

DAFTAR PUSTAKA

- Abuharfeil, N., Al-Oran, R., Abo-Shehada, M., 1999. The effect of bee honey on the proliferative activity of human B- and T-Lymphocytes and the activity of phagocytes. *Food Agr. Immunol.* 11(2): 169-177.
- Allen, K., Vázquez-Medina, J. P., 2021. Reactive oxygen species, redox signaling, and regulation of vascular endothelial signaling. In: Chatterje Endothelial (Ed.): *Signaling in Vascular Dysfunction and Disease: From Bench to Bedside*, pp.37-45 Academic press, Philadelphia.
- Almasaudi, S., el-shitany, N., Abbas, A., Abdel-Dayem, M., Ali Abdulhadi, S., AL Jaouni, S., *et al.*, 2016. Antioxidant, Anti-inflammatory, and Antiulcer Potential of Manuka Honey against Gastric Ulcer in Rats. *Oxid. Med. Cell. Longev.* 2016(1): 1-10.
- Andersen, M. H., Schrama, D., Thor Straten, P., Becker, J. C., 2006. Cytotoxic T cells. *J. Investig. Dermatol.* 126(1): 32–41.
- Andreicuț, A. D., Fischer-Fodor, E., Pârvu, A. E., Țigu, A. B., Cenariu, M., Pârvu, M., *et al.*, 2019. Antitumoral and Immunomodulatory Effect of *Mahonia aquifolium* Extracts. *Oxid. Med. Cell. Longev.* 2019: 6439021.
- Anita, D., 2021. Aktivitas mencari makan lebah madu (*Apis cerana* F.) dan tanaman potensial sumber pakan di hutan Pendidikan Wanagama I Gunungkidul Yogyakarta [Tesis]. Universitas Gadjah Mada, Yogyakarta.
- Ardawi, M. S. M., 1988. Glutamine and glucose metabolism in human peripheral lymphocytes. *Metabolism* 37(1): 99–103.
- Atsaves, V., Leventaki, V., Rassidakis, G. Z., Claret, F. X. 2019., AP-1 Transcription Factors as Regulators of Immune Responses in Cancer. *Cancers* 11(7): 1037.
- Baine, M. J., Mallya, K., Batra, S. K., 2013. Quantitative real-time PCR expression analysis of peripheral blood mononuclear cells in pancreatic cancer patients. *Methods Mol. Biol.* 980: 157–173.
- Behbahani, M., 2014. Anti-HIV-1 activity of eight monofloral Iranian honey types. *PloS ONE.* 9(10): e108195.

- Bhattacharyya, S., Deb, J., Patra, A. K., Thuy Pham, D. A., Chen, W., Vaeth, M., *et al.*, 2011. NFATc1 affects mouse splenic B cell function by controlling the calcineurin--NFAT signaling network. *J. Exp. Med.* 208(4): 823–839
- Bianchi, R., Giambanco, I., & Donato, R., 2010. S100B/RAGE-dependent activation of microglia via NF- κ B and AP-1. *Neurobiol. Aging* 31(4): 665–677.
- Bittersohl, H., Steimer, W., 2016. Intracellular concentrations of immunosuppressants. In: Oellerich, M., Dasgupta, A. (Ed.): *Personalized Immunosuppression in Transplantation*, pp: 199–226. Elsevier, Amsterdam.
- Bondy, S., Maiese, K., 2010. Aging and age-related disorders. Humana press, London.
- Brand, K., 1985. Glutamine and glucose metabolism during thymocyte proliferation. Pathways of glutamine and glutamate metabolism. *Biochem. J.* 228(2): 353–361.
- Brudzynski, K., 2020. A current perspective on hydrogen peroxide production in honey. *Food Chem.* 332: 127229.
- Buck, M.D., O'Sullivan, D., Pearce, E.L., 2015. T cell metabolism drives immunity. *J. Exp. Med.* 212(9): 1345-1360.
- Camperio, C., Caristi, S., Fanelli, G., Soligo, M., Del Porto, P., Piccolella, E. (2012). Forkhead transcription factor FOXP3 upregulates CD25 expression through cooperation with RelA/NF- κ B. *PloS one* 7(10): e48303.
- Casella-Martins, A., Ayres, L. R., Burin, S. M., Morais, F. R., Pereira, J. C., Faccioli, L. H., *et al.*, 2015. Immunomodulatory activity of Tityus serrulatus scorpion venom on human T lymphocytes. *J. Venom. Anim. Toxins. Incl. Trop Dis.* 21: 46.
- Chang, H. C., Tan, K., Ouyang, J., Parisini, E., Liu, J. H., Le, Y., *et al.*, 2005. Structural and mutational analyses of a CD8alphabeta heterodimer and comparison with the CD8alphaalpha homodimer. *Immunity* 23(6): 661–671.
- Chaplin, D. D., 2010. Overview of the immune response. *J. Allergy Clin. Immunol.* 125(2 Suppl 2): S3–S23.

Chauhan, D., Kharbanda, S. M., Rubin, E., Barut, B. A., Mohrbacher, A., Kufe, D. W., *et al.*, 1993. Regulation of c-jun gene expression in human T lymphocytes. *Blood* 81(6): 1540–1548.

Chiang, L. C., Ng, L. T., Chiang, W., Chang, M. Y., Lin, C. C., 2003. Immunomodulatory activities of flavonoids, monoterpenoids, triterpenoids, iridoid glycosides and phenolic compounds of *Plantago* species. *Planta Med.*, 69(7): 600–604.

Chin, N., Sowndhararajan, K., 2020. A Review on Analytical Methods for Honey Classification, Identification and Authentication. 10.5772/intechopen.90232.

Cianciosi, D., Forbes-Hernández, T. Y., Afrin, S., Gasparrini, M., Reboredo-Rodriguez, P., Manna, P. P., *et al.*, 2018. Phenolic Compounds in Honey and Their Associated Health Benefits: A Review. *Molecules* 23(9): 2322.

