

LIST OF PUBLICATIONS

2000-2005

76. Hino, A., Igarashi, O., Tagawa, Y., Iwakura, Y., and Nariuchi, H. Interferon- γ priming is not critical for IL-12 production of murine spleen cells. *Cytokine*, **12**, 12-20 (2000).
77. Horai, R., Saijo, S., Tanioka, H., Nakae, S., Sudo, K., Okahara, A., Ikuse, T., Asano, M., and Iwakura, Y. Development of chronic inflammatory arthropathy resembling rheumatoid arthritis in IL-1 receptor antagonist-deficient mice. *J. Exp. Med.*, **191**, 313-320 (2000).
78. Tagawa, Y., Matthys, P., Heremans, H., Dillen, C., Zaman, Z., Iwakura, Y., and Billiau, A. Bimodal role of endogenous interleukin-6 in concanavalin A-induced hepatitis in mice. *J. Leukocyte Biology*, **67**, 90-96 (2000).
79. Miyazato, A., Kawakami, K., Iwakura, Y., and Saito, A. Chemokine synthesis and cellular inflammatory changes in lungs of mice bearing $p40^{tax}$ of human T-lymphotropic virus type 1. *Clin. Exp. Immunol.*, **120**, 113-124 (2000).
80. Nishihori, H., Tsuji, H., Wang, H., Tahara, H., Akiyama, M., Ogawa, Y., Matsushima, K., Iwakura, Y., and Mukaida, N. Participation of endogenously produced IFN- γ in interleukin 4-mediated tumor rejection. *Human Gene Therapy*, **11**, 659-668 (2000).
81. Ohkusu, K., Yoshimoto, T., Takeda, K., Ogura, T., Kashiwamura, S., Iwakura, Y., Akira, S., Okamura, H., and Nakanishi, K. Potentiality of interleukin-18 as a useful reagent for treatment and prevention of *Leishmania major* infection. *Infect. Immun.*, **68**, 2449-2456 (2000).
82. Sasaki, S., Nishikawa, S., Miura, T., Mizuki, M., Yamada, K., Madarame, H., Tagawa, Y., Iwakura, Y., and Nakane, A. Interleukin-4 and interleukin-10 are involved in host resistance to *Staphylococcus aureus* infection through regulation of gamma interferon. *Infect. Immun.*, **68**, 2424-2430 (2000).

83. Yamada, H., Mizumo, S., Horai, R., Iwakura, Y., and Sugawara, I. Protective role of interleukin-1 in mycobacterial infection in IL-1 alpha/beta double-knockout mice. *Lab. Invest.*, **80**, 759-67 (2000).
84. Uetani, N., Kato, K., Ogura, K., Mizuno, H., Kawano, K., Mikoshiba, K., Yakura, H., Asano, M., and Iwakura, Y. Impaired learning with enhanced hippocampal long-term potentiation in PTP δ -deficient mice. *EMBO J.*, **19**, 2775-2785 (2000).
85. Serizawa, S., Ishii, T., Nakatani, H., Tsuboi, A., Nagawa, F., Asano, M., Sudo, K., Sakagami, J., Sakano, H., Ijiri, T., Matsuda, Y., Suzuki, M., Yamamori, T., Iwakura, Y., and Sakano, H. Mutually exclusive expression of odorant receptor transgenes. *Nature Neuroscience*, **3**, 687-693 (2000).
86. Ohta, A., Sekimoto, M., Sato, M., Koda, T., Nishimura, S., Iwakura, Y., Sekikawa, K., and Nishimura, T. Indispensable role for TNF- α and IFN- γ at the effector phase of liver injury mediated by Th1 cells specific to hepatitis B virus surface antigen. *J. Immunol.*, **165**, 956-961 (2000).
87. Kawakami, K., Koguchi, Y., Qureshi, M. H., Miyazato, A., Yara, S., Kinjo, Y., Iwakura, Y., Takeda, K., Akira, S., Kurimoto, M., and Saito, A. IL-18 contributes to host resistance against infection with *Cryptococcus neoformans* in mice with defective IL-12 synthesis through induction of IFN- γ production by NK Cells. *J. Immunol.*, **165**, 941-947 (2000).
88. Tanaka, J., Ozaki, H., Yasuda, J., Horai, R., Tagawa, Y., Asano, M., Saijo, S., Imai, M., Sekikawa, K., Kopf, M., and Iwakura, Y. Lipopolysaccharide-induced HIV-I expression in transgenic mice is mediated by tumor necrosis factor- α and interleukin-1, but not by interferon- γ nor interleukin-6. *AIDS*, **14**, 1299-1307 (2000).
89. Kido, M., Asano, M., Iwakura, Y., Ichinose, M., Miki, K., and Furukawa, K. Presence of a higher molecular weight β -1, 4-galactosyltransferase in mouse liver. *Acta Histochem. Cytochem.*, **33**, 215-221 (2000).

90. Miura, T., Nishikawa, S., Sasaki, S., Yamada, K., Hasegawa, S., Mizuki, D., Mizuki, M., Hatayama, I., Sekikawa, K., Tagawa, Y., Iwakura, Y., and Nakane, A. Roles of endogenous cytokines in liver apoptosis of mice in lethal *Listeria monocytogenes* infection. *FEMS Immunol. Med. Microbiol.*, **28**, 335-41 (2000).
91. Yamaguchi, K., Motegi, K., Iwakura, Y., and Endo, Y. Involvement of interleukin-1 in the inflammatory actions of aminobisphosphonates in mice. *Br. J. Pharmacol.*, **130**, 1646-1654 (2000).
92. Igarashi, I., Asaba, U., Xuan, X., Omata, Y., Saito, A., Nagasawa, H., Fujisaki, K., Suzuki, N., Iwakura, Y., and Mikami, T. Immunization with recombinant surface antigens p26 with Freund's adjuvants against *Babesia rodhaini* infection. *J. Vet. Med. Sci.* **62**, 717-723 (2000).
93. Mun, H.-S., Aosai, F., Norose, K., Chen, M., Hata, H., Tagawa, Y., Iwakura, Y., Byun, D.-S., and Yano, A. *Toxoplasma gondii* Hsp70 as a danger signal in *Toxoplasma gondii*-infected mice. *Cell Stress & Chaperones*, **5**, 328-335 (2000).
94. Sugawara, I., Ymamada, H., Mizuno, S., and Iwakura, Y. IL-4 is required for defense against Mycobacterial infection. *Microbiol. Immunol.*, **44**, 971-979 (2000).
95. Hayashi, K., Natsume, W., Watanabe, T., Abe, N., Iwai, N., Okada, H., Ito, Y., Asano, M., Iwakura, Y., Habu, S., Takehama, Y., and Satake, M. Diminution of the AML1 transcription factor function causes differential effects on the fates of CD4 and CD8 single positive T cells. *J. Immunol.*, **165**, 6816-6824 (2000).
96. Takeda, K., Hayakawa, Y., Smyth, M. J., Kayagaki, N., Yamaguchi, N., Kakuta, S., Iwakura, Y., Yagita, H., and Okumura, K. Involvement of tumor necrosis factor-related apoptosis-inducing ligand in surveillance of tumor metastasis by liver natural killer cells. *Nature Medicine*, **7**, 94-100 (2001).
97. Fukumauchi, F., Aihara, O., Wang, Y. J., Akasaka, K., Takeda, Y., Horie, M., Kawano, H., Sudo, K., Asano, M., Watababe, K., and

