REFERENCES

Abbas, A.R., Baldwin, D., Ma, Y., Ouyang, W., Gurney, A., Martin, F., Fong, S., van Lookeren Campagne, M., Godowski, P., Williams, P.M., Chan, A.C., Clark, H.F., 2005, Immune response in silico (IRIS): immune-specific genes identified from a compendium of microarray expression data. Genes Immun 6: 319-331.

Agematsu, K., Hokibara, S., Nagumo, H., Komiyama, A., 2000, CD27: a memory B-cell marker. Immunol Today 21: 204-206.

Agematsu, K., Nagumo, H., Yang, F.C., Nakazawa, T., Fukushima, K., Ito, S., Sugita, K., Mori, T., Kobata, T., Morimoto, C., Komiyama, A., 1997, B cell subpopulations separated by CD27 and crucial collaboration of CD27+ B cells and helper T cells in immunoglobulin production. Eur J Immunol 27: 2073-2079.

Ahuja, A., Shupe, J., Dunn, R., Kashgarian, M., Kehry, M.R., Shlomchik, M.J., 2007, Depletion of B cells in murine lupus: efficacy and resistance. J Immunol 179: 3351-3361.

Akiba, H., Nakano, H., Nishinaka, S., Shindo, M., Kobata, T., Atsuta, M., Morimoto, C., Ware, C.F., Malinin, N.L., Wallach, D., Yagita, H., Okumura, K., 1998, CD27, a member of the tumor necrosis factor receptor superfamily, activates NF-kappaB and stress-activated protein kinase/c-Jun N-terminal kinase via TRAF2, TRAF5, and NF-kappaB-inducing kinase. J Biol Chem 273: 13353-13358.

Alouf, J.E., Muller-Alouf, H., 2003, Staphylococcal and streptococcal superantigens: molecular, biological and clinical aspects. Int J Med Microbiol 292: 429-440.

Arens, R., Baars, P.A., Jak, M., Tesselaar, K., van der Valk, M., van Oers, M.H., van Lier, R.A., 2005, Cutting edge: CD95 maintains effector T cell homeostasis in chronic immune activation. J Immunol 174: 5915-5920.

Arstila, T.P., Casrouge, A., Baron, V., Even, J., Kanellopoulos, J., Kourilsky, P., 1999, A direct estimate of the human alphabeta T cell receptor diversity. Science 286: 958-961.

Ashburner, M., Ball, C.A., Blake, J.A., Botstein, D., Butler, H., Cherry, J.M., Davis, A.P., Dolinski, K., Dwight, S.S., Eppig, J.T., Harris, M.A., Hill, D.P., Issel-Tarver, L., Kasarskis, A., Lewis, S., Matese, J.C., Richardson, J.E., Ringwald, M., Rubin, G.M., Sherlock, G., 2000, Gene ontology: tool for the unification of biology. The Gene Ontology Consortium. Nat Genet 25: 25-29.

Ashour, H.M., Seif, T.M., 2007, The role of B cells in the induction of peripheral T cell tolerance. J Leukoc Biol 82: 1033-1039.

Attinger, A., Acha-Orbea, H., MacDonald, H.R., 2000, Cutting edge: cell autonomous rather than environmental factors control bacterial superantigen-induced T cell anergy in vivo. J Immunol 165: 1171-1174.

Avalos, A.M., Latz, E., Mousseau, B., Christensen, S.R., Shlomchik, M.J., Lund, F., Marshak-Rothstein, A., 2009, Differential cytokine production and bystander activation of autoreactive B cells in response to CpG-A and CpG-B oligonucleotides. J Immunol 183: 6262-6268.

Banchereau, J., Briere, F., Liu, Y.J., Rousset, F., 1994, Molecular control of B lymphocyte growth and differentiation. Stem Cells 12: 278-288.

Bekeredjian-Ding, I.B., Wagner, M., Hornung, V., Giese, T., Schnurr, M., Endres, S., Hartmann, G., 2005, Plasmacytoid dendritic cells control TLR7 sensitivity of naive B cells via type I IFN. J Immunol 174: 4043-4050.

Bennett, S.R., Carbone, F.R., Toy, T., Miller, J.F., Heath, W.R., 1998, B cells directly tolerize CD8(+) T cells. J Exp Med 188: 1977-1983.

Berg, E.L., Goldstein, L.A., Jutila, M.A., Nakache, M., Picker, L.J., Streeter, P.R., Wu, N.W., Zhou, D., Butcher, E.C., 1989, Homing receptors and vascular addressins: cell adhesion molecules that direct lymphocyte traffic. Immunol Rev 108: 5-18.

Bergmann, C.C., Ramakrishna, C., Kornacki, M., Stohlman, S.A., 2001, Impaired T cell immunity in B cell-deficient mice following viral central nervous system infection. J Immunol 167: 1575-1583.

Bhardwaj, N., Young, J.W., Nisanian, A.J., Baggers, J., Steinman, R.M., 1993, Small amounts of superantigen, when presented on dendritic cells, are sufficient to initiate T cell responses. J Exp Med 178: 633-642.

Boackle, S.A., Morris, M.A., Holers, V.M., Karp, D.R., 1998, Complement opsonization is required for presentation of immune complexes by resting peripheral blood B cells. J Immunol 161: 6537-6543.

Bofill, M., Janossy, G., Janossa, M., Burford, G.D., Seymour, G.J., Wernet, P., Kelemen, E., 1985, Human B cell development. II. Subpopulations in the human fetus. J Immunol 134: 1531-1538.

Bohnhorst, J.O., Bjorgan, M.B., Thoen, J.E., Natvig, J.B., Thompson, K.M., 2001, Bm1-Bm5 classification of peripheral blood B cells reveals circulating germinal center founder cells in healthy individuals and disturbance in the B cell subpopulations in patients with primary Sjogren's syndrome. J Immunol 167: 3610-3618.

Borchert, G.M., Holton, N.W., Edwards, K.A., Vogel, L.A., Larson, E.D., Histone H2A and H2B are monoubiquitinated at AID-targeted loci. PLoS One 5: e11641.

Bouaziz, J.D., Yanaba, K., Tedder, T.F., 2008, Regulatory B cells as inhibitors of immune responses and inflammation. **Immunol Rev** 224: 201-214.

Bouaziz, J.D., Yanaba, K., Venturi, G.M., Wang, Y., Tisch, R.M., Poe, J.C., Tedder, T.F., 2007, Therapeutic B cell depletion impairs adaptive and autoreactive CD4+ T cell activation in mice. **Proc Natl Acad Sci U S A** 104: 20878-20883.

Bourdette, D., Yadav, V., 2008, B-cell depletion with rituximab in relapsing-remitting multiple sclerosis. **Curr Neurol Neurosci Rep** 8: 417-418.

Breloer, M., Kretschmer, B., Luthje, K., Ehrlich, S., Ritter, U., Bickert, T., Steeg, C., Fillatreau, S., Hoehlig, K., Lampropoulou, V., Fleischer, B., 2007, CD83 is a regulator of murine B cell function in vivo. **Eur J Immunol** 37: 634-648.

Brown, P.J., Ashe, S.L., Leich, E., Burek, C., Barrans, S., Fenton, J.A., Jack, A.S., Pulford, K., Rosenwald, A., Banham, A.H., 2008, Potentially oncogenic B-cell activation-induced smaller isoforms of FOXP1 are highly expressed in the activated B cell-like subtype of DLBCL. **Blood** 111: 2816-2824.

Brusko, T.M., Hulme, M.A., Myhr, C.B., Haller, M.J., Atkinson, M.A., 2007, Assessing the in vitro suppressive capacity of regulatory T cells. **Immunol Invest** 36: 607-628.

Campana, D., Janossy, G., Bofill, M., Trejdosiewicz, L.K., Ma, D., Hoffbrand, A.V., Mason, D.Y., Lebacq, A.M., Forster, H.K., 1985, Human B cell development. I. Phenotypic differences of B lymphocytes in the bone marrow and peripheral lymphoid tissue. **J Immunol** 134: 1524-1530.

Carpenter, E.L., Mick, R., Ruter, J., Vonderheide, R.H., 2009, Activation of human B cells by the agonist CD40 antibody CP-870,893 and augmentation with simultaneous toll-like receptor 9 stimulation. **J Transl Med** 7: 93.

Carsetti, R., Kohler, G., Lamers, M.C., 1995, Transitional B cells are the target of negative selection in the B cell compartment. **J Exp Med** 181: 2129-2140.

Cauley, L.S., Cauley, K.A., Shub, F., Huston, G., Swain, S.L., 1997, Transferable anergy: superantigen treatment induces CD4+ T cell tolerance that is reversible and requires CD4-CD8- cells and interferon gamma. **J Exp Med** 186: 71-81.

Cauley, L.S., Miller, E.E., Yen, M., Swain, S.L., 2000, Superantigen-induced CD4 T cell tolerance mediated by myeloid cells and IFN-gamma. **J Immunol** 165: 6056-6066.

Chen, L.C., Delgado, J.C., Jensen, P.E., Chen, X., 2009, Direct expansion of human allospecific FoxP3+CD4+ regulatory T cells with allogeneic B cells for therapeutic application. **J Immunol** 183: 4094-4102.

Chen, X., Laur, O., Kambayashi, T., Li, S., Bray, R.A., Weber, D.A., Karlsson, L., Jensen, P.E., 2002, Regulated expression of human histocompatibility leukocyte antigen (HLA)-DO during antigen-dependent and antigen-independent phases of B cell development. J Exp Med 195: 1053-1062.

Choi, Y.W., Herman, A., DiGiusto, D., Wade, T., Marrack, P., Kappler, J., 1990, Residues of the variable region of the T-cell-receptor beta-chain that interact with S. aureus toxin superantigens. Nature 346: 471-473.

Chu, Y., Vahl, J.C., Kumar, D., Heger, K., Bertossi, A., Wojtowicz, E., Soberon, V., Schenten, D., Mack, B., Reutelshofer, M., Beyaert, R., Amann, K., van Loo, G., Schmidt-Supprian, M., B cells lacking the tumor suppressor TNFAIP3/A20 display impaired differentiation and hyperactivation and cause inflammation and autoimmunity in aged mice. Blood 117: 2227-2236.

Chung, J.B., Silverman, M., Monroe, J.G., 2003, Transitional B cells: step by step towards immune competence. Trends Immunol 24: 343-349.

Clark, A.G., Chen, S., Zhang, H., Brady, G.F., Ungewitter, E.K., Bradley, J.K., Sackey, F.N., Foster, M.H., 2007, Multifunctional regulators of cell growth are differentially expressed in anergic murine B cells. Mol Immunol 44: 1274-1285.

Coffman, R.L., Cohn, M., 1977, The class of surface immunoglobulin on virgin and memory B lymphocytes. J Immunol 118: 1806-1815.

Cohen, S.B., Emery, P., Greenwald, M.W., Dougados, M., Furie, R.A., Genovese, M.C., Keystone, E.C., Loveless, J.E., Burmester, G.R., Cravets, M.W., Hessey, E.W., Shaw, T., Totoritis, M.C., 2006, Rituximab for rheumatoid arthritis refractory to anti-tumor necrosis factor therapy: Results of a multicenter, randomized, double-blind, placebo-controlled, phase III trial evaluating primary efficacy and safety at twenty-four weeks. Arthritis Rheum 54: 2793-2806.

Cole, B.C., Griffiths, M.M., 1993, Triggering and exacerbation of autoimmune arthritis by the Mycoplasma arthritidis superantigen MAM. Arthritis Rheum 36: 994-1002.

Collins, R.A., Oldham, G., 1995, Effect of recombinant bovine IL-1 and IL-2 on B cell proliferation and differentiation. Vet Immunol Immunopathol 44: 141-150.