Cole, D. K., Laugel, B., Clement, M., Price, D. A., Wooldridge, L., Sewell, A. K., 2012. The molecular determinants of CD8 co-receptor function. *Immunology* 137(2): 139–148.

Costantini, M., 2014. Bodily self and immune self: is there a link?. *Front. Hum. Neurosci.* 8: 138.

Crevel, R., 2005., Lymphocyte Proliferation. In: Vohr HW. (Ed.): *Encyclopedic Reference of Immunotoxicology*, pp: 43-75. Springer, Berlin.

Cui, J., Chen, Y., Wang, H. Y., Wang, R. F., 2014. Mechanisms and pathways of innate immune activation and regulation in health and cancer. *Hum. Vaccin. Immunother.* 10(11): 3270–3285.

De Kleer, I., Willems, F., Lambrecht, B., Goriely, S., 2014. Ontogeny of myeloid cells. *Front. Immunol.* 5: 423.

Delgoffe, G. M., & Powell, J. D., 2015. Feeding an army: The metabolism of T cells in activation, anergy, and exhaustion. *Mol. Immunol.* 68(2): 492–496.

DePalma, L., Brown, E., Baker, R., 1998. c-fos and c-jun mRNA expression in activated cord and adult lymphocytes: an analysis by Northern hybridization. *Vox Sang.* 75(2): 134–138.

Descotes, J., 2014. Immune system. In: Wexler, P (Ed.): *Encyclopedia of Toxicology*, pp. 573-596. Academic Press, Cambridge.

- Dhama, K., Saminathan, M., Susan, S., Singh, M., Karthik, K., Amarpal., 2015. Effect of Immunomodulation and Immunomodulatory Agents on Health with some Bioactive Principles, Modes of Action and Potent Biomedical Applications. *Int. J. Pharmacol.* 11(4): 253-290.
- Di Marzo, N., Chisci, E., Giovannoni, R., 2018. The Role of Hydrogen Peroxide in Redox-Dependent Signaling: Homeostatic and Pathological Responses in Mammalian Cells. *Cells* 7(10): 156.
- Dimeloe, S., Burgener, A. V., Grähler, J., Hess, C., 2017. T-cell metabolism governing activation, proliferation and differentiation; a modular view. *Immunology* 150(1): 35–44.
- Dimitriou, I. D., Clemenza, L., Scotter, A. J., Chen, G., Guerra, F. M., Rottapel, R., 2008. Putting out the fire: coordinated suppression of the innate and adaptive immune systems by SOCS1 and SOCS3 proteins. *Immunol. Rev.* 224: 265–283.
- Donato, R., 2007. RAGE: A Single Receptor for Several Ligands and Different Cellular Responses: The Case of Certain S100 Proteins. *Curr. Mol. Med.* 7(8): 711–724.
- Ellrichmann, G., Thöne, J., Lee, D. H., Rupec, R. A., Gold, R., & Linker, R. A., 2012. Constitutive activity of NF-kappa B in myeloid cells drives pathogenicity of monocytes and macrophages during autoimmune neuroinflammation. *J. Neuroinflammation* 9: 15.
- Escriche, I., Kadar, M., Juan-Borrás, M., Domenech, E. 2014. Suitability of antioxidant capacity, flavonoids and phenolic acids for floral authentication of honey. Impact of industrial thermal treatment. *Food Chem.* 142(4): 35–143.
- Faadhilah, A., 2018. Pengelolaan lebah madu di Kawasan hutan dengan tujuan khusus Wanagama I oleh masyarakat dusun Banaran I kabupaten Gunungkidul Yogyakarta [Skripsi]. Universitas Gadjah Mada, Yogyakarta.
- Feinerman, O., Jentsch, G., Tkach, K. E., Coward, J. W., Hathorn, M. M., Sneddon, M. W., *et al.*, 2010. Single-cell quantification of IL-2 response by effector and regulatory T cells reveals critical plasticity in immune response. *Mol. Syst. Biol.* 6: 437.
- Ferreira, P. M., Lima, D. J., Debiasi, B. W., Soares, B. M., Machado, K., Noronha, J., *et al.*, 2013. Antiproliferative activity of *Rhinella marina* and *Rhaebo guttatus* venom extracts from Southern Amazon. *Toxicon* 72: 43-51.

- Frauwirth, K. A., Riley, J. L., Harris, M. H., Parry, R. V., Rathmell, J. C., Plas, D. R., *et al.*, 2002. The CD28 Signaling Pathway Regulates Glucose Metabolism. *Immunity* 16(6): 769–777.
- Fukuda, M., Kobayashi, K., Hirono, Y., Miyagawa, M., Ishida, T., Ejiogu, *et al.*, 2011. Jungle honey enhances immune function and antitumor activity. *Evid. Based Complementary Altern. Med.* 2011: 908743.
- Gandhi, G. R., Neta, M., Sathiyabama, R. G., Quintans, J., de Oliveira E Silva, *Et al.*, 2018. Flavonoids as Th1/Th2 cytokines immunomodulators: A systematic review of studies on animal models. *Phytomedicine*. 44: 74–84.
- Gannabathula, S., Skinner, M. A., Rosendale, D., Greenwood, J. M., Mutukumira, A. N., Steinhorn, G., *et al.*, 2012. Arabinogalactan proteins contribute to the immunostimulatory properties of New Zealand honeys. *Immunopharmacol. Immunotoxicol.* 34(4): 598–607.
- Gaudino, S.J., Kumar, P., 2019. Cross-Talk Between Antigen Presenting Cells and T Cells Impacts Intestinal Homeostasis, Bacterial Infections, and Tumorigenesis. *Front. Immunol.* (10): 360.
- Gazon, H., Barbeau, B., Mesnard, J. M., Peloponese, J. M., Jr 2018. Hijacking of the AP-1 Signaling Pathway during Development of ATL. *Front. Microbiol.* 8: 2686.
- Ghaffari, S., Torabi-Rahvar, M., Aghayan, S., Jabbarpour, Z., Moradzadeh, K., Omidkhoda, *et al.*, 2021. Optimizing interleukin-2 concentration, seeding density and bead-to-cell ratio of T-cell expansion for adoptive immunotherapy. *BMC Immunol.* 22: 43.
- Giampaolo, S., 2022. Role of the transcription factor NFATc1 during the early stages of thymocyte development [tesis]. Univ. of Würzburg, Würzburg.
- Gibson, J. N., Beesetty, P., Sulentic, C., Kozak, J. A., 2016. Rapid Quantification of Mitogen-induced Blastogenesis in T Lymphocytes for Identifying Immunomodulatory Drugs. *J. Vis. Exp.* 118: 55212.
- Gilston, V., Williams, M. A., Newland, A. C., Winyard, P. G., 2001. *Hydrogen peroxide and tumour necrosis factor- α induce NF- κ B-DNA binding in primary human T lymphocytes in addition to T cell lines.* *Free Radic. Res.* 35(6): 681–691.