- Iwakura, Y. TAG-1-deficient mice have marked elevation of adenosine A1 receptors in the hippocampus. *Biochem. Biophys. Res. Commun.*, **281**, 220-226 (2001).
98. Seino, K., Fukao, K., Muramoto, K., Yanagisawa, K., Takada, Y., Kakuta, S., Iwakura, Y., Van Kaer, L., Takeda, K., Nakayama, T., Taniguchi, M., Bashuda, H., Yagita, H., and Okumura, K. Requirement for NKT cells in the induction of allograft tolerance. *Proc. Natl. Acad. U. S. A.*, **98**, 2577-2581 (2001).
99. Ishii, T., Serizawa, S., Kohda, A., Nakatani, H., Shiroishi, T., Okumura, K., Iwakura, Y., Nagawa, F., Tsuboi, A., and Sakano, H. Projection of three subsets of olfactory neurons expressing the odorant receptor transgene and the two cognate endogenous alleles. *Genes to Cell*, **6**, 71-78 (2001).
100. Naruse-Nakajima, C., Asano, M., and Iwakura, Y. Involvement of EphA2 in the formation of the tail notochord via interaction with ephrinA1. *Mech. Develop.*, **102**, 95-105 (2001).
101. Ozaki, H., Watanabe, Y., Takahashi, K., Kitamura, K., Tanaka, A., Urase, K., Momoi, T., Sudo, K., Sakagami, J., Asano, M., Iwakura, Y., and Kawakami, K. *Six-4*, a putative *myogenin* gene regulator, is not essential for mouse embryonal development. *Mol. Cell. Biol.*, **21**, 3343-3350 (2001).
102. Norose, K., Mun, H. S., Aosai, F., Chen, M., Hata, H., Tagawa, Y., Iwakura, Y., Yano, A. Organ infectivity of *Toxoplasma gondii* in interferon- γ knockout mice. *J. Parasitol.*, **87**, 447-52 (2001).
103. Yoneto, T., Waki, S., Takai, T., Tagawa, Y., Iwakura, Y., Mizuguchi, J., Nariuchi, H., and Yoshimoto, T. A critical role of Fc receptor-mediated antibody-dependent phagocytosis in the host resistance to blood-stage *Plasmodium berghei* XAT infection. *J. Immunol.*, **166**, 6236-6241 (2001).
104. Hayakawa, Y., Takeda, K., Yagita, H., Kakuta, S., Iwakura, Y., Van Kaer, L., Saiki, I., and Okumura, K. Critical contribution of IFN-gamma and NK cells, but not perforin-mediated cytotoxicity, to

- anti-metastatic effect of alpha-galactosylceramide. *Eur J Immunol.*, **31**, 1720-1727 (2001).
105. Shibata, S., Kakuta, S., Hamada, K., Sokawa, Y., and Iwakura, Y. Cloning of a novel 2', 5'-oligoadenylate synthetase-like molecule, Oasl5 in mice. *Gene*, **271**, 261-271 (2001).
106. Nakae, S., Asano, M., Horai, R., Sakaguchi, N., and Iwakura, Y. IL-1 enhances T cell-dependent antibody production through induction of CD40L and OX40 on T cells. *J. Immunol.*, **167**, 90-97 (2001).
107. Yasuda, J., Miyao, T., Kamata, M., Aida, Y., and Iwakura, Y. T cell apoptosis causes peripheral T cell depletion in mice transgenic for the HIV-1 *vpr*. *Virology*, **285**, 181-192 (2001).
108. Kotani, N., Asano, M., Iwakura, Y., and Takasaki, S. Knockout of mouse β 1,4-galactosyltransferase-1 gene results in a dramatic shift of outer chain moieties of N-glycans from type 2 to type 1 chains in hepatic membrane and plasma glycoproteins. *Biochem J.*, **357**, 827-834 (2001).
109. Boutin, H., LeFeuvre, R. A., Horai, R., Asano, M., Iwakura, Y., and Rothwell, N. Role of IL-1 α and IL-1 β in ischaemic brain damage. *J. Neuroscience*, **21**, 5528-5534 (2001).
110. Morita, Y., Maravei, D. V., Bergeron, L., Wang, S., Perez, G. I., Tsutsumi, O., Taketani, Y., Asano, M., Horai, R., Korsmeyer, S. J., Iwakura, Y., Yuan, J., and Tilly, J. L. Caspase-2 deficiency prevents programmed germ cell death resulting from cytokine insufficiency but not meiotic defects caused by loss of ataxia telangiectasia-mutated (Atm) gene function. *Cell Death Differ.*, **8**, 614-620 (2001).
111. Sato, M., Chamoto, K., Tsuji, T., Iwakura, Y., Togashi, Y., Koda, T., and Nishimura, T. Th1 cytokine-conditioned bone marrow-derived dendritic cells can bypass the requirement for Th functions during the generation of CD8(+) CTL. *J. Immunol.*, **167**, 3687-3691 (2001).