Collins, T., Korman, A.J., Wake, C.T., Boss, J.M., Kappes, D.J., Fiers, W., Ault, K.A., Gimbrone, M.A., Jr., Strominger, J.L., Pober, J.S., 1984, Immune interferon activates multiple class II major histocompatibility complex genes and the associated invariant chain gene in human endothelial cells and dermal fibroblasts. Proc Natl Acad Sci U S A 81: 4917-4921.

Constant, S., Schweitzer, N., West, J., Ranney, P., Bottomly, K., 1995, B lymphocytes can be competent antigen-presenting cells for priming CD4+ T cells to protein antigens in vivo. J Immunol 155: 3734-3741.

Croft, M., Joseph, S.B., Miner, K.T., 1997, Partial activation of naive CD4 T cells and tolerance induction in response to peptide presented by resting B cells. J Immunol 159: 3257-3265.

Crotty, S., Aubert, R.D., Glidewell, J., Ahmed, R., 2004, Tracking human antigen-specific memory B cells: a sensitive and generalized ELISPOT system. J Immunol Methods 286: 111-122.

Curtsinger, J.M., Mescher, M.F., Inflammatory cytokines as a third signal for T cell activation. Curr Opin Immunol 22: 333-340.

Daubeuf, S., Puaux, A.L., Joly, E., Hudrisier, D., 2006, A simple trogocytosis-based method to detect, quantify, characterize and purify antigen-specific live lymphocytes by flow cytometry, via their capture of membrane fragments from antigen-presenting cells. Nat Protoc 1: 2536-2542.

de Hoon, M.J., Imoto, S., Nolan, J., Miyano, S., 2004, Open source clustering software. Bioinformatics 20: 1453-1454.

Del Prete, G., De Carli, M., D'Elios, M.M., Fleckenstein, I.M., Fickenscher, H., Fleckenstein, B., Almerigogna, F., Romagnani, S., 1994, Polyclonal B cell activation induced by herpesvirus saimiri-transformed human CD4+ T cell clones. Role for membrane TNF-alpha/TNF-alpha receptors and CD2/CD58 interactions. J Immunol 153: 4872-4879.

Dellabona, P., Peccoud, J., Kappler, J., Marrack, P., Benoist, C., Mathis, D., 1990, Superantigens interact with MHC class II molecules outside of the antigen groove. Cell 62: 1115-1121.

Denzin, L.K., Fallas, J.L., Prendes, M., Yi, W., 2005, Right place, right time, right peptide: DO keeps DM focused. Immunol Rev 207: 279-292.

Di Rosa, F., Matzinger, P., 1996, Long-lasting CD8 T cell memory in the absence of CD4 T cells or B cells. J Exp Med 183: 2153-2163.

Dinges, M.M., Orwin, P.M., Schlievert, P.M., 2000, Exotoxins of Staphylococcus aureus. Clin Microbiol Rev 13: 16-34, table of contents.

Dinkel, A., Aicher, W.K., Haas, C., Zipfel, P.F., Peter, H.H., Eibel, H., 1997, Transcription factor Egr-1 activity down-regulates Fas and CD23 expression in B cells. J Immunol 159: 2678-2684.

Dorner, M., Zucol, F., Berger, C., Byland, R., Melroe, G.T., Bernasconi, M., Speck, R.F., Nadal, D., 2008, Distinct ex vivo susceptibility of B-cell subsets to epstein-barr virus infection according to differentiation status and tissue origin. J Virol 82: 4400-4412.

Dorner, T., Isenberg, D., Jayne, D., Wiendl, H., Zillikens, D., Burmester, G., 2009, Current status on B-cell depletion therapy in autoimmune diseases other than rheumatoid arthritis. **Autoimmun Rev** 9: 82-89.

Douagi, I., Gujer, C., Sundling, C., Adams, W.C., Smed-Sorensen, A., Seder, R.A., Karlsson Hedestam, G.B., Lore, K., 2009, Human B cell responses to TLR ligands are differentially modulated by myeloid and plasmacytoid dendritic cells. **J Immunol** 182: 1991-2001.

Duty, J.A., Szodoray, P., Zheng, N.Y., Koelsch, K.A., Zhang, Q., Swiatkowski, M., Mathias, M., Garman, L., Helms, C., Nakken, B., Smith, K., Farris, A.D., Wilson, P.C., 2009, Functional anergy in a subpopulation of naive B cells from healthy humans that express autoreactive immunoglobulin receptors. **J Exp Med** 206: 139-151.

Eki, T., Okumura, K., Abe, M., Kagotani, K., Taguchi, H., Murakami, Y., Pan, Z.Q., Hanaoka, F., 1998, Mapping of the human genes encoding cyclin H (CCNH) and the CDK-activating kinase (CAK) assembly factor MAT1 (MNAT1) to chromosome bands 5q13.3-q14 and 14q23, respectively. **Genomics** 47: 115-120.

Eming, R., Nagel, A., Wolff-Franke, S., Podstawa, E., Debus, D., Hertl, M., 2008, Rituximab exerts a dual effect in pemphigus vulgaris. **J Invest Dermatol** 128: 2850-2858.

Epstein, M.M., Di Rosa, F., Jankovic, D., Sher, A., Matzinger, P., 1995, Successful T cell priming in B cell-deficient mice. **J Exp Med** 182: 915-922.

Evans, D.E., Munks, M.W., Purkerson, J.M., Parker, D.C., 2000, Resting B lymphocytes as APC for naive T lymphocytes: dependence on CD40 ligand/CD40. **J Immunol** 164: 688-697.

Eynon, E.E., Parker, D.C., 1992, Small B cells as antigen-presenting cells in the induction of tolerance to soluble protein antigens. **J Exp Med** 175: 131-138.

Eynon, E.E., Parker, D.C., 1993, Parameters of tolerance induction by antigen targeted to B lymphocytes. **J Immunol** 151: 2958-2964.

Fathman, C.G., Lineberry, N.B., 2007, Molecular mechanisms of CD4+ T-cell anergy. **Nat Rev Immunol** 7: 599-609.

Fecteau, J.F., Cote, G., Neron, S., 2006, A new memory CD27-IgG+ B cell population in peripheral blood expressing VH genes with low frequency of somatic mutation. **J Immunol** 177: 3728-3736.

Fecteau, J.F., Neron, S., 2003, CD40 stimulation of human peripheral B lymphocytes: distinct response from naive and memory cells. **J Immunol** 171: 4621-4629.

Feunou, P., Poulin, L., Habran, C., Le Moine, A., Goldman, M., Braun, M.Y., 2003, CD4+CD25+ and CD4+CD25- T cells act respectively as inducer and effector T suppressor cells in superantigen-induced tolerance. **J Immunol** 171: 3475-3484.

Fiorina, P., Vergani, A., Dada, S., Jurewicz, M., Wong, M., Law, K., Wu, E., Tian, Z., Abdi, R., Guleria, I., Rodig, S., Dunussi-Joannopoulos, K., Bluestone, J., Sayegh, M.H., 2008, Targeting CD22 reprograms B-cells and reverses autoimmune diabetes. Diabetes 57: 3013-3024.

Fischer, H., Dohlsten, M., Lindvall, M., Sjogren, H.O., Carlsson, R., 1989, Binding of staphylococcal enterotoxin A to HLA-DR on B cell lines. J Immunol 142: 3151-3157.

Flaishon, L., Hershkoviz, R., Lantner, F., Lider, O., Alon, R., Levo, Y., Flavell, R.A., Shachar, I., 2000, Autocrine secretion of interferon gamma negatively regulates homing of immature B cells. J Exp Med 192: 1381-1388.

Fleischer, B., Schrezenmeier, H., 1988, T cell stimulation by staphylococcal enterotoxins. Clonally variable response and requirement for major histocompatibility complex class II molecules on accessory or target cells. J Exp Med 167: 1697-1707.

Florquin, S., Amraoui, Z., Goldman, M., 1996, Persistent production of TH2-type cytokines and polyclonal B cell activation after chronic administration of staphylococcal enterotoxin B in mice. J Autoimmun 9: 609-615.

Floyd, S.R., Porro, E.B., Slepnev, V.I., Ochoa, G.C., Tsai, L.H., De Camilli, P., 2001, Amphiphysin 1 binds the cyclin-dependent kinase (cdk) 5 regulatory subunit p35 and is phosphorylated by cdk5 and cdc2. J Biol Chem 276: 8104-8110.

Fraser, J.D., 1989, High-affinity binding of staphylococcal enterotoxins A and B to HLA-DR. Nature 339: 221-223.

Frazer, J.K., LeGros, J., de Bouteiller, O., Liu, Y.J., Banchereau, J., Pascual, V., Capra, J.D., 1997, Identification and cloning of genes expressed by human tonsillar B lymphocyte subsets. Ann N Y Acad Sci 815: 316-318.

Freedman, A.S., Freeman, G., Whitman, J., Segil, J., Daley, J., Nadler, L.M., 1988, Pre-exposure of human B cells to recombinant IL-1 enhances subsequent proliferation. J Immunol 141: 3398-3404.

Frenzel, L.P., Patz, M., Pallasch, C.P., Brinker, R., Claasen, J., Schulz, A., Hallek, M., Kashkar, H., Wendtner, C.M., Novel X-linked inhibitor of apoptosis inhibiting compound as sensitizer for TRAIL-mediated apoptosis in chronic lymphocytic leukaemia with poor prognosis. Br J Haematol 152: 191-200.

Friedl, P., den Boer, A.T., Gunzer, M., 2005, Tuning immune responses: diversity and adaptation of the immunological synapse. Nat Rev Immunol 5: 532-545.

Fu, Y.X., Huang, G., Wang, Y., Chaplin, D.D., 1998, B lymphocytes induce the formation of follicular dendritic cell clusters in a lymphotoxin alpha-dependent fashion. J Exp Med 187: 1009-1018.

Fuchs, E.J., Matzinger, P., 1992, B cells turn off virgin but not memory T cells. Science 258: 1156-1159.

Gallegos, A.M., Bevan, M.J., 2006, Central tolerance: good but imperfect. Immunol Rev 209: 290-296.

Geiger, R., Duhen, T., Lanzavecchia, A., Sallusto, F., 2009, Human naive and memory CD4+ T cell repertoires specific for naturally processed antigens analyzed using libraries of amplified T cells. J Exp Med 206: 1525-1534.

Gilbert, K.M., Weigle, W.O., 1994, Tolerogenicity of resting and activated B cells. J Exp Med 179: 249-258.

Giordani, L., Sanchez, M., Libri, I., Quaranta, M.G., Mattioli, B., Viora, M., 2009, IFN-alpha amplifies human naive B cell TLR-9-mediated activation and Ig production. J Leukoc Biol 86: 261-271.

Girschick, H.J., Grammer, A.C., Nanki, T., Mayo, M., Lipsky, P.E., 2001, RAG1 and RAG2 expression by B cell subsets from human tonsil and peripheral blood. J Immunol 166: 377-386.

Glimcher, L.H., Kara, C.J., 1992, Sequences and factors: a guide to MHC class-II transcription. Annu Rev Immunol 10: 13-49.

Goldrath, A.W., Bevan, M.J., 1999, Selecting and maintaining a diverse T-cell repertoire. Nature 402: 255-262.

Golovkina, T.V., Shlomchik, M., Hannum, L., Chervonsky, A., 1999, Organogenic role of B lymphocytes in mucosal immunity. Science 286: 1965-1968.