- Giridharan, S., & Srinivasan, M., 2018. Mechanisms of NF- κ B p65 and strategies for therapeutic manipulation. *J. Inflamm.* 11: 407–419.
- Giuliani C., 2019. The Flavonoid Quercetin Induces AP-1 Activation in FRTL-5 Thyroid Cells. *Antioxidants* 8(5): 112.
- Giuliani, C., Bucci, I., Napolitano, G., 2018. The Role of the Transcription Factor Nuclear Factor-kappa B in Thyroid Autoimmunity and Cancer. *Front. Endocrinol.* 9: 471.
- Glatzová, D., Cebecauer, M., 2019. Dual Role of CD4 in Peripheral T Lymphocytes. *Frontiers Immunol.* 10: 618.
- Gonzalez, S., González-Rodríguez, A. P., Suárez-Álvarez, B., López-Soto, A., Huergo-Zapico, L., Lopez-Larrea, C., 2011. Conceptual aspects of self and nonself discrimination. *Self/nonself* 2(1): 19–25.
- Gosselin, K., Touzet, H., Abbadie, C., 2004. Rel/NF-kappaB target genes. *Bonsai Bioinformatics* (Software). Available from: URL: <https://bioinfo.lifl.fr/NF-KB/>
- Granado-Serrano, A. B., Martín, M. A., Haegeman, G., Goya, L., Bravo, L., Ramos, S., 2010. Epicatechin induces NF-kappaB, activator protein-1 (AP-1) and nuclear transcription factor erythroid 2p45-related factor-2 (Nrf2) via phosphatidylinositol-3-kinase/protein kinase B (PI3K/AKT) and extracellular regulated kinase (ERK) signalling in HepG2 cells. *Br. J. Nutr.* 103(2): 168–179.
- Granado-Serrano, A. B., Martín, M. A., Bravo, L., Goya, L., Ramos, S., 2010. Quercetin Modulates NF- κ B and AP-1/JNK Pathways to Induce Cell Death in Human Hepatoma Cells. *Nutr. Cancer* 62(3): 390–401.
- Grumont, R., Lock, P., Mollinari, M., Shannon, F. M., Moore, A., Gerondakis, S., 2004. The mitogen-induced increase in T cell size involves PKC and NFAT activation of Rel/NF-kappaB-dependent c-myc expression. *Immunity* 21(1): 19–30.
- Gulden, G., Sert, B., Teymur, T., Ay, Y., Tiryaki, N. N., Mishra, A. K., *et al.*, 2023. CAR-T Cells with Phytohemagglutinin (PHA) Provide Anti-Cancer Capacity with Better Proliferation, Rejuvenated Effector Memory, and Reduced Exhausted T Cell Frequencies. *Vaccines* 11(2): 313.

- Haas, A., Zimmermann, K., Oxenius, A., 2011. Antigen-dependent and -independent mechanisms of T and B cell hyperactivation during chronic HIV-1 infection. *J. Virol.* 85(23): 12102–12113.
- Harcourt, N. R., 2005. The effects of honey on the inflammatory response of cells with respect to wound healing [tesis]. Univ. of Waikato, Hamilton.
- Hein, Gert., Franke, S., 2002. Are advanced glycation end-product-modified proteins of pathogenetic importance in fibromyalgia?. *Rheumatology* 41: 1163–1167.
- Higdon, L.E., Lee, K., Tang, Q., Maltzman, J.S., 2016. Virtual global transplant laboratory standard operating procedures for blood collection, PBMC isolation, and storage. *Transplant Direct.* 2(9): e101.
- Hughes-Fulford, M., Chang, T. T., Martinez, E. M., Li, C. F., 2015. Spaceflight alters expression of microRNA during T-cell activation. *FASEB J.* 29(12): 4893–4900.
- Iles, K. E., Dickinson, D. A., Watanabe, N., Iwamoto, T., & Forman, H. J., 2002. AP-1 activation through endogenous H₂O₂ generation by alveolar macrophages. *Free Radic. Biol. Med.* 32(12): 1304–1313.
- Ingebritsen, T.S., 2013. Serine/Threonine Phosphatases. In: Lennarz, W.J dan Lane, W.D (Ed): *Encyclopedia of Biological Chemistry (Second Edition)*, pp: 219–223. Academic Press, London.
- Islam, A., Khalil, I., Islam, N., Moniruzzaman, M., Mottalib, A., *et al.* Physicochemical and antioxidant properties of Bangladeshi honeys stored for more than one year. *BMC Complement Altern. Med.* 12: 177 (2012)
- Ito, T., Connett, J.M., Kunkel, S.L., Matsukawa, A., 2013. The linkage of innate and adaptive immune response during granulomatous development. *Front. Immun.* 4: 10.
- Iurlina, M. O., Saiz, A. I., Fritz, R., Manrique, G. D., 2009. *Major flavonoids of Argentinean honeys. Optimisation of the extraction method and analysis of their content in relationship to the geographical source of honeys.* *Food Chem.* 115(3): 1141–1149.
- Jackson, K. J., Kidd, M. J., Wang, Y., Collins, A. M., 2013. The shape of the lymphocyte receptor repertoire: lessons from the B cell receptor. *Front. Immunol.* 4: 263.

