



DAFTAR PUSTAKA

- Aaro, T., Jaana, R., Reidar, G., Kari, S., & Stina, S. 2017. Epstein-Barr virus (EBV)-encoded small RNAs (EBERs) associated with poor prognosis of head and neck carcinomas. *Oncotarget*, 8(16): 27328–27338. doi: 10.18632/oncotarget.16033.
- Adam, A. A. M., Abdullah, N. E., El Hassan, L. A. M., Elamin, E. M., Ibrahim, M. E., & El Hassan, A. M. 2014. Detection of Epstein-Barr Virus in Nasopharyngeal Carcinoma in Sudanese by in Situ Hybridization. *Journal of Cancer Therapy*, 05(06), 517–522. <https://doi.org/10.4236/jct.2014.56059>.
- Adham, M., Greijer, A. E., Verkuijlen, S. A. W. M., Juwana, H., Fleig, S., Rachmadi, L., Malik, O., Kurniawan, A. N., Roezin, A., Gondhowiardjo, S., Atmakusumah, D., Stevens, S. J. C., Hermani, B., Bing Tan, I., & Middeldorp, J. M. 2013. Epstein-barr virus DNA load in nasopharyngeal brushings and whole blood in nasopharyngeal carcinoma patients before and after treatment. *Clinical Cancer Research*, 19(8), 2175–2186. <https://doi.org/10.1158/1078-0432.CCR-12-2897>.
- Adham, M., Kurniawan, A. N., Muhtadi, A. I., Roezin, A., Hermani, B., Gondhowiardjo, S., Tan, I. B., & Middeldorp, J. M. 2012. Nasopharyngeal Carcinoma in Indonesia: epidemiology, incidence, signs and symptoms at presentation. *Chinese Journal of Cancer*, 31(4), 185–196.
- Aga, M., Bentz, G. L., Raffa, S., Torrisi, M. R., Kondo, S., Wakisaka, N., Yoshizaki, T., Pagano, J. S., & Shackelford, J. 2014. Exosomal HIF1 α supports invasive potential of nasopharyngeal carcinoma-associated LMP1-positive exosomes. *Oncogene*, 33(37), 4613–4622. <https://doi.org/10.1038/onc.2014.66>.
- Aggarwal, B. B. 2003. Signalling pathways of the TNF superfamily: A double-edged sword. *Nature Reviews Immunology*, 3(9), 745–756. <https://doi.org/10.1038/nri1184>.
- Ahmed, W., Philip, P. S., Tariq, S., & Khan, G. 2014. Epstein-Barr virus-encoded small RNAs (EBERs) are present in fractions related to exosomes released by EBV-transformed cells. *PLoS ONE*, 9(6). <https://doi.org/10.1371/journal.pone.0099163>.
- Aliyah, S., Ardiyan, Y., Mardhiyah, I., Herdini, camelia, Dwianingsih, E., Aning, S., Handayani, N. S., Asmara, W., Fachiroh, J., & Paramita, D. 2021. The Distribution of M2 Macrophage and Treg in Nasopharyngeal Carcinoma Tumor Tissue and the Correlation with TNM Status and Clinical Stage. *Asian Pacific Journal of Cancer Prevention*, 22(11), 3447–3453. <https://doi.org/10.31557/apjcp.2021.22.11.3447>.
- Anita, K. W., Putranto, B. E., Prasetyo, A., & Paramita, D. K. 2015. *Ekspresi EBER pada Berbagai Tipe Histopatologi Karsinoma Nasofaring*. 24(1), 7–11.
- Ataie-Kachoie, P., Pourgholami, M. H., & Morris, D. L. 2013. Inhibition of the IL-6 signaling pathway: A strategy to combat chronic inflammatory diseases and cancer. *Cytokine and Growth Factor Reviews*. 24(2): 163-173. <https://doi.org/10.1016/j.cytogfr.2012.09.001>.
- Azuma, M., Matsuo, A., Fujimoto, Y., Fukase, K., Hazeki, K., Hazeki, O.,

- Matsumoto, M., & Seya, T. 2007. Inhibition of lipid A-mediated type I interferon induction by Bactericidal/permeability-increasing protein (BPI). *Biochemical and Biophysical Research Communications*, 354(2):574-578. <https://doi.org/10.1016/j.bbrc.2007.01.019>.
- Balkwill, F. 2009. Tumour necrosis factor and cancer. *Nature Reviews Cancer*, 9(5), 361–371. <https://doi.org/10.1038/nrc2628>.
- Baumforth, K. R. N., Birgersdotter, A., Reynolds, G. M., Wei, W., Kapatai, G., Flavell, J. R., Kalk, E., Piper, K., Lee, S., Machado, L., Hadley, K., Sundblad, A., Sjoberg, J., Bjorkholm, M., Porwit, A. A., Yap, L. F., Teo, S., Grundy, R. G., Young, L. S., Murray, P. G. 2008. Expression of the Epstein-Barr virus-encoded Epstein-Barr virus nuclear antigen 1 in Hodgkin's lymphoma cells mediates up-regulation of CCL20 and the migration of regulatory T cells. *American Journal of Pathology*. 173(1):195-204. <https://doi.org/10.2353/ajpath.2008.070845>.
- Birbrair, A., Zhang, T., Wang, Z.-M., Messi, M. L., Olson, J. D., Mintz, A., & Delbono, O. 2014. Type-2 pericytes participate in normal and tumoral angiogenesis. *AJP: Cell Physiology*. 307(1):C25-38. <https://doi.org/10.1152/ajpcell.00084.2014>.
- Biswas, S. K., & Mantovani, A. 2010. Macrophage plasticity and interaction with lymphocyte subsets: Cancer as a paradigm. *Nature Immunology*. 11(10): 889-896. <https://doi.org/10.1038/ni.1937>.
- Bray, F., Ferlay, J., & Soerjomataram, I. 2018. Global Cancer Statistics 2018: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA: a cancer journal for clinicians*, 68(6), 394–424. <https://doi.org/10.3322/caac.21492>.
- Brown, J., Wang, H., Hajishengallis, G. N., & Martin, M. 2011. TLR-signaling networks: An integration of adaptor molecules, kinases, and cross-talk. *Journal of Dental Research*. 90(4): 417-427. <https://doi.org/10.1177/0022034510381264>.
- Bugge, M., Bergstrom, B., Eide, O. K., Solli, H., Kjønstad, I. F., Stenvik, J., Espevik, T., & Nilsen, N. J. 2017. Surface toll-like receptor 3 expression in metastatic intestinal epithelial cells induces inflammatory cytokine production and promotes invasiveness. *Journal of Biological Chemistry*, 292(37):15408-15425. <https://doi.org/10.1074/jbc.M117.784090>.
- Cai, L. M., Lyu, X. M., Luo, W. R., Cui, X. F., Ye, Y. F., Yuan, C. C., Peng, Q. X., Wu, D. H., Liu, T. F., Wang, E., Marincola, F. M., Yao, K. T., Fang, W. Y., Cai, H. B., & Li, X. 2015. EBV-miR-BART7-3p promotes the EMT and metastasis of nasopharyngeal carcinoma cells by suppressing the tumor suppressor PTEN. *Oncogene*. 34(17):2155-2166. <https://doi.org/10.1038/onc.2014.341>.
- Cai, L., Ye, Y., Jiang, Q., Chen, Y., Lyu, X., Li, J., Wang, S., Liu, T., Cai, H., Yao, K., Li, J. L., & Li, X. 2015. Epstein-Barr virus-encoded microRNA BART1 induces tumour metastasis by regulating PTEN-dependent pathways in nasopharyngeal carcinoma. *Nature Communications*. 2(6):7353. <https://doi.org/10.1038/ncomms8353>
- Cai, T. T., Ye, S. B., Liu, Y. N., He, J., Chen, Q. Y., Mai, H. Q., Zhang, C. X., Cui,



- J., Zhang, X. S., Busson, P., Zeng, Y. X., & Li, J. 2017. LMP1-mediated glycolysis induces myeloid-derived suppressor cell expansion in nasopharyngeal carcinoma. *PLoS Pathogens*, 13(7):e1006503. <https://doi.org/10.1371/journal.ppat.1006503>.
- Cao, S.M., Liu, Z., Jia, W.-H., Huang, Q.-H., Liu, Q., Guo, X., Huang, T.-B., Ye, W., & Hong, M.-H. 2011. Fluctuations of Epstein-Barr Virus Serological Antibodies and Risk for Nasopharyngeal Carcinoma: A Prospective Screening Study with a 20-Year Follow-Up. *PLoS ONE*. 6(4):e19100. <https://doi.org/10.1371/journal.pone.0019100>.
- Chan, J. Y. W., Gao, W., Ho, W. K., Wei, W. I., & Wong, T. S. 2012. Overexpression of epstein-barr virus-encoded microRNA-BART7 in undifferentiated nasopharyngeal carcinoma. *Anticancer Research*. 32(8):3201-3210. <https://doi.org/32/8/3201>.
- Chang, A. L., Miska, J., Wainwright, D. A., Dey, M., Rivetta, C. V., Yu, D., Kanojia, D., Pituch, K. C., Qiao, J., Pytel, P., Han, Y., Wu, M., Zhang, L., Horbinski, C. M., Ahmed, A. U., & Lesniak, M. S. 2016. CCL2 produced by the glioma microenvironment is essential for the recruitment of regulatory t cells and myeloid-derived suppressor cells. *Cancer Research*. 76(19):5671-5682. <https://doi.org/10.1158/0008-5472.CAN-16-0144>.
- Chang, K. P., Chang, Y. T., Wu, C. C., Liu, Y. L., Chen, M. C., Tsang, N. M., Hsu, C. L., Chang, Y. S., & Yu, J. S. 2011. Multiplexed immunobead-based profiling of cytokine markers for detection of nasopharyngeal carcinoma and prognosis of patient survival. *Head and Neck*. 33(6):886-897. <https://doi.org/10.1002/hed.21557>.
- Chao, T. Y., Chow, K. C., Chang, J. Y., Wang, C. C., Tsao, T. Y., Harn, H. J., & Chi, K. H. 1996. Expression of Epstein-Barr virus-encoded RNAs as a marker for metastatic undifferentiated nasopharyngeal carcinoma. *Cancer*, 78(1). [https://doi.org/10.1002/\(SICI\)1097-0142\(19960701\)78:1<24::AID-NCR5>3.0.CO;2-H](https://doi.org/10.1002/(SICI)1097-0142(19960701)78:1<24::AID-NCR5>3.0.CO;2-H).
- Chaudhary, B., & Elkord, E. 2016. Regulatory T Cells in the Tumor Microenvironment and Cancer Progression: Role and Therapeutic Targeting. *Vaccines*. 4(3):28. <https://doi.org/10.3390/vaccines4030028>.
- Chen, F., Zhuang, X., Lin, L., Yu, P., Wang, Y., Shi, Y., Hu, G., & Sun, Y. 2015. New horizons in tumor microenvironment biology: challenges and opportunities. *BMC Medicine*. 13:45. <https://doi.org/10.1186/s12916-015-0278-7>.
- Chen, J., Li, G., Meng, H., Fan, Y., Song, Y., Wang, S., Zhu, F., Guo, C., Zhang, L., & Shi, Y. 2012. Upregulation of B7-H1 expression is associated with macrophage infiltration in hepatocellular carcinomas. *Cancer Immunology, Immunotherapy*. 61(1):101-108. <https://doi.org/10.1007/s00262-011-1094-3>.
- Chen, L., Li, N., & Luo, C. 2012. Vaccines and Antiviral Drugs for Diseases Associated with the Epstein-Barr Virus. *Viral Genomes - Molecular Structure, Diversity, Gene Expression Mechanisms and Host-Virus Interactions*. <https://doi.org/10.5772/26735>.



