

10-02011 STROBER ADDITIONAL SUPPLEMENTARY REFERENCES

51. Pickert G, Neufert C, Leppkes M, Zheng Y, Wittkopf N, Warntjen M, Lehr H-A, Hirth S, Weigmann B, Wirtz S, Ouyang W, Neurath MF, Becker C. STAT3 links IL-22 signaling in intestinal epithelial cells to mucosal wound healing. *JEM* 2009; 206: 1465-1472.
52. Klatt NR, Harris LD, Vinton CL, Sung H, Briant JA, Tabb B, Morcock D, McGinty JW, Lifson JD, Lafont BA, Martin MA, Levine AD, Estes JD, Brenchley JM. Compromised gastrointestinal integrity in pigtail macaques is associated with increased microbial translocation, immune activation, and IL-17 production in the absence of SIV infection. *Mucosal Immunol* 2010; 3: 387-398.
53. Strober W, Fuss IJ, Mannon P. The fundamental basis of inflammatory bowel disease. *J Clin Invest* 2007; 117: 514-521.
54. Bouma G, Kaushiva A, Strober W. Experimental murine colitis is regulated by two genetic loci, including one on chromosome 11 that regulates IL-12 responses. *Gastroenterology* 2002; 123: 554-565.
55. Fichtner-Feigl S, Fuss IJ, Preiss JC, Strober W, Kitani A. Treatment of murine Th1- and Th2-mediated inflammatory bowel disease with NF-kappa B decoy oligonucleotides. *J Clin Invest* 2005; 115: 3057-3071.
56. Parello T, Monteleone G, Cucchiara S, Monteleone I, Sebkova L, Doldo P, Luzzza F, Pallone F. Up-regulation of the IL-12 receptor beta 2 chain in Crohn's disease. *J Immunol* 2000 165: 7234-7239.
57. Fujino S, Ando A, Bamba S, Ogawa A, Hata K, Araki Y, Bamba T, Fujiyama Y. Increased expression of interleukin 17 in inflammatory bowel disease. *Gut* 2003; 52: 65-70.
58. Nielsen OH, Kiman I, Rüdiger N, Hendel J, Vainer B. Upregulation of interleukin-12 and -17 in active inflammatory bowel disease. *Scand J Gastroenterol* 2003; 38: 180-185.

59. Kobayashi T, Okoamoto S, Hisamatsu T, Kamada N, Chinen H, Saito R, Kitazume MT, Nakazawa A, Sugita A, Koganei I, Isobe K, Hibi T. IL23 differentially regulates the Th1/Th17 balance in ulcerative colitis and Crohn's disease. *Gut* 2008; 57: 1682-1689.
60. Duerr RH, Taylor KD, Brant SR, Rioux JD, Silverberg MS, Daly MJ, Steinhart AH, Abraham C, Regueiro M, Griffiths A, Dassopoulos T, Bitton A, Yang H, Targan S, Datta LW, Kistner EO, Schumm LP, Lee AT, Gregersen PK, Bamada MM, Rotter JI, Nicolae DL, Cho JH. A genome-wide association study identifies IL23R as an inflammatory bowel disease gene. *Science* 2006; 314: 1461-1463.
61. Sakuraba A, Sato T, Kamada N, Kitazume M, Sugita A, Hibi T. Th1/Th17 immune response is induced by mesenteric lymph node dendritic cells in Crohn's disease. *Gastroenterology* 2009; 137: 1736-1745.
62. Kleinschek MA, Boniface K, Sadekova S, Grein J, Murphy EE, Turner SP, Raskin L, Desai B, Faubion WA, de Waal Malefyt R, Pierce RH, McClanahan T, Kastelein RA. Circulating and gut-resident human Th17 cells express CD161 and promote intestinal inflammation. *J Exp Med* 2009; 206: 525-534.
63. Jarry A, Bossard C, Bou-Hanna C, Masson D, Espaze E, Denis MG, Laboisse CL. Mucosal IL-10 and TGF-beta play crucial roles in preventing LPS-driven, IFN-gamma-mediated epithelial damage in human colon explants. *J Clin Invest* 2008; 118: 1132-1142.
64. Strober W, Fuss IJ, Blumberg RS. The immunology of mucosal models of inflammation. *Ann Rev Immunol* 2002; 20: 495-549.
65. Boirivant M, Fuss IJ, Chu A, Strober W. Oxazolone colitis: A murine model of T helper cell type 2 colitis treatable with antibodies to interleukin 4. *J Exp Med* 1998; 188: 1929-1939.
66. Heller F, Fuss IJ, Nieuwenhuis EE, Blumberg RS, Strober W. Oxazolone colitis, a Th2 colitis model resembling ulcerative colitis, is mediated by IL-13-producing NK-T cells. *Immunity* 2002; 17: 629-638.
67. Heller F, Florian P, Bojarski C, Richter J, Christ M, Hillenbrand B, Mankertz J, Gitter AH, Bürgei N, Fromm M, Zeitz M, Fuss IJ, Strober W, Schulzke JD. Interleukin-13 is the key effector Th2 cytokine in