- Jenkins, M. K., Moon, J. J., 2012. The role of naive T cell precursor frequency and recruitment in dictating immune response magnitude. *J. Immunol.* 188(9): 4135–4140.
- Lord, J. D., McIntosh, B. C., Greenberg, P. D., Nelson, B. H. 2000., The IL-2 receptor promotes lymphocyte proliferation and induction of the c-myc, bcl-2, and bcl-x genes through the trans-activation domain of Stat5. *J. Immunol.* 164(5): 2533–2541.
- Janeway Jr, C.A., Travers, P., Walport, M., Shlomchik, M., 2001. Immunobiology: The Immune System in Health and Disease. 5th ed. Garland Science, New York.
- Jantan, I., Ahmad, W., Bukhari, S. N., 2015. Plant-derived immunomodulators: an insight on their preclinical evaluation and clinical trials. *Front. Plant Sci.* 6: 655.
- Jasmi., 2013. Hamuli Lebah madu Apis (Hymenoptera: Apidae) pada beberapa ketinggian di Sumatera Barat. *J. Sains Teknol.* 5(1): 71-77.
- Jenkins, M. K., & Moon, J. J., 2012. The role of naive T cell precursor frequency and recruitment in dictating immune response magnitude. *J. Immunol.* 188(9): 4135–4140.
- Jeong, W.-S., Kim, I.-W., Hu, R., & Kong, A.-N. T., 2004. Modulation of AP-1 by Natural Chemopreventive Compounds in Human Colon HT-29 Cancer Cell Line. *Pharm. Res.* 21(4): 649–660.
- John, S., Robbins, C. M., Leonard, W. J., 1996. An IL-2 response element in the human IL-2 receptor alpha chain promoter is a composite element that binds Stat5, Elf-1, HMG-I(Y) and a GATA family protein. *EMBO J.* 15(20): 5627–5635.
- Justiz-Vaillant, A.A, Sabir, S., Jan, A., 2021. Physiology, Immune Response. StatPearls [serial online] [cited 2021 Aug 28]. Available from: URL: <https://www.ncbi.nlm.nih.gov/books/NBK539801/>
- Kalia, V., Sarkar, S., 2018. Regulation of Effector and Memory CD8 T Cell Differentiation by IL-2-A Balancing Act. *Front. Immunol.* 9: 2987.
- Kardan, M., Rafiei, A., Ghaffari, J., Valadan, R., Morsaljahan, Z., Haj-Ghorbani, S. T., 2019. Effect of ginger extract on expression of GATA3, T-bet and ROR-

γ t in peripheral blood mononuclear cells of patients with Allergic Asthma. *Allergol. Immunopathol.* 47(4): 378–385.

Kim, H. P., Kelly, J., Leonard, W. J., 2001. The basis for IL-2-induced IL-2 receptor alpha chain gene regulation: importance of two widely separated IL-2 response elements. *Immunity* 15(1): 159–172.

Kim, H.P., & Leonard, W.J., 2002. The basis for TCR-mediated regulation of the IL-2 receptor alpha chain gene: role of widely separated regulatory elements. *EMBO J.* 21(12): 3051-3059.

Klein-Hessling, S., Muhammad, K., Klein, M., Pusch, T., Rudolf, R., Flöter, J., *et al.*, 2017. NFATc1 controls the cytotoxicity of CD8⁺ T cells. *Nat. Commun.* 8(1): 511-526.

Kolan, S. S., Li, G., Wik, J. A., Malachin, G., Guo, S., Kolan, P., *et al.*, 2020. Cellular metabolism dictates T cell effector function in health and disease. *Scand. J. Immunol.* 92(5): e12956.

Kotak D.J., Todke P.A., Dandekar P., Devarajan P.V., 2019. CD Receptor and Targeting Strategies. In: Devarajan P., Dandekar P., D'Souza A. (Ed.): *Targeted Intracellular Drug Delivery by Receptor Mediated Endocytosis*. Springer, Cham.

Lamb, J. R., Skidmore, B. J., Green, N., Chiller, J. M., Feldmann, M., 1983. Induction of tolerance in influenza virus-immune T lymphocyte clones with synthetic peptides of influenza hemagglutinin. *J. Exp. Med.* 157(5): 1434–1447.

Lee, J. U., Kim, L. K., & Choi, J. M., 2018. Revisiting the Concept of Targeting NFAT to Control T Cell Immunity and Autoimmune Diseases. *Front. Immunol.* 9: 2747.

Lee, J. Y., Lee, J. H., Park, J. H., Kim, S. Y., Choi, J. Y., *et al.*, 2009. Liquiritigenin, a licorice flavonoid, helps mice resist disseminated candidiasis due to *Candida albicans* by Th1 immune response, whereas liquiritin, its glycoside form, does not. *Int. Immunopharmacol.* 9(5), 632–638.

Liu, H., Pan, W., Tang, C., Tang, Y., Wu. H., Yoshimura. A., *et al.*, 2021. The methods and advances of adaptive immune receptors repertoire sequencing. *Theranostics* 11(18): 8945-8963.