- Chen, Y., Song, Y., Du, W., Gong, L., Chang, H., & Zou, Z. 2019. Tumor-associated macrophages: An accomplice in solid tumor progression. *Journal of Biomedical Science*, 26(1):78. <https://doi.org/10.1186/s12929-019-0568-z>.
- Cheng, J., Cai, Y., Zheng, Y., Li, J., & Mo, Y. 2009. Analysis of serum levels of IgA antibodies to Epstein-Barr virus capsid antigens in spouses and children of patients with nasopharyngeal carcinoma. *Chinese Journal of Clinical Oncology*, 36(18):267-270. <https://doi.org/10.3969/j.issn.1000-8179.2009.18.006>.
- Chew, V., Tow, C., Huang, C., Bard-Chapeau, E., Copeland, N. G., Jenkins, N. A., Weber, A., Lim, K. H., Toh, H. C., Heikenwalder, M., Ng, I. O. L., Nardin, A., & Abastado, J. P. 2012. Toll-like receptor 3 expressing tumor parenchyma and infiltrating natural killer cells in hepatocellular carcinoma patients. *Journal of the National Cancer Institute*, 104(23). <https://doi.org/10.1093/jnci/djs436>.
- Cho, H. J., Jung, J. I., Lim, D. Y., Kwon, G. T., Her, S., Park, J. H., & Park, J. H. Y. 2012. Bone marrow-derived, alternatively activated macrophages enhance solid tumor growth and lung metastasis of mammary carcinoma cells in a Balb/C mouse orthotopic model. *Breast Cancer Research: BCR*. 14(3):R18. <https://doi.org/10.1186/bcr3195>.
- Chow, K. C., Chiou, S. H., Ho, S. P., Tsai, M. H., Chen, C. L., Wang, L. S., & Chi, K. H. 2003. The elevated serum interleukin-6 correlates with the increased serum butyrate level in patients with nasopharyngeal carcinoma. *Oncology Reports*, 10(4), 813–819. <https://doi.org/10.3892/or.10.4.813>.
- Choy, E. Y.W., Siu, K.L., Kok, K.H., Lung, R. W.M., Tsang, C. M., To, K.F., Kwong, D. L.-W., Tsao, S. W., & Jin, D.-Y. 2008. An Epstein-Barr virus-encoded microRNA targets PUMA to promote host cell survival. *The Journal of Experimental Medicine*. 205(11):2551-2560. <https://doi.org/10.1084/jem.20072581>.
- Chrestella, J., Farhat, F., Daulay, E. R., Asnir, R. A., Yudhistira, A., & Nasution, I. A. 2018. Cyclooxygenase-2 Expression and Its Correlation with Primary Tumor Size and Lymph Node Involvement in Nasopharyngeal Carcinoma. *Open Access Maced J Med Sci.*, 6(11), 2001–2005.
- Chua, D. T. T., Sham, J. S. T., Kwong, D. L. W., & Au, G. K. H. 2003. Treatment outcome after radiotherapy alone for patients with Stage I-II nasopharyngeal carcinoma. *Cancer*. 98(1):74-80. <https://doi.org/10.1002/cncr.11485>.
- Chua, M. L. K., Wee, J. T. S., Hui, E. P., & Chan, A. T. C. 2016. Nasopharyngeal carcinoma. *The Lancet*, 387(10022), 1012–1024. [https://doi.org/10.1016/S0140-6736\(15\)00055-0](https://doi.org/10.1016/S0140-6736(15)00055-0).
- Chuang, H. C., Chou, M. H., Chien, C. Y., Chuang, J. H., & Liu, Y. L. 2018. Triggering TLR3 pathway promotes tumor growth and cisplatin resistance in head and neck cancer cells. *Oral Oncology*, 86:141-149. <https://doi.org/10.1016/j.oraloncology.2018.09.015>.
- Clarke, P. A., Sharp, N. A., & Clemens, M. J. 1990. Translational control by the Epstein-Barr virus small RNA EBER-1: Reversal of the double-stranded RNA-induced inhibition of protein synthesis in reticulocyte lysates. *European*



- Journal of Biochemistry.* 193(3):635-641. <https://doi.org/10.1111/j.1432-1033.1990.tb19381.x>.
- Clear, A. J., Lee, A. M., Calaminici, M., Ramsay, A. G., Morris, K. J., Hallam, S., Kelly, G., MacDougall, F., Lister, T. A., & Gribben, J. G. 2010. Increased angiogenic sprouting in poor prognosis FL is associated with elevated numbers of CD163+ macrophages within the immediate sprouting microenvironment. *Blood.* 115(24):5053-5056. <https://doi.org/10.1182/blood-2009-11-253260>.
- Condeelis, J., & Pollard, J. W. 2006. Macrophages: Obligate partners for tumor cell migration, invasion, and metastasis. *Cell.* 124(2):263-266. <https://doi.org/10.1016/j.cell.2006.01.007>.
- Conroy, H., Marshall, N. A., & Mills, K. H. G. 2008. TLR ligand suppression or enhancement of Treg cells? A double-edged sword in immunity to tumours. *Oncogene.* 27(2):168-180. <https://doi.org/10.1038/sj.onc.1210910>.
- Correia, S., Bridges, R., Wegner, F., Venturini, C., Palser, A., Middeldorp, J. M., Cohen, J. I., Lorenzetti, M. A., Bassano, I., White, R. E., Kellam, P., Breuer, J., & Farrell, J. 2018. Sequence Variation of Epstein-Barr Virus: Viral Types, Geography, Codon Usage, and Diseases. *Journal of virology,* 92(22), e01132-18. <https://doi.org/10.1128/JVI.01132-18>.
- Curiel, T. J., Coukos, G., Zou, L., Alvarez, X., Cheng, P., Mottram, P., Evdemon-Hogan, M., Conejo-Garcia, J. R., Zhang, L., Burow, M., Zhu, Y., Wei, S., Kryczek, I., Daniel, B., Gordon, A., Myers, L., Lackner, A., Disis, M. L., Knutson, K. L., Zou, W. 2004. Specific recruitment of regulatory T cells in ovarian carcinoma fosters immune privilege and predicts reduced survival. *Nature Medicine.* 10(9):942-929. <https://doi.org/10.1038/nm1093>.
- Daurkin, I., Eruslanov, E., Stoffs, T., Perrin, G. Q., Algood, C., Gilbert, S. M., Rosser, C. J., Su, L. M., Vieweg, J., & Kusmartsev, S. 2011. Tumor-associated macrophages mediate immunosuppression in the renal cancer microenvironment by activating the 15-lipoxygenase-2 pathway. *Cancer Research.* 71(20):6400-6409. <https://doi.org/10.1158/0008-5472.CAN-11-1261>.
- De Bock, K., Cauwenberghs, S., & Carmeliet, P. 2011. Vessel abnormalization: Another hallmark of cancer? Molecular mechanisms and therapeutic implications. *Current Opinion in Genetics and Development.* 21(1): 73-79. <https://doi.org/10.1016/j.gde.2010.10.008>.
- de Martel, C., & Franceschi, S. 2009. Infections and cancer: Established associations and new hypotheses. *Critical Reviews in Oncology/Hematology.* 70(3):183-194. <https://doi.org/10.1016/j.critrevonc.2008.07.021>.
- Denning, T. L., Wang, Y. C., Patel, S. R., Williams, I. R., & Pulendran, B. 2007. Lamina propria macrophages and dendritic cells differentially induce regulatory and interleukin 17-producing T cell responses. *Nature Immunology.* 8(10):1086-1094. <https://doi.org/10.1038/ni1511>.
- Devi, B. C. R., Pisani, P., Tang, T. S., & Parkin, D. M. 2004. High incidence of nasopharyngeal carcinoma in native people of Sarawak, Borneo Island. *Cancer Epidemiology Biomarkers and Prevention.* 13(3):482-486.



- Ding, N., Yu, R. T., Subramaniam, N., Sherman, M. H., Wilson, C., Rao, R., Leblanc, M., Coulter, S., He, M., Scott, C., Lau, S. L., Atkins, A. R., Barish, G. D., Gunton, J. E., Liddle, C., Downes, M., & Evans, R. M. 2013. A vitamin D receptor/SMAD genomic circuit gates hepatic fibrotic response. *Cell.* 153(3):601-613. <https://doi.org/10.1016/j.cell.2013.03.028>.
- Dirk M. Pegtel, Jaap Middeldorp, and D. A. T.-L. 2004. Epstein-Barr Virus Infection in Ex Vivo Tonsil Epithelial Cell Cultures of Asymptomatic Carriers. *Journal of Virology.* 78(22):12613-24. <https://doi.org/10.1128/JVI.78.22.12613-12624.2004>.
- Dong, H., Strome, S. E., Salomao, D. R., Tamura, H., Hirano, F., Flies, D. B., Roche, P. C., Lu, J., Zhu, G., Tamada, K., Lennon, V. A., Celis, E., & Chen, L. 2002. Tumor-associated B7-H1 promotes T-cell apoptosis: a potential mechanism of immune evasion. *Nature Medicine.* 8(8):793-800. <https://doi.org/10.1038/nm730>.
- Donohoe, C. L., Ofarrell, N. J., Doyle, S. L., & Reynolds, J. V. 2014. The role of obesity in gastrointestinal cancer: Evidence and opinion. *Therapeutic Advances in Gastroenterology.* 7(1):38-50. <https://doi.org/10.1177/1756283X13501786>.
- Dranoff, G. 2004. Cytokines in cancer pathogenesis and cancer therapy. *Nature Reviews Cancer.* 4(1):11-22. <https://doi.org/10.1038/nrc1252>.
- Duan, Y., Li, Z., Cheng, S., Chen, Y., Zhang, L., He, J., Liao, Q., Yang, L., Gong, Z., & Sun, L.Q. 2015. Nasopharyngeal carcinoma progression is mediated by EBER-triggered inflammation via the RIG-I pathway. *Cancer Letters.* 361(1), 67–74. <https://doi.org/10.1016/j.canlet.2015.02.037>.
- Dunn, G. P., Old, L. J., & Schreiber, R. D. 2004. The Three Es of Cancer Immunoediting. *Annual Review of Immunology.* 22:329-60 <https://doi.org/10.1146/annurev.immunol.22.012703.104803>.
- EI-Naggar A.K., Chan J.K.C., Grandis J.R., Takata T., S. P. J. (Eds). 2017. WHO classification of Head and neck Tumors (4th edition). In *WHO classification of Head and neck Tumors (4th edition)*.
- Erreni, M., Mantovani, A., & Allavena, P. 2011. Tumor-associated macrophages (TAM) and inflammation in colorectal cancer. *Cancer Microenvironment.* 4(2): 141-154. <https://doi.org/10.1007/s12307-010-0052-5>.
- Ewald, S. E., Engel, A., Lee, J., Wang, M., Bogyo, M., & Barton, G. M. 2011. Nucleic acid recognition by Toll-like receptors is coupled to stepwise processing by cathepsins and asparagine endopeptidase. *The Journal of Experimental Medicine,* 208(4), 643–651. <https://doi.org/10.1084/jem.20100682>.
- Facciabene, A., Motz, G. T., & Coukos, G. 2013. T Regulatory Cells: Key Players in Tumor Immune Escape and Angiogenesis Andrea. *Cancer Res.*, 72(9), 2162–2171. <https://doi.org/10.1158/0008-5472.CAN-11-3687>.
- Fachiroh, J., Paramita, D. K., Hariwiyanto, B., Harijadi, A., Dahlia, H. L., Indrasari, S. R., Kusumo, H., Zeng, Y. S., Schouten, T., Mubarika, S., & Middeldorp, J. M. 2006. Single-assay combination of Epstein-Barr virus (EBV) EBNA1- and viral capsid antigen-p18-derived synthetic peptides for measuring anti-EBV