112. Imaizumi, Y., Mizushima, H., Matsumoto, H., Dohi, K., Motsumoto, K., Ohtaki, H., Funahashi, H., Matsunaga, S., Horai, R., Asano, M., Iwakura, Y., and Shioda, S. Increased expression of interleukin-1 β in mouse hippocampus after global cerebral ischemia. *Acta Histochem. Cytochem.*, **34**, 357-362 (2001).
113. Dal, J. H., Iwatani, Y., Ishida, T., Terunuma, H., Kasai, H., Iwakura, Y., Fujiwara, H., and Ito, M. Glycyrrhizin enhances interleukin-12 production in peritoneal macrophage. *Immunology*, **103**, 235-243 (2001).
114. Miura, T., Kudo, T., Matsuki, A., Sekikawa, K., Tagawa, Y., Iwakura, Y., Nakane, A. Effect of 6-Hydroxydopamine on host resistance against *Listeria monocytogenes* infection. *Infect. Immun.*, **69**, 7234-7241 (2001).
115. Le Feuvre, R. A., Brough, D., Iwakura, Y., Takeda, K., Rothwell, N. J. Priming of macrophages with LPS potentiates P2X7 mediated cell death via a caspase-1 dependent mechanism, independently of cytokine production. *J. Biol. Chem.*, **277**, 3210-3218 (2001).
116. Nakae, S., Naruse-Nakajima, C., Sudo, K., Horai, R., Asano, M., and Iwakura, Y. IL-1 α , but not IL-1 β , is required for contact-allergen-specific T cell activation during the sensitization phase in contact hypersensitivity. *Int. Immunol.*, **13**, 1471-1478 (2001).
117. Kyuwa, S., Kawamura, S., Shibata, S., Machii, K., Tagawa, Y., Iwakura, Y., and Urano, T. The severity of hepatic lesion after intraperitoneal JHMV infection in IFN- γ deficient mice is parallel to viral replication in hepatocytes *in vitro*. *Adv Exp Med Biol.*, **494**, 95-99 (2001).
118. Moshkin, M. P., Tamagawa, A., Kolosova, I. E., Gerlinskaya, L. A., Iwakura, Y., and Endo, Y. Social behavior in male mice deficient in genes for interleukin-1. *Med. Immunol.*, **3**, 449-457 (2001).

119. Nakae, S., Asano, M., Horai, R., and Iwakura, Y. Interleukin-1 β , but not interleukin-1 α , is required for T cell-dependent antibody production. *Immunology*, **104**, 402-409 (2001).
120. Yoshida, K., Matsumoto, T., Tateda, K., Uchida, K., Tsujimoto, S., Iwakura, Y., and Yamaguchi, K. Protection against pulmonary infection with *Klebsiella pneumoniae* in mice by interferon-gamma through activation of phagocytic cells and stimulation of production of other cytokines. *J. Med. Microbiol.*, **50**, 959-964 (2001).
121. Moshkin, M. P., Tamagawa, A., Kolosova, I. E., Gerlinskaya, L. A., Iwakura, Y., and Endo, Y. Behavioral and endocrine effects of endotoxin in wild-type mice and mice deficient in interleukin 1: sickness behavior or adaptive response? *Dokl. Biol. Sci.*, **379**, 322-324 (2001).
122. Yokoyama, H., Yasuda, J., Okamoto, H., and Iwakura, Y. Pathological changes of renal epithelial cells in mice transgenic for the TT virus ORF1 gene. *J. Gen. Virol.*, **83**, 141-150 (2002).
123. Saijo, S., Asano, M., Horai, R., Yamamoto, H., and Iwakura, Y. Suppression of autoimmune arthritis in IL-1-deficient mice in which T cell activation is impaired due to low levels of CD40L and OX40 expression on T cells. *Arth. Rheum.*, **46**, 533-544 (2002).
124. Kakuta, S., Tagawa, Y., Shibata, S., Nanno, M., and Iwakura, Y. Inhibition of B16 melanoma experimental metastasis by interferon- γ through direct inhibition of cell proliferation and activation of anti-tumor host mechanisms. *Immunology*, **105**, 92-100 (2002).
125. Brough, D., LeFeuvre, R. A., Iwakura, Y., and Rothwell, N. J. Purinergic (P2X7) receptor activation of microglia induces cell death via an interleukin-1-independent mechanism. *Mol. Cell Neurosci.*, **19**, 272-280 (2002).
126. Nagai, Y., Shimazu, R., Ogata, H., Akashi, S., Sudo, K., Yamasaki, H., Hayashi, S., Iwakura, Y., Kimoto, M., and Miyake, K. Requirement for MD-1 in cell surface expression of RP105/CD180

and B-cell responsiveness to lipopolysaccharide. *Blood*, **99**,1699-1705 (2002).

127. Kyuwa, S., Shibata, S., Tagawa, Y., Iwakura, Y., Machii, K., and Urano, T. Acute hepatic failure in IFN- γ -deficient BALB/c mice after murine coronavirus infection. *Virus Research*, **83**, 169-177 (2002).
128. Shinozawa, Y., Matsumoto, T., Uchida, K., Tsujimoto, S., Iwakura, Y., and Yamaguchi, K. Role of interferon- γ in inflammatory responses in murine respiratory infection with *Legionella pneumophila*. *J. Med. Microbiol.*, **51**, 225-230 (2002).
129. Furuzawa, M., Kuwahara, M., Ishii, K., Iwakura, Y., and Tsubone, H. Diurnal variation of heart rate, locomotor activity, and body temperature in interleukin-1 alpha/beta doubly deficient mice. *Exp. Anim.*, **51**, 49-56 (2002).
130. Asahi, Y., Yoshikawa, T., Watanabe, I., Iwasaki, T., Hasegawa, H., Sato, Y., Shimada, S., Nanno, M., Matsuoka, Y., Ohwaki, M., Iwakura, Y., Suzuki, Y., Aizawa, C., Sata, T., Kurata, T. and Tamura, S. Protection against influenza virus infection in polymeric Ig receptor knockout mice immunized intranasally with adjuvant-combined vaccines. *J. Immunol.*, **168**, 2930-2938 (2002).
131. Battsetseg, B., Mamiro, K., Inoue, N., Makala, L., Nagasanw, H., Iwakura, Y., Toyoda, Y., Mikami, T., Fujisaki, K. Immune responses of interferon gamma (IFN- γ) knock out mice to repeated *Haemaphysalis longicornis* (Acari: Ixodidae) nymph infestations. *J. Med. Entomol.*, **39**, 173-176 (2002).
132. Oguro, T., Takahashi, Y., Ashino, T., Takaki, A., Shioda, S., Horai, R., Asano, M., Sekikawa, K., Iwakura, Y., and Yoshida, T. Involvement of tumor necrosis factor α , rather than interleukin-1 or nitric oxides in the HEME Oxygenase-1 gene expression by lipopolysaccharide in the mouse liver. *FEBS Letters*, **516**, 63-66 (2002).

