

DAFTAR PUSTAKA

- Abbas, A.K., Lichtman, A.H., Pillai, S., Baker, D.L., Baker, A., 2015. Cellular and Molecular Immunology, 8th ed. Elsevier Saunders, Philadelphia.
- Abbas, N., Shakoori, A.R., 2007. Hepatitis B Virus : X Gene. Pak. J. Zool. 27, 127–136.
- Abe, A., Kazuaki, I., Take, A.T., Junko, K., Nooki, K., Satoshi, T., Mkoto, Y., Michinori, K., 1999. Quantification of Hepatitis B virus genomic DNA by Real-Time detection. J. Clin. Microbiol. 37, 2899–2903. <https://doi.org/10.1016/j.jhep.2012.02.010>
- Al-qahtani, A.A., Al-anazi, M.R., Nazir, N., Ghai, R., Ayman, A., Bohol, F., Al-ahdal, M.N., 2017. Hepatitis B virus (HBV) X gene mutations and their association with liver disease progression in HBV-infected patients. Oncotarget 8, 105115–105125.
- Al-sadeq, D.W., Taleb, S.A., Zaied, R.E., Fahad, S.M., Smatti, M.K., Rizeq, B.R., Thani, A.A. Al, Yassine, H.M., Nasrallah, G.K., 2019. Hepatitis B Virus Molecular Epidemiology, Diagnosis in the MENA Region : An Update. Pathogens 8, 1–22.
- Alberts, B., Johnson, A., Lewis, J., Morgan, D., Raff, M., Roberts, K., Walter, P., 2015. Molecular Biology of The Cell, 6th Editio. ed. Garland Science, Taylor & Francis Group, New York.
- Ali, A., Abdel-hafiz, H., Suhail, M., Al-mars, A., Zakaria, M.K., Fatima, K., Ali, A., Suhail, M., Al-mars, A., Ahmad, S., 2014. Hepatitis B virus , HBx mutants and their role in hepatocellular carcinoma. World J. Gastroenterol. 20, 10238–10248. <https://doi.org/10.3748/wjg.v20.i30.10238>
- An, N., 2015. Oral Contraceptives Use and Liver Cancer Risk. Medicine (Baltimore). 94, 1–7. <https://doi.org/10.1097/MD.0000000000001619>
- An, P., Xu, J., Yu, Y., Winkler, C.A., 2018. Host and Viral Genetic Variation in HBV-Related Hepatocellular Carcinoma. Front. Genet. 9, 1–15. <https://doi.org/10.3389/fgene.2018.00261>
- Andrisani, O.M., Barnabas, S., 1999. The transcriptional function of the hepatitis B virus X protein and its role in hepatocarcinogenesis (Review). Int. J. Oncol. 15, 373–379.
- Arbuthnot, P., Capovilla, A., Kew, M., 2000. Putative role of hepatitis B virus X protein in hepatocarcinogenesis : Effects on apoptosis , DNA repair , mitogen-activated protein kinase and JAK / STAT pathways. J. Gastroenterol. Hepatol. 15, 357–368.
- Aroucha, D.C., Carmo, R.F., Silva, L.R.V., Lima, R.E., Mendonca Furtado, T., Arnez, L.E., Cavalcanti, M. do S.M., Muniz, M.T.C., Aroucha, M.L., Pereira, E.R.S.L.B., Moura, P., Pereira, L.M.M.B., Coelho, M.R., 2016. TNF-a and IL-10 Polymorphisms Increase the Risk to Hepatocellular Carcinoma in HCV Infected Individuals. J. Med. Virol. 88, 1587–95.
- Aroucha, D.C.B.L., Carmo, R.F., Moura, P., Silva, J.L.A., Vasconcelos, L.R.S.,