- immunoglobulin G (IgG) and IgA antibody levels in sera from nasopharyngeal carcinoma patients. *Journal of Clinical Microbiology.* 44(4):1459-1467. <https://doi.org/10.1128/JCM.44.4.1459-1467.2006>.
- Fachiroh, J., Schouten, T., Hariyanto, B., Paramita, D. K., Harijadi, A., Haryana, S. M., Ng, M. H., & Middeldorp, J. M. 2004. Molecular Diversity of Epstein-Barr Virus IgG and IgA Antibody Responses in Nasopharyngeal Carcinoma: A Comparison of Indonesian, Chinese, and European Subjects. *Journal of Infectious Diseases,* 190(1), 53–62. <https://doi.org/10.1086/421245>.
- Fang, R., Jiang, Q., Guan, Y., Gao, P., Zhang, R., Zhao, Z., & Jiang, Z. 2021. Golgi apparatus-synthesized sulfated glycosaminoglycans mediate polymerization and activation of the cGAMP sensor STING. *Immunity,* 54(5):962-957. <https://doi.org/10.1016/j.immuni.2021.03.011>.
- Farhat, A. R. A., Yudhistira, A., Susilo, R. R., Daulay, E. R., & Chrestella, J. 2018. Correlation of TNF- α expression to clinical stadium in Nasopharyngeal Carcinoma (NPC). *Stem Cell Oncology.* 129-132. <https://doi.org/10.1201/9781351190152-28>.
- Farias, T. P., Dias, F. L., Lima, R. A., Kligerman, J., De Sá, G. M., Barbosa, M. M., & Goncalves, J. F. B. 2003. Prognostic factors and outcome for nasopharyngeal carcinoma. *Archives of Otolaryngology - Head and Neck Surgery.* 129(7):794-799. <https://doi.org/10.1001/archotol.129.7.794>.
- Fles, R., Wildeman, M. A., Sulistiono, B., Haryana, S. M., & Tan, I. B. 2010. Knowledge of general practitioners about nasopharyngeal cancer at the Puskesmas in Yogyakarta, Indonesia. *BMC Medical Education.* 10:81. <https://doi.org/10.1186/1472-6920-10-81>.
- Foong, Y. T., Cheng, H. M., Sam, C. K., Dillner, J., Hinderer, W., & Prasad, U. 1990. Serum and salivary IgA antibodies against a defined epitope of the Epstein-Barr virus nuclear antigen (EBNA) are elevated in nasopharyngeal carcinoma. *International Journal of Cancer,* 45(6):1061-1064. <https://doi.org/10.1002/ijc.2910450614>.
- Frappier, L. 2012. Contributions of Epstein-Barr nuclear antigen 1 (EBNA1) to cell immortalization and survival. *Viruses.* 4(9):1537-1547. <https://doi.org/10.3390/v4091537>.
- Fu, S., Li, J. S., Dias-Ribeiro, E., Freire, J. C. P., Sun, S., & Fan, S. 2019. Aggressive surgical resection of enormous cervical metastasis from nasopharyngeal carcinoma. *Acta Stomatologica Croatica,* 53(2), 168–173. <https://doi.org/10.15644/asc53/2/9>.
- Fu, X. L., Duan, W., Su, C. Y., Mao, F. Y., Lv, Y. P., Teng, Y. S., Yu, P. W., Zhuang, Y., & Zhao, Y. L. 2017. Interleukin 6 induces M2 macrophage differentiation by STAT3 activation that correlates with gastric cancer progression. *Cancer Immunology, Immunotherapy.* 66(12):1597-1608. <https://doi.org/10.1007/s00262-017-2052-5>.
- Galdiero, M. R., Garlanda, C., Jaillon, S., Marone, G., & Mantovani, A. 2013. Tumor associated macrophages and neutrophils in tumor progression. *Journal of*



- Cellular Physiology*, 228(7), 1404–1412. <https://doi.org/10.1002/jcp.24260>.
- Hamid, G. A. 2021. Epidemiology and Outcomes of Nasopharyngeal Carcinoma. Pharynx - Diagnosis and Treatment. *InTechOpen*. <https://doi.org/10.5772/intechopen.96802>.
- Garrido, F., Romero, I., Aptsiauri, N., & Garcia-Lora, A. M. 2016. Generation of MHC class I diversity in primary tumors and selection of the malignant phenotype. *International Journal of Cancer*. 138(2):271-280. <https://doi.org/10.1002/ijc.29375>.
- Gilbert, C. A., & Slingerland, J. M. 2013. Cytokines, Obesity, and Cancer: New Insights on Mechanisms Linking Obesity to Cancer Risk and Progression. *Annual Review of Medicine*. 64:45-57. <https://doi.org/10.1146/annurev-med-121211-091527>.
- Gobert, M., Treilleux, I., Bendriss-Vermare, N., Bachelot, T., Goddard-Leon, S., Arfl, V., Biota, C., Doffin, A. C., Durand, I., Olive, D., Perez, S., Pasqual, N., Faure, C., Ray-Coquard, I., Puisieux, A., Caux, C., Blay, J. Y., & Ménétrier-Caux, C. 2009. Regulatory T cells recruited through CCL22/CCR4 are selectively activated in lymphoid infiltrates surrounding primary breast tumors and lead to an adverse clinical outcome. *Cancer Research*. 69(5):2000-2009. <https://doi.org/10.1158/0008-5472.CAN-08-2360>.
- Goodwin, P. J., & Stambolic, V. 2015. Impact of the Obesity Epidemic on Cancer. *Annual Review of Medicine*. 66:281-296. <https://doi.org/10.1146/annurev-med-051613-012328>.
- Gourzane, C., Barjon, C., & Busson, P. 2012. Host-tumor interactions in nasopharyngeal carcinomas. *Seminars in Cancer Biology*. 22(2):127-136. <https://doi.org/10.1016/j.semcaner.2012.01.002>.
- Gout, S., & Huot, J. 2008. Role of cancer microenvironment in metastasis: Focus on colon cancer. In *Cancer Microenvironment*. 1(1):69-83. <https://doi.org/10.1007/s12307-008-0007-2>.
- Grivennikov, S. I., Greten, F. R., & Karin, M. 2010. Immunity, Inflammation, and Cancer. 140(6):883-899. *Cell*. <https://doi.org/10.1016/j.cell.2010.01.025>.
- Gunawardene, A. R., Corfe, B. M., & Staton, C. A. 2011. Classification and functions of enteroendocrine cells of the lower gastrointestinal tract. In *International Journal of Experimental Pathology*. 92(4):219-231. <https://doi.org/10.1111/j.1365-2613.2011.00767.x>.
- Haan, K. M., Kyeong Lee, S., & Longnecker, R. 2001. Different functional domains in the cytoplasmic tail of glycoprotein B are involved in Epstein-Barr virus-induced membrane fusion. *Virology*. 290(1):106-114. <https://doi.org/10.1006/viro.2001.1141>.
- Haas, M., Dimmler, A., Hohenberger, W., Grabenbauer, G. G., Niedobitek, G., & Distel, L. V. 2009. Stromal regulatory T-cells are associated with a favourable prognosis in gastric cancer of the cardia. *BMC Gastroenterology*. 9:65. <https://doi.org/10.1186/1471-230X-9-65>.
- Hammerschmidt, W., & Sugden, B. 2013. Replication of Epstein-Barr viral DNA.



- Cold Spring Harbor Perspectives in Biology. 5(1):a013029. <https://doi.org/10.1101/cshperspect.a013029>.
- Hanahan, D., & Folkman, J. 1996. Patterns and emerging mechanisms of the angiogenic switch during tumorigenesis. *Cell.* 86(3):353-364. [https://doi.org/10.1016/S0092-8674\(00\)80108-7](https://doi.org/10.1016/S0092-8674(00)80108-7).
- Hanahan, D., & Weinberg, R. A. 2011. Hallmarks of cancer: The next generation. In *Cell.* 144(5):646-74. doi: 10.1016/j.cell.2011.02.013.
- He, K. F., Zhang, L., Huang, C. F., Ma, S. R., Wang, Y. F., Wang, W. M., Zhao, Z. L., Liu, B., Zhao, Y. F., Zhang, W. F., & Sun, Z. J. 2014. CD163+ tumor-associated macrophages correlated with poor prognosis and cancer stem cells in oral squamous cell carcinoma. *BioMed Research International.* 2014:838632. <https://doi.org/10.1155/2014/838632>.
- Henle, G., & Henle, W. 1976. Epstein-barr virus-specific IgA serum antibodies as an outstanding feature of nasopharyngeal carcinoma. *International Journal of Cancer.* 17(1):1-7. <https://doi.org/10.1002/ijc.2910170102>.
- Herdini, C., Hutajulu, S., Indrasari, S. R., Hariwiyanto, B., Fachiro, J., Mubarika, S., & Middeldorp, J. 2011. Uji serologi IgA karakter KNF EBNA1+VCA p-18 pada penderita keluhan kronis kepala leher. *Oto Rhino Laryngologica Indonesiana,* 41(2), 105. <https://doi.org/10.32637/orli.v41i2.46>.
- Hildesheim, A., & Wang, C. P. 2012. Genetic predisposition factors and nasopharyngeal carcinoma risk: A review of epidemiological association studies, 2000-2011. Rosetta Stone for NPC: Genetics, viral infection, and other environmental factors. In *Seminars in Cancer Biology.* 22 (2):107–116. <https://doi.org/10.1016/j.semcan.2012.01.007>.
- Hildesheim, A., West, S., DeVeyra, E., De Guzman, M. F., Jurado, A., Jones, C., Imai, J., & Hinuma, Y. 1992. Herbal Medicine Use, Epstein-Barr Virus, and Risk of Nasopharyngeal Carcinoma. *Cancer Research.* 52(11):3048-51.
- Hori, S., Nomura, T., & Sakaguchi, S. 2017. Control of regulatory T cell development by the transcription factor Foxp3. *Journal of Immunology,* 198(3), 981–985. <https://doi.org/10.1126/science.1079490>.
- Howe, J. G., & Shu, M. 1988. Isolation and Characterization of the Genes for Two Small RNAs of Herpesvirus Papio and Their Comparison with Epstein-Barr Virus-Encoded EBER RNAs. *Journal of Virology,* 62(8), 2790–2798. doi: 10.1128/JVI.62.8.2790-2798.1988.
- Hsiao, S. H., Lee, M. S., Lin, H. Y., Su, Y. C., Ho, H. C., Hwang, J. H., Lee, C. C., & Hung, S. K. 2009. Clinical significance of measuring levels of tumor necrosis factor-alpha and soluble interleukin-2 receptor in nasopharyngeal carcinoma. *Acta Oto-Laryngologica,* 129(12), 1519–1523. <https://doi.org/10.3109/00016480902849427>.
- Hsu, C. Y., Yi, Y. H., Chang, K. P., Chang, Y. S., Chen, S. J., & Chen, H. C. 2014. The Epstein-Barr Virus-Encoded MicroRNA MiR-BART9 Promotes Tumor Metastasis by Targeting E-Cadherin in Nasopharyngeal Carcinoma. *PLoS Pathogens.* 10(2): e1003974. <https://doi.org/10.1371/journal.ppat.1003974>.