- Liu, Y., Wang, C., Dong, X., Cheng, D., Zhou, T., 2015. Immunomodulatory effects of epicatechin-(2 β →O→7, 4 β →8)-ent-epicatechin isolated from *Rhododendron spiciferum* in vitro. *Immunopharmacol. Immunotoxicol.* 37(6): 527–534.
- Liu, Y. N., Zha, W. J., Ma, Y., Chen, F. F., Zhu, W., *et al.*, 2015. Galangin attenuates airway remodelling by inhibiting TGF- β 1-mediated ROS generation and MAPK/Akt phosphorylation in asthma. *Sci. Rep.* 5: 11758.
- Liu, T., Zhang, L., Joo, D., Sun, S. C., 2017. NF- κ B signaling in inflammation. *Signal Transduct. Target. Ther.* 2: 17023.
- Los, M., Dröge, W., Stricker, K., Baeuerle, P. A., Schulze-Osthoff, K., 1995. *Hydrogen peroxide as a potent activator of T lymphocyte functions.* *Eur. J. Immunol.* 25(1): 159–165.
- Machiyama, H., Yamaguchi, T., Watanabe, T. M., Yanagida, T., Fujita, H., 2021. Activation probability of a single naïve T cell upon TCR ligation is controlled by T cells interacting with the same antigen-presenting cell. *FEBS Lett.* 595(11): 1512–1524.
- Macian, F., 2005. NFAT proteins: key regulators of T-cell development and function. Nature reviews. *Nat. Rev. Immunol.* 5(6): 472–484.
- Macian, F., 2016. Nuclear Factor of Activated T Cells and Tolerance. In: Bradshaw, R.A., Stahl, P. (Ed.): *Encyclopedia of Cell Biology*, pp: 573–579. Elsevier, USA
- MacIver, N. J., Michalek, R. D., Rathmell, J. C., 2013. Metabolic Regulation of T Lymphocytes. *Annu. Rev. Immunol.* 31(1): 259–283.
- Maher, M., Al-Dabbas, M., Otoom, H., 2019. Impact of honey color from Jordanian flora on total phenolic and flavonoids contents and antioxidant activity. *Fresenius Environmental Bulletin.* 28: 6898-6907.
- Majtan, J., Kováčová, E., Bíliková, K., & Simúth, J., 2006. The immunostimulatory effect of the recombinant apalbumin 1-major honeybee royal jelly protein-on TNF α release. *Int. Immunopharm.* 6(2): 269–278.
- Majtan, J., 2014. Honey: An immunomodulator in wound healing. *Wound Repair and Regen.* 22(2): 187–192.

- Mak, T.W., Saunders, M.E., 2006. *The Immune Response: Basic and Clinical Principles*. 1st ed. Academic Press, Toronto.
- Martino, A., Holmes, J. H., 4th, Lord, J. D., Moon, J. J., Nelson, B. H., 2001. Stat5 and Sp1 regulate transcription of the cyclin D2 gene in response to IL-2. *J. Immunol.* 166(3): 1723–1729
- Marshall, J. S., Warrington, R., Watson, W., Kim, H. L., 2018. An introduction to immunology and immunopathology. *Allergy Asthma Clin. Immunol.* 14(Suppl 2): 49.
- Martin, E. W., Chakraborty, S., Presman, D. M., Tomassoni Ardori, F., Oh, K. S., Kaileh, M., *et al.*, 2019. Assaying Homodimers of NF- κ B in Live Single Cells. *Front. Immunol.* 10: 2609.
- Martinez, G. J., Hu, J. K., Pereira, R. M., Crampton, J. S., Togher, S., Bild, N., Crotty, S., & Rao, A. (2016). Cutting Edge: NFAT Transcription Factors Promote the Generation of Follicular Helper T Cells in Response to Acute Viral Infection. *J. Immunol.* 196(5): 2015–2019.
- Masad, R. J., Haneefa, S. M., Mohamed, Y. A., Al-Sbiei, A., Bashir, G., Fernandez-Cabezudo, *et al.*, 2021. The Immunomodulatory Effects of Honey and Associated Flavonoids in Cancer. *Nutrients* 13(4): 1269.
- McIntyre, O. R., & Cole, A. F., 1969. Variation in the response of normal lymphocytes to PHA. *Int. Arch. Allergy appl. Immunol.* 35(2): 105–118.
- Medina K. L., 2016. Overview of the immune system. *Handb. Clin. Neurol.* 133: 61–76.
- Meininger, I. & Krappmann, D., 2016. Lymphocyte signaling and activation by the CARMA1-BCL10-MALT1 signalosome. *Biol. Chem.* 397(12): 1315–1333.
- Michalek, R. D., & Rathmell, J. C., 2010. The metabolic life and times of a T-cell. *Immunol. Rev.* 236: 190–202.
- Michalek, R. D., Gerriets, V. A., Jacobs, S. R., Macintyre, A. N., MacIver, N. J., Mason, E. F., *et al.*, 2011. Cutting edge: distinct glycolytic and lipid oxidative metabolic programs are essential for effector and regulatory CD4+ T cell subsets. *J. Immunol.* 186(6): 3299–3303.
- Miguel, M. G., Antunes, M. D., Faleiro, M. L., 2017. Honey as a Complementary Medicine. *Integr. Med. Insights.* 12: 1–15.

- Mishima, T., Fukaya, S., Toda, S., Ando, Y., Matsunaga, T., Inobe, M., 2017. Rapid G0/1 transition and cell cycle progression in CD8⁺ T cells compared to CD4⁺ T cells following in vitro stimulation. *Microbiol. Immunol.* 61(5): 168–175.
- Mognol, G. P., Carneiro, F. R., Robbs, B. K., Faget, D. V., Viola, J. P., 2016. Cell cycle and apoptosis regulation by NFAT transcription factors: new roles for an old player. *Cell Death Dis.* 7(4): e2199.
- Mognol, G. P., González-Avalos, E., Ghosh, S., Spreafico, R., Gudlur, A., Rao, A., *et al.*, 2019. Targeting the NFAT:AP-1 transcriptional complex on DNA with a small-molecule inhibitor. *Proc. Natl. Acad. Sci. U S A.* 116(20): 9959–9968.
- Morath, A., Deswal S., Schamel W.W.A., 2018. CD3. In: Choi S. (Ed.): *Encyclopedia of Signaling Molecules*. Springer, New York.
- Moriggl, R., Topham, D. J., Teglund, S., Sexl, V., McKay, C., Wang, D., *et al.*, 1999. Stat5 is required for IL-2-induced cell cycle progression of peripheral T cells. *Immunity* 10(2): 249–259.
- Mukherjee, P., Nema, N., Bhadra, S., Mukherjee, D., Braga, F., Matsabisa, M., 2014. Immunomodulatory leads from medicinal plants. *Indian J. Tradit. Knowl.* 13(2): 235-256.
- Muñoz-Carrillo, J.L., Rodriguez, F.P.C., Coronado, O.G., García, M.A.M., Cordero, J.F.C., 2017. Physiology and Pathology of Innate Immune Response Against Pathogens, Physiology and Pathology of Immunology. IntechOpen [serial online] [cited 2021 Aug 28] Available from: URL: <https://www.intechopen.com/chapters/56849>
- Muhammad, K., Alrefai, H., Marienfeld, R., Pham, D. A., Murti, K., Patra, A. K., *et al.*, 2014. NF- κ B factors control the induction of NFATc1 in B lymphocytes. *Eur. J. Immunol.* 44(11): 3392–3402.
- Nagoba, B., Davane, M., 2018. Natural Immunomodulators. *J. Immunol. Microbiol.* 2(1): 2
- Nazir, N., Koul, S., Qurishi, M. A., Taneja, S. C., Ahmad, S. F., *et al.*, 2009. Immunomodulatory activity of isoflavones isolated from *Iris germanica* (Iridaceae) on T-lymphocytes and cytokines. *Phytotherapy res.* 23(3), 428–433.