133. Asada, H., Kishida, T., Hirai, H., Satoh, E., Ohashi, S., Takeuchi, M., Kubo, T., Kita, M., Iwakura, Y., Imanishi, J., and Mazda, O. Significant antitumor effects obtained by autologous tumor cell vaccine engineered to secrete interleukin (IL)-12 and IL-18 by means of the EBV/lipoplex. *Molec. Therapy*, **5**, 609-616, (2002).
134. Mizushima, H., Cheng, J-Z., Dohi, K., Horai, R., Asano, M., Iwakura, Y., Hirabayashi, T., Arata, S., Nakajo, S., Takaki, A., Ohtaki, H., and Shioda, S. Reduced postischemic apoptosis in the hippocampus of mice deficient in interleukin-1. *J. Comparative Neurol.*, **448**, 203-216 (2002).
135. Yamamoto, S., Oka, S., Inoue, M., Shimuta, M., Manabe, T., Takahashi, H., Miyamoto, M., Asano, M., Sakagami, J., Sudo, K., Iwakura, Y., and Kawasaki, T. Mice deficient in nervous system-specific carbohydrate epitope HNK-1 exhibit impaired synaptic plasticity and spatial learning. *J. Biol. Chem.*, **277**, 27227-27231 (2002).
136. Nagai, Y., Akashi, S., Nagafuku, M., Ogata, M., Iwakura, Y., Akira, S., Kitamura, T., Kosugi, A., Kimoto, M., and Miyake, K. Essential role of MD-2 in LPS responsiveness and TLR4 distribution. *Nature Immunol.*, **3**, 667-672 (2002).
137. Sasaki, S., Omoe, K., Tagawa, Y., Iwakura, Y., Sekikawa, K., Shinagawa, K., and Nakane, A. Roles of gamma interferon and tumor necrosis factor-alpha in shiga toxin lethality. *Microb. Pathog.*, **33**, 43-47 (2002).
138. Konishi, H., Tsutsui, H., Murakami, T., Yumikura-Futatsugi, S., Yamanaka, K., Tanaka, M., Iwakura, Y., Suzuki, N., Fuchs, E. V., Takeda, K., Akira, S., Nakanishi, K., and Mizutani, H. IL-18 contributes to the spontaneous development of atopic dermatitis-like inflammatory skin lesion independently of IgE/stat6 under specific pathogen-free conditions. *Proc. Natl. Acad. Sci. USA*, **99**, 11340-11345 (2002).

139. Ishida, Y., Kondo, T., Ohshima, T., Fujiwara, H., Iwakura, Y., and Mukaida, N. A pivotal involvement of IFN- γ in the pathogenesis of acetaminophen-induced acute liver injury. *FASEB J.*, **16**, 1227-1236 (2002).
140. Minami, M., Kita, M., Yan, X.-Q., Yamamoto, T., Iida, T., Sekikawa, K., Iwakura, Y., and Imanishi, J. Role of IFN- γ and tumor necrosis factor- α in herpes simplex virus type I infection. *J. Interferon Cytokine Res.*, **22**, 671-676, (2002).
141. Shiraishi, K., Hanada, K., Iwakura, Y., and Ikeda, H. Roles of RecJ, RecO, and RecR in RecET-mediated illegitimate recombination in *Escherichia coli*. *J. Bacteriol.*, **184**, 4715-4721 (2002).
142. Mizuki, M., Nakane, A., Sekikawa, K., Tagawa, Y. -I., and Iwakura, Y. Comparison of host resistance to primary and secondary *Listeria monocytogenes* infections in mice by intranasal and intravenous routes. *Infect. Immun.*, **70**, 4805-4811 (2002).
143. Iwakura, Y. Roles of IL-1 in the development of rheumatoid arthritis: Consideration from mouse models. *Cytokine Growth Factor Rev.*, **13**, 341-355 (2002).
144. Yan, X., Kita, M., Minami, M., Yamamoto, T., Kuriyama, H., Ohno, T., Iwakura, Y., and Imanishi, J. Antibacterial effect of Kampo herbal formulation Hochu-ekki-to (Bu-Zhong-Yi-Qi-Tang) on *Helicobacter pylori* infection in mice. *Microbiol. Immunol.*, **46**, 475-482 (2002).
145. Nakae, S., Komiyama, Y., Nambu, A., Sudo, K., Iwase, M., Homma, I., Sekikawa, K., Asano, M., and Iwakura, Y. Antigen-specific T cell sensitization is impaired in IL-17-deficient mice, resulting in the suppression of allergic cellular and humoral responses. *Immunity*, **17**, 375-387 (2002).
146. Sakamaki, K., Inoue, T., Asano, M., Sudo, K., Kazama, H., Sakagami, J., Sakata, S., Ozaki, M., Nakamura, S., Toyokuni, S., Osumi, N., Iwakura, Y. and Yonehara, S. *Ex vivo* whole-embryo culture of caspase-8-deficient embryos normalize their aberrant phenotypes in

the developing neural tube and heart. *Cell Death Differ.*, **9**, 1196-1206 (2002).