- Hsu, M. M., Hsu, W. C., Sheen, T. S., & Kao, C. L. 2001. Specific IgA antibodies to recombinant early and nuclear antigens of Epstein-Barr virus in nasopharyngeal carcinoma. *Clinical Otolaryngology and Allied Sciences*, 26(4):334-338.. <https://doi.org/10.1046/j.1365-2273.2001.00489.x>.
- Huang, D., Song, S., Wu, Z., Wu, W., Cui, X., Chen, J., Zeng, M., & Su, S. 2017. Epstein-Barr Virus-Induced VEGF and GM-CSF Drive Nasopharyngeal Carcinoma Metastasis via Recruitment and Activation of Macrophages. *Cancer research*, 77(13), 3591–3604. <https://doi.org/10.1158/0008-5472.CAN-16-2706>.
- Huang, H., Liu, X., Zhao, F., Lu, J., Zhang, B., Peng, X., Zhang, M., Chen, X., Li, G., & Li, X. 2017. M2-polarized tumour-associated macrophages in stroma correlate with poor prognosis and Epstein-Barr viral infection in nasopharyngeal carcinoma. *Acta Oto-Laryngologica*. 137(8): 888–894. <https://doi.org/10.1080/00016489.2017.1296585>.
- Huang, J., Wan, B., Li, S., Liu, G., Pang, Q., Wu, J., Bao, E., Sun, C., Qin, Y., Wang, K., Yang, F., Wu, Y., Zhang, F., & Yang, B. 2021. High expression of heme oxygenase-1 in tumor-associated macrophages characterizes a poor-prognosis subtype in nasopharyngeal carcinoma. *Aging*. 13(4): 5674–5685. <https://doi.org/10.18632/aging.202492>.
- Huang, S. C. M., Tsao, S. W., & Tsang, C. M. 2018. Interplay of viral infection, host cell factors and tumor microenvironment in the pathogenesis of nasopharyngeal carcinoma. *Cancers*, 10(4): 106. <https://doi.org/10.3390/cancers10040106>.
- Hutajulu, S. H., Howdon, D., Taroen-Hariadi, K. W., Hardianti, M. S., Purwanto, I., Indrasari, S. R., Herdini, C., Hariwiyanto, B., Ghozali, A., Kusumo, H., Dhamiyati, W., Dwidanarti, S. R., Bing Tan, I., Kurnianda, J., & Allsop, M. J. 2021. Survival outcome and prognostic factors of patients with nasopharyngeal cancer in Yogyakarta, Indonesia: A hospital-based retrospective study. *PLoS ONE*. 16(2):e0246638. <https://doi.org/10.1371/journal.pone.0246638>.
- Ishida, T., Ishii, T., Inagaki, A., Yano, H., Komatsu, H., Iida, S., Inagaki, H., & Ueda, R. 2006. Specific recruitment of CC chemokine receptor 4-positive regulatory T cells in Hodgkin lymphoma fosters immune privilege. *Cancer Research*. 66(11):5716-5722. <https://doi.org/10.1158/0008-5472.CAN-06-0261>.
- Iwakiri, D. 2014. Epstein-Barr Virus-Encoded RNAs: Key Molecules in Viral Pathogenesis. *Cancers*. 6(3): 1615–1630. <https://doi.org/10.3390/cancers6031615>.
- Iwakiri, D., Sheen, T. S., Chen, J. Y., Huang, D. P., & Takada, K. 2005. Epstein-Barr virus-encoded small RNA induces insulin-like growth factor 1 and supports growth of nasopharyngeal carcinoma-derived cell lines. *Oncogene*. 24(10): 1767–1773. <https://doi.org/10.1038/sj.onc.1208357>.
- Iwakiri, D., Zhou, L., Samanta, M., Matsumoto, M., Ebihara, T., Seya, T., Imai, S., Fujieda, M., Kawa, K., & Takada, K. 2009. Epstein-Barr virus (EBV)-encoded small RNA is released from EBV-infected cells and activates signaling from toll-like receptor 3. *Brief Definitive Report*, 206(10), 2091–2099. <https://doi.org/10.1084/jem.20081761>.



- Iwasaki, A., & Medzhitov, R. 2004. Toll-like receptor control of the adaptive immune responses. *Nature Immunology*. 5(10): 987–995. <https://doi.org/10.1038/ni1112>.
- Ji, M. F., Wang, D. K., Yu, Y. L., Guo, Y. Q., Liang, J. S., Cheng, W. M., Zong, Y. S., Chan, K. H., Ng, S. P., Wei, W. I., Chua, D., Sham, J., & Ng, M. H. 2007. Sustained elevation of Epstein-Barr virus antibody levels preceding clinical onset of nasopharyngeal carcinoma. *British Journal of Cancer*, 96, 623–630. <https://doi.org/10.1038/sj.bjc.6603609>.
- Jia, D., Yang, W., Li, L., Liu, H., Tan, Y., Ooi, S., Chi, L., Filion, L. G., Figeys, D., & Wang, L. 2015. β -Catenin and NF- κ B co-activation triggered by TLR3 stimulation facilitates stem cell-like phenotypes in breast cancer. *Cell Death and Differentiation*, 22(2): 298–310. <https://doi.org/10.1038/cdd.2014.145>.
- Jia, Deyong, & Wang, L. 2015. The other face of TLR3: A driving force of breast cancer stem cells. *Molecular and Cellular Oncology*, 2(4):e981443. <https://doi.org/10.4161/23723556.2014.981443>.
- Jia, W. H., & Qin, H. De. 2012. Non-viral environmental risk factors for nasopharyngeal carcinoma: A systematic review. *Seminars in Cancer Biology*. ;22(2):117-126. <https://doi.org/10.1016/j.semcan.2012.01.009>.
- Karikó, K., Ni, H., Capodici, J., Lamphier, M., & Weissman, D. 2004. mRNA Is an Endogenous Ligand for Toll-like Receptor 3. *Journal of Biological Chemistry*, 279(13): 12542–12550. <https://doi.org/10.1074/jbc.M310175200>.
- Kawai, T., & Akira, S. 2011. Toll-like Receptors and Their Crosstalk with Other Innate Receptors in Infection and Immunity. *Immunity*. 34(5): 637–650. <https://doi.org/10.1016/j.immuni.2011.05.006>.
- Ke, K. J., Wang, H. Y., Fu, S., Zhang, Z. C., Duan, L. P., Liu, D. B., & Ye, J. 2014. Epstein-Barr virus-encoded RNAs as a survival predictor in nasopharyngeal carcinoma. *Chinese Medical Journal*, 127(2), 294–299. <https://doi.org/10.3760/cma.j.issn.0366-6999.20132206>.
- Key, T. J., Appleby, P. N., Reeves, G. K., Roddam, A., Dorgan, J. F., Longcope, C., Stanczyk, F. Z., Stephenson, H. E., Falk, R. T., Miller, R., Schatzkin, A., Allen, D. S., Fentiman, I. S., Wang, D. Y., Dowsett, M., Thomas, H. V., Hankinson, S. E., Toniolo, P., Akhmedkhanov, A., Miller, S. R. 2003. Body mass index, serum sex hormones, and breast cancer risk in postmenopausal women. *Journal of the National Cancer Institute*. 95(16): 1218–1226. <https://doi.org/10.1093/jnci/djg022>.
- Kieff, E., & Rickinson, A. B. 2007. Epstein-Barr virus and its replication. *Fields Virology 5 ed: Vol. I*. Lippincott Williams & Wilkins, Philadelphia.
- Kikuchi, K., Inoue, H., Miyazaki, Y., Ide, F., Kojima, M., & Kusama, K. 2017. Epstein–Barr virus (EBV)-associated epithelial and non-epithelial lesions of the oral cavity. *Japanese Dental Science Review*. 53(3): 95–109.. <https://doi.org/10.1016/j.jdsr.2017.01.002>.
- Kim, J. M., & Rudensky, A. 2006. The role of the transcription factor Foxp3 in the development of regulatory T cells. *Immunological Reviews*. 212:86-98.. <https://doi.org/10.1111/j.0105-2896.2006.00426.x>.



- Kim, R. 2007. Cancer Immunoediting: From Immune Surveillance to Immune Escape. *Cancer Immunotherapy*. 3(11): 991–998. <https://doi.org/10.1016/B978-012372551-6/50066-3>.
- Kitamura, T., Qian, B. Z., Soong, D., Cassetta, L., Noy, R., Sugano, G., Kato, Y., Li, J., & Pollard, J. W. 2015. CCL2-induced chemokine cascade promotes breast cancer metastasis by enhancing retention of metastasis-associated macrophages. *Journal of Experimental Medicine*. 212(7): 1043–1059. <https://doi.org/10.1084/jem.20141836>.
- Kolonin, M. G., Evans, K. W., Mani, S. A., & Gomer, R. H. 2012. Alternative origins of stroma in normal organs and disease. *Stem Cell Research*. 8(2):312-23. <https://doi.org/10.1016/j.scr.2011.11.005>.
- Kong, Q. L., Hu, L. J., Cao, J. Y., Huang, Y. J., Xu, L. H., Liang, Y., Xiong, D., Guan, S., Guo, B. H., Mai, H. Q., Chen, Q. Y., Zhang, X., Li, M. Z., Shao, J. Y., Qian, C. N., Xia, Y. F., Song, L. B., Zeng, Y. X., & Zeng, M. S. 2010. Epstein-barr virus-encoded LMP2A induces an epithelial- mesenchymal transition and increases the number of side population stem-like cancer cells in nasopharyngeal carcinoma. *PLoS Pathogens*. 6(6):e1000940. <https://doi.org/10.1371/journal.ppat.1000940>.
- Kridel, R., Xerri, L., Gelas-Dore, B., Tan, K., Feugier, P., Vawda, A., Canioni, D., Farinha, P., Boussetta, S., Moccia, A. A., Brice, P., Chavez, E. A., Kyle, A. H., Scott, D. W., Sanders, A. D., Fabiani, B., Slack, G. W., Minchinton, A. I., Haioun, C., Salles, G. 2015. The prognostic impact of CD163-positive macrophages in follicular Lymphoma: A study from the BC cancer agency and the lymphoma study association. *Clinical Cancer Research*. 21(15):3428-3435. <https://doi.org/10.1158/1078-0432.CCR-14-3253>.
- Kuraishi, A., Karin, M., & Grivennikov, S. I. 2013. Tumor Promotion via Injury- and Death-induced Inflammation Ali. *Immunity*, 35(4): 467–477. <https://doi.org/10.1016/j.immuni.2011.09.006>.
- Kwok Fung Lo, A., Wai Lo, K., Tsao, S. W., Wong, H. L., Ying Hui, J. W., To, K. F., Hayward, S. D., Chui, Y. L., Lau, Y. L., Takada, K., & Huang, D. P. 2006. Epstein-Barr Virus Infection Alters Cellular Signal Cascades in Human Nasopharyngeal Epithelial Cells. *Neoplasia*. 8(3):173-180. <https://doi.org/10.1593/neo.05625>.
- Lao, T. D., Nguyen, D. H., Nguyen, T. M., & Le, T. A. H. 2017. Molecular Screening for Epstein-Barr virus (EBV): Detection of Genomic EBNA-1, EBNA-2, LMP-1, LMP-2 Among Vietnamese Patients with Nasopharyngeal Brush Samples. *Asian Pacific Journal of Cancer Prevention: APJCP*. 18(6):1675-1679. <https://doi.org/10.22034/APJCP.2017.18.6.1675>.
- Laoui, D., Van Overmeire, E., Movahedi, K., Van den Bossche, J., Schouppé, E., Mommer, C., Nikolaou, A., Morias, Y., De Baetselier, P., & Van Ginderachter, J. A. 2011. Mononuclear phagocyte heterogeneity in cancer: Different subsets and activation states reaching out at the tumor site. *Immunobiology*. 216(11):1192-1202. <https://doi.org/10.1016/j.imbio.2011.06.007>.