- Cavalcanti, M.S.M., Muniz, M.T.C., Aroucha, M.L., Siqueira, E.R.F., Cahú, G.G.O.M., Pereira, L.M.M.B., Coêlho, M.R.C.D., 2013. Cytokine High tumor necrosis factor- α / interleukin-10 ratio is associated with hepatocellular carcinoma in patients with chronic hepatitis C. *Cytokine* 62, 421–425. <https://doi.org/10.1016/j.cyto.2013.03.024>
- Artarini, A., Jessica, H.G., Kartikasari, R.R., Riani, C., Retnoningrum, D.S., 2016. Detection of Hepatitis B Virus X Gene Mutation from Local Clinical Samples. *Microbiol. Indones.* 10, 9–14. <https://doi.org/10.5454/mi.10.1.2>
- Ashari, M.A., 2012. Hubungan Kadar dan Polimorfisme Transforming Growth Factor – β 1 dengan Kejadian Osteoporosis pada Wanita. Universitas Gadjah Mada.
- Avci, E., Avci, G.A., Ozcelik, B., Cevher, S.C., Suicmez, M., 2017. Transforming growth factor beta-1 An important biomarker for developing cardiovascular diseases in chronic renal failure. *Bratisl Med J* 118, 175 – 178.
- Ayub, A., Ashfaq, U.A., Haque, A., 2013. Review Article HBV Induced HCC : Major Risk Factors from Genetic to Molecular Level. *Biomed Res. Int.* 2013, 1–14.
- Baig, S., 2009. Gender disparity in infections of hepatitis B virus. *J. Coll. Physicians Surg. Pakistan* 19, 598–600. <https://doi.org/09.2009/JCPSP.598600>
- Balmasova, I.P., Yushchuk, N.D., Mynbaev, O.A., Alla, N.R., Malova, E.S., Shi, Z., 2014. Immunopathogenesis of chronic hepatitis B. *World J. Gastroenterol.* 20, 14156–14171. <https://doi.org/10.3748/wjg.v20.i39.14156>
- Banday, M.Z., Balkhi, H.M., Hamid, Z., Sameer, A.S., Chowdri, N.A., Haq, E., 2016. Tumor necrosis factor-Alpha (TNF-Alpha)-308G/A promoter polymorphism in colorectal cancer in ethnic Kashmiri population - A case control study in a detailed perspective. *Meta Gene* 9, 128–136. <https://doi.org/10.1016/j.mgene.2016.06.001>
- Baptista, M., Kramvis, A., Kew, M.C., 1999. High prevalence of 1762(T) 1764(A) mutations in the basic core promoter of hepatitis B virus isolated from black Africans with hepatocellular carcinoma compared with asymptomatic carriers. *Hepatology* 29, 946–953. <https://doi.org/10.1002/hep.510290336>
- Barbini, L., Tadey, L., Fernandez, S., Bouzas, B., Campos, R., 2012. Molecular characterization of hepatitis B virus X gene in chronic hepatitis B patients. *Viol. J.* 9, 1–7.
- Baumert, T.F., Thimme, R., Weizsäcker, F. Von, Baumert, T.F., Thimme, R., Weizsäcker, F. Von, 2007. Pathogenesis of hepatitis B virus infection. *World J. Gastroenterol.* 13, 82–90.
- Belbacha, I., Cherkaoui, I., Akrim, M., Dooley, K.E., Aouad, R. El, 2007. Seroprevalence of hepatitis B and C among barbers and their clients in the Rabat region of Morocco. *East. Mediterr. J.* 17, 911–919.
- Bharadwaj, M., Roy, G., Dutta, K., Misbah, M., Husain, M., Hussain, S., 2013. Tackling hepatitis B virus-associated hepatocellular carcinoma - The future is

- now. *Cancer Metastasis Rev.* 32, 229–268. <https://doi.org/10.1007/s10555-012-9412-6>
- Bhutta, R.A., Syed, N.A., Ahmad, A., Khan, S., 2019. Hepatitis B Virus [WWW Document]. URL <http://www.labpedia.net/test/223>. Diakses pada: 22 April 2017
- Biazar, T., Yahyapour, Y., Roushan, M.R.H., Rajabnia, R., Sadeghi, M., Taheri, H., Ranaei, M., Bayani, M., 2015. Relationship between hepatitis B DNA viral load in the liver and its histology in patients with chronic hepatitis B. *Casp. J Intern Med* 6, 209–212.
- Bisceglie, A.M. Di, 2009. Hepatitis B And Hepatocellular Carcinoma. *Hepatology* 49, S56–S60. <https://doi.org/10.1002/hep.22962>.Hepatitis
- Bissell, D.M., 2001. Chronic liver injury, TGF-beta, and cancer. *Exp. Mol. Med.* 33, 179–90. <https://doi.org/10.1038/emm.2001.31>
- Bordiny, M. El, Hanafy, S.M., Abdo, A., 2011. Impact of single nucleotide polymorphism of TGF- β 1 gene (SNP-Codon10) on hepatocellular carcinoma risk in Egyptian patients following HCV infection. *Aust. J. Basic Appl. Sci.* 5, 1814–1821.
- Borrás, C., Gambini, J., López-grueso, R., Pallardó, F. V, Viña, J., 2010. Biochimica et Biophysica Acta Direct antioxidant and protective effect of estradiol on isolated mitochondria. *BBA - Mol. Basis Dis.* 1802, 205–211. <https://doi.org/10.1016/j.bbadis.2009.09.007>
- Bortolotti, F., Guido, M., 2007. Reversal of liver cirrhosis: A desirable clinical outcome and its pathogenic background. *J. Pediatr. Gastroenterol. Nutr.* 44, 401–406. <https://doi.org/10.1097/MPG.0b013e318032069a>
- Botros, M., Sikaris, K.A., 2013. The de ritis ratio: The test of time. *Clin. Biochem. Rev.* 34, 117–130.
- Cai, G., Chen, Y., Li, L., Zhou, B., Hu, C., Yu, Y., Xu, M., Wang, Zhengting, Liu, K., Wang, Zhifang, Jiang, Z., 2018. Global Journal of