147. Kakuta, S., Shibata, S., and Iwakura, Y. Genomic structure of the mouse 2', 5'-oligoadenylate synthetase gene family. *J. Interferon Cytokine Res.*, **22**, 981-993 (2002).
148. Oguri, S., Motegi, K., Iwakura, Y., and Endo, Y. Primary role of interleukin-1 α and Interleukin-1 β in lipopolysaccharide-induced hypoglycemia in mice. *Clin. Diagn. Lab. Immunol.*, **9**, 1307-1312 (2002).
149. Yoshida, M., Shirai, Y., Watanabe, T., Yamori, M., Iwakura, Y., Chiba T., Kita, T., and Wakatsuki, Y. Differential localization of colitogenic Th1 and Th2 cells monospecific to a microflora-associated antigen in mice. *Gastroenterology*. **123**, 1949-1961 (2002).
150. Desaki, M., Sugawara, I., Iwakura, Y., Yamamoto, K., and Takizawa, H. Role of interferon-gamma in the development of murine bronchus-associated lymphoid tissues induced by silica *in vivo*. *Toxicol. Appl. Pharmacol.*, **185**, 1-7 (2002).
151. Yano, A., Mun, H.S., Chin, M., Norose, K., Hata, K., Kobayashi, M., Aosai, F., and Iwakura, Y. Roles of IFN- γ on stage conversion of an obligate intracellular protozoan parasite, *Toxoplasma gondii*. *Int. Rev. Immunol.*, **21**, 405-421 (2002).
152. Kurisaki, T., Masuda, A., Sudo, K., Sakagami, J., Higashiyama, S., Matsuda, Y., Nagabukuro, A., Tsuji, A., Nabeshima, Y., Asano, M., Iwakura, Y., and Sehara-Fujisawa, A. Phenotypic analysis of Meltrin α (ADAM12)-deficient mice: involvement of Meltrin α in adipogenesis and myogenesis. *Mol. Cell. Biol.*, **23**, 55-61 (2003).
153. Ikegaya, Y., Delcroix, I., Iwakura, Y., Matsuki, N., and Nishiyama, N. Interleukin-1 β abrogates long-term depression of hippocampal CA1 synaptic transmission. *Synapse*, **47**, 54-57 (2003).
154. Nakae, S., Komiyama, Y., Narumi, S., Sudo, K., Horai, R., Tagawa, Y., Sekikawa, K., Matsushima, K., Asano, M., and Iwakura, Y.

IL-1-induced TNF α elicits inflammatory cell infiltration in the skin by inducing interferon- γ -inducible protein-10 in the elicitation phase of contact hypersensitivity response. *Int. Immunol.*, **15**, 251-260 (2003).

155. Iwakura, Y. Autoimmune chronic inflammatory arthropathy in mice transgenic for the HTLV-I *tax* gene. In “*Two decades of adult T-cell leukemia and HTLV-I research*”, (eds. K. Sugamura, R. Uchiyama, M. Matsuoka, and M. Kannagi), *Gann Monograph on Cancer Research*, **50**, Japan Scientific Societies Press and Karger, Tokyo, pp. 197-218 (2003).
156. Nakae, S., Horai, R., Komiyama, Y., Nambu, A., Asano, M., Nakane, A., and Iwakura, Y. The role of IL-1 in the immune system. In “*Cytokine Knockouts*”, (ed. G. Fantuzzi), Humana Press, Totowa, NJ, pp. 95-109 (2003).
157. Tanaka, J., Ishida, T., Choi, B.-I., Watanabe, T., Yasuda, J., and Iwakura, Y. Latent HIV-1 reactivation in transgenic mice requires cell cycle-dependent demethylation of CREB/ATF sites in the LTR. *AIDS*, **17**, 165-175 (2003).
158. Li, H., Takeda, Y., Niki, H., Ogawa, J., Kobayashi, S., Kai, N., Akasaka, K., Asano, M., Sudo, K., Iwakura, Y., and Watanabe K. Aberrant responses to acoustic stimuli in mice deficient for neural recognition molecule NB-2. *Eur. J. Neurosci.*, **17**, 929-936 (2003).
159. Sashinami, H., Nakane, A., Iwakura, Y., and Sasaki, M. Effective induction of acquired resistance to *Listeria monocytogenes* by immunizing mice with *in vivo*-infected dendritic cells. *Infect. Immun.*, **71**, 117-125 (2003).
160. Ohtaki, H., Funahashi, H., Dohi, K., Oguro, T., Horai, R., Asano, M., Iwakura, Y., Yin, L., Matsunaga, M., Goto, N., and Shioda, S. Suppression of oxidative neuronal damage after transient middle cerebral artery occlusion in mice lacking interleukin-1. *Neuroscience Res.*, **45**, 313-324 (2003).

161. Nakae, S., Komiyama, Y., Yokoyama, H., Nambu, A., Umeda, M., Iwase, M., Homma, I., Sudo, K., Horai, R., Asano, M. and Iwakura, Y. Interleukin-1 is required for allergen-specific Th2 cell activation and the development of airway hypersensitivity response. *Int. Immunol.*, **15**, 483-490 (2003).
162. Voronov, E., Shouval, D. S., Krelin, Y., Cagnano, E., Benharroch, D., Iwakura, Y., Dinarello, C. A., and Apte, R. N. Interleukin 1 is required for tumor invasiveness and angiogenesis. *Proc. Natl. Acad. Sci. USA*, **100**, 2645-2650 (2003).
163. Kyuwa, S., Kawamura, S., Tagawa, Y., Iwakura, Y., Urano, T., and Yoshikawa, Y. Differences between BALB/c and C57BL/6 mice in mouse hepatitis virus replication in primary hepatocyte culture. *Exp. Anim.*, **52**, 81-84 (2003).
164. Kirii, H., Niwa, T., Yamada, Y., Wada, H., Saito, K., Iwakura, Y., Asano, M., Moriwaki, H., and Seshima, M. Lack of interleukin-1 β decreases the severity of atherosclerosis in apolipoprotein E-deficient mice. *Arterioscler. Thromb. Vasc. Biol.*, **23**, 656-660 (2003).
165. Nakae, S., Saijo, S., Horai, R., Sudo, K., Mori, S., and Iwakura, Y. IL-17 production from activated T cells is required for the spontaneous development of destructive arthritis in mice deficient in IL-1 receptor antagonist. *Proc. Natl. Acad. Sci. USA*, **100**, 5986-5990 (2003).
166. Asano, M., Nakae, S., Kotani, N., Shirafuji, N., Nambu, A., Hashimoto, N., Kawashima, H., Hirose, M., Miyasaka, M., Takasaki, S., and Iwakura, Y. Impaired selectin ligand biosynthesis and reduced inflammatory responses in β -1,4-galactosyltransferase-I-deficient mice. *Blood*, **102**, 1678-1685 (2003).
167. Wheeler, R. D., Brough, D., Le Feuvre, R. A., Takeda, K., Iwakura, Y., Luheshi, G. N., Rothwell, N. J. Interleukin-18 induces expression and release of cytokines from murine glial cells:

interactions with interleukin-1 β . *J. Neurochem.*, **85**, 1412-1420 (2003).