- Nikaein, D., Khosravi, A.R., Moosavi, Z., Shokri, H., Erfanmanesh, A., Ghorbani-Choboghlo, H., *et al.*, 2014. Effect of honey as an immunomodulator against invasive aspergillosis in BALB/c mice. *J. Apic. Res.* 53(1): 84-90
- Obst, R., 2015. The Timing of T Cell Priming and Cycling. *Front. Immunol.* 6: 563
- Oeckinghaus, A., Ghosh, S., 2009. The NF-kappaB family of transcription factors and its regulation. *Cold Spring Harb Perspect Biol.* 1(4): a000034.
- Oh, H., Ghosh, S., 2013. NF- κ B: roles and regulation in different CD4(+) T-cell subsets. *Immunol. Rev.* 252(1): 41–51.
- Olaitan, P. B., Adeleke, O. E., Ola, I. O., 2007. Honey: a reservoir for microorganisms and an inhibitory agent for microbes. *Afr. Health Sci.* 7(3): 159–165.
- Ott, C., Jacobs, K., Haucke, E., Navarrete Santos, A., Grune, T., Simm, A., 2014. Role of advanced glycation end products in cellular signaling. *Redox Biol.* 2: 411–429.
- Pamungkas, Z.Y., 2019. Potensi produksi madu hutan serta tegakan sebagai sumber polen dan nectar di hutan pendidikan Wanagama Gunungkidul Yogyakarta [Skripsi]. Universitas Gadjah Mada, Yogyakarta.
- Pavlova, T., Stamatovska, V., Stamatovska., Kalevska, T, Dimov, I., Nakov, G., 2019. Quality Characteristics of Honey: A Review. *Proc. Univ. RUSE.* 57(10): 31-37.
- Penhale, W. J., Farmer, A., Maccuish, A. C., Irvine, W. J., 1974. A rapid micro-method for the phytohaemagglutinin-induced human lymphocyte transformation test. *Clinic. Exp. Immunol.* 18(1): 155–167.
- Peng, Y., Kim, J. M., Park, H. S., Yang, A., Islam, C., Lakatta, E. G., *et al.*, 2016. AGE-RAGE signal generates a specific NF- κ B RelA "barcode" that directs collagen I expression. *Sci. Rep.* 6: 18822.
- Pennock, N. D., White, J. T., Cross, E. W., Cheney, E. E., Tamburini, B. A., Kedl, R. M., 2013. T cell responses: naive to memory and everything in between. *Adv. Physiology. Educ.* 37(4): 273–283.
- Podtschaske, M., Benary, U., Zwinger, S., Höfer, T., Radbruch, A., Baumgrass, R., 2007. Digital NFATc2 activation per cell transforms graded T cell receptor activation into an all-or-none IL-2 expression. *PloS one* 2(9): e935.

- Pont, J. N., McArdle, C. A., López Bernal, A., 2012. Oxytocin-stimulated NFAT transcriptional activation in human myometrial cells. *Mol. Endocrinol.* 26(10): 1743–1756.
- Powell, J. D., Lerner, C. G., Schwartz, R. H., 1999. Inhibition of cell cycle progression by rapamycin induces T cell clonal anergy even in the presence of costimulation. *J. Immunol.* 162(5): 2775–2784.
- Priatna, D. H., 2020. Pengaruh ekstraksi pemerasan dengan pemanasan dan tanpa pemanasan terhadap kualitas Madu Hutan Wanagama I desa Banaran kabupaten Gunungkidul Yogyakarta [Tugas akhir]. Universitas Gadjah Mada, Yogyakarta.
- Ramalingam, S., Cai, B., Wong, J., Twomey, M., Chen, R., Boote, T., *et al.*, 2018. Antiviral innate immune response in non-myeloid cells is augmented by chloride ions via an increase in intracellular hypochlorous acid levels. *Sci. Rep.* 8(1): 13630.
- Raynaud, A., Ghezali, L., Gloaguen, V., Liagre, B., Quero, F., Petit, J. M., 2013. Honey-induced macrophage stimulation: AP-1 and NF- κ B activation and cytokine production are unrelated to LPS content of honey. *Int. Immunopharmacol.* 17(3): 874–879.
- Reddy, S. P., Mossman, B. T. 2002., Role and regulation of activator protein-1 in toxicant-induced responses of the lung. *Am. J. Physiol. Lung cell. Mol. Physiol.* 283(6): L1161–L1178.
- Rhew, K. Y., & Han, Y., 2012. Immunoadjuvant activity of icariin that induces Th1-type antibody in mice. *Arch.Pharm. Res.* 35(9): 1685–1691
- Rivera, A., Siracusa, M., Yap, G., Gause, W.C., 2016. Innate cell communication kick-starts pathogen-specific immunity. *Nat. Immunol.* 17(4): 356–363.
- Rincón, M., & Flavell, R. A., 1994. AP-1 transcriptional activity requires both T-cell receptor-mediated and co-stimulatory signals in primary T lymphocytes. *EMBO J.* 13(18): 4370–4381.
- Rogerio, A. P., Kanashiro, A., Fontanari, C., da Silva, E. V., Lucisano-Valim, Y. M., *et al.*, 2007. Anti-inflammatory activity of quercetin and isoquercitrin in experimental murine allergic asthma. *Inflamm. Res.* 56(10): 402–408.