- Law, H. K. W., Cheung, C. Y., Sia, S. F., Chan, Y. O., Peiris, J. S. M., & Lau, Y. L. 2009. Toll-like receptors, chemokine receptors and death receptor ligands responses in SARS coronavirus infected human monocyte derived dendritic cells. *BMC Immunology*. 10:35. <https://doi.org/10.1186/1471-2172-10-35>.
- Lee, A. W. M., Foo, W., Mang, O., Sze, W. M., Chappell, R., Lau, W. H., & Ko, W. M. 2003. Changing epidemiology of nasopharyngeal carcinoma in Hong Kong over a 20-year period (1980-99): An encouraging reduction in both incidence and mortality. *International Journal of Cancer*. 103(5):680-5. <https://doi.org/10.1002/ijc.10894>.
- Lee, D. C. W., Chua, D. T. T., Wei, W. I., Sham, J. S. T., & Lau, A. S. Y. 2007. Induction of matrix metalloproteinases by Epstein-Barr virus latent membrane protein 1 isolated from nasopharyngeal carcinoma. *Biomedicine and Pharmacotherapy*. 61(9): 520–526. <https://doi.org/10.1016/j.biopha.2007.08.007>.
- Lei, T., Yuen, K. S., Xu, R., Tsao, S. W., Chen, H., Li, M., Kok, K. H., & Jin, D. Y. 2013. Targeting of DICE1 tumor suppressor by Epstein-Barr virus-encoded miR-BART3 microRNA in nasopharyngeal carcinoma. *International Journal of Cancer*. 133(1): 79–87. <https://doi.org/10.1002/ijc.28007>.
- Li, B., Huang, G., Zhang, X., Li, R., Wang, J., Dong, Z., & He, Z. 2013. Increased phosphorylation of histone H3 at serine 10 is involved in Epstein-Barr virus latent membrane protein-1-induced carcinogenesis of nasopharyngeal carcinoma. *BMC Cancer*. 13. 124. <https://doi.org/10.1186/1471-2407-13-124>.
- Li, D., Gu, R., Yang, X., Hu, C., Li, Y., Gao, M., & Yu, Y. 2014. TLR3 correlated with cervical lymph node metastasis in patients with papillary thyroid cancer. *International Journal of Clinical and Experimental Medicine*. 7(12): 5111–5117.
- Li, Z., Duan, Y., Cheng, S., Chen, Y., Hu, Y., Zhang, L., He, J., Liao, Q., Yang, L., & Sun, L.-Q. 2015. EBV-encoded RNA via TLR3 induces inflammation in nasopharyngeal carcinoma. *Oncotarget*. 6(27): 24291–24303. <https://doi.org/10.18632/oncotarget.4552>.
- Liao, Q., Guo, X., Li, X., Li, X., Chen, P., Liang, F., Tang, H., Deng, M., Wu, M., Ma, J., Xiong, W., & Li, G. 2012. Analysis of the contribution of nasopharyngeal epithelial cancer cells to the induction of a local inflammatory response. *Journal of Cancer Research and Clinical Oncology*. 138(1): 57–64. <https://doi.org/10.1007/s00432-011-1066-1>.
- Lin, J.-C., Jan, J.S., Hsu, C.Y., Liang, W.M., Jiang, R.S., & Wang, W.Y. 2003. Phase III study of concurrent chemoradiotherapy versus radiotherapy alone for advanced nasopharyngeal carcinoma: positive effect on overall and progression-free survival. *Journal of Clinical Oncology : Official Journal of the American Society of Clinical Oncology*. 21(4): 631–637. <https://doi.org/10.1200/JCO.2003.06.158>.
- Lin, K.T., Huang, W.Y., Lin, C.C., Jen, Y.M., Lin, C.S., Lo, C.H., & Kao, C.H. 2015. Subsequent risk of nasopharyngeal carcinoma among patients with allergic rhinitis: A nationwide population-based cohort study. *Head Neck*. 37(3): 413–

417. <https://doi.org/10.1002/hed.23617>.
- Lippitz, B. E., & Harris, R. A. 2016. Cytokine patterns in cancer patients : A review of the correlation between interleukin 6 and prognosis. *OncoImmunology*, 5(5): 1–12. <https://doi.org/10.1080/2162402X.2015.1093722>.
- Liu, Y., Huang, Q., Liu, W., Liu, Q., Jia, W., Chang, E., Chen, F., Liu, Z., Guo, X., Mo, H., Chen, J., Rao, D., Ye, W., Cao, S., & Hong, M. 2012. Establishment of VCA and EBNA1 IgA-based combination by enzyme-linked immunosorbent assay as preferred screening method for nasopharyngeal carcinoma: A two-stage design with a preliminary performance study and a mass screening in southern China. *International Journal of Cancer*. 131(2): 406–416. <https://doi.org/10.1002/ijc.26380>.
- Lo, A. K.-F., Lo, K.-W., Ko, C.-W., Young, L. S., & Dawson, C. W. 2013. Inhibition of the LKB1-AMPK pathway by the Epstein-Barr virus-encoded LMP1 promotes proliferation and transformation of human nasopharyngeal epithelial cells. *The Journal of Pathology*. 230(3): 336–346. <https://doi.org/10.1002/path.4201>.
- Lo, A. K. F., To, K. F., Lo, K. W., Lung, R. W. M., Hui, J. W. Y., Liao, G., & Hayward, S. D. 2007. Modulation of LMP1 protein expression by EBV-encoded microRNAs. *Proceedings of the National Academy of Sciences*. 104(41): 16164–16169. <https://doi.org/10.1073/pnas.0702896104>.
- Lo, Angela Kwok Fung, Dawson, C. W., Lung, H. L., Wong, K. L., & Young, L. S. 2021. The Role of EBV-Encoded LMP1 in the NPC Tumor Microenvironment: From Function to Therapy. *Frontiers in Oncology*. 11: 640207.. <https://doi.org/10.3389/fonc.2021.640207>.
- Lo, K. W., To, K. F., & Huang, D. P. 2004. Focus on nasopharyngeal carcinoma. *Cancer Cell*. 5(5): 423–428. [https://doi.org/10.1016/s1535-6108\(04\)00119-9](https://doi.org/10.1016/s1535-6108(04)00119-9).
- Ma, J., Li, J., Hao, Y., Nie, Y., Li, Z., Qian, M., Liang, Q., Yu, J., Zeng, M., & Wu, K. 2017. Differentiated tumor immune microenvironment of Epstein-Barr virus-associated and negative gastric cancer: implication in prognosis and immunotherapy. *Oncotarget*, 8(40): 67094–67103. <https://doi.org/10.18632/oncotarget.17945>.
- Ma, Y., Yang, Y., Wang, F., Zhang, P., Shi, C., Zou, Y., & Qin, H. 2013. Obesity and Risk of Colorectal Cancer: A Systematic Review of Prospective Studies. *PLoS ONE*. 8(1):e53916. <https://doi.org/10.1371/journal.pone.0053916>.
- Mahdavifar, N., Ghoncheh, M., Mohammadian-Hafshejani, A., Khosravi, B., & Salehiniya, H. 2016. Epidemiology and Inequality in the Incidence and Mortality of Nasopharynx Cancer in Asia. *Osong Public Health and Research Perspectives*, 7(6): 360–372. <https://doi.org/10.1016/j.phrp.2016.11.002>.
- Mantovani, A., Allavena, P., Sica, A., & Balkwill, F. 2008. Cancer-related inflammation. *Nature*. 454(7203), 436–444. <https://doi.org/10.1038/nature07205>.
- Mantovani, A., & Sica, A. 2010. Macrophages, innate immunity and cancer: balance,

- tolerance, and diversity. *Current Opinion in Immunology.* 22(2): 231–237. <https://doi.org/10.1016/j.coи.2010.01.009>.
- Mantovani, A., Sica, A., Allavena, P., Garlanda, C., & Locati, M. 2009. Tumor-associated macrophages and the related myeloid-derived suppressor cells as a paradigm of the diversity of macrophage activation. *Human Immunology.* 70(5): 325–330. <https://doi.org/10.1016/j.humimm.2009.02.008>.
- Mantovani, A., Sozzani, S., Locati, M., Allavena, P., & Sica, A. 2002. Macrophage polarization: Tumor-associated macrophages as a paradigm for polarized M2 mononuclear phagocytes. *Trends in Immunology.* 23(11): 549–555. [https://doi.org/10.1016/S1471-4906\(02\)02302-5](https://doi.org/10.1016/S1471-4906(02)02302-5).
- Mardhiyah, I., Ardiyan, Y. N., Aliyah, S. H., Sitepu, E. C., Herdini, C., Dwianingsih, E. K., Asfarina, F., Sumartiningsih, S., Fachiroh, J., & Paramita, D. K. 2021. Necrosis Factor- α (TNF- α) and the Presence of Macrophage M2 and T Regulatory Cells in Nasopharyngeal Carcinoma. *Asian Pacific Journal of Cancer Prevention.* 22(8):2363-2370. <https://doi.org/10.31557/APJCP.2021.22.8.2363>.
- Marshall, N. A., Vickers, M. A., & Barker, R. N. 2003. Regulatory T Cells Secreting IL-10 Dominate the Immune Response to EBV Latent Membrane Protein 1. *The Journal of Immunology.* 170(12): 6183–6189. <https://doi.org/10.4049/jimmunol.170.12.6183>.
- Matijevic, T., & Pavelic, J. 2011. The dual role of TLR3 in metastatic cell line. *Clin Exp Metastasis,* 28:701–712. <https://doi.org/10.1007/s10585-011-9402-z>.
- Meylan, E., & Tschoopp, J. 2006. Toll-Like Receptors and RNA Helicases : Two Parallel Ways to Trigger Antiviral Responses. *Molecular Cell.* 22(5): 561–569. <https://doi.org/10.1016/j.molcel.2006.05.012>.
- Middeldorp, J. M., Brink, A. A. T. P., Van den Brule, A. J. C., & Meijer, C. J. L. M. 2003. Pathogenic roles for Epstein-Barr virus (EBV) gene products in EBV-associated proliferative disorders. 45(1): 1–36. *Critical Reviews in Oncology/Hematology.* [https://doi.org/10.1016/S1040-8428\(02\)00078-1](https://doi.org/10.1016/S1040-8428(02)00078-1).
- Moore, P. S., & Chang, Y. 2013. Why do viruses cause cancer? Highlights of the first century of human tumour virology. *Nat Rev Cancer,* 10(12): 878–889. <https://doi.org/10.1038/nrc2961>.Why.
- Morales-Sánchez, A., & Fuentes-Pananá, E. M. 2014. Human viruses and cancer. *Viruses,* 6(10): 4047–4079. <https://doi.org/10.3390/v6104047>.
- Mozes, T., Barath, I., Gornicsar, K., Grosz, A., Gondocs, C., Szephalmi, P., Gaal, K., & Madarasz, E. 2011. Deviations in Circulating TNF α Levels and TNF α Production by mononuclear cell. *Mediators of Inflammation,* 1–8.
- Murakami, M., Harada, M., Kamimura, D., Ogura, H., Okuyama, Y., Kumai, N., Okuyama, A., Singh, R., Jiang, J. J., Atsumi, T., Shiraya, S., Nakatsuji, Y., Kinoshita, M., Kohsaka, H., Nishida, M., Sakoda, S., Miyasaka, N., Yamaguchi-Takahara, K., & Hirano, T. 2013. Disease-association analysis of an inflammation-related feedback loop. *Cell Reports.* 3(3): 946–959. <https://doi.org/10.1016/j.celrep.2013.01.028>.