168. Isoda, K., Shiigai, M., Ishigami, N., Matsuki, T., Horai, R., Nishikawa, K., Kusuhara, M., Nishida, Y., Iwakura, Y., Ohsuzu, F. Deficiency of interleukin-1 receptor antagonist promotes neointimal formation after injury. *Circulation*, **108**, 516-518 (2003).
169. Matsuki, T., Horai, R., Sudo, K., and Iwakura, Y. IL-1 plays an important role in lipid metabolism by regulating insulin levels under physiological conditions. *J. Exp. Med.*, **198**, 877-888 (2003).
170. Miyake-Nishijima, R., Iwata, S., Saijo, S., Kobayashi, H., Kobayashi, S., Souta-Kuribara, A., Hosono, O., Kawasaki, H., Tanaka, H., Ikeda, E., Okada, Y., Iwakura, Y., and Morimoto, C. Role of Crk-associated substrate lymphocyte type in the pathophysiology of rheumatoid arthritis in *tax* transgenic mice and in humans. *Arthritis Rheum.*, **48**, 1890-1900 (2003).
171. Takeda, Y., Akasaka, K., Lee, S., Kobayashi, S., Kawano, H., Murayama, S., Takahashi, N., Hashimoto, K., Kano, M., Asano, M., Sudo, K., Iwakura, K., and Watanabe, K. Impaired motor coordination in mice lacking neural recognition molecule NB-3 of the Contactin/F3 subgroup. *J. Neurobiol.*, **56**, 252-265 (2003).
172. Traka, M., Goutebroge, L., Denisenko, N., Bessa, M., Nifli, A., Havaki, S., Iwakura, Y., Fukamauchi, F., Watanabe, K., Soliven, B., Girault, J. A., and Karagogeos, D. Association of Tag-1 with Caspr 2 is essential for the molecular organization of juxtaparanodal regions of myelinated fibers. *J. Cell Biol.*, **162**, 1161-1172 (2003).
173. Mun, H. S., Aosai, F., Chen, M., Piao, L. X., Norose, K., Iwakura, Y., and Yano, A. Pathogenicity of *Toxoplasma gondii* through B-2 cell-mediated downregulation of host defense responses. *Microbiol. Immunol.*, **47**, 533-542 (2003).
174. Kariyone, A., Tamura, T., Kano, H., Iwakura, Y., Takeda, K., Akira, S., and Takatsu, K. Immunogenicity of peptide-25 of Ag85B in Th1 development: role of IFN- γ . *Int. Immunol.*, **15**, 1183-1194 (2003).

175. Norose, K., Mun, H. S., Aosai, F., Chen, M., Piao, L. X., Kobayashi, M., Iwakura, Y., and Yano, A. IFN- γ -regulated *Toxoplasma gondii* distribution and load in the murine eye. *Invest. Ophthalmol. Vis. Sci.*, **44**, 4375-4381 (2003).
176. Nakae, S., Nambu, A., Sudo, K., and Iwakura, Y. Suppression of immune induction of collagen-induced arthritis in IL-17-deficient mice. *J. Immunol.*, **171**, 6173-6177 (2003).
177. Ohtaki H, Takaki A, Yin L, Dohi K, Nakamachi T, Matsunaga M, Horai R, Asano M, Iwakura Y, and Shioda S. Suppression of oxidative stress after transient focal ischemia in interleukin-1 knockout mice. *Acta Neurochir., Suppl.*, **86**, 191-194 (2003).
178. Ozaki, O., Nakamura, K., Funahashi, J., Ikeda, I., Yamada, G., Tokano, H., Okamura, H., Kitamura, K., Muto, S., Kotaki, H., Sudo, K., Horai, R., Iwakura, Y., and Kawakami, K. *Six1* controls patterning of the mouse otic vesicle. *Development*, **131**, 551-562 (2003).
179. Ono, Y., Ogihara, Y., Saijo, S., Iwakura, Y., and Inoue, M. Evaluation of Kampo medicines used to treat rheumatoid arthritis in collagen-induced arthritis and pX transgenic mice. *Mod. Rheumatol.*, **13**, 50-56 (2003).
180. Kobari, Y., Misaki, Y., Setoguchi, K., Zhao, W., Komagata, Y., Kawahata, K., Iwakura, Y., and Yamamoto, K. T cells accumulating in the inflamed joints of a spontaneous murine model of rheumatoid arthritis become restricted to common clonotypes during disease progression. *Int. Immunol.*, **16**, 131-138 (2004).
181. Ishida, Y., Kondo, T., Takayasu, T., Iwakura, Y., and Mukaida, N. The essential involvement of cross-talk between IFN- γ and TGF- β in the skin wound-healing process. *J. Immunol.*, **172**, 1848-1855 (2004).
182. Kurohara, K., Komatsu, K., Kurisaki, T., Masuda, A., Irie, N., Asano, M., Sudo, K., Nabeshima, Y., Iwakura, Y., and Sehara-Fujisawa, A.

Essential roles of Meltrin beta (ADAM19) in heart development. *Dev. Biol.*, **267**, 14-28 (2004).