- Rojas, A., Figueroa, H., & Morales, E., 2009. Fueling inflammation at tumor microenvironment: the role of multiligand/rage axis. *Carcinogenesis* 31(3): 334–341.
- Ronnekleiv-Kelly, S. M., Nukaya, M., Díaz-Díaz, C. J., Megna, B. W., Carney, P. R., Geiger, P. G., & Kennedy, G. D. (2016). Aryl hydrocarbon receptor-dependent apoptotic cell death induced by the flavonoid chrysin in human colorectal cancer cells. *Cancer lett.* 370(1): 91–99.
- Roth-Walter, F., Jensen-Jarolim, E., Stockinger, H., 2013. Principles and Comparative Aspects of Adaptive Immunity. In: Jarolim, E.J (Ed.): *Comparative Medicine: Anatomy and Physiology*, pp: 243-266. Springer, Vienna.
- Salih, K., 2008. Effect of honey on the human lymphocytes culture and induced chronic inflammation in mice. *Al- Mustansiriya J. Sci.* 19(6): 1-10.
- Samarghandian, S., Farkhondeh, T., Samini, F., 2017. Honey and Health: A Review of Recent Clinical Research. *Pharmacogn. Res.* 9(2): 121–127.
- Sasaki, Y., & Iwai, K., 2015. Roles of the NF- κ B Pathway in B-Lymphocyte Biology. *Curr. Top. Microbiol. Immunol.* 393: 177–209.
- Schietinger, A., & Greenberg, P. D., 2014. Tolerance and exhaustion: defining mechanisms of T cell dysfunction. *Trends Immunol.* 35(2): 51–60.
- Schreck, R., Rieber, P., Baeuerle, P. A., 1991. Reactive oxygen intermediates as apparently widely used messengers in the activation of the NF-kappa B transcription factor and HIV-1. *EMBO J.* 10(8): 2247–2258.
- Shatrova, A. N., Mityushova, E. V., Vassilieva, I. O., Aksenov, N. D., Zenin, V. V., Nikolsky, N. N., *et al.*, 2016. Time-Dependent Regulation of IL-2R α -Chain (CD25) Expression by TCR Signal Strength and IL-2-Induced STAT5 Signaling in Activated Human Blood T Lymphocytes. *PloS one* 11(12): e0167215.
- Shi, M., Lin, T. H., Appell, K. C., Berg, L. J., 2009. Cell cycle progression following naive T cell activation is independent of Jak3/common gamma-chain cytokine signals. *J. Immunol.* 183(7): 4493–4501.
- Shin, S., Ye, M., Son, H., Kim, Y., 2017. Comparison of Manuka, Kanuka, and Black Locust honey on the production of chemical mediators by peripheral blood mononuclear cells. *J. Rhinol.* 24(2): 104-111.

- Silva, B., Biluca, F. C., Gonzaga, L. V., Fett, R., Dalmarco, E. M., Caon, T., *et al.*, 2021. In vitro anti-inflammatory properties of honey flavonoids: A review. *Food Res. Int.* 141: 110086.
- Smith, K., 2006. The quantal theory of immunity. *Cell Res.* 16: 11–19.
- Sparvero, L. J., Asafu-Adjei, D., Kang, R., Tang, D., Amin, N., Im, J., *et al.*, 2009. RAGE (Receptor for Advanced Glycation Endproducts), RAGE ligands, and their role in cancer and inflammation. *J. Transl. Med.* 7: 17
- Svehlikova, V., 2004. Interactions between sulforaphane and apigenin in the induction of UGT1A1 and GSTA1 in CaCo-2 cells. *Carcinog.* 25(9): 1629–1637.
- Tóbon-Velasco, J. C., Cuevas, E., Torres-Ramos, M. A., 2014., Receptor for AGEs (RAGE) as mediator of NF- κ B pathway activation in neuroinflammation and oxidative stress. *CNS Neurol. Disord. Drug Targets* 13(9): 1615–1626.
- Tomczyk, M., Tarapatsky, M., Dżugan, M., 2019. The influence of geographical origin on honey composition studied by Polish and Slovak honeys. *Czech J. Food Sci.* 37(4): 232-238.
- Tonks, A., Cooper, R. A., Price, A. J., Molan, P. C., Jones, K. P., 2001. Stimulation of TNF- α release in monocytes by honey. *Cytokine* 14(4): 240–242.
- Tonks, A. J., Dudley, E., Porter, N. G., Parton, J., Brazier, J., Smith, E. L., *et al.*, 2007. A 5.8-kDa component of manuka honey stimulates immune cells via TLR4. *J. Leukoc. Biol.* 82(5): 1147–1155.
- Tyagi, A., Agarwal, R., & Agarwal, C. , 2003. Grape seed extract inhibits EGF-induced and constitutively active mitogenic signaling but activates JNK in human prostate carcinoma DU145 cells: possible role in antiproliferation and apoptosis. *Oncogene* 22(9): 1302–1316
- Varadhachary, A. S., Perdow, S. N., Hu, C., Ramanarayanan, M., Salgame, P., 1997. Differential ability of T cell subsets to undergo activation-induced cell death. *Proc. Natl. Acad. Sci. USA.* 94(11): 5778–5783.
- Verhoeckx, K., Cotter, P., López-Expósito, I., Kleiveland, C., Lea, T., Mackie, A., *et al.* (Eds.), 2015. *The Impact of Food Bioactives on Health: in vitro and ex vivo models*. Springer, New York.

