

CLIFFORD M. SNAPPER, M.D.

EDUCATION:

1975 Brooklyn College, City University of New York, Brooklyn, NY – B.S. - Physics
1981 Albany Medical College of Union University, Albany, NY – MD - Medicine
1982 Certification, National Board of Medical Examiners
1985 Board Certification in Anatomic Pathology

PROFESSIONAL POSITIONS:

1981-82 Intern, Internal Medicine, Albany Medical Center, Albany, NY
1982-85 Resident, Dept. of Pathology, The New York Hospital-Cornell Medical Center, New York, NY
1985-88 Medical Staff Fellow, Lab. of Immunology, NIAID, NIH, Bethesda, MD (Lab: William E. Paul)
1988-92 Assistant Professor, Dept of Pathology, USUHS, Bethesda, MD
1992-94 Associate Professor, Dept. of Pathology, USUHS, Bethesda, MD
1994-Pres Professor, Dept. of Pathology, USUHS, Bethesda, MD
1994-Pres Professor, Cell and Molecular Biology Program, USUHS, Bethesda, MD
1997-Pres Professor, Dept. of Medicine, USUHS, Bethesda, MD
2000-Pres Professor, Emerging Infectious Diseases Program, USUHS, Bethesda, MD
2000-Pres Director, Institute for Vaccine Research, USUHS, Bethesda, MD

HONORS/AWARDS: B.S. Magna Cum Laude (1975), American Assoc. of Immunologists (1988), Burroughs Wellcome Fund Developing Investigator Award, Immunopharmacology of Allergic Diseases (1989), Associate Editor Journal of Immunology (1991-1993), The Jeffrey Modell Foundation Lifetime Achievement Award (1992), American Association of University Pathologists (1993), Editorial Board, Infection and Immunity (2004-2008), Outstanding biomedical graduate educator award (USUHS, 2006).

RESEARCH PROJECTS ONGOING OR COMPLETED DURING THE LAST 3 YEARS:

"Dendritic and T cells in anti-bacterial Ig responses", Principal Investigator: Clifford M. Snapper, M.D., Agency: NIH; Type: 2R01 AI049192-06; Period: 4/15/06-3/31/11; The role of this project is to elucidate the ability by which murine dendritic and T cells are able to process and present protein and polysaccharide antigens to the immune system for induction of antigen-specific Ig isotype production.

"Developing of Novel Adjuvants for Augmenting Humoral Immunity", Principal Investigator: Clifford M. Snapper, M.D., Agency: USUHS; Period: 9/1/05-8/31/08; The role of this project is to develop novel approaches to augmenting protective antibody responses to protein and/or polysaccharide antigens, expressed by pathogens, for development of improved vaccines.

"Toll-like Receptors and Anti-bacterial Ig Responses "; Principal Investigator: Clifford M. Snapper, M.D., Agency: USUHS; Period: 10/1/06-9/30/09. The purpose of this grant is to determine the role of Toll-like receptors in mediating innate and adaptive immunity to *Streptococcus pneumoniae*.

"Dengue virus vaccines and diagnostics"; Principal Investigator: Kanakatte Raviprakash, Ph.D., Agency: Office of Naval Research; Period: 10/1/05-9/30/08. The purpose of this project is to develop a protective, antibody-based tetravalent vaccine against dengue virus.

SELECTED BIBLIOGRAPHY (45 out of 104 publications)

Snapper, C.M., and Paul W.E. 1987. Interferon gamma and B cell stimulatory factor-1 reciprocally regulate Ig isotype expression. *Science*. 236:944.

Snapper, C. M., Finkelman, F. D., and Paul, W.E. 1988. Differential regulation of IgG1 and IgE synthesis by interleukin 4. *J. Exp. Med.* 167:183.

Snapper, C. M., Hornbeck, P. V., Atasoy, U., Pereira, G. M. B., Paul, W. E. 1988. Interleukin 4 induces membrane Thy-1 expression on normal murine B cells. *Proc. Natl. Acad. Sci. USA.* 85:6107.