- Nakao, K., Yuge, T., Mochiki, M., Nibu, K. ichi, & Sugasawa, M. 2003. Detection of Epstein-Barr virus in metastatic lymph nodes of patients with nasopharyngeal carcinoma and a primary unknown carcinoma. *Archives of Otolaryngology - Head and Neck Surgery*, 129(3):338–340. <https://doi.org/10.1001/archotol.129.3.338>.
- Nanbo, A., Inoue, K., Adachi-Takasawa, K., & Takada, K. 2002. Epstein-Barr virus RNA confers resistance to interferon- α -induced apoptosis in Burkitt's lymphoma. *EMBO Journal*. 21(5): 954–965. <https://doi.org/10.1093/emboj/21.5.954>.
- Nanbo, A., & Takada, K. 2002. The role of Epstein-Barr virus-encoded small RNAs (EBERs) in oncogenesis. *Reviews in medical virology*, 12(5), 321–326. <https://doi.org/10.1002/rmv.363>.
- Napetschnig, J., & Wu, H. 2013. Molecular basis of NF- κ B signaling. *Annual Review of Biophysics*, 42(1): 443–468. <https://doi.org/10.1146/annurev-biophys-083012-130338>.
- Nathan, C., & Ding, A. 2010. Nonresolving Inflammation. 40(6): 871–882. *Cell*. <https://doi.org/10.1016/j.cell.2010.02.029>.
- Neuhierl, B., Baldwin, G., Rickinson, A. B., & Delecluse, H. 2006. Resting B cells as a transfer vehicle for Epstein-Barr virus infection of epithelial cells. *Proceedings of the National Academy of Sciences of the United States of America*. 103(18): 7065–7070. <https://doi.org/10.1073/pnas.0510512103>.
- Ng, M. H., Chen, H. L., Luo, R. X., Chan, K. H., Woo, P. C. Y., Sham, J. S. T., Huang, J., Seto, W. H., Smith, P., & Griffin, B. E. 1998. Serological diagnosis of nasopharyngeal carcinoma by enzyme linked immunosorbant assay: Optimization, standardization and diagnostic criteria. *Chinese Medical Journal*. 111(6), 531–536.
- Nicholls, J. M., Agathangelou, A., Fung, K., Xiangguo, Z., & Niedobitek, G. 1997. The association of squamous cell carcinomas of the nasopharynx with epstein-barr virus shows geographical variation reminiscent of burkitt's lymphoma. *Journal of Pathology*, 183(2): 164–168. [https://doi.org/10.1002/\(SICI\)1096-9896\(199710\)183:2<164::AID-PATH919>3.0.CO;2-J](https://doi.org/10.1002/(SICI)1096-9896(199710)183:2<164::AID-PATH919>3.0.CO;2-J).
- O'Neil, J. D., Owen, T. J., Wood, V. H. J., Date, K. L., Valentine, R., Chukwuma, M. B., Arrand, J. R., Dawson, C. W., & Young, L. S. 2008. Epstein-Barr virus-encoded EBNA1 modulates the AP-1 transcription factor pathway in nasopharyngeal carcinoma cells and enhances angiogenesis in vitro. *Journal of General Virology*. 89(Pt 11): 2833–2842. <https://doi.org/10.1099/vir.0.2008/003392-0>.
- Oganesyan, G., Saha, S. K., Guo, B., He, J. Q., Shahangian, A., Zarnegar, B., Perry, A., & Cheng, G. 2006. Critical role of TRAF3 in the Toll-like receptor-dependent and -independent antiviral response. *Nature*. 439(7073): 208–211. <https://doi.org/10.1038/nature04374>.
- Ok, C. Y. 2016. EBV-positive diffuse large B-cell lymphoma of the elderly. *Hematologic Cancers: From Molecular Pathobiology to Targeted Therapeutics*.



- 122(3): 328–341. https://doi.org/10.1007/978-94-007-5028-9_5.
- Ooft, M. L., van Ipenburg, J. A., Sanders, M. E., Kranendonk, M., Hofland, I., de Bree, R., Koljenović, S., & Willems, S. M. 2018. Prognostic role of tumour-associated macrophages and regulatory T cells in EBV-positive and EBV-negative nasopharyngeal carcinoma. *Journal of Clinical Pathology*. 71(3): 267–274. <https://doi.org/10.1136/jclinpath-2017-204664>.
- Pagès, F., Berger, A., Camus, M., Sanchez-Cabo, F., Costes, A., Molidor, R., Mlecnik, B., Kirilovsky, A., Nilsson, M., Damotte, D., Meatchi, T., Bruneval, P., Cugnenc, P.-H., Trajanoski, Z., Fridman, W.-H., & Jérôme Galon. 2015. Effector Memory T Cells, Early Metastasis, and Survival in Colorectal Cancer. *New England Journal of Medicine*. 353(25): 2654–2666. <https://doi.org/10.1056/NEJMoa051424> PM - 16371631.
- Pai, T., Gupta, S., Gurav, M., Nag, S., Shet, T., Patil, A., & Desai, S. 2018. Evidence for the association of Epstein-Barr Virus in breast cancer in Indian patients using in-situ hybridization technique. *Breast Journal*. 24(1): 16–22. <https://doi.org/10.1111/tbj.12828>.
- Paramita, D. K., Fachiroh, J., Artama, W. T., Van Benthem, E., Haryana, S. M., & Middeldorp, J. M. 2007. Native early antigen of Epstein-Barr virus, a promising antigen for diagnosis of nasopharyngeal carcinoma. *Journal of Medical Virology*. 79(11): 1710–1721.. <https://doi.org/10.1002/jmv.20987>.
- Paramita, D. K., Fachiroh, J., Haryana, S. M., & Middeldorp, J. M. 2009. Two-step epstein-barr virus immunoglobulin A enzyme-linked immunosorbent assay system for serological screening and confirmation of nasopharyngeal carcinoma. *Clinical and Vaccine Immunology*. 16(5): 706–711. <https://doi.org/10.1128/CVI.00425-08>.
- Pardede, S. A. 2014. Korelasi Antara Ekspresi TNF- α dan Microvessel Density Pada Penderita Karsinoma Nasofaring di RSUP H. Adam Malik Medan. *Tesis*.
- Parkin, D. M., Bray, F., Ferlay, J., & Pisani, P. 2005. Global cancer statistics, 2002. *CA: A Cancer Journal for Clinicians*, 55(2): 74–108. <https://doi.org/10.3322/canjclin.55.2.74>.
- Pathak, B. R., Breed, A. A., Apte, S., Acharya, K., & Mahale, S. D. 2016. Cysteine-rich secretory protein 3 plays a role in prostate cancer cell invasion and affects expression of PSA and ANXA1. *Molecular and Cellular Biochemistry*. 411(1-2):11-21. <https://doi.org/10.1007/s11010-015-2564-2>.
- Paul, P., Rouas-Freiss, N., Khalil-Daher, I., Moreau, P., Riteau, B., Le Gal, F. A., Avril, M. F., Dausset, J., Guillet, J. G., & Carosella, E. D. 1998. HLA-G expression in melanoma: a way for tumor cells to escape from immunosurveillance. *Proceedings of the National Academy of Sciences of the United States of America*. 95(8):4510–4515. <https://doi.org/10.1073/pnas.95.8.4510>.
- Piotrowski, I., Kulcenty, K., & Suchorska, W. 2020. Interplay between inflammation and cancer. In *Reports of Practical Oncology and Radiotherapy*. 25(3): 422–427. <https://doi.org/10.1016/j.rpor.2020.04.004>.



- Port, R. J., Pinheiro-Maia, S., Hu, C., Arrand, J. R., Wei, W., Young, L. S., & Dawson, C. W. 2013. Epstein-Barr virus induction of the Hedgehog signalling pathway imposes a stem cell phenotype on human epithelial cells. *Journal of Pathology*. 231(3): 367–377. <https://doi.org/10.1002/path.4245>.
- Prasad, U., & Pua, K. C. 2000. Nasopharyngeal carcinoma: a delay in diagnosis. *The Medical Journal of Malaysia*, 55(2), 230–235.
- Qian, B. Z., & Pollard, J. W. 2010. Macrophage Diversity Enhances Tumor Progression and Metastasis. *Cell*. 141(1): 39–51. <https://doi.org/10.1016/j.cell.2010.03.014>.
- Qing, W., Fang, W.-Y., Ye, L., Shen, L.-Y., Zhang, X.-F., Fei, X.-C., Chen, X., Wang, W.-Q., Li, X.-Y., Xiao, J.-C., & Ning, G. 2012. Density of Tumor-Associated Macrophages Correlates with Lymph Node Metastasis in Papillary Thyroid Carcinoma. *Thyroid*, 22(9), 905–910. <https://doi.org/10.1089/thy.2011.0452>.
- Rajala, M. W., & Scherer, P. E. 2003. Minireview: The adipocyte - At the crossroads of energy homeostasis, inflammation, and atherosclerosis. *Endocrinology*. 144(9): 3765–3773. <https://doi.org/10.1210/en.2003-0580>.
- Ramayanti, O., Juwana, H., Verkuijlen, S. A. M. W., Adham, M., Pegtel, M. D., Greijer, A. E., & Middeldorp, J. M. 2017. Epstein-Barr virus mRNA profiles and viral DNA methylation status in nasopharyngeal brushings from nasopharyngeal carcinoma patients reflect tumor origin. *International Journal of Cancer*. 140(1):149–162. <https://doi.org/10.1002/ijc.30418>.
- Ravishankaran, P., & Karunanithi, R. 2011. Clinical significance of preoperative serum interleukin-6 and C-reactive protein level in breast cancer patients. *World Journal of Surgical Oncology*. 9:8. <https://doi.org/10.1186/1477-7819-9-18>.
- Reina-Campos, M., Moscat, J., & Diaz-Meco, M. 2017. Metabolism shapes the tumor microenvironment. *Current Opinion in Cell Biology*. 48: 47–53. <https://doi.org/10.1016/j.ceb.2017.05.006>.
- Ricciardi, M., Zanotto, M., Malpeli, G., Bassi, G., Perbellini, O., Chilosi, M., Bifari, F., & Krampera, M. 2015. Epithelial-to-mesenchymal transition (EMT) induced by inflammatory priming elicits mesenchymal stromal cell-like immune-modulatory properties in cancer cells. *British Journal of Cancer*. 112(6): 1067–1075. <https://doi.org/10.1038/bjc.2015.29>.
- Rovedo, M., & Longnecker, R. 2007. Epstein-Barr Virus Latent Membrane Protein 2B (LMP2B) Modulates LMP2A Activity. *Journal of Virology*. 81(1): 84–94. <https://doi.org/10.1128/JVI.01302-06>.
- Ruffell, B., Affara, N. I., & Coussens, L. M. 2012. Differential macrophage programming in the tumor microenvironment. *Trends in Immunology*. 33(3): 119–126. <https://doi.org/10.1016/j.it.2011.12.001>.
- Saikia, A., Raphael, V., Shunyu, N.-B., Khonglah, Y., Mishra, J., Jitani, A.-K., & Medhi, J. 2016. Analysis of Epstein Barr Virus Encoded RNA Expression in Nasopharyngeal Carcinoma in North-Eastern India: A Chromogenic In Situ Hybridization Based Study. *Iranian Journal of Otorhinolaryngology*, 28(87):