- Virtue, A., Wang, H., & Yang, X. F., 2012. MicroRNAs and toll-like receptor/interleukin-1 receptor signaling. *J. Hematol. Oncol.* 5: 66.
- Vollgraf, U., Wegner, M., & Richter-Landsberg, C., 1999. Activation of AP-1 and nuclear factor-kappaB transcription factors is involved in hydrogen peroxide-induced apoptotic cell death of oligodendrocytes. *J. Neurochem.* 73(6): 2501–2509.
- Von Brandenstein, M. G., Ngum Abety, A., Depping, R., Roth, T., Koehler, M., Dienes, H. P., et al., 2008. A p38-p65 transcription complex induced by endothelin-1 mediates signal transduction in cancer cells. *Biochim. Biophys. Acta.* 1783(9): 1613–1622.
- Wan Yusuf, W. N., Wan Mohammad, W., Gan, S. H., Mustafa, M., Abd Aziz, C. B., Sulaiman, S. A., 2018. Tualang honey ameliorates viral load, CD4 counts and improves quality of life in asymptomatic human immunodeficiency virus infected patients. *J. Tradit. Complement. Med.* 9(4): 249–256.
- Wang, R., Natarajan, K., Margulies, D. H., 2009. Structural basis of the CD8 alpha beta/MHC class I interaction: focused recognition orients CD8 beta to a T cell proximal position. *J. Immunol.* 183(4): 2554–2564.
- Wook Chung, Y., Jeong, D., Yun Won, J., Choi, E.-J., Hyun Choi, Y., & Young Kim, I., 2002. H₂O₂-induced AP-1 activation and its effect on p21WAF1/CIP1-mediated G2/M arrest in a p53-deficient human lung cancer cell. *Biochem. Biophys. Res. Commun.* 293(4): 1248–1253.
- Wolf, T., Jin, W., Zoppi, G., Vogel, I.A, Akhmedov, M., Bleck, C.K.E., et al., 2020. Dynamics in protein translation sustaining T cell preparedness. *Nat. Immunol.* 21: 927–937.
- Wu, Z., Nicoll, M., & Ingham, R. J. 2021., AP-1 family transcription factors: a diverse family of proteins that regulate varied cellular activities in classical hodgkin lymphoma and ALK+ ALCL. *Exp. Hematol. Oncol.* 10(1): 4.
- Xia, F., Qian, C. R., Xun, Z., Hamon, Y., Sartre, A. M., Formisano, A., et al., 2018. TCR and CD28 concomitant stimulation elicits a distinctive calcium response in naive T cells. *Front. Immunol.* 9: 2864.
- Xiao, Z. J., Liu, J., Wang, S. Q., Zhu, Y., Gao, X. Y., Tin, V. P., et al., 2017. NFATc2 enhances tumor-initiating phenotypes through the NFATc2/SOX2/ALDH axis in lung adenocarcinoma. *eLife* 6: e26733.

- Xu, Z., Bu, Y., Chitnis, N., Koumenis, C., Fuchs, S. Y., Diehl, J. A., 2016. miR-216b regulation of c-Jun mediates GADD153/CHOP-dependent apoptosis. *Nat. Commun.* 7: 11422
- Yang, Z. Z., Grote, D. M., Ziesmer, S. C., Manske, M. K., Witzig, T. E., Novak, *et al.*, 2011. Soluble IL-2R α facilitates IL-2-mediated immune responses and predicts reduced survival in follicular B-cell non-Hodgkin lymphoma. *Blood* 118(10): 2809–2820.
- Yano, T., Hagiwara, Y., Ando, A., Kanazawa, K., Koide, M., Sekiguchi, T., *et al.*, 2020. RAGE-dependent NF- κ B inflammation processes in the capsule of frozen shoulders. *J. Shoulder Elbow Surg.* 29(9): 1884–1891.
- Yazdi, A. S., Drexler, S. K., Tschopp, J., 2010. The role of the inflammasome in nonmyeloid cells. *J. Clin. Immunol.* 30(5): 623–627.
- Ye, N., Ding, Y., Wild, C., Shen, Q., & Zhou, J., 2014. Small molecule inhibitors targeting activator protein 1 (AP-1). *J. Med. Chem.* 57(16): 6930–6948.
- Yeh, J. H., Spicuglia, S., Kumar, S., Sanchez-Sevilla, A., Ferrier, P., Imbert, J., 2002. Control of IL-2R α gene expression: structural changes within the proximal enhancer/core promoter during T-cell development. *Nucleic Acids Res.* 30(9), 1944–1951.
- Yelin, A., Kuntadi., 2019. *Phytochemical identification of honey from several regions in Java and Sumbawa. International Conference On Biology And Applied Science (ICOBAS).*
- Yi, B., Hu, X., Zhang, H., Huang, J., Liu, J., Hu, *et al.*, 2014. Nuclear NF- κ B p65 in peripheral blood mononuclear cells correlates with urinary MCP-1, RANTES and the severity of type 2 diabetic nephropathy. *PloS one.* 9(6): e99633.
- Yin, J., Duan, J., Cui, Z., Ren, W., Li, T., & Yin, Y., 2015. Hydrogen peroxide-induced oxidative stress activates NF- κ B and Nrf2/Keap1 signals and triggers autophagy in piglets. *RSC Adv.* 5(20): 15479–15486.
- Yoshida, H., Nishina, H., Takimoto, H., Marengère, L. E., Wakeham, A. C., Bouchard, D., *et al.*, 1998. The transcription factor NF-ATc1 regulates lymphocyte proliferation and Th2 cytokine production. *Immunity* 8(1): 115–124

- Yoshimura, T., Galligan, C., Takahashi, M., Chen, K., Liu, M., Tessarollo, L., *et al.*, 2014. Non-myeloid cells are major contributors to innate immune responses via production of monocyte chemoattractant protein-1/CCL2. *Front. Immunol.* 4: 482.
- Yu, H., Lin, L., Zhang, Z., Zhang, H., & Hu, H., 2020. Targeting NF- κ B pathway for the therapy of diseases: mechanism and clinical study. *Signal Transduct Target Ther.* 5(1): 209.
- Yukawa, M., Jagannathan, S., Vallabh, S., Kartashov, A. V., Chen, X., Weirauch, M. T., *et al.*, 2020. AP-1 activity induced by co-stimulation is required for chromatin opening during T cell activation. *J. Exp. Med.* 217(1): e20182009.