183. Ishida, Y., Maegawa, T., Kondo, T., Kimura, A., Iwakura, Y., Nakamura, S., and Mukaida, N. Essential involvement of IFN- γ in *Clostridium difficile* toxin A-induced enteritis. *J. Immunol.*, **172**, 3018-3025 (2004).
184. Ishihara, K., Sawa, S. I., Ikushima, H., Hirota, S., Atsumi, T., Kamimura, D., Park, S. J., Murakami, M., Kitamura, Y., Iwakura, Y., and Hirano, T. The point mutation of tyrosine 759 of the IL-6 family cytokine receptor gp130 synergizes with HTLV-1 *pX* in promoting rheumatoid arthritis-like arthritis. *Int. Immunol.*, **16**, 455-465 (2004).
185. Wu, X., Yoshida, A., Sasano, T., Iwakura, Y., and Endo, Y. Histamine production via mast cell-independent induction of histidine decarboxylase in response to lipopolysaccharide and interleukin-1. *Int. Immuno-pharmacology*, **4**, 513-520 (2004).
186. Timoshanko, J. R., Kitching, A. R., Iwakura, Y., Holdsworth, S., R., and Tipping, P. G. Contributions of IL-1 β and IL-1 α to crescentic glomerulonephritis in mice. *J. Am. Soc. Nephrol.*, **15**, 910-918 (2004).
187. Nakaya, T. A., Kita, M., Kuriyama, H., Iwakura, Y., and Imanishi, J. Panax ginseng induces production of proinflammatory cytokines via Toll-like receptor. *J. Interferon Cytokine Res.*, **24**, 93-100 (2004).
188. Li, Y., Ishii, K., Hisaeda, H., Hamano, S., Zhang, M., Nakanishi, K., Yoshimoto, T., Hemmi, H., Takeda, K., Akira, S., Iwakura, Y., and Himeno, K. IL-18 gene therapy develops Th1-type immune responses in *Leishmania major*-infected BALB/c mice: is the effect mediated by the CpG signaling TLR9? *Gene Ther.*, **11**, 941-948 (2004).
189. Belal, U. S., Norose, K., Aosai, F., Mun, H. S., Ahmed, A. K., Chen, M., Mohamed, R. M., Piao, L. X., Iwakura, Y., and Yano, A. Evaluation of the effects of sulfamethoxazole on *Toxoplasma gondii*

loads and stage conversion in IFN- γ knockout mice using QC-PCR. *Microbiol. Immunol.*, **48**, 185-193 (2004).

190. Kawakami, K., Kinjo, Y., Uezu, K., Miyagi, K., Kinjo, T., Yara, S., Koguchi, Y., Miyazato, A., Shibuya, K., Iwakura, Y., Takeda, K., Akira, S., and Saito, A. Interferon- γ production and host protective response against *Mycobacterium tuberculosis* in mice lacking both IL-12p40 and IL-18. *Microbes Infect.* **6**, 339-349 (2004).
191. Timoshanko, J. R., Kitching, A. R., Iwakura, Y., Holdsworth, S. R., and Tipping, P. G. Leukocyte derived IL-1 β interacts with renal IL-1 receptor I to promote renal TNF and glomerular injury in murine crescentic glomerulonephritis. *Am. J. Physiol.*, **164**, 1967-1977 (2004).
192. Kotani, N., Asano, M., Inoue, N., Iwakura, Y., and Takasaki, S. Polylactosamine synthesis and branch formation of N-glycans in β 1, 4-galactosyltransferase-1-deficient mice. *Arch. Biochem. Biophys.*, **426**, 258-265 (2004).
193. Joosten, L. A. B., Smeets, R. L., Koenders, M. I., van den Bersselaar, L. A. M., Helsen, M. M. A., Oppers-Walgreen, B., Lubberts, E., Iwakura, Y., van de Loo, F. A., J., and van den Berg, W. B. IL-18 promotes joint inflammation and induces IL-1 driven cartilage destruction. *Am. J. Pathol.*, **165**, 959-967 (2004).
194. Isoda, K., Sawada, S., Ishigami, N., Matsuki, T., Miyazaki, K., Kusuhara, M., Iwakura, Y., and Ohsuzu, F. Lack of Interleukin-1 receptor antagonist modulates plaque composition in apolipoprotein E-deficient mice. *Arterioscler. Thromb. Vasc. Biol.*, **24**, 1068-1073 (2004).
195. Ashino, T., Oguro, T., Shioda, S., Horai, R., Asano, M., Sekikawa, K., Iwakura, Y., Numazawa, S., and Yoshida, T. Involvement of IL-6 and TNF in CYP 3A11 and 2C29 down-regulation by BCG and LPS in mouse liver. *Drug Metabolism and Disposition*, **32**, 707-714 (2004).

196. Saito, T., Okumura, A., Watanabe, H., Asano, M., Ishida-Okawara, A., Sakagami, J., Sudo, K., Hatano, Y., Abo, T., Iwakura, Y., Suzuki, K., and Yamagoe, S. Increase of hepatic NKT cells in LECT2-deficient mice contributes to severe Concanavalin A-induced hepatitis. *J. Immunol.*, **173**, 579-585 (2004).
197. Umemura, M., Kawabe, T., Shudo, K., Kidoya, H., Fukui, M., Asano, M., Iwakura, Y., Matsuzaki, G., Imamura, R., and Suda, T. Involvement of IL-17 in Fas ligand-induced inflammation. *Int Immunol.* **16**, 1099-1108 (2004).
198. Kagiwada, K., Chida, D., Sakatani, T., Asano, M., Nambu, A., Kakuta, S., and Iwakura, Y. *IL-6*, but not *IL-1*, induction in the brain downstream of Cox-2 is essential for the induction of febrile response against peripheral IL-1 α . *Endocrinology*, **145**, 5044-5048 (2004).
199. Hata, H., Sakaguchi, N., Yoshitomi, H., Iwakura, Y., Sekikawa, K., Azuma, Y., Kanai, C., Moriizumi, E., Nomura, T., Nakamura, T., and Sakaguchi, S. Distinct contribution of IL-6, TNF- α , IL-1, and IL-10 to T cell-mediated spontaneous autoimmune arthritis in mice. *J. Clin. Invest.*, **114**, 582-588 (2004).
200. Yoshimoto, T., Okada, K., Morishima, N., Kamiya, S., Owaki, T., Asakawa, M., Iwakura, Y., Fukai, F., and Mizuguchi, J. Induction of IgG2a class switching in B cells by IL-27. *J. Immunol.*, **173**, 2479-2485 (2004).
201. Uekawa, N., Nishikimi, A., Isobe, K., Iwakura, Y., and Maruyama, M. Involvement of IL-1 family proteins in p38 linked cellular senescence of mouse embryonic fibroblasts. *FEBS Lett.*, **575**, 30-34, (2004).
202. Kudo, M., Aosai, F., Mun, H. S., Norose, K., Akira, S., Iwakura, Y., and Yano, A. The role of IFN- γ and Toll-like receptors in nephropathy induced by *Toxoplasma gondii* infection. *Microbiol. Immunol.*, **48**, 617-628 (2004).
203. Asahi-Ozaki, Y., Yoshikawa, T., Iwakura, Y., Suzuki, Y., Tamura, S., Kurata, T., and Sata, T. Secretory IgA antibodies provide

cross-protection against infection with different strains of influenza B virus. *J. Med. Virol.*, **74**, 328-335 (2004).