ulcerative colitis that affects epithelial tight junctions, apoptosis, and cell restitution. *Gastroenterology* 2005; 129: 550-564.

68. Rachitskaya AV, Hansen AM, Horai R, Li Z, Villasmil R, Luger D, Nussenblatt RB, Caspi RR. Cutting edge: NK T cells constitutively express IL-23 receptor and ROR γ and rapidly produce IL-17 upon receptor ligation in an IL-6 dependent fashion. *J Immunol* 2008; 180: 5167-5171.

69. Mannon PJ, Hornung RL, Yang Z, Yi C, Groden C, Friend J, Yao M, Strober W, Fuss IJ. Suppression of inflammation in ulcerative colitis by interferon-beta-1a is accompanied by inhibition of IL-13 production. *Gut* 2011; In press.

70. Meng G, Zhang F, Fuss IJ, Kitani A, Strober W. A mutation in the Nirp3 gene causing inflammasome hyperactivation potentiates Th17 cell-dominant immune responses. *Immunity* 2009; 30: 860-874.

71. Prehn JL, Thomas LS, Landers CJ, Yu QT, Michelsen KS, Targan SR. The T cell costimulator TL1A is induced by Fc γ R signaling in human monocytes and dendritic cells. *J Immunol* 2007; 178: 4033-4038.

72. Kamada N, Hisamatsu T, Honda H, Kobayashi T, Chinen H, Takayama T, Kitazume MT, Okamoto S, Koganei K, Sugita A, Kanai T, Hibi T. TL1A produced by lamina propria macrophages induces Th1 and Th17 immune responses in cooperation with IL-23 in patients with Crohn's disease. *Inflamm Bowel Dis* 2010; 16: 568-575.

73. Hidetoshi T, Michelsen KS, Wei B, Landers CJ, Thomas LS, Dhall D, Braun J, Targan SR. TL1A (TNFSF15) regulates the development of chronic colitis by modulating both T helper (T_H) 1 and T_H17 activation. *Gastroenterology* 135: 552-5567.

