. Cyclosporin A reduces expression of adhesion molecules in the kidney of rats with chronic serum sickness. *Clin Exp Immunol* 2000;121:391-8.