Gong, Q., Ou, Q., Ye, S., Lee, W.P., Cornelius, J., Diehl, L., Lin, W.Y., Hu, Z., Lu, Y., Chen, Y., Wu, Y., Meng, Y.G., Gribling, P., Lin, Z., Nguyen, K., Tran, T., Zhang, Y., Rosen, H., Martin, F., Chan, A.C., 2005, Importance of cellular microenvironment and circulatory dynamics in B cell immunotherapy. J Immunol 174: 817-826.

Gonnella, P.A., Waldner, H.P., Weiner, H.L., 2001, B cell-deficient (mu MT) mice have alterations in the cytokine microenvironment of the gut-associated lymphoid tissue (GALT) and a defect in the low dose mechanism of oral tolerance. J Immunol 166: 4456-4464.

Good, K.L., Avery, D.T., Tangye, S.G., 2009, Resting human memory B cells are intrinsically programmed for enhanced survival and responsiveness to diverse stimuli compared to naive B cells. J Immunol 182: 890-901.

Gros, M.J., Naquet, P., Guinamard, R.R., 2008, Cell intrinsic TGF-beta 1 regulation of B cells. J Immunol 180: 8153-8158.

Grundstrom, S., Cederbom, L., Sundstedt, A., Scheipers, P., Ivars, F., 2003, Superantigen-induced regulatory T cells display different suppressive functions in the presence or absence of natural CD4+CD25+ regulatory T cells in vivo. J **Immunol** 170: 5008-5017.

Grundstrom, S., Dohlsten, M., Sundstedt, A., 2000, IL-2 unresponsiveness in anergic CD4+ T cells is due to defective signaling through the common gamma-chain of the IL-2 receptor. J **Immunol** 164: 1175-1184.

Gujer, C., Sandgren, K.J., Douagi, I., Adams, W.C., Sundling, C., Smed-Sorensen, A., Seder, R.A., Hedestam, G.B., Lore, K., IFN-{alpha} produced by human plasmacytoid dendritic cells enhances T cell-dependent naive B cell differentiation. **J Leukoc Biol**.

Hamel, K., Doodes, P., Cao, Y., Wang, Y., Martinson, J., Dunn, R., Kehry, M.R., Farkas, B., Finnegan, A., 2008, Suppression of proteoglycan-induced arthritis by anti-CD20 B Cell depletion therapy is mediated by reduction in autoantibodies and CD4+ T cell reactivity. J **Immunol** 180: 4994-5003.

Hanten, J.A., Vasilakos, J.P., Riter, C.L., Neys, L., Lipson, K.E., Alkan, S.S., Birmachu, W., 2008, Comparison of human B cell activation by TLR7 and TLR9 agonists. **BMC Immunol** 9: 39.

Hao, Z., Duncan, G.S., Seagal, J., Su, Y.W., Hong, C., Haight, J., Chen, N.J., Elia, A., Wakeham, A., Li, W.Y., Liepa, J., Wood, G.A., Casola, S., Rajewsky, K., Mak, T.W., 2008, Fas receptor expression in germinal-center B cells is essential for T and B lymphocyte homeostasis. **Immunity** 29: 615-627.

Hardy, R.R., Hayakawa, K., Parks, D.R., Herzenberg, L.A., 1983, Demonstration of B-cell maturation in X-linked immunodeficient mice by simultaneous three-colour immunofluorescence. **Nature** 306: 270-272.

Harper, J.W., Adami, G.R., Wei, N., Keyomarsi, K., Elledge, S.J., 1993, The p21 Cdk-interacting protein Cip1 is a potent inhibitor of G1 cyclin-dependent kinases. **Cell** 75: 805-816.

Harris, D.P., Goodrich, S., Gerth, A.J., Peng, S.L., Lund, F.E., 2005a, Regulation of IFN-gamma production by B effector 1 cells: essential roles for T-bet and the IFN-gamma receptor. J **Immunol** 174: 6781-6790.

Harris, D.P., Goodrich, S., Mohrs, K., Mohrs, M., Lund, F.E., 2005b, Cutting edge: the development of IL-4-producing B cells (B effector 2 cells) is controlled by IL-4, IL-4 receptor alpha, and Th2 cells. **J Immunol** 175: 7103-7107.

Harris, D.P., Haynes, L., Sayles, P.C., Duso, D.K., Eaton, S.M., Lepak, N.M., Johnson, L.L., Swain, S.L., Lund, F.E., 2000, Reciprocal regulation of polarized cytokine production by effector B and T cells. **Nat Immunol** 1: 475-482.

Hartwig, U.F., Gerlach, D., Fleischer, B., 1994, Major histocompatibility complex class II binding site for streptococcal pyrogenic (erythrogenic) toxin A. **Med Microbiol Immunol** 183: 257-264.

Hase, H., Kanno, Y., Kojima, H., Morimoto, C., Okumura, K., Kobata, T., 2002, CD27 and CD40 inhibit p53-independent mitochondrial pathways in apoptosis of B cells induced by B cell receptor ligation. **J Biol Chem** 277: 46950-46958.

Hauser, S.L., Waubant, E., Arnold, D.L., Vollmer, T., Antel, J., Fox, R.J., Bar-Or, A., Panzara, M., Sarkar, N., Agarwal, S., Langer-Gould, A., Smith, C.H., 2008, B-cell depletion with rituximab in relapsing-remitting multiple sclerosis. **N Engl J Med** 358: 676-688.

Herve, M., Isnardi, I., Ng, Y.S., Bussel, J.B., Ochs, H.D., Cunningham-Rundles, C., Meffre, E., 2007, CD40 ligand and MHC class II expression are essential for human peripheral B cell tolerance. **J Exp Med** 204: 1583-1593.

Hewitt, C.R., Lamb, J.R., Hayball, J., Hill, M., Owen, M.J., O'Hehir, R.E., 1992, Major histocompatibility complex independent clonal T cell anergy by direct interaction of Staphylococcus aureus enterotoxin B with the T cell antigen receptor. **J Exp Med** 175: 1493-1499.

Hollsberg, P., Batra, V., Dressel, A., Hafler, D.A., 1996, Induction of anergy in CD8 T cells by B cell presentation of antigen. **J Immunol** 157: 5269-5276.

Homann, D., Tishon, A., Berger, D.P., Weigle, W.O., von Herrath, M.G., Oldstone, M.B., 1998, Evidence for an underlying CD4 helper and CD8 T-cell defect in B-cell-deficient mice: failure to clear persistent virus infection after adoptive immunotherapy with virus-specific memory cells from muMT/muMT mice. **J Virol** 72: 9208-9216.

Hu, C.Y., Rodriguez-Pinto, D., Du, W., Ahuja, A., Henegariu, O., Wong, F.S., Shlomchik, M.J., Wen, L., 2007, Treatment with CD20-specific antibody prevents and reverses autoimmune diabetes in mice. **J Clin Invest** 117: 3857-3867.

Hu, H., Wu, X., Jin, W., Chang, M., Cheng, X., Sun, S.C., Noncanonical NF-{kappa}B regulates inducible costimulator (ICOS) ligand expression and T follicular helper cell development. **Proc Natl Acad Sci U S A**.

Huang da, W., Sherman, B.T., Lempicki, R.A., 2009a, Bioinformatics enrichment tools: paths toward the comprehensive functional analysis of large gene lists. **Nucleic Acids Res** 37: 1-13.

Huang da, W., Sherman, B.T., Lempicki, R.A., 2009b, Systematic and integrative analysis of large gene lists using DAVID bioinformatics resources. **Nat Protoc** 4: 44-57.

Hudrisier, D., Riond, J., Garidou, L., Duthoit, C., Joly, E., 2005, T cell activation correlates with an increased proportion of antigen among the materials acquired from target cells. **Eur J Immunol** 35: 2284-2294.

Huggins, J., Pellegrin, T., Felgar, R.E., Wei, C., Brown, M., Zheng, B., Milner, E.C., Bernstein, S.H., Sanz, I., Zand, M.S., 2007, CpG DNA activation and plasma-cell differentiation of CD27- naive human B cells. **Blood** 109: 1611-1619.

Ishisaki, A., Yamato, K., Nakao, A., Nonaka, K., Ohguchi, M., ten Dijke, P., Nishihara, T., 1998, Smad7 is an activin-inducible inhibitor of activin-induced growth arrest and apoptosis in mouse B cells. **J Biol Chem** 273: 24293-24296.

Isnardi, I., Ng, Y.S., Menard, L., Meyers, G., Saadoun, D., Srdanovic, I., Samuels, J., Berman, J., Buckner, J.H., Cunningham-Rundles, C., Meffre, E., Complement receptor 2/CD21- human naive B cells contain mostly autoreactive unresponsive clones. **Blood** 115: 5026-5036.

Ivars, F., 2007, Superantigen-induced regulatory T cells in vivo. **Chem Immunol Allergy** 93: 137-160.

Izcue, A., Morales, G., Minguet, S., Sanchez-Movilla, A., Morales, P., Martinez, M.J., Gaspar, M.L., Marcos, M.A., 2001, Both B and gammadelta TCR(+) lymphocytes regulate alphabeta TCR(+) lymphocytes involved in superantigen specific responses. **Eur J Immunol** 31: 2811-2817.

Jabara, H.H., Chaudhuri, J., Dutt, S., Dedeoglu, F., Weng, Y., Murphy, M.M., Franco, S., Alt, F.W., Manis, J., Geha, R.S., 2008, B-cell receptor cross-linking delays activation-induced cytidine deaminase induction and inhibits class-switch recombination to IgE. **J Allergy Clin Immunol** 121: 191-196 e192.

Jabara, H.H., Geha, R.S., 1996, The superantigen toxic shock syndrome toxin-1 induces CD40 ligand expression and modulates IgE isotype switching. **Int Immunol** 8: 1503-1510.

Jacquot, S., Kobata, T., Iwata, S., Morimoto, C., Schlossman, S.F., 1997, CD154/CD40 and CD70/CD27 interactions have different and sequential functions in T cell-dependent B cell responses: enhancement of plasma cell differentiation by CD27 signaling. **J Immunol** 159: 2652-2657.

Jahrsdorfer, B., Muhlenhoff, L., Blackwell, S.E., Wagner, M., Poeck, H., Hartmann, E., Jox, R., Giese, T., Emmerich, B., Endres, S., Weiner, G.J., Hartmann, G., 2005, B-cell lymphomas differ in their responsiveness to CpG oligodeoxynucleotides. **Clin Cancer Res** 11: 1490-1499.

Jain, N., Cho, H., O'Connell, M., Lee, J.K., 2005, Rank-invariant resampling based estimation of false discovery rate for analysis of small sample microarray data. **BMC Bioinformatics** 6: 187.

Jarraud, S., Peyrat, M.A., Lim, A., Tristan, A., Bes, M., Mougel, C., Etienne, J., Vandenesch, F., Bonneville, M., Lina, G., 2001, egc, a highly prevalent operon of enterotoxin gene, forms a putative nursery of superantigens in Staphylococcus aureus. **J Immunol** 166: 669-677.

Jelinek, D.F., Splawski, J.B., Lipsky, P.E., 1986, Human peripheral blood B lymphocyte subpopulations: functional and phenotypic analysis of surface IgD positive and negative subsets. **J Immunol** 136: 83-92.

Jiang, H., Chess, L., 2000, The specific regulation of immune responses by CD8+ T cells restricted by the MHC class Ib molecule, Qa-1. **Annu Rev Immunol** 18: 185-216.

Jiang, H., Ware, R., Stall, A., Flaherty, L., Chess, L., Pernis, B., 1995, Murine CD8+ T cells that specifically delete autologous CD4+ T cells expressing V beta 8 TCR: a role of the Qa-1 molecule. **Immunity** 2: 185-194.