Snapper, C. M., Hooley, J. J., Urban, J. F., Jr., and Finkelman, F. D. 1991. Lack of FcεRII expression by murine B cells after in vivo immunization is directly associated with Ig secretion and not Ig isotype switching. *J. Immunol.* 146:2161.

Snapper, C. M., McIntyre, T. M., Mandler, R., Peçanha, L. M. T., Finkelman, F. D., Lees, A., and Mond, J. J. 1992. Induction of IgG3 secretion by IFN-γ: A model for T cell-independent class switching in response to T cell-independent type-2 antigens. *J. Exp. Med.* 175:1367.

- Snapper, C. M., Yamada, H., Smoot, D., Sneed, R., and Mond, J. J. 1993. Comparative in vitro analysis of proliferation, Ig secretion, and Ig class switching by murine marginal zone and follicular B cells. *J. Immunol.* 150:2737.
- McIntyre, T. M., Klinman, D. R., Rothman, P., Lugo, M., Dasch, J. R., Mond, J. J., and Snapper, C. M. 1993. Transforming growth factor b1 selectively stimulates immunoglobulin G2b secretion by lipopolysaccharide-activated murine B cells. *J. Exp. Med.* 177:1031.
- Mandler, R., Chu, C., Paul, W. E., Max, E., and Snapper, C. M. 1993. Interleukin 5 induces Su-Sg1 DNA rearrangement by B cells activated with dextran-anti-IgD antibodies and interleukin-4: A 3 component model for Ig class switching. *J. Exp. Med.* 178:1577.
- Snapper, C. M., Yamaguchi, H., Sneed, R., Smoot, D., and Mond, J. J. 1993. Natural killer cells induce activated murine B cells to secrete Ig. *J. Immunol.* 151:5251.
- Snapper, C. M., Yamaguchi, H., Moorman, M. A., and Mond, J. J. 1994. An in vitro model for T cell-independent induction of humoral immunity: A key role for natural killer cells. *J. Immunol.* 152:4884.
- Snapper, C. M., Kehry, M. R., Castle, B. E., and Mond, J. J. 1995. Multivalent, but not bivalent, antigen receptor crosslinkers synergize with CD40 ligand for induction of Ig synthesis and class switching in normal murine B cells. A redefinition of the TI-2 versus TD antigen dichotomy. *J. Immunol.* 154:1177.
- McIntyre, T. M., Kehry, and Snapper, C. M. 1995. Novel in vitro model for high-rate IgA class switching. *J. Immunol.* 154:3156.
- Snapper, C. M., Moorman, M. A., Kehry, M. R., Maliszewski, C. R., and Mond, J. J. 1995. IL-3 and GM-CSF strongly induce Ig secretion by sort-purified murine B cells activated through the membrane Ig, but not the CD40, signaling pathway. *J. Immunol.* 154:5842.
- Snapper, C. M., Rosas, F. R., Kehry, M. R., and Mond, J. J. 1995. Bacterial lipoproteins may substitute for cytokines in the humoral immune response to T cell-independent type II antigens. *J. Immunol.* 155:5582.
- Shparago, N., Zelazowski, P., Jin, L., McIntyre, T. M., Eckhard, S., Peçanha, L. M. T., Kehry, M. R., Mond, J. J., Max, E. E., and Snapper, C. M. 1996. Interleukin-10 selectively regulates murine Ig isotype switching. *Int. Immunol.* 8:781.