204. Hasegawa, S., Nishikawa, S., Miura, T., Saito, Y., Madarame, H., Sekikawa, K., Tagawa, Y., Iwakura, Y., and Nakane, A. Tumor necrosis factor- α is required for gastritis induced by *Helicobacter felis* infection in mice. *Microb. Pathog.*, **37**, 119-124 (2004).
205. Park, S. J., Nakagawa, T., Kitamura, H., Atsumi, T., Kamon, H., Sawa, S., Kamimura, D., Ueda, N., Iwakura, Y., Ishihara, K., Murakami, M., and Hirano, T. IL-6 regulates *in vivo* dendritic cell differentiation through STAT3 activation. *J. Immunol.*, **173**, 3844-3854 (2004).
206. Yamamoto, T., Kita, M., Ohno, T., Iwakura, Y., Sekikawa, K., and Imanishi, J. Role of tumor necrosis factor-alpha and interferon-gamma in *Helicobacter pylori* infection. *Microbiol. Immunol.*, **48**, 647-654, (2004).
207. Horai, R., Nakajima, A., Habiro, K., Kotani, M., Nakae, S., Matsuki, T., Nambu, A., Saijo, S., Kotaki, H., Sudo, K., Okahara, A., Tanioka, H., Ikuse, T., Ishii, N., Schwartzberg, P. L., Abe, R., and Iwakura, Y. TNF α is crucial for the development of autoimmune arthritis in IL-1 receptor antagonist-deficient mice. *J. Clin. Invest.*, **114**, 1603-1611 (2004).
208. Yasuda, T., Shirakata, M., Iwama, A., Ishii, A., Ebihara, Y., Osawa, M., Honda, K., Shinohara, H., Sudo, K., Tsuji, K., Nakauchi, H., Iwakura, Y., Hirai, H., Oda, H., Yamamoto, T., and Yamanashi, Y. Role of Dok-1 and Dok-2 in myeloid homeostasis and suppression of leukemia. *J. Exp. Med.*, **200**, 1681-1687 (2004).
209. Sakuraba, H., Ishiguro, Y., Yamagata, K., Tagawa, Y., Iwakura, Y., Sekikawa, K., Munakata, A., and Nakane, A. Transforming growth factor- β regulates susceptibility of epithelial apoptosis in murine model of colitis. *Ann. N. Y. Acad. Sci.*, **1029**, 382-384 (2004).
210. Tanabe, M., Matsumoto, T., Shibuya, K., Tateda, K., Miyazaki, S., Nakane, A., Iwakura, Y., and Yamaguchi, K. Compensatory

- response of IL-1 gene knockout mice after pulmonary infection with *Klebsiella pneumoniae*. *J. Med. Microbiol.*, **54**, 7-13 (2005).
211. Wakabayashi, T., Hu, D. L., Tagawa, Y, Sekikawa, K., Iwakura, Y., Hanada, K., and Nakane, A. IFN- γ and TNF- α are involved in urushiol-induced contact hypersensitivity in mice. *Immunol. Cell Biol.*, **83**, 18-24 (2005).
 212. Kohu, K., Sato, T., Ohno, S., Hayashi, K., Uchino, R., Abe, N., Nakazato, M., Yoshida, N., Kikuchi, T., Iwakura, Y., Inoue, Y., Watanabe, T., Habu, S., and Satake, M. Over-expression of the Runx3 transcription factor increases the proportion of mature thymocytes of the CD8 single positive lineage. *J. Immunol.*, **174**, 2627-2636 (2005).
 213. Isoda K, Sawada S, Ayaori M, Matsuki T, Horai R, Kagata Y, Miyazaki K, Kusuvara M, Okazaki M, Matsubara O, Iwakura Y, Ohsuzu F. Deficiency of interleukin-1 receptor antagonist deteriorates fatty-liver and cholesterol metabolism in hypercholesterolemic mice. *J. Biol. Chem.*, **280**, 7002-7009 (2005).
 214. Shinohara, H., Inoue, A., Toyama-Sorimachi, N., Nagai, Y., Yasuda, T., Suzuki, H., Horai, R., Iwakura, Y., Yamamoto, T., Karasuyama, H., Miyake, K., and Yamanashi, Y. Dok-1 and Dok-2 are negative regulators of lipopolysaccharide-induced signaling. *J. Exp. Med.*, **201**, 333-339 (2005).
 215. Horino. T., Matsumoto, T., Uramatsu, M., Tanabe, M., Tateda, K., Miyazaki, S., Nakane, A., Iwakura, Y., and Yamaguchi, K. Interleukin-1-deficient mice exhibit high sensitivity to gut-derived sepsis caused by *Pseudomonas aeruginosa*. *Cytokine*, **30**, 339-346 (2005).
 216. Matsuki, T., Isoda, K., Horai, R., Nakajima, A., Aizawa, Y., Suzuki, K., Ohsuzu, F., and Iwakura, Y. Involvement of TNF α in the development of T cell-dependent aortitis in IL-1 receptor antagonist-deficient mice. *Circulation*, **112**, 1323-1331 (2005).

217. Hedtjarn, M., Mallard, C., Iwakura, Y., and Hagberg, H. Combined deficiency of IL-1 β , but not IL-1 α , reduces susceptibility to hypoxia-ischemia in the immature brain. *Dev. Neurosci.*, **27**, 143-148 (2005).
218. Zhou, F., He, X., Iwakura, Y., Horai, R., and Stuart, J. M. Arthritis in mice that are deficient in IL-1 receptor antagonist is dependent on genetic background. *Arth. Rheum.*, **52**, 3731-3738 (2005).
219. Chida, D., Imaki, T., Suda, T., and Iwakura, Y. Involvement of CRH- and IL-6-dependent proopiomelanocortin induction in the anterior pituitary during hypothalamic-pituitary-adrenal axis activation by IL-1 α . *Endocrinology*, **146**, 5496-5502 (2005).