Jiang, W., Lederman, M.M., Harding, C.V., Rodriguez, B., Mohner, R.J., Sieg, S.F., 2007, TLR9 stimulation drives naive B cells to proliferate and to attain enhanced antigen presenting function. **Eur J Immunol** 37: 2205-2213.

Jiang, W., Lederman, M.M., Harding, C.V., Sieg, S.F., Presentation of soluble antigens to CD8+ T cells by CpG oligodeoxynucleotide-primed human naive B cells. **J Immunol** 186: 2080-2086.

Jin, S., Antinore, M.J., Lung, F.D., Dong, X., Zhao, H., Fan, F., Colchagie, A.B., Blanck, P., Roller, P.P., Fornace, A.J., Jr., Zhan, Q., 2000, The GADD45 inhibition of Cdc2 kinase correlates with GADD45-mediated growth suppression. **J Biol Chem** 275: 16602-16608.

Joao, C., Ogle, B.M., Gay-Rabinstein, C., Platt, J.L., Cascalho, M., 2004, B cell-dependent TCR diversification. **J Immunol** 172: 4709-4716.

Johansson-Lindbom, B., Ingvarsson, S., Borrebaeck, C.A., 2003, Germinal centers regulate human Th2 development. **J Immunol** 171: 1657-1666.

Johnson, W.E., Li, C., Rabinovic, A., 2007, Adjusting batch effects in microarray expression data using empirical Bayes methods. **Biostatistics** 8: 118-127.

Joly, E., Hudrisier, D., 2003, What is trogocytosis and what is its purpose? **Nat Immunol** 4: 815.

Juszczynski, P., Chen, L., O'Donnell, E., Polo, J.M., Ranuncolo, S.M., Dalla-Favera, R., Melnick, A., Shipp, M.A., 2009, BCL6 modulates tonic BCR signaling in diffuse large B-cell lymphomas by repressing the SYK phosphatase, PTPROt. **Blood** 114: 5315-5321.

Kappler, J., Kotzin, B., Herron, L., Gelfand, E.W., Bigler, R.D., Boylston, A., Carrel, S., Posnett, D.N., Choi, Y., Marrack, P., 1989, V beta-specific stimulation of human T cells by staphylococcal toxins. **Science** 244: 811-813.

Kaur, K., Chowdhury, S., Greenspan, N.S., Schreiber, J.R., 2007, Decreased expression of tumor necrosis factor family receptors involved in humoral immune responses in preterm neonates. **Blood** 110: 2948-2954.

Kawabe, Y., Ochi, A., 1991, Programmed cell death and extrathymic reduction of Vbeta8+ CD4+ T cells in mice tolerant to Staphylococcus aureus enterotoxin B. **Nature** 349: 245-248.

Kawai, K., Tsuno, N.H., Matsuhashi, M., Kitayama, J., Osada, T., Yamada, J., Tsuchiya, T., Yoneyama, S., Watanabe, T., Takahashi, K., Nagawa, H., 2005, CD11b-mediated migratory property of peripheral blood B cells. **J Allergy Clin Immunol** 116: 192-197.

Kearney, E.R., Walunas, T.L., Karr, R.W., Morton, P.A., Loh, D.Y., Bluestone, J.A., Jenkins, M.K., 1995, Antigen-dependent clonal expansion of a trace population of antigen-specific CD4+ T cells in vivo is dependent on CD28 costimulation and inhibited by CTLA-4. **J Immunol** 155: 1032-1036.

Kinoshita, K., Harigai, M., Fagarasan, S., Muramatsu, M., Honjo, T., 2001, A hallmark of active class switch recombination: transcripts directed by I promoters on looped-out circular DNAs. **Proc Natl Acad Sci U S A** 98: 12620-12623.

Kissner, T.L., Ruthel, G., Alam, S., Ulrich, R.G., Fernandez, S., Saikh, K.U., Activation of MyD88 signaling upon staphylococcal enterotoxin binding to MHC class II molecules. **PLoS One** 6: e15985.

Klein, U., Dalla-Favera, R., 2008, Germinal centres: role in B-cell physiology and malignancy. **Nat Rev Immunol** 8: 22-33.

Klein, U., Kuppers, R., Rajewsky, K., 1994, Variable region gene analysis of B cell subsets derived from a 4-year-old child: somatically mutated memory B cells accumulate in the peripheral blood already at young age. **J Exp Med** 180: 1383-1393.

Klein, U., Rajewsky, K., Kuppers, R., 1998, Human immunoglobulin (Ig)M+IgD+ peripheral blood B cells expressing the CD27 cell surface antigen carry somatically mutated variable region genes: CD27 as a general marker for somatically mutated (memory) B cells. **J Exp Med** 188: 1679-1689.

Klein, U., Tu, Y., Stolovitzky, G.A., Keller, J.L., Haddad, J., Jr., Miljkovic, V., Cattoretti, G., Califano, A., Dalla-Favera, R., 2003, Transcriptional analysis of the B cell germinal center reaction. **Proc Natl Acad Sci U S A** 100: 2639-2644.

Knoechel, B., Lohr, J., Kahn, E., Abbas, A.K., 2005, The link between lymphocyte deficiency and autoimmunity: roles of endogenous T and B lymphocytes in tolerance. **J Immunol** 175: 21-26.

Kobata, T., Jacquot, S., Kozlowski, S., Agematsu, K., Schlossman, S.F., Morimoto, C., 1995, CD27-CD70 interactions regulate B-cell activation by T cells. **Proc Natl Acad Sci U S A** 92: 11249-11253.

Koelsch, K., Zheng, N.Y., Zhang, Q., Duty, A., Helms, C., Mathias, M.D., Jared, M., Smith, K., Capra, J.D., Wilson, P.C., 2007, Mature B cells class switched to IgD are autoreactive in healthy individuals. **J Clin Invest** 117: 1558-1565.

Kuo, T.C., Shaffer, A.L., Haddad, J., Jr., Choi, Y.S., Staudt, L.M., Calame, K., 2007, Repression of BCL-6 is required for the formation of human memory B cells in vitro. **J Exp Med** 204: 819-830.

Kuppers, R., Zhao, M., Hansmann, M.L., Rajewsky, K., 1993, Tracing B cell development in human germinal centres by molecular analysis of single cells picked from histological sections. **EMBO J** 12: 4955-4967.

Labeur, M.S., Roters, B., Pers, B., Mehling, A., Luger, T.A., Schwarz, T., Grabbe, S., 1999, Generation of tumor immunity by bone marrow-derived dendritic cells correlates with dendritic cell maturation stage. **J Immunol** 162: 168-175.

Lagresle, C., Bella, C., Defrance, T., 1993, Phenotypic and functional heterogeneity of the IgD- B cell compartment: identification of two major tonsillar B cell subsets. **Int Immunol** 5: 1259-1268.

Lamphear, J.G., Stevens, K.R., Rich, R.R., 1998, Intercellular adhesion molecule-1 and leukocyte function-associated antigen-3 provide costimulation for superantigen-induced T lymphocyte proliferation in the absence of a specific presenting molecule. **J Immunol** 160: 615-623.

Langford, M.P., Stanton, G.J., Johnson, H.M., 1978, Biological effects of staphylococcal enterotoxin A on human peripheral lymphocytes. **Infect Immun** 22: 62-68.

Langhorne, J., Cross, C., Seixas, E., Li, C., von der Weid, T., 1998, A role for B cells in the development of T cell helper function in a malaria infection in mice. **Proc Natl Acad Sci U S A** 95: 1730-1734.

Lazarus, A.H., Kawauchi, K., Rapoport, M.J., Delovitch, T.L., 1993, Antigen-induced B lymphocyte activation involves the p21ras and ras.GAP signaling pathway. **J Exp Med** 178: 1765-1769.

Lee, H.H., Dempsey, P.W., Parks, T.P., Zhu, X., Baltimore, D., Cheng, G., 1999, Specificities of CD40 signaling: involvement of TRAF2 in CD40-induced NF-kappaB activation and intercellular adhesion molecule-1 up-regulation. **Proc Natl Acad Sci U S A** 96: 1421-1426.

Lee, J., Kuchen, S., Fischer, R., Chang, S., Lipsky, P.E., 2009, Identification and characterization of a human CD5+ pre-naive B cell population. **J Immunol** 182: 4116-4126.

Lee, W.T., Vitetta, E.S., 1992, Memory T cells are anergic to the superantigen staphylococcal enterotoxin B. **J Exp Med** 176: 575-579.

Lens, S.M., Tesselaar, K., den Drijver, B.F., van Oers, M.H., van Lier, R.A., 1996, A dual role for both CD40-ligand and TNF-alpha in controlling human B cell death. **J Immunol** 156: 507-514.

Levesque, M.C., 2009, Translational Mini-Review Series on B Cell-Directed Therapies: Recent advances in B cell-directed biological therapies for autoimmune disorders. **Clin Exp Immunol** 157: 198-208.

Levesque, M.C., St Clair, E.W., 2008, B cell-directed therapies for autoimmune disease and correlates of disease response and relapse. **J Allergy Clin Immunol** 121: 13-21; quiz 22-13.

Li, H., Llera, A., Tsuchiya, D., Leder, L., Ysern, X., Schlievert, P.M., Karjalainen, K., Mariuzza, R.A., 1998, Three-dimensional structure of the complex between a T cell receptor beta chain and the superantigen staphylococcal enterotoxin B. **Immunity** 9: 807-816.

Li, P.L., Tiedemann, R.E., Moffat, S.L., Fraser, J.D., 1997, The superantigen streptococcal pyrogenic exotoxin C (SPE-C) exhibits a novel mode of action. **J Exp Med** 186: 375-383.

Li, Y., Li, H., Dimasi, N., McCormick, J.K., Martin, R., Schuck, P., Schlievert, P.M., Mariuzza, R.A., 2001, Crystal structure of a superantigen bound to the high-affinity, zinc-dependent site on MHC class II. **Immunity** 14: 93-104.

Liang, L., Porter, E.M., Sha, W.C., 2002, Constitutive expression of the B7h ligand for inducible costimulator on naive B cells is extinguished after activation by distinct B cell receptor and interleukin 4 receptor-mediated pathways and can be rescued by CD40 signaling. **J Exp Med** 196: 97-108.

Liossis, S.N., Sfikakis, P.P., 2008, Rituximab-induced B cell depletion in autoimmune diseases: potential effects on T cells. **Clin Immunol** 127: 280-285.

Liu, Y.J., Barthelemy, C., de Bouteiller, O., Arpin, C., Durand, I., Banchereau, J., 1995, Memory B cells from human tonsils colonize mucosal epithelium and directly present antigen to T cells by rapid up-regulation of B7-1 and B7-2. **Immunity** 2: 239-248.

Longo, N.S., Lugar, P.L., Yavuz, S., Zhang, W., Krijger, P.H., Russ, D.E., Jima, D.D., Dave, S.S., Grammer, A.C., Lipsky, P.E., 2009, Analysis of somatic hypermutation in X-linked hyper-IgM syndrome shows specific deficiencies in mutational targeting. **Blood** 113: 3706-3715.

Lu, H., Crawford, R.B., North, C.M., Kaplan, B.L., Kaminski, N.E., 2009, Establishment of an immunoglobulin m antibody-forming cell response model for characterizing immunotoxicity in primary human B cells. **Toxicol Sci** 112: 363-373.

Lund, F.E., 2008, Cytokine-producing B lymphocytes-key regulators of immunity. **Curr Opin Immunol** 20: 332-338.

Lund, F.E., Randall, T.D., Effector and regulatory B cells: modulators of CD4(+) T cell immunity. **Nat Rev Immunol** 10: 236-247.