- Snapper, C. M., Moorman, M. A., Kehry, M. R., Mond, J. J., Maliszewski, C. R. 1996. IFN-g is a potent inducer of Ig secretion by B murine cells activated through the mIg-, but not CD40 signaling pathway. *Int. Immunol.* 8:877.
- Snapper, C. M. and Mond, J. J. 1996. A model for induction of T cell-independent humoral immunity in response to polysaccharide antigens. *J. Immunol.* 157: 2229.
- Snapper, C. M., Rosas, F. R., Zelazowski, P., Moorman, M. A., Kehry, M. R., Bravo, R., and Weih, F. 1996. B cells lacking relB are defective in proliferative responses, but undergo normal B cell maturation to Ig secretion and Ig class switching. *J. Exp. Med.* 184:1537.
- Snapper, C. M., Zelazowski, P., Rosas, F. R., Kehry, M. R., Baltimore, D., and Sha, B. 1996. B cells from p50/NF-kB knockout mice have selective defects in proliferation, differentiation, germline CH transcription and Ig class switching. *J. Immunol.* 156:183.
- Snapper, C. M., Marcu, K. B., and Zelazowski, P. 1997. Ig class switching: Beyond accessibility. *Immunity.* 6:217.
- Snapper, C. M., Rosas, F. R., Moorman, M. A., Kehry, M. R., and Mond, J. J. 1997. Restoration of T cell-independent type 2 induction of Ig secretion by murine neonatal B cells in vitro. *J. Immunol.* 158:2731.
- Snapper, C. M., Rosas, F. R., Kehry, M. R., Mond, J. J., and Wetzler, L. M. 1997. Neisserial porins may provide critical second signals to polysaccharide-activated murine B cells for induction of Ig. *Infect. Immun.* 65:3203.
- Horwitz, B. H., Zelazowski, P., Shen, Y., Scott, M. L., Baltimore, D., and Snapper, C. M. 1999. The p65 subunit of NF-kB is redundant with p50 during B cell proliferative responses, and is required for germline CH transcription and class switching to IgG3. *J. Immunol.* 162:1941.
- Wu, Z-Q., Vos, Q., Shen, Y., Lees, A., Wilson, S. R., Briles, D. E., Gause, W. C., Mond, J. J., and Snapper, C. M. 1999. In vivo polysaccharide-specific IgG responses to intact *Streptococcus pneumoniae* are T cell-dependent and require CD40- and B7-ligand interactions. *J. Immunol.* 163:659.
- Wu, Z-Q, Khan, A. Q., Shen, Y., Schartmann, J., Peach, R., Lees, A., Mond, J. J., Gause, W. C., and Snapper, C. M. 2000. B7 requirements for primary and secondary protein- and polysaccharide-specific Ig isotype responses to *Streptococcus pneumoniae*. *J. Immunol.* 165:6840.
- Snapper, C. M., Shen, Y., Khan, A. Q., Colino, J., Zelazowski, P., Mond, J. J., Gause, W. C., and Wu, Z-Q. 2001. Distinct types of T-cell help for the induction of a humoral immune response to *Streptococcus pneumoniae*. *Trends in Immunology.* 22:308.