- 267–26774. <https://doi.org/10.22038/ijorl.2016.7036>.
- Schmidt, A., Zhang, X. M., Joshi, R. N., Iqbal, S., Wahlund, C., Gabrielsson, S., Harris, R. A., & Tegnér, J. 2016. Human macrophages induce CD4 + Foxp3 + regulatory T cells via binding and re-release of TGF- β . *Immunology and Cell Biology*. 94(8): 747–762. <https://doi.org/10.1038/icb.2016.34>.
- Sethi, G., Sung, B., & Aggarwal, B. B. 2008. TNF: A master switch for inflammation to cancer. *Frontiers in bioscience : a journal and virtual library*, 13: 5094–5107. <https://doi.org/10.2741/3066>.
- Seto, E., Ooka, T., Middeldorp, J., & Takada, K. 2008. Reconstitution of nasopharyngeal carcinoma-type EBV infection induces tumorigenicity. *Cancer Research*. 68(4): 1030–1036. <https://doi.org/10.1158/0008-5472.CAN-07-5252>.
- Shen, Y., Zhang, S., Sun, R., Wu, T., & Qian, J. 2015. Understanding the interplay between host immunity and Epstein-Barr virus in NPC patients. *Emerging Microbes and Infections*. 4(3), e20. <https://doi.org/10.1038/emi.2015.20>.
- Shitara, K., & Nishikawa, H. 2016. Regulatory T cells: A potential target in cancer immunotherapy. *Annals of the New York Academy of Sciences*. 1417(1): 104–115.. <https://doi.org/10.1111/nyas.13625>.
- Sivachandran, N., Wang, X., & Frappier, L. 2012. Functions of the Epstein-Barr Virus EBNA1 Protein in Viral Reactivation and Lytic Infection. *Journal of Virology*. 86(11): 6146–6158. <https://doi.org/10.1128/jvi.00013-12>.
- Sivachandran, Nirojini, Sarkari, F., & Frappier, L. 2008. Epstein-Barr nuclear antigen 1 contributes to nasopharyngeal carcinoma through disruption of PML nuclear bodies. *PLoS Pathogens*. 4(10): e1000170. <https://doi.org/10.1371/journal.ppat.1000170>.
- Siveen, K. S., & Kuttan, G. 2009. Role of macrophages in tumour progression. *Immunol. Lett.* 123(2): 97–102. <https://doi.org/10.1016/j.imlet.2009.02.011>.
- Song, Y., Li, X., Zeng, Z., Li, Q., Gong, Z., Liao, Q., Li, X., Chen, P., Xiang, B., Zhang, W., Xiong, F., Zhou, Y., Zhou, M., Ma, J., Li, Y., Chen, X., Li, G., & Xiong, W. 2016. Epstein-Barr virus encoded miR-BART11 promotes inflammationinduced carcinogenesis by targeting FOXP1. *Oncotarget*. 7(24): 36783–36799. <https://doi.org/10.18632/oncotarget.9170>.
- Stevens, S. J. C., Verkuijen, S. A. W. M., Hariwiyanto, B., Harijadi, Paramita, D. K., Fachiroh, J., Adham, M., Tan, I. B., Haryana, S. M., & Middeldorp, J. M. 2006. Noninvasive diagnosis of nasopharyngeal carcinoma: Nasopharyngeal brushings reveal high Epstein-Barr virus DNA load and carcinoma-specific viral BARF1 mRNA. *International Journal of Cancer*. 119(3): 608–614. <https://doi.org/10.1002/ijc.21914>.
- Su, Z. Y., Siak, P. Y., Leong, C. O., & Cheah, S. C. 2022. Nasopharyngeal Carcinoma and Its Microenvironment: Past, Current, and Future Perspectives. *Frontiers in Oncology*. 12: 840467. <https://doi.org/10.3389/fonc.2022.840467>.
- Sumitomo, R., Hirai, T., Fujita, M., Murakami, H., Otake, Y., & Huang, C. 2019. M2 tumor-associated macrophages promote tumor progression in non-small-cell lung cancer. *Experimental And Therapeutic Medicine*, 18, 4490–4498.



- [https://doi.org/10.3892/etm.2019.8068.](https://doi.org/10.3892/etm.2019.8068)
- Sun, W., Liu, D. B., Li, W. W., Zhang, L. L., Long, G. X., Wang, J. F., Mei, Q., & Hu, G. Q. 2014. Interleukin-6 promotes the migration and invasion of nasopharyngeal carcinoma cell lines and upregulates the expression of MMP-2 and MMP-9. *Int J Oncol.* <https://doi.org/10.3892/ijo.2014.2323>.
- Susilo, R., Farhat, Asnir, R. A., Yudhistira, A., Daulay, E. R., & Chrestella, J. 2020. Correlation of Tnf-A Expression To Clinical Stadium in Nasopharyngeal Carcinoma. *International Journal of Nasopharyngeal Carcinoma (Ijnpc).* 44(5), 1551–1560. <https://doi.org/10.32734/ijnpc.v2i01.3503>.
- Takada, K. 2012. Role of EBER and BARF1 in nasopharyngeal carcinoma (NPC) tumorigenesis. *Seminars in Cancer Biology.* 22(2): 162–165. <https://doi.org/10.1016/j.semcaner.2011.12.007>.
- Takeda, K., Kaisho, T., & Akira, S. 2003. Toll-like receptors," Annual Review of Immunology,. *Annual Review of Immunology.* 21, 335–376. <https://doi.org/10.1146/annurev.immunol.21.120601.141126>.
- Takeuchi, Y., & Nishikawa, H. 2016. Roles of regulatory T cells in cancer immunity. *International Immunology.* 28(8): 401–409.. <https://doi.org/10.1093/intimm/dxw025>.
- Tan, E. L., Selvaratnam, G., Kananathan, R., & Sam, C. K. 2006. Quantification of Epstein-Barr virus DNA load, interleukin-6, interleukin-10, transforming growth factor- β 1 and stem cell factor in plasma of patients with nasopharyngeal carcinoma. *BMC Cancer,* 6:7. <https://doi.org/10.1186/1471-2407-6-227>.
- Tan, G., Visser, L., Tan, L., Berg, A., & Diepstra, A. 2018. The Microenvironment in Epstein–Barr Virus-Associated Malignancies. *Pathogens.* 7(2): 40. <https://doi.org/10.3390/pathogens7020040>.
- Tang, L.-L., Chen, W.-Q., Xue, W.-Q., He, Y.-Q., Zheng, R.-S., Zeng, Y.-X., & Jia, W.-H. 2016. Global trends in incidence and mortality of nasopharyngeal carcinoma. *Cancer Letters.* 374(1): 22–30. <https://doi.org/10.1016/j.canlet.2016.01.040>.
- Tang, L., Li, L., Mao, Y., Liu, L., Liang, S., Chen, Y., Sun, Y., Liao, X., Tian, L., Lin, A., Liu, M., & Ma, J. 2008. Retropharyngeal lymph node metastasis in nasopharyngeal carcinoma detected by magnetic resonance imaging: Prognostic value and staging categories. *Cancer.* 113(2): 347–354. <https://doi.org/10.1002/cncr.23555>.
- Tang, Y., Cai, W., & Xu, B. 2015. Profiles of phenolics, carotenoids and antioxidative capacities of thermal processed white, yellow, orange and purple sweet potatoes grown in Guilin, China. *Food Science and Human Wellness,* 4(3): 123–132. <https://doi.org/10.1016/j.fshw.2015.07.003>.
- Tao, M., Liu, L., Shen, M., Zhi, Q., Gong, F. R., Zhou, B. P., Wu, Y., Liu, H., Chen, K., Shen, B., Wu, M. Y., Shou, L. M., & Li, W. 2016. Inflammatory stimuli promote growth and invasion of pancreatic cancer cells through NF- κ B pathway dependent repression of PP2Ac. *Cell Cycle.* 15(3): 381–393. <https://doi.org/10.1080/15384101.2015.1127468>.



- Thorley-Lawson, D. A. 2005. EBV the prototypical human tumor virus - Just how bad is it? *Journal of Allergy and Clinical Immunology*. 116(2): 251–262. <https://doi.org/10.1016/j.jaci.2005.05.038>.
- Thorley-Lawson, D. A., & Gross, A. 2004. Persistence of the Epstein–Barr Virus and the Origins of Associated Lymphomas. *New England Journal of Medicine*. 350(13):1328–1337. <https://doi.org/10.1056/NEJMra032015>
- Tiainen, S., Tumelius, R., Rilla, K., Hääläinen, K., Tammi, M., Tammi, R., Kosma, V. M., Oikari, S., & Auvinen, P. 2015. High numbers of macrophages, especially M2-like (CD163-positive), correlate with hyaluronan accumulation and poor outcome in breast cancer. *Histopathology*. 66(6): 873–883. <https://doi.org/10.1111/his.12607>.
- Topping, K. D., & Kelly, D. G. 2019. Investigation of binding characteristics of immobilized toll-like receptor 3 with poly(I:C) for potential biosensor application. *Analytical Biochemistry*, 564–565. <https://doi.org/10.1016/j.ab.2018.05.023>.
- Tsai, S. T., Jin, Y. T., Mann, R. B., & Ambinder, R. F. 1998. Epstein-Barr virus detection in nasopharyngeal tissues of patients with suspected nasopharyngeal carcinoma. *Cancer*, 564-565: 133–140.. [https://doi.org/10.1002/\(SICI\)1097-0142\(19980415\)82:8<1449::AID-CNCR3>3.0.CO;2-4](https://doi.org/10.1002/(SICI)1097-0142(19980415)82:8<1449::AID-CNCR3>3.0.CO;2-4).
- Tsao, S. W., Tsang, C. M., & Lo, K. W. 2017. Epstein – Barr virus infection and nasopharyngeal carcinoma. *Philosophical transactions of the Royal Society of London. Series B, Biological sciences*. 372(1732): 20160270. <https://doi.org/10.1098/rstb.2016.0270>.
- Tsao, S. W., Tsang, C. M., Pang, P. S., Zhang, G., Chen, H., & Lo, K. W. 2012. The biology of EBV infection in human epithelial cells. *Seminars in Cancer Biology*. 22(2): 137–143. <https://doi.org/10.1016/j.semcan.2012.02.004>.
- Tsao, S. W., Tsang, C. M., To, K. F., & Lo, K. W. 2015. The role of Epstein-Barr virus in epithelial malignancies. *Journal of Pathology*. 235(2): 323–333. <https://doi.org/10.1002/path.4448>.
- Tsao, S. W., Yip, Y. L., Tsang, C. M., Pang, P. S., Lau, V. M. Y., Zhang, G., & Lo, K. W. 2014. Etiological factors of nasopharyngeal carcinoma. *Oral Oncology*. 50(5): 330–338. <https://doi.org/10.1016/j.oraloncology.2014.02.006>.
- Tzellos, S., & Farrell, P. J. 2012. Epstein-barr virus sequence variation-biology and disease. *Pathogens*. 1(2): 156–174.. <https://doi.org/10.3390/pathogens1020156>.
- Vérrillaud, B., Gressette, M., Morel, Y., Paturel, C., Herman, P., Lo, K., Tsao, S., Waslef, M., Jimenez-Pailhes, A.-S., & Busson, P. 2012. Toll-like receptor 3 in Epstein-Barr virus-associated nasopharyngeal carcinomas: consistent expression and cytotoxic effects of its synthetic ligand poly(A:U) combined to a Smac-mimetic. *Infectious Agents and Cancer*, 7(1): 36. <https://doi.org/10.1186/1750-9378-7-36>.
- Veyrat, M., Durand, S., Classe, M., Glavan, T. M., Oker, N., Kapetanakis, N. I., Jiang, X., Gelin, A., Herman, P., Casiraghi, O., Zagzag, D., Enot, D., Busson, P., & Vérrillaud, B. 2016. Stimulation of the toll-like receptor 3 promotes metabolic