Maeda, H., Fujimoto, S., Greene, M.I., 2000, Suppressor T cells regulate the nonanergic cell population that remains after peripheral tolerance is induced to the Mls-1 antigen in T cell receptor Vbeta 8.1 transgenic mice. **Proc Natl Acad Sci U S A** 97: 13257-13262.

Mahnke, K., Johnson, T.S., Ring, S., Enk, A.H., 2007, Tolerogenic dendritic cells and regulatory T cells: a two-way relationship. **J Dermatol Sci** 46: 159-167.

Manders, S.M., 1998, Toxin-mediated streptococcal and staphylococcal disease. **J Am Acad Dermatol** 39: 383-398; quiz 399-400.

Marino, E., Villanueva, J., Walters, S., Liuwantara, D., Mackay, F., Grey, S.T., 2009, CD4(+)CD25(+) T-cells control autoimmunity in the absence of B-cells. **Diabetes** 58: 1568-1577.

Marrack, P., Kappler, J., 1990, The staphylococcal enterotoxins and their relatives. **Science** 248: 705-711.

Martin, H.J., Lee, J.M., Walls, D., Hayward, S.D., 2007, Manipulation of the toll-like receptor 7 signaling pathway by Epstein-Barr virus. **J Virol** 81: 9748-9758.

Martinez-Valdez, H., Guret, C., de Bouteiller, O., Fugier, I., Banchereau, J., Liu, Y.J., 1996, Human germinal center B cells express the apoptosis-inducing genes Fas, c-myc, P53, and Bax but not the survival gene bcl-2. **J Exp Med** 183: 971-977.

Matsushita, T., Yanaba, K., Bouaziz, J.D., Fujimoto, M., Tedder, T.F., 2008, Regulatory B cells inhibit EAE initiation in mice while other B cells promote disease progression. **J Clin Invest** 118: 3420-3430.

Matzinger, P., 2002, An innate sense of danger. **Ann N Y Acad Sci** 961: 341-342.

Maurer, D., Fischer, G.F., Fae, I., Majdic, O., Stuhlmeier, K., Von Jeney, N., Holter, W., Knapp, W., 1992, IgM and IgG but not cytokine secretion is restricted to the CD27+ B lymphocyte subset. **J Immunol** 148: 3700-3705.

Mauri, C., Ehrenstein, M.R., 2008, The 'short' history of regulatory B cells. **Trends Immunol** 29: 34-40.

McCormack, J.E., Callahan, J.E., Kappler, J., Marrack, P.C., 1993, Profound deletion of mature T cells in vivo by chronic exposure to exogenous superantigen. **J Immunol** 150: 3785-3792.

McHeyzer-Williams, L.J., McHeyzer-Williams, M.G., 2005, Antigen-specific memory B cell development. **Annu Rev Immunol** 23: 487-513.

Melamed, D., Messika, O., Glass-Marmor, L., Miller, A., 2006, Modulation of matrix metalloproteinase-9 (MMP-9) secretion in B lymphopoiesis. **Int Immunol** 18: 1355-1362.

Menard, L.C., Minns, L.A., Darche, S., Mielcarz, D.W., Foureau, D.M., Roos, D., Dzierszinski, F., Kasper, L.H., Buzoni-Gatel, D., 2007, B cells amplify IFN-gamma production by T cells via a TNF-alpha-mediated mechanism. **J Immunol** 179: 4857-4866.

Meyaard, L., 2008, The inhibitory collagen receptor LAIR-1 (CD305). **J Leukoc Biol** 83: 799-803.

Miethke, T., Wahl, C., Gaus, H., Heeg, K., Wagner, H., 1994, Exogenous superantigens acutely trigger distinct levels of peripheral T cell tolerance/immunosuppression: dose-response relationship. **Eur J Immunol** 24: 1893-1902.

Miethke, T., Wahl, C., Heeg, K., Wagner, H., 1995, Bacterial superantigens induce T cell unresponsiveness in B cell-deficient mice. **Eur J Immunol** 25: 3187-3190.

Miller, C., Ragheb, J.A., Schwartz, R.H., 1999, Anergy and cytokine-mediated suppression as distinct superantigen-induced tolerance mechanisms in vivo. J Exp Med 190: 53-64.

Miyawaki, T., Uehara, T., Nibu, R., Tsuji, T., Yachie, A., Yonehara, S., Taniguchi, N., 1992, Differential expression of apoptosis-related Fas antigen on lymphocyte subpopulations in human peripheral blood. J Immunol 149: 3753-3758.

Mizoguchi, A., Bhan, A.K., 2006, A case for regulatory B cells. J Immunol 176: 705-710.

Mooney, N.A., Grillot-Courvalin, C., Hivroz, C., Ju, L.Y., Charron, D., 1990, Early biochemical events after MHC class II-mediated signaling on human B lymphocytes. J Immunol 145: 2070-2076.

Morris, S.C., Lees, A., Holmes, J.M., Jeffries, R.D., Finkelman, F.D., 1994, Induction of B cell and T cell tolerance in vivo by anti-CD23 mAb. J Immunol 152: 3768-3776.

Muraille, E.M., De Becker, G., Bakkus, M., Thielemans, K., Urbain, J., Moser, M., Leo, O., 1995, Co-stimulation lowers the threshold for activation of naive T cells by bacterial superantigens. Int Immunol 7: 295-304.

Nagumo, H., Agematsu, K., Kobayashi, N., Shinozaki, K., Hokibara, S., Nagase, H., Takamoto, M., Yasui, K., Sugane, K., Komiyama, A., 2002, The different process of class switching and somatic hypermutation; a novel analysis by CD27(-) naive B cells. Blood 99: 567-575.

Nakata, Y., Matsuda, K., Uzawa, A., Nomura, M., Akashi, M., Suzuki, G., 1995, Administration of recombinant human IL-1 by Staphylococcus enterotoxin B prevents tolerance induction in vivo. J Immunol 155: 4231-4235.

Nambu, A., Nakae, S., IL-1 and Allergy. Allergol Int 59: 125-135.

Newell, K.A., Asare, A., Kirk, A.D., Gisler, T.D., Bourcier, K., Suthanthiran, M., Burlingham, W.J., Marks, W.H., Sanz, I., Lechler, R.I., Hernandez-Fuentes, M.P., Turka, L.A., Seyfert-Margolis, V.L., Identification of a B cell signature associated with renal transplant tolerance in humans. J Clin Invest 120: 1836-1847.

Ng, Y.S., Wardemann, H., Chelnis, J., Cunningham-Rundles, C., Meffre, E., 2004, Bruton's tyrosine kinase is essential for human B cell tolerance. J Exp Med 200: 927-934.

Ngo, V.N., Cornall, R.J., Cyster, J.G., 2001, Splenic T zone development is B cell dependent. J Exp Med 194: 1649-1660.

Nicholson, I.C., 2002, CD62L (L-selectin). J Biol Regul Homeost Agents 16: 144-146.

Noble, A., Pestano, G.A., Cantor, H., 1998a, Suppression of immune responses by CD8 cells. I. Superantigen-activated CD8 cells induce unidirectional Fas-mediated apoptosis of antigen-activated CD4 cells. J Immunol 160: 559-565.

Noble, A., Zhao, Z.S., Cantor, H., 1998b, Suppression of immune responses by CD8 cells. II. Qa-1 on activated B cells stimulates CD8 cell suppression of T helper 2 responses. **J Immunol** 160: 566-571.

Noh, J., Lee, J.H., Noh, G., Bang, S.Y., Kim, H.S., Choi, W.S., Cho, S., Lee, S.S., Characterisation of allergen-specific responses of IL-10-producing regulatory B cells (Br1) in Cow Milk Allergy. **Cell Immunol**.

Noorchashm, H., Moore, D.J., Noto, L.E., Noorchashm, N., Reed, A.J., Reed, A.L., Song, H.K., Mozaffari, R., Jevnikar, A.M., Barker, C.F., Naji, A., 2000, Impaired CD4 T cell activation due to reliance upon B cell-mediated costimulation in nonobese diabetic (NOD) mice. **J Immunol** 165: 4685-4696.

Nurieva, R.I., Chung, Y., Hwang, D., Yang, X.O., Kang, H.S., Ma, L., Wang, Y.H., Watowich, S.S., Jetten, A.M., Tian, Q., Dong, C., 2008, Generation of T follicular helper cells is mediated by interleukin-21 but independent of T helper 1, 2, or 17 cell lineages. **Immunity** 29: 138-149.

Palanichamy, A., Barnard, J., Zheng, B., Owen, T., Quach, T., Wei, C., Looney, R.J., Sanz, I., Anolik, J.H., 2009, Novel human transitional B cell populations revealed by B cell depletion therapy. **J Immunol** 182: 5982-5993.

Pallasch, C.P., Schulz, A., Kutsch, N., Schwamb, J., Hagist, S., Kashkar, H., Ultsch, A., Wickenhauser, C., Hallek, M., Wendtner, C.M., 2008, Overexpression of TOSO in CLL is triggered by B-cell receptor signaling and associated with progressive disease. **Blood** 112: 4213-4219.

Papageorgiou, A.C., Acharya, K.R., Shapiro, R., Passalacqua, E.F., Brehm, R.D., Tranter, H.S., 1995, Crystal structure of the superantigen enterotoxin C2 from Staphylococcus aureus reveals a zinc-binding site. **Structure** 3: 769-779.

Papageorgiou, A.C., Collins, C.M., Gutman, D.M., Kline, J.B., O'Brien, S.M., Tranter, H.S., Acharya, K.R., 1999, Structural basis for the recognition of superantigen streptococcal pyrogenic exotoxin A (SpeA1) by MHC class II molecules and T-cell receptors. **EMBO J** 18: 9-21.

Pape, K.A., Taylor, J.J., Maul, R.W., Gearhart, P.J., Jenkins, M.K., Different B cell populations mediate early and late memory during an endogenous immune response. **Science** 331: 1203-1207.

Parekh, V.V., Prasad, D.V., Banerjee, P.P., Joshi, B.N., Kumar, A., Mishra, G.C., 2003, B cells activated by lipopolysaccharide, but not by anti-Ig and anti-CD40 antibody, induce anergy in CD8+ T cells: role of TGF-beta 1. **J Immunol** 170: 5897-5911.

Park, C.K., Shin, Y.K., Kim, T.J., Park, S.H., Ahn, G.H., 1999, High CD99 expression in memory T and B cells in reactive lymph nodes. **J Korean Med Sci** 14: 600-606.

Parker, D.C., Greiner, D.L., Phillips, N.E., Appel, M.C., Steele, A.W., Durie, F.H., Noelle, R.J., Mordes, J.P., Rossini, A.A., 1995, Survival of mouse pancreatic islet allografts in recipients treated with allogeneic small lymphocytes and antibody to CD40 ligand. **Proc Natl Acad Sci U S A** 92: 9560-9564.

Pascual, V., Liu, Y.J., Magalski, A., de Bouteiller, O., Banchereau, J., Capra, J.D., 1994, Analysis of somatic mutation in five B cell subsets of human tonsil. **J Exp Med** 180: 329-339.

Patil, S., Wildey, G.M., Brown, T.L., Choy, L., Derynck, R., Howe, P.H., 2000, Smad7 is induced by CD40 and protects WEHI 231 B-lymphocytes from transforming growth factor-beta -induced growth inhibition and apoptosis. **J Biol Chem** 275: 38363-38370.

Peavy, D.L., Adler, W.H., Smith, R.T., 1970, The mitogenic effects of endotoxin and staphylococcal enterotoxin B on mouse spleen cells and human peripheral lymphocytes. **J Immunol** 105: 1453-1458.