74. Meylan F, Song Y-J, Fuss IJ, Villarreal S, Kahle E, Malm I-J, Acharya K, Ramos HL, Lo L, Mentink-Kane MM, Wynn TA, Migone T-S, Strober W, and Siegel RM. The TNF-family cytokine TL1A drives IL-13-dependent small intestinal inflammation. *Mucosal Immunology* 2010 In press.
75. Meylan F, Davidson TS, Kahle E, Kinder M, Acharya K, Jankovic D, Bundoc V, Hodges M, Shevach EM, Keane-Myers A, Wang E, Siegel RM. The TNF-family receptor DR3 is essential for diverse T cell-mediated inflammatory diseases. *Immunity* 2008; 29: 79-89.
76. Schreiber TH, Wolf D, Tsai MS, Chirinos J, Deyev VV, Gonzalez L, Malek TR, Levy RB, Podack ER. Therapeutic Treg expansion in mice by TNFRSF25 prevents allergic lung inflammation. *J Clin Invest* 2010; 120: 3629-3640.
77. Prehn JL, Mehdizadeh S, Landers CJ, Luo X, Cha SC, Wei P, Targan SR. Potential role for TL1A, the new TNF-family member and potent costimulator of IFN-gamma, in mucosal inflammation. *Clin Immunol* 2004; 112: 66-77.
78. Bamias G, Martin C 3rd, Marini M, Hoang S, Mishina M, Ross WG, Sachedina MA, Friel CM, Mize J, Bickston SJ, Pizarro TT, Wei P, Cominelli F. Expression, localization, and functional activity of TL1A, a novel Th1-polarizing cytokine in inflammatory bowel disease. *J Immunol* 2003; 171: 4868-4874.
79. Michelson KS, Thomas LS, Taylor KD, Yu QT, Mei L, Landers CJ, Derkowski C, McGovern DP, Rotter JL, Targan SR. IBD-associated TL1A gene (TNFSF15) haplotypes determine increased expression of TL1A proteins. *PLoS One* 2009; 4: e4719.
80. Peyrin-Biroulet L, Deltenre P, de Suray N, Branche J, Sandborn WJ, Colombel JF. Efficacy and safety of tumor necrosis factor antagonists in Crohn's disease: meta-analysis of placebo-controlled trials. *Clin Gastroenterol Hepatol* 2008; 6: 644-653.
81. Tilig H, Moschen A, Kaser A. Mode of function of biological anti-TNF agents in the treatment of inflammatory bowel diseases. *Expert Opin Biol Ther* 2007; 7: 1051-1059.

82. Mitoma H, Horiuchi T, Hatta N, Tsukamoto H, Harashima S, Kikuchi Y, Otsuka J, Okamura S, Fujita S, Harada M. Infliximab induces potent anti-inflammatory responses by outside-to-inside signals through transmembrane TNF- α . *Gastroenterology* 2005; 128: 376-392.
83. Panaccione R, Sandborn W, Gordon G, Lee S, Safdi A, Sedghi S, Feagan B, Hanauer S, Kumar A, Carcereri R. Briakinumab (Anti-interleukin 12/23 P40, ABT874) for treatment of Crohn's disease. Highlights from ACG 2010. *Gastroenterology & Hepatol* 2010; 12: Suppl 17 pg 17.
84. Reinisch W, de Villiers W, Bene L, Simon L, Racz I, Katz S, Altoraj I, Faegan B, Riff D, Berstein CN, Hommes D, Rutgeerts P, Cortot A, Gaspari M, Cheng M, Pearce T, Sands BE. Fontolizumab in moderate to severe Crohn's disease: a phase 2, randomized, double-blind, placebo-controlled, multiple-dose study. *Inflamm Bowel Dis* 2010; 16: 233-242.
85. Fuss IJ, Marth T, Neurath MF, Pearlstein GR, Jain A, Strober W. Anti-interleukin 12 treatment regulates apoptosis of Th1 T cells in experimental colitis in mice. *Gastroenterology* 1999; 117: 1078-1088.
86. Nishimoto N, Kishimoto T. Humanized antihuman IL-6 receptor antibody, tocilizumab. *Handb Exp Pharmacol* 2008; 181: 151-160.
87. Nishimoto N, Kishimoto T. Inhibition of IL-6 for the treatment of inflammatory diseases. *Curr Opin Pharmacol* 2004; 4: 386-391.
88. Atreya R, Mudter J, Finotto S, Mullberg J, Jostock T, Wirtz S, Schutz M, Bartsch B, Holtmann M, Becker C, Strand D, Czaja J, Schlaak JF, Lehr HA, Autschbach F, Schurmann G, Nishimoto N, Yoshizaki K, Ito H, Kishimoto T, Galle PR, Rose-John S, Neurath MF. Blockade of interleukin 6 trans signaling suppresses T-cell resistance against apoptosis in chronic intestinal inflammation: evidence in Crohn's disease and experimental colitis in vivo.