- Khan, A. Q., Shen, Y., Wu, Z-Q., Wynn, T. A., and Snapper, C. M. 2002. Endogenous pro-inflammatory and anti-inflammatory cytokines differentially regulate an in vivo humoral response to *Streptococcus pneumoniae*. *Infect. Immun.* 70:749.
- Colino, J., Shen, Y., and Snapper, C. M. 2002. Dendritic cells pulsed with intact *Streptococcus pneumoniae* elicit both protein- and polysaccharide-specific immunoglobulin isotype responses in vivo through distinct mechanisms. *J. Exp. Med.* 195: 1.
- Wu, Z.-Q., Shen, Y., Chu, C-L., Riese, R., Chapman, H.A., Kanagawa, O., and Snapper, C. M. 2002. The mechanism underlying T cell help for induction of an antigen-specific in vivo humoral immune response to *Streptococcus pneumoniae* is dependent on the type of antigen. *J. Immunol.* 168: 5551.
- Wu, Z.-Q., Khan, A. Q., Shen, Y., Dawicki, W., Watts, T. H., Mittler, R. S., and Snapper, C. M. 2003. 4-1BB (CD137) differentially regulates murine in vivo protein- and polysaccharide-specific immunoglobulin isotype responses to *Streptococcus pneumoniae*. *Infect. Immun.* 71: 196.
- Colino, J. and Snapper, C. M. 2003. Opposing signals from Pathogen-Associated Molecular Patterns and IL-10 are critical for optimal dendritic cell induction of in vivo humoral immunity to *Streptococcus pneumoniae*. *J. Immunol.* 171: 3508.
- Colino, J. and Snapper, C. M. 2003. Two distinct mechanisms for induction of dendritic cell apoptosis in response to intact *Streptococcus pneumoniae*. *J. Immunol.* 171: 2354.
- Colino, J. and Snapper, C. M. 2003. Dendritic cells, new tools for vaccination. *Microbes and Infection* 5:311.
- Khan, A. Q., Lees, A., and Snapper, C. M. 2004. Differential regulation of IgG anti-capsular polysaccharide and anti-protein responses to intact *Streptococcus pneumoniae* in the presence of cognate CD4⁺ T cell help. *J. Immunol.* 172:532.
- Sen, G., Flora, M., Chattopadhyay, G., Klinman, D. M., Lees, A., Mond, J. J., and Snapper, C. M. 2004. The critical DNA flanking sequences of a CpG oligodeoxynucleotides, but not the 6 base CpG motif, can be replaced with RNA without quantitative or qualitative changes in Toll-like receptor 9-mediated activity. *Cell. Immunol.* 232: 64.
- Khan, A. Q., Chen, Q., Wu, Z-Q., Paton, J. C., and Snapper, C. M. 2005. Innate and type 1 humoral immunity to *Streptococcus pneumoniae* are both mediated by MyD88, but differ in their relative dependence on Toll-like receptor 2. *Infect. Immun.* 73:298.
- Lee, K. S., Sen, G., and Snapper, C. M. 2005. Endogenous CD4⁺CD25⁺ regulatory T cells (Tregs) play no apparent role in the acute humoral response to *Streptococcus pneumoniae*. *Infect. Immun.* In press.
- Sen, G, Khan, A. Q., Chen, Q., and Snapper, C. M. 2005. In vivo IgG responses to isolated pneumococcal polysaccharides are critically dependent on the presence of associated Toll-like receptor ligands. *J. Immunol.* 173:7084.
- Khan, A.Q., Sen, G., Guo, S., Witte, O.N., Snapper, C.M. 2006. Induction of CD4⁺ T cell-dependent IgG anti-polysaccharide (PS) responses to intact *Streptococcus pneumoniae* or to a soluble pneumococcal PS-protein conjugate is more heavily dependent on Btk-mediated BCR signaling than anti-protein responses. *Infect. Immun.* 74:1419.
- Sen, G., Chen, Q., and Snapper, C.M. 2006. Immunization of aged mice with a pneumococcal conjugate vaccine when combined with an unmethylated CpG-containing oligodeoxynucleotide restores defective IgG anti-PPS14 responses and PspA-specific CD4⁺ T cell priming to young adult levels. *Infect. Immun.* 74:2177.
- Colino, J, and Snapper, C. M. 2006. Exosomes from bone marrow dendritic cells pulsed with Diphtheria toxoid preferentially induce type 1 antigen-specific IgG responses in naïve recipients in the absence of free antigen. *J. Immunol.* 177: 3757
- Chen, Q., Sen, G., and Snapper, C. M. 2006. IL-1R1 is critical for cognate, but not non-cognate, CD4⁺ T cell help for induction of both type 1 and type 2 humoral immunity in response to intact *Streptococcus pneumoniae*. *J. Immunol.* 177: 6044.
- Colino, J., and Snapper, C. M. 2007. Dendritic cell derived exosomes express a *Streptococcus pneumoniae* capsular polysaccharide type 14 cross-reactive antigen that induces protective immunoglobulin responses against pneumococcal infection in mice. *Infect. Immun.* 75: 220.
- Goldblatt, D. and Snapper, C. M. 2007. Immunobiology of pneumococcal polysaccharides and conjugate vaccines. In Pneumococcal Vaccines: The Impact of Conjugate Vaccine. Eds. G. Siber, K. Klugman, and H. Makela, ASM Press.
- Chattopadhyay, G., Khan, A. Q., Dubois, W., Potter, M., Snapper, C. M. 2007. Transgenic expression of bcl-xL or bcl2 by murine B cells enhances the in vivo anti-polysaccharide, but not anti-protein response to intact *Streptococcus pneumoniae*. *J. Immunol.* 179: 7523.