Pecanha, L.M., Yamaguchi, H., Lees, A., Noelle, R.J., Mond, J.J., Snapper, C.M., 1993, Dextran-conjugated anti-IgD antibodies inhibit T cell-mediated IgE production but augment the synthesis of IgM and IgG. J **Immunol** 150: 2160-2168.

Pentcheva-Hoang, T., Egen, J.G., Wojnoonski, K., Allison, J.P., 2004, B7-1 and B7-2 selectively recruit CTLA-4 and CD28 to the immunological synapse. **Immunity** 21: 401-413.

Pers, J.O., Jamin, C., Lydyard, P.M., Charreire, J., Youinou, P., 2002, The H2 haplotype regulates the distribution of B cells into B-1a, B-1b and B-2 subsets. **Immunogenetics** 54: 208-211.

Pescovitz, M.D., Greenbaum, C.J., Krause-Steinrauf, H., Becker, D.J., Gitelman, S.E., Goland, R., Gottlieb, P.A., Marks, J.B., McGee, P.F., Moran, A.M., Raskin, P., Rodriguez, H., Schatz, D.A., Wherrett, D., Wilson, D.M., Lachin, J.M., Skyler, J.S., 2009, Rituximab, B-lymphocyte depletion, and preservation of beta-cell function. **N Engl J Med** 361: 2143-2152.

Petersson, K., Forsberg, G., Walse, B., 2004, Interplay between superantigens and immunoreceptors. **Scand J Immunol** 59: 345-355.

Petersson, K., Hakansson, M., Nilsson, H., Forsberg, G., Svensson, L.A., Liljas, A., Walse, B., 2001, Crystal structure of a superantigen bound to MHC class II displays zinc and peptide dependence. **EMBO** J 20: 3306-3312.

Phillips, J.A., Romball, C.G., Hobbs, M.V., Ernst, D.N., Shultz, L., Weigle, W.O., 1996, CD4+ T cell activation and tolerance induction in B cell knockout mice. **J Exp Med** 183: 1339-1344.

Pillai, S., Cariappa, A., 2009, The follicular versus marginal zone B lymphocyte cell fate decision. **Nat Rev Immunol** 9: 767-777.

Poeck, H., Wagner, M., Battiany, J., Rothenfusser, S., Wellisch, D., Hornung, V., Jahrsdorfer, B., Giese, T., Endres, S., Hartmann, G., 2004, Plasmacytoid dendritic cells, antigen, and CpG-C

license human B cells for plasma cell differentiation and immunoglobulin production in the absence of T-cell help. **Blood** 103: 3058-3064.

Prazma, C.M., Yazawa, N., Fujimoto, Y., Fujimoto, M., Tedder, T.F., 2007, CD83 expression is a sensitive marker of activation required for B cell and CD4+ T cell longevity in vivo. J **Immunol** 179: 4550-4562.

Proft, T., Moffatt, S.L., Berkahn, C.J., Fraser, J.D., 1999, Identification and characterization of novel superantigens from Streptococcus pyogenes. J **Exp Med** 189: 89-102.

Proft, T., Webb, P.D., Handley, V., Fraser, J.D., 2003, Two novel superantigens found in both group A and group C Streptococcus. **Infect Immun** 71: 1361-1369.

Quach, T.D., Manjarrez-Orduno, N., Adlowitz, D.G., Silver, L., Yang, H., Wei, C., Milner, E.C., Sanz, I., Anergic Responses Characterize a Large Fraction of Human Autoreactive Naive B Cells Expressing Low Levels of Surface IgM. J **Immunol**.

Quah, B.J., Warren, H.S., Parish, C.R., 2007, Monitoring lymphocyte proliferation in vitro and in vivo with the intracellular fluorescent dye carboxyfluorescein diacetate succinimidyl ester. **Nat Protoc** 2: 2049-2056.

Raimondi, G., Zanoni, I., Citterio, S., Ricciardi-Castagnoli, P., Granucci, F., 2006a, Induction of peripheral T cell tolerance by antigen-presenting B cells. I. Relevance of antigen presentation persistence. J **Immunol** 176: 4012-4020.

Raimondi, G., Zanoni, I., Citterio, S., Ricciardi-Castagnoli, P., Granucci, F., 2006b, Induction of peripheral T cell tolerance by antigen-presenting B cells. II. Chronic antigen presentation overrules antigen-presenting B cell activation. J **Immunol** 176: 4021-4028.

Rajagopalan, G., Smart, M.K., Patel, R., David, C.S., 2006, Acute systemic immune activation following conjunctival exposure to staphylococcal enterotoxin B. **Infect Immun** 74: 6016-6019.

Rajewsky, K., 1996, Clonal selection and learning in the antibody system. **Nature** 381: 751-758.

Reichardt, P., Dornbach, B., Gunzer, M., 2007a, The molecular makeup and function of regulatory and effector synapses. **Immunol Rev** 218: 165-177.

Reichardt, P., Dornbach, B., Rong, S., Beissert, S., Gueler, F., Loser, K., Gunzer, M., 2007b, Naive B cells generate regulatory T cells in the presence of a mature immunologic synapse. **Blood** 110: 1519-1529.

Robert C. Hsueh, T.I.A.R., Keng-Mean Lin, Timothy D. O'Connell, Heping Han, Zhen Yan, 2002, Purification and Characterization of Mouse Splenic B Lymphocytes. **AfCS Research Reports** 1: 11.

Ruprecht, C.R., Lanzavecchia, A., 2006, Toll-like receptor stimulation as a third signal required for activation of human naive B cells. **Eur J Immunol** 36: 810-816.

Saadoun, D., Rosenzwajg, M., Landau, D., Piette, J.C., Klatzmann, D., Cacoub, P., 2008, Restoration of peripheral immune homeostasis after rituximab in mixed cryoglobulinemia vasculitis. **Blood** 111: 5334-5341.

Saeed, A.I., Sharov, V., White, J., Li, J., Liang, W., Bhagabati, N., Braisted, J., Klapa, M., Currier, T., Thiagarajan, M., Sturn, A., Snuffin, M., Rezantsev, A., Popov, D., Ryltsov, A., Kostukovich, E., Borisovsky, I., Liu, Z., Vinsavich, A., Trush, V., Quackenbush, J., 2003, TM4: a free, open-source system for microarray data management and analysis. **Biotechniques** 34: 374-378.

Sarma, V., Lin, Z., Clark, L., Rust, B.M., Tewari, M., Noelle, R.J., Dixit, V.M., 1995, Activation of the B-cell surface receptor CD40 induces A20, a novel zinc finger protein that inhibits apoptosis. J **Biol Chem** 270: 12343-12346.

Sato, K., Fujita, S., 2007, Dendritic cells: nature and classification. **Allergol Int** 56: 183-191.

Sato, S., Fujimoto, M., Hasegawa, M., Takehara, K., 2004, Altered blood B lymphocyte homeostasis in systemic sclerosis: expanded naive B cells and diminished but activated memory B cells. **Arthritis Rheum** 50: 1918-1927.

Schiffenbauer, J., Johnson, H.M., Butfiloski, E.J., Wegrzyn, L., Soos, J.M., 1993, Staphylococcal enterotoxins can reactivate experimental allergic encephalomyelitis. **Proc Natl Acad Sci U S A** 90: 8543-8546.

Schneider, E., Montenarh, M., Wagner, P., 1998, Regulation of CAK kinase activity by p53. **Oncogene** 17: 2733-2741.

Schultze, J.L., Michalak, S., Lowne, J., Wong, A., Gilleece, M.H., Gribben, J.G., Nadler, L.M., 1999, Human non-germinal center B cell interleukin (IL)-12 production is primarily regulated by T cell signals CD40 ligand, interferon gamma, and IL-10: role of B cells in the maintenance of T cell responses. **J Exp Med** 189: 1-12.

Seyfert, V.L., McMahon, S., Glenn, W., Cao, X.M., Sukhatme, V.P., Monroe, J.G., 1990, Egr-1 expression in surface Ig-mediated B cell activation. Kinetics and association with protein kinase C activation. **J Immunol** 145: 3647-3653.

Sfikakis, P.P., Boletis, J.N., Lionaki, S., Vigklis, V., Fragiadaki, K.G., Iniotaki, A., Moutsopoulos, H.M., 2005, Remission of proliferative lupus nephritis following B cell depletion therapy is preceded by down-regulation of the T cell costimulatory molecule CD40 ligand: an open-label trial. **Arthritis Rheum** 52: 501-513.

Sfikakis, P.P., Souliotis, V.L., Fragiadaki, K.G., Moutsopoulos, H.M., Boletis, J.N., Theofilopoulos, A.N., 2007, Increased expression of the FoxP3 functional marker of regulatory T cells

following B cell depletion with rituximab in patients with lupus nephritis. **Clin Immunol** 123: 66-73.

Shah, S., Qiao, L., 2008, Resting B cells expand a CD4+CD25+Foxp3+ Treg population via TGF-beta3. **Eur J Immunol** 38: 2488-2498.

Shen, H., Whitmire, J.K., Fan, X., Shedlock, D.J., Kaech, S.M., Ahmed, R., 2003, A specific role for B cells in the generation of CD8 T cell memory by recombinant Listeria monocytogenes. J **Immunol** 170: 1443-1451.

Slifka, M.K., Whitton, J.L., 2000, Antigen-specific regulation of T cell-mediated cytokine production. **Immunity** 12: 451-457.

Stark Aroeira, L., Williams, O., Borlado, L.R., Carrera, A.C., Martinez, C., 1997, Evidence for B cell participation in the in vitro and in vivo maintenance of in vivo staphylococcal enterotoxin B-induced T cell anergy. **Int Immunol** 9: 65-72.

Stashenko, P., Nadler, L.M., Hardy, R., Schlossman, S.F., 1981, Expression of cell surface markers after human B lymphocyte activation. **Proc Natl Acad Sci U S A** 78: 3848-3852.

Stasi, R., Del Poeta, G., Stipa, E., Evangelista, M.L., Trawinska, M.M., Cooper, N., Amadori, S., 2007, Response to B-cell depleting therapy with rituximab reverts the abnormalities of T-cell subsets in patients with idiopathic thrombocytopenic purpura. **Blood** 110: 2924-2930.

Stohl, W., Elliott, J.E., 1995, Differential human T cell-dependent B cell differentiation induced by staphylococcal superantigens (SAg). Regulatory role for SAg-dependent B cell cytolysis. J **Immunol** 155: 1838-1850.

Stohl, W., Elliott, J.E., Linsley, P.S., 1994, Human T cell-dependent B cell differentiation induced by staphylococcal superantigens. J **Immunol** 153: 117-127.

Streilein, J.W., 1999, Regional immunity and ocular immune privilege. **Chem Immunol** 73: 11-38.

Su, T.T., Rawlings, D.J., 2002, Transitional B lymphocyte subsets operate as distinct checkpoints in murine splenic B cell development. **J Immunol** 168: 2101-2110.

Sugimoto, K., Ogawa, A., Shimomura, Y., Nagahama, K., Mizoguchi, A., Bhan, A.K., 2007, Inducible IL-12-producing B cells regulate Th2-mediated intestinal inflammation. **Gastroenterology** 133: 124-136.

Sun, J.B., Flach, C.F., Czerkinsky, C., Holmgren, J., 2008, B lymphocytes promote expansion of regulatory T cells in oral tolerance: powerful induction by antigen coupled to cholera toxin B subunit. **J Immunol** 181: 8278-8287.

Sundberg, E., Jardetzky, T.S., 1999, Structural basis for HLA-DQ binding by the streptococcal superantigen SSA. **Nat Struct Biol** 6: 123-129.