- reprogramming in head and neck carcinoma cells. *Oncotarget*, 7(50): 82580–82593.. <https://doi.org/10.18632/oncotarget.12892>.
- Wang, J., Huang, H., Lu, J., Bi, P., Wang, F., Liu, X., Zhang, B., & Luo, Y. 2017. *Tumor cells induced-M2 macrophage favors accumulation of Treg in nasopharyngeal carcinoma.* 10(8), 8389–8401.
- Wang, J., Luo, Y., Bi, P., Lu, J., Wang, F., Liu, X., Zhang, B., & Li, X. 2020. Mechanisms of Epstein-Barr virus nuclear antigen 1 favor Tregs accumulation in nasopharyngeal carcinoma. *Cancer Medicine*. 9(15): 5598–5608. <https://doi.org/10.1002/cam4.3213>.
- Wang, M., Zhao, J., Zhang, L., Wei, F., Lian, Y., Wu, Y., Gong, Z., Zhang, S., Zhou, J., Cao, K., Li, X., Xiong, W., Li, G., Zeng, Z., & Guo, C. 2017. Role of tumor microenvironment in tumorigenesis. *Journal of Cancer*. 8(5): 761–773. <https://doi.org/10.7150/jca.17648>.
- Wang, N., Liang, H., & Zen, K. 2014. Molecular mechanisms that influence the macrophage M1-M2 polarization balance. *Frontiers in Immunology*. 5: 614. <https://doi.org/10.3389/fimmu.2014.00614>.
- Wang, X., & Lin, Y. 2008. Tumor necrosis factor and cancer, buddies or foes? *Acta Pharmacologica Sinica*. 29(11): 1275–1288. <https://doi.org/10.1111/j.1745-7254.2008.00889.x>.
- Waters, J. P., Pober, J. S., & Bradley, J. R. 2013. Tumour necrosis factor and cancer. *Journal of Pathology*. 230(3): 241–248. <https://doi.org/10.1002/path.4188>.
- Watson, P. F., & Petrie, A. 2010. Method agreement analysis: A review of correct methodology. *Theriogenology*. 73(9): 1167–1179.. <https://doi.org/10.1016/j.theriogenology.2010.01.003>.
- Wee, J. T. S., Ha, T. C., Loong, S. L. E., & Qian, C. N. 2010. Is nasopharyngeal cancer really a “Cantonese cancer”? *Chinese Journal of Cancer*. 29(5): 517–526. <https://doi.org/10.5732/cjc.009.10329>.
- Whiteside, T. L. 2008. The tumor microenvironment and its role in promoting tumor growth. *Oncogene*. 27(45): 5904–5912. <https://doi.org/10.1038/onc.2008.271>.
- Wong, E. H. C., Tan, H. Y., Dompok, T. M., Mohamad Ishak, L. A., & Loong, S. P. 2021. The First Report on Incidence of Nasopharyngeal Carcinoma in Sabah, Borneo. *Orl*. 83(4): 258–262. <https://doi.org/10.1159/000516597>.
- Wong, H. L., Wang, X., Chang, R. C. C., Jin, D. Y., Feng, H., Wang, Q., Lo, K. W., Huang, D. P., Yuen, P. W., Takada, K., Wong, Y. C., & Tsao, S. W. 2005. Stable expression of EBVs in immortalized nasopharyngeal epithelial cells confers resistance to apoptotic stress. *Molecular Carcinogenesis*. 44(2): 92–101. <https://doi.org/10.1002/mc.20133>.
- Wu, Y., & Zhou, B. P. 2010. TNF- α /NF κ -B/Snail pathway in cancer cell migration and invasion. *British Journal of Cancer*. 102(4): 639–644. <https://doi.org/10.1038/sj.bjc.6605530>.
- Wu, Z. M., Dai, C., Huang, Y., Zheng, C. F., Dong, Q. Z., Wang, G., Li, X. W., Zhang, X. F., Li, B., & Chen, G. 2011. Anti-cancer effects of p21WAF1/CIP1 transcriptional activation induced by dsRNAs in human hepatocellular



- carcinoma cell lines. *Acta Pharmacologica Sinica.* 32(7): 939–946. <https://doi.org/10.1038/APS.2011.28>.
- Xie, S. H., Yu, I. T. S., Tse, L. A., Mang, O. W. K., & Yue, L. 2013. Sex difference in the incidence of nasopharyngeal carcinoma in Hong Kong 1983-2008: Suggestion of a potential protective role of oestrogen. *European Journal of Cancer.* 49(1): 150–155. <https://doi.org/10.1016/j.ejca.2012.07.004>.
- Xu, L., Peng, Q., Xuan, W., Feng, X., Kong, X., Zhang, M., Tan, W., Xue, M., & Wang, F. 2016. Interleukin-29 Enhances Synovial Inflammation and Cartilage Degradation in Osteoarthritis. *Mediators of Inflammation,* 2016. <https://doi.org/10.1155/2016/9631510>.
- Xu, Y., Shi, Y., Yuan, Q., Liu, X., Yan, B., Chen, L., Tao, Y., & Cao, Y. 2013. Epstein-Barr Virus encoded LMP1 regulates cyclin D1 promoter activity by nuclear EGFR and STAT3 in CNE1 cells. *Journal of Experimental and Clinical Cancer Research.* 2016: 9631510. <https://doi.org/10.1186/1756-9966-32-90>.
- Xue, W., Qin, H., Ruan, H., Shugart, Y. Y., & Jia, W. 2013. *Systematic Reviews and Meta- and Pooled Analyses Quantitative Association of Tobacco Smoking With the Risk of Nasopharyngeal Carcinoma: A Comprehensive Meta-Analysis of Studies Conducted Between 1979 and 2011.* 178(3): 325–338. <https://doi.org/10.1093/aje/kws479>.
- Yajima, M., Kanda, T., & Takada, K. 2005. Critical Role of Epstein-Barr Virus (EBV)-Encoded RNA in Efficient EBV-Induced B-Lymphocyte Growth Transformation. *Journal of Virology.* 79(7): 4298–4307. <https://doi.org/10.1128/jvi.79.7.4298-4307.2005>.
- Yamamoto, M., Sato, S., Hemmi, H., Hoshino, K., Kaisho, T., Sanjo, H., Takeuchi, O., Sugiyama, M., Okabe, M., Takeda, K., & Akira, S. 2003. Role of adaptor TRIF in the MyD88-independent toll-like receptor signaling pathway. *Science,* 301(5633): 640–643.. <https://doi.org/10.1126/science.1087262>.
- Yan, Q., Zeng, Z., Gong, Z., Zhang, W., Li, X., He, B., Song, Y., Li, Q., Zeng, Y., Liao, Q., Chen, P., Shi, L., Fan, S., Xiang, B., Ma, J., Zhou, M., Li, X., Yang, J., Xiong, W., & Li, G. 2015. EBV-miR-BART10-3p facilitates epithelial-mesenchymal transition and promotes metastasis of nasopharyngeal carcinoma by targeting BTRC. *Oncotarget,* 6(39): 41766–41782. <https://doi.org/10.18632/oncotarget.6155>.
- Ye, Y., Zhou, Y., Zhang, L., Chen, Y., Lyu, X., Cai, L., Lu, Y., Deng, Y., Wang, J., Yao, K., Fang, W., Cai, H., & Li, X. 2013. EBV-miR-BART1 is involved in regulating metabolism-associated genes in nasopharyngeal carcinoma. *Biochemical and Biophysical Research Communications.* 436(1): 19–24. <https://doi.org/10.1016/j.bbrc.2013.05.008>.
- Yi, M., Cai, J., Li, J., CHen, S., Zeng, Z., Peng, Q., & Al, E. 2017. Rediscovery of NF-κB Signaling in Nasopharyngeal Caiernoma: How Genetic Defect of NF-κB Pathway Interplay with EBV in Driving Oncogenesis. *Journal of Cellular Physiology.* 233(8): 5537–5549.. [https://doi.org/doi: \[10.1002/jcp.26410\]](https://doi.org/doi: [10.1002/jcp.26410]).
- Yoshida, T., Miura, T., Matsumiya, T., Yoshida, H., Morohashi, H., Sakamoto, Y.,



- Kurose, A., Imaizumi, T., & Hakamada, K. 2020. Toll-like receptor 3 as a recurrence risk factor and a potential molecular therapeutic target in colorectal cancer. In *Clinical and Experimental Gastroenterology* (Vol. 13). <https://doi.org/10.2147/CEG.S252157>.
- Yoshizaki, T., Kondo, S., Endo, K., Nakanishi, Y., Aga, M., Kobayashi, E., Hirai, N., Sugimoto, H., Hatano, M., Ueno, T., Ishikawa, K., & Wakisaka, N. 2018. Modulation of the tumor microenvironment by Epstein-Barr virus latent membrane protein 1 in nasopharyngeal carcinoma. *Cancer Sci.* 109(2):272–278. <https://doi.org/10.1111/cas.13473>.
- Young, L. S., & Dawson, C. W. 2014. Epstein-Barr virus and nasopharyngeal carcinoma. *Chinese Journal of Cancer.* 33(12): 581–590. <https://doi.org/10.5732/cjc.014.10197>.
- Young, L. S., & Rickinson, A. B. 2004. Epstein-Barr virus: 40 Years on. *Nature Reviews Cancer.* 4(10): 757–768. <https://doi.org/10.1038/nrc1452>.
- Yu, P. H., Chou, S. F., Chen, C. L., Hung, H., Lai, C. Y., Yang, P. M., Jeng, Y. M., Liaw, S. F., Kuo, H. H., Hsu, H. C., Chen, J. Y., & Wang, W. B. 2013. Upregulation of endocan by epstein-barr virus latent membrane protein 1 and its clinical significance in nasopharyngeal Carcinoma. *PLoS ONE.* 8(12): e82254. <https://doi.org/10.1371/journal.pone.0082254>.
- Yu, Y., Ke, L., Lv, X., Ling, Y. H., Lu, J., Liang, H., Qiu, W., Huang, X., Liu, G., Li, W., Guo, X., Xia, W., & Xiang, Y. 2018a. The prognostic significance of carcinoma-associated fibroblasts and tumor-associated macrophages in nasopharyngeal carcinoma. 10: 1935–1946. *Cancer Management and Research.* <https://doi.org/10.2147/CMAR.S167071>.
- Yu, Y., Ke, L., Lv, X., Ling, Y. H., Lu, J., Liang, H., Qiu, W., Huang, X., Liu, G., Li, W., Guo, X., Xia, W., & Xiang, Y. 2018b. The prognostic significance of carcinoma-associated fibroblasts and tumor-associated macrophages in nasopharyngeal carcinoma. *Cancer Management and Research.* 10: 1935–1946 <https://doi.org/10.2147/CMAR.S167071>.
- Zeng, Z., Zhang, S. F. X., Zhou, S. L. M., & Xiong, W. 2015. Epstein – Barr virus-encoded small RNA 1 (EBER-1) could predict good prognosis in nasopharyngeal carcinoma. *Clin Transl Oncol,* 1, 1–6. <https://doi.org/10.1007/s12094-015-1354-3>.
- Zhang, G., Tsang, C. M., Deng, W., Yip, Y. L., Lui, V. W. Y., Wong, S. C. C., Cheung, A. L. M., Hau, P. M., Zeng, M., Lung, M. L., Chen, H., Lo, K. W., Takada, K., & Tsao, S. W. 2013. Enhanced IL-6/IL-6R Signaling Promotes Growth and Malignant Properties in EBV-Infected Premalignant and Cancerous Nasopharyngeal Epithelial Cells. *PLoS ONE,* 8(5), 1–13. <https://doi.org/10.1371/journal.pone.0062284>.
- Zhang, H., Wang, J., Yu, D., Liu, Y., Xue, K., & Zhao, X. 2017. Role of Epstein-Barr virus in the development of nasopharyngeal carcinoma. *Open Medicine (Poland),* 12(1), 171–176. <https://doi.org/10.1515/med-2017-0025>.
- Zhao, R., Liu, Y., Wang, H., Yang, J., Niu, W., Fan, S., Xiong, W., Ma, J., Li, X.,



- Phillips, J. B., Tan, M., Qiu, Y., Li, G., & Zhou, M. 2017. BRD7 plays an anti-inflammatory role during early acute inflammation by inhibiting activation of the NF-κB signaling pathway. *Cellular and Molecular Immunology*. 14(10): 830–841. <https://doi.org/10.1038/cmi.2016.31>.
- Zheng, Y. M., Tuppin, P., Hubert, A., Jeannel, D., Pan, Y. J., Zeng, Y., & de Thé, G. 1994. Environmental and dietary risk factors for nasopharyngeal carcinoma: A case-control study in Zangwu County, Guangxi, China. *British Journal of Cancer*. 69(3): 508–514. <https://doi.org/10.1038/bjc.1994.92>.
- Zuo, L., Yue, W., Du, S., Xin, S., Zhang, J., Liu, L., Li, G., & Lu, J. 2017. An update: Epstein-Barr virus and immune evasion via microRNA regulation. *Virologica Sinica*. 32(3):175-187. <https://doi.org/10.1007/s12250-017-3996-5>.