Sundberg, E.J., Sawicki, M.W., Southwood, S., Andersen, P.S., Sette, A., Mariuzza, R.A., 2002, Minor structural changes in a mutated human melanoma antigen correspond to dramatically enhanced stimulation of a CD4+ tumor-infiltrating lymphocyte line. J Mol Biol 319: 449-461.

Sundstedt, A., Dohlsten, M., Hedlund, G., Hoiden, I., Bjorklund, M., Kalland, T., 1994, Superantigens anergize cytokine production but not cytotoxicity in vivo. Immunology 82: 117-125.

Sundstedt, A., Hoiden, I., Rosendahl, A., Kalland, T., van Rooijen, N., Dohlsten, M., 1997, Immunoregulatory role of IL-10 during superantigen-induced hyporesponsiveness in vivo. J Immunol 158: 180-186.

Takahashi, K., Kozono, Y., Waldschmidt, T.J., Berthiaume, D., Quigg, R.J., Baron, A., Holers, V.M., 1997, Mouse complement receptors type 1 (CR1;CD35) and type 2 (CR2;CD21): expression on normal B cell subpopulations and decreased levels during the development of autoimmunity in MRL/lpr mice. J Immunol 159: 1557-1569.

Tamimoto, Y., Horiuchi, T., Tsukamoto, H., Otsuka, J., Mitoma, H., Kimoto, Y., Nakashima, H., Muta, K., Abe, Y., Kiyohara, C., Ueda, A., Nagasawa, K., Yoshizawa, S., Shimoda, T., Harada, M., 2008, A dose-escalation study of rituximab for treatment of systemic lupus erythematosus and Evans' syndrome: immunological analysis of B cells, T cells and cytokines. Rheumatology (Oxford) 47: 821-827.

Tang, Y.C., Thoman, M., Linton, P.J., Deisseroth, A., 2009, Use of CD40L immunoconjugates to overcome the defective immune response to vaccines for infections and cancer in the aged. Cancer Immunol Immunother 58: 1949-1957.

Tangye, S.G., Avery, D.T., Hodgkin, P.D., 2003, A division-linked mechanism for the rapid generation of Ig-secreting cells from human memory B cells. J Immunol 170: 261-269.

Tangye, S.G., Good, K.L., 2007, Human IgM+CD27+ B cells: memory B cells or "memory" B cells? J Immunol 179: 13-19.

Tangye, S.G., Hodgkin, P.D., 2004, Divide and conquer: the importance of cell division in regulating B-cell responses. Immunology 112: 509-520.

Tangye, S.G., Liu, Y.J., Aversa, G., Phillips, J.H., de Vries, J.E., 1998, Identification of functional human splenic memory B cells by expression of CD148 and CD27. J Exp Med 188: 1691-1703.

Taylor, R.P., Lindorfer, M.A., 2008, Immunotherapeutic mechanisms of anti-CD20 monoclonal antibodies. Curr Opin Immunol 20: 444-449.

Thomas, M.D., Srivastava, B., Allman, D., 2006, Regulation of peripheral B cell maturation. Cell Immunol 239: 92-102.

Tian, J., Zekzer, D., Hanssen, L., Lu, Y., Olcott, A., Kaufman, D.L., 2001, Lipopolysaccharide-activated B cells down-regulate Th1 immunity and prevent autoimmune diabetes in nonobese diabetic mice. **J Immunol** 167: 1081-1089.

Townsend, S.E., Goodnow, C.C., 1998, Abortive proliferation of rare T cells induced by direct or indirect antigen presentation by rare B cells in vivo. **J Exp Med** 187: 1611-1621.

Tsai, L.H., Delalle, I., Caviness, V.S., Jr., Chae, T., Harlow, E., 1994, p35 is a neural-specific regulatory subunit of cyclin-dependent kinase 5. **Nature** 371: 419-423.

Tsitoura, D.C., Yeung, V.P., DeKruyff, R.H., Umetsu, D.T., 2002, Critical role of B cells in the development of T cell tolerance to aeroallergens. **Int Immunol** 14: 659-667.

Tu, W., Lau, Y.L., Zheng, J., Liu, Y., Chan, P.L., Mao, H., Dionis, K., Schneider, P., Lewis, D.B., 2008, Efficient generation of human alloantigen-specific CD4+ regulatory T cells from naive precursors by CD40-activated B cells. **Blood** 112: 2554-2562.

Valencic, E., Piscianz, E., Tommasini, A., Granzotto, M., 2007, T cells stimulated in vitro have a suppressive function but do not contain only regulatory T cells. **Clin Exp Immunol** 150: 561-566.

Vallerskog, T., Gunnarsson, I., Widhe, M., Risselada, A., Klareskog, L., van Vollenhoven, R., Malmstrom, V., Trollmo, C., 2007, Treatment with rituximab affects both the cellular and the humoral arm of the immune system in patients with SLE. **Clin Immunol** 122: 62-74.

van der Vuurst de Vries, A.R., Clevers, H., Logtenberg, T., Meyaard, L., 1999, Leukocyte-associated immunoglobulin-like receptor-1 (LAIR-1) is differentially expressed during human B cell differentiation and inhibits B cell receptor-mediated signaling. **Eur J Immunol** 29: 3160-3167.

van Zelm, M.C., Szczepanski, T., van der Burg, M., van Dongen, J.J., 2007, Replication history of B lymphocytes reveals homeostatic proliferation and extensive antigen-induced B cell expansion. **J Exp Med** 204: 645-655.

Vella, A.T., McCormack, J.E., Linsley, P.S., Kappler, J.W., Marrack, P., 1995, Lipopolysaccharide interferes with the induction of peripheral T cell death. **Immunity** 2: 261-270.

Vidakovics, M.L., Jendholm, J., Morgelin, M., Mansson, A., Larsson, C., Cardell, L.O., Riesbeck, K., B cell activation by outer membrane vesicles--a novel virulence mechanism. **PLoS Pathog** 6: e1000724.

Vigna-Perez, M., Hernandez-Castro, B., Paredes-Saharopulos, O., Portales-Perez, D., Baranda, L., Abud-Mendoza, C., Gonzalez-Amaro, R., 2006, Clinical and immunological effects of Rituximab in patients with lupus nephritis refractory to conventional therapy: a pilot study. **Arthritis Res Ther** 8: R83.

Vugmeyster, Y., Howell, K., Bakshi, A., Flores, C., Hwang, O., McKeever, K., 2004, B-cell subsets in blood and lymphoid organs in Macaca fascicularis. Cytometry A 61: 69-75.

Wagner, E.F., Hanna, N., Fast, L.D., Kouttab, N., Shank, P.R., Vazquez, A., Sharma, S., 2000, Novel diversity in IL-4-mediated responses in resting human naive B cells versus germinal center/memory B cells. J Immunol 165: 5573-5579.

Wagner, M., Poeck, H., Jahrsdoerfer, B., Rothenfusser, S., Prell, D., Bohle, B., Tuma, E., Giese, T., Ellwart, J.W., Endres, S., Hartmann, G., 2004, IL-12p70-dependent Th1 induction by human B cells requires combined activation with CD40 ligand and CpG DNA. J Immunol 172: 954-963.

Wahl, C., Miethke, T., Heeg, K., Wagner, H., 1993, Clonal deletion as direct consequence of an in vivo T cell response to bacterial superantigen. Eur J Immunol 23: 1197-1200.

Waldschmidt, T.J., Conrad, D.H., Lynch, R.G., 1988, The expression of B cell surface receptors. I. The ontogeny and distribution of the murine B cell IgE Fc receptor. J Immunol 140: 2148-2154.

Wang, K., Yin, X.M., Chao, D.T., Milliman, C.L., Korsmeyer, S.J., 1996, BID: a novel BH3 domain-only death agonist. Genes Dev 10: 2859-2869.

Wang, Z.Q., Orlikowsky, T., Dudhane, A., Trejo, V., Dannecker, G.E., Pernis, B., Hoffmann, M.K., 1998, Staphylococcal enterotoxin B-induced T-cell anergy is mediated by regulatory T cells. Immunology 94: 331-339.

Watson, A.R., Lee, W.T., 2006, Defective T cell receptor-mediated signal transduction in memory CD4 T lymphocytes exposed to superantigen or anti-T cell receptor antibodies. Cell Immunol 242: 80-90.

Watt, V., Ronchese, F., Ritchie, D., 2007, Resting B cells suppress tumor immunity via an MHC class-II dependent mechanism. J Immunother 30: 323-332.

Webb, S., Morris, C., Sprent, J., 1990, Extrathymic tolerance of mature T cells: clonal elimination as a consequence of immunity. Cell 63: 1249-1256.

Weller, S., Braun, M.C., Tan, B.K., Rosenwald, A., Cordier, C., Conley, M.E., Plebani, A., Kumararatne, D.S., Bonnet, D., Tournilhac, O., Tchernia, G., Steiniger, B., Staudt, L.M., Casanova, J.L., Reynaud, C.A., Weill, J.C., 2004, Human blood IgM "memory" B cells are circulating splenic marginal zone B cells harboring a prediversified immunoglobulin repertoire. Blood 104: 3647-3654.

White, J., Herman, A., Pullen, A.M., Kubo, R., Kappler, J.W., Marrack, P., 1989, The V beta-specific superantigen staphylococcal enterotoxin B: stimulation of mature T cells and clonal deletion in neonatal mice. Cell 56: 27-35.

Wieneke, A.A., Roberts, D., Gilbert, R.J., 1993, Staphylococcal food poisoning in the United Kingdom, 1969-90. **Epidemiol Infect** 110: 519-531.

Wirths, S., Lanzavecchia, A., 2005, ABCB1 transporter discriminates human resting naive B cells from cycling transitional and memory B cells. **Eur J Immunol** 35: 3433-3441.

Wojciechowski, W., Harris, D.P., Sprague, F., Mousseau, B., Makris, M., Kusser, K., Honjo, T., Mohrs, K., Mohrs, M., Randall, T., Lund, F.E., 2009, Cytokine-producing effector B cells regulate type 2 immunity to H. polygyrus. **Immunity** 30: 421-433.

Wulff, H., Knaus, H.G., Pennington, M., Chandy, K.G., 2004, K+ channel expression during B cell differentiation: implications for immunomodulation and autoimmunity. **J Immunol** 173: 776-786.

Xiao, Y., Hendriks, J., Langerak, P., Jacobs, H., Borst, J., 2004, CD27 is acquired by primed B cells at the centroblast stage and promotes germinal center formation. **J Immunol** 172: 7432-7441.

Xiu, Y., Wong, C.P., Bouaziz, J.D., Hamaguchi, Y., Wang, Y., Pop, S.M., Tisch, R.M., Tedder, T.F., 2008, B lymphocyte depletion by CD20 monoclonal antibody prevents diabetes in nonobese diabetic mice despite isotype-specific differences in Fc gamma R effector functions. **J Immunol** 180: 2863-2875.

Yamazaki, T., Nagumo, H., Hayashi, T., Sugane, K., Agematsu, K., 2005, CD72-mediated suppression of human naive B cell differentiation by down-regulating X-box binding protein 1. **Eur J Immunol** 35: 2325-2334.

Yanaba, K., Bouaziz, J.D., Haas, K.M., Poe, J.C., Fujimoto, M., Tedder, T.F., 2008, A regulatory B cell subset with a unique CD1dhiCD5+ phenotype controls T cell-dependent inflammatory responses. **Immunity** 28: 639-650.

Yanaba, K., Hamaguchi, Y., Venturi, G.M., Steeber, D.A., St Clair, E.W., Tedder, T.F., 2007, B cell depletion delays collagen-induced arthritis in mice: arthritis induction requires synergy between humoral and cell-mediated immunity. **J Immunol** 179: 1369-1380.

Yefenof, E., Sanders, V.M., Snow, E.C., Noelle, R.J., Oliver, K.G., Uhr, J.W., Vitetta, E.S., 1985, Preparation and analysis of antigen-specific memory B cells. **J Immunol** 135: 3777-3784.

Yin, T.G., 1990, Characterization of IL-6 production by B cells. **Immunol Invest** 19: 413-419.

Young, A.J., Marston, W.L., Dessing, M., Dudler, L., Hein, W.R., 1997, Distinct recirculating and non-recirculating B-lymphocyte pools in the peripheral blood are defined by coordinated expression of CD21 and L-selectin. **Blood** 90: 4865-4875.

Yu, S., Dunn, R., Kehry, M.R., Braley-Mullen, H., 2008, B cell depletion inhibits spontaneous autoimmune thyroiditis in NOD.H-2h4 mice. **J Immunol** 180: 7706-7713.

Yuan, D., Vitetta, E.S., Kettman, J.R., 1977, Cell surface immunoglobulin. XX. Antibody responsiveness of subpopulations of B lymphocytes bearing different isotypes. J Exp Med 145: 1421-1435.

Yurasov, S., Wardemann, H., Hammersen, J., Tsuiji, M., Meffre, E., Pascual, V., Nussenzweig, M.C., 2005, Defective B cell tolerance checkpoints in systemic lupus erythematosus. J Exp Med 201: 703-711.

Yuschenkoff, V.N., Sethna, M.P., Freeman, G.J., Parker, D.C., 1996, Coexpression of B7-1 and antigen blocks tolerance induction to antigen presented by resting B cells. J Immunol 157: 1987-1995.

Yusuf, I., Kharas, M.G., Chen, J., Peralta, R.Q., Maruniak, A., Sareen, P., Yang, V.W., Kaestner, K.H., Fruman, D.A., 2008, KLF4 is a FOXO target gene that suppresses B cell proliferation. Int Immunol 20: 671-681.

Yusuf, I., Zhu, X., Kharas, M.G., Chen, J., Fruman, D.A., 2004, Optimal B-cell proliferation requires phosphoinositide 3-kinase-dependent inactivation of FOXO transcription factors. Blood 104: 784-787.

Zandvoort, A., Lodewijk, M.E., de Boer, N.K., Dammers, P.M., Kroese, F.G., Timens, W., 2001, CD27 expression in the human splenic marginal zone: the infant marginal zone is populated by naive B cells. Tissue Antigens 58: 234-242.

Zazzeroni, F., Papa, S., Algeciras-Schimnich, A., Alvarez, K., Melis, T., Bubici, C., Majewski, N., Hay, N., De Smaele, E., Peter, M.E., Franzoso, G., 2003, Gadd45 beta mediates the protective effects of CD40 costimulation against Fas-induced apoptosis. Blood 102: 3270-3279.

Zhan, Q., Antinore, M.J., Wang, X.W., Carrier, F., Smith, M.L., Harris, C.C., Fornace, A.J., Jr., 1999, Association with Cdc2 and inhibition of Cdc2/Cyclin B1 kinase activity by the p53-regulated protein Gadd45. Oncogene 18: 2892-2900.

Zhang, S., Iandolo, J.J., Stewart, G.C., 1998, The enterotoxin D plasmid of Staphylococcus aureus encodes a second enterotoxin determinant (sej). FEMS Microbiol Lett 168: 227-233.

Zhu, J., Yamane, H., Paul, W.E., Differentiation of effector CD4 T cell populations (*). Annu Rev Immunol 28: 445-489.

Zhu, N., Shao, Y., Xu, L., Yu, L., Sun, L., 2009, Gadd45-alpha and Gadd45-gamma utilize p38 and JNK signaling pathways to induce cell cycle G2/M arrest in Hep-G2 hepatoma cells. Mol Biol Rep 36: 2075-2085.

Zhu, Y.X., Benn, S., Li, Z.H., Wei, E., Masih-Khan, E., Trieu, Y., Bali, M., McGlade, C.J., Claudio, J.O., Stewart, A.K., 2004, The SH3-SAM adaptor HACS1 is up-regulated in B cell activation signaling cascades. J Exp Med 200: 737-747.

Zinkel, S., Gross, A., Yang, E., 2006, BCL2 family in DNA damage and cell cycle control. **Cell Death Differ** 13: 1351-1359.

Zinkernagel, R.M., Ehl, S., Aichele, P., Oehen, S., Kundig, T., Hengartner, H., 1997, Antigen localisation regulates immune responses in a dose- and time-dependent fashion: a geographical view of immune reactivity. **Immunol Rev** 156: 199-209.

Zuber, C.E., Galizzi, J.P., Valle, A., Harada, N., Howard, M., Banchereau, J., 1990, Interleukin 4 receptors on normal human B lymphocytes: characterization and regulation. **Eur J Immunol** 20: 551-555.

Zuniga, E., Rabinovich, G.A., Iglesias, M.M., Gruppi, A., 2001, Regulated expression of galectin-1 during B-cell activation and implications for T-cell apoptosis. **J Leukoc Biol** 70: 73-79.

APPENDICES

APPENDIX A

REAGENTS, ANTIBODIES, MATERIALS AND INSTRUMENTS

A. REAGENTS

Alkaline Phosphatase (AP) conjugate Substrate Kit (Bio Rad Labs., Hercules, CA)

Anti-PE Microbeads (Miltenyi Biotec, Auburn, USA)

Carboxyfluorescein succinimidyl ester (CFSE) (Invitrogen, Merelbeke, Belgium)

CD14 MicroBeads (Miltenyi Biotec, Auburn, USA)

Cyclosporin A (Sigma, UK)

DMSO (Sigma, UK)

Fetal Bovine Serum (Bio Whittaker, Maryland, U.S.A)

Ficoll-Hypaque Isoprep (Robbins Scientific, Sunnyvale, CA)

Foxp3 Staining kit (eBioscience, CA, USA)

Granulocyte macrophage colony-stimulating factor (GM-CSF) cytokines (BD Biosciences)

Human $CD4^{+}CD25^{+}CD127^{lo}$T cell isolation kit (Miltenyi Biotec, Auburn, USA)

Interleukin 2 (IL-2) (Genzyme, U.S.A)

Interleukin 4 (IL-4) (Genzyme, U.S.A)

L-Glutamine (Sigma, UK)

PBS (Sigma, UK)

Penicillin G (General Drugs House, Thailand)

RPMI 1640 with L-glutamine (Invitrogen GIBCO, Grand Island, NY)

RPMI medium1640 (GIBCO, U.S.A)

Staphylococcus enterotoxin B (Sigma-Aldrich)

Streptomycin (General Drugs House, Thailand)

Trypan blue (Sigma, UK)

B. ANTIBODIES

Antigen Specificity	Clone	Fluorescence conjugated	Source
Surface antigens			
CD3	ucht1	PerCP	BD Biosciences, Sanjose, CA
CD4	RFT-4G	APC	BD Biosciences, Sanjose, CA
CD11c	b-ly6	APC	BD Biosciences, Sanjose, CA
CD14	M5E2	APC	BD Biosciences, Sanjose, CA
CD19	4g7	PerCP	BD Biosciences, Sanjose, CA
CD25	m-a251	FITC, APC	BD Biosciences, Sanjose, CA
CD27	3A12	FITC	Sanquin, Amsterdam, Netherlands
CD40	5C3	FITC	BD Biosciences, Sanjose, CA
CD45RA	hi100	FITC	BD Biosciences, Sanjose, CA
CD45RO	UCHL1	PE	BD Biosciences, Sanjose, CA
CD62L	SK11	PE	BD Biosciences, Sanjose, CA
CD69	FN50	FITC, APC	BD Biosciences, Sanjose, CA
CD80	L307.4	PE	BD Biosciences, Sanjose, CA
CD83	HB15e	FITC	BD Biosciences, Sanjose, CA
CD86	IT2.2	APC	BD Biosciences, Sanjose, CA
CD95 (FAS)	DX2	PE	BD Biosciences, Sanjose, CA
CD127	R34.34	PE	Immunotech, Quebec, Canada
HLA-DP, -DQ, -DR	tu39	FITC	BD Biosciences, Sanjose, CA
Intracellular antigens			
Foxp3	PCH101	PE	eBioscience, San Diego, CA
IL-2	5344.1111	FITC, PE	BD Biosciences, Sanjose, CA
IL-4	8D4-8	FITC	BD Biosciences, Sanjose, CA
IL-10	JES3-19F1	PE	BD Biosciences, Sanjose, CA
IFN-γ	4SB3	FITC, PE	BD Biosciences, Sanjose, CA
TNF-α	MAb11	FITC, PE	BD Biosciences, Sanjose, CA

FITC - Fluorescein isothiocyanate, PE - Phycoerythrin, PerCP - Peridinin chlorophyll protein, APC - Allophycocyanin

C. MATERIALS

24-well flat plate (Costar, U.S.A)

96-well U plate (Costar, U.S.A)

Heparinized tube (Becton-Dickinson, U.S.A)

Automatic pipette (Gilson, France)

Conical tube 50, 15 ml (Falcon, U.S.A)

Counting chamber

Cryotube (Sarstedt, Germany)

Disposable serological pipette 25, 10, 5, 2, 1 ml (Costar, U.S.A)

EDTA tube (Becton-Dickinson, U.S.A)

ELISpot plate (Millipore, U.S.A)

Flask 25,75 cm^3 (Nunc, Denmark)

Glove

Lead shield

Multichannel Autopipettor

Microcentrifuge (Eppendrof, U.S.A)

Microcentrifuge tube

Pipette boy

Pipette tip

D. INSTRUMENTS

Biological Safety Cabinet Class II

Centrifuge

CO_2 incubator (Forma Scientific, U.S.A)

ELISpot Automatic reader (Carl Zeiss, Germany)

ELISpot washer

Freezer – 70°C

Gamma counter

Geiger counter (Ludlum, U.S.A)

Mixer-Vortex-Genic (Scienfic industries, U.S.A)

Refrigerator

Water bath (Shel-lab, U.S.A)

APPENDIX B

ENGINES AND R-PACKAGES

A. ENGINES

Name	Links
DAVID Bioinformatics Database	http://david.abcc.ncifcrf.gov/
Gene Expression Onimbus	http://www.ncbi.nlm.nih.gov/geo/

B. DOWLOADABLE PROGRAMS

Name	Links
Cluster 3.0	http://bonsai.hgc.jp/~mdehoon/software/cluster/software.htm
MultiExperiment Viewer	http://www.tm4.org/mev/
Java TreeView	http://jtreeview.sourceforge.net/
R-Bioconductor	http://www.bioconductor.org/install/

C. R-PACKAGES

Name	Sources
affy	http://www.bioconductor.org/packages/release/bioc/html/affy.html
ComBat	http://statistics.byu.edu/johnson/ComBat/ComBat_Old.R
gcrma	http://www.bioconductor.org/packages/release/bioc/html/gcrma.html
LPE	http://www.bioconductor.org/packages/release/bioc/html/LPE.html
LPEadj	http://www.bioconductor.org/packages/release/bioc/html/LPEadj.html

VITAE

Mr Kaj Chokeshai-u-saha was born on April 24th 1982 in Samutsongkram province, Thailand. He graduated with Degree of Doctor of Veterinary Medicine (DVM) with the 1st honour from Faculty of Veterinary Science, Chulalongkorn University, in 2006. In 2008, he received a Ph.D. student grant support through Chulalongkorn University to perform a doctoral degree of Philosophy Program in Biomedical Sciences Program in Interdisciplinary Program, Graduate School, Chulalongkorn University, Bangkok, Thailand. His focus research is about in vitro characterization of naïve B cell antigen presentation in human of which the data is still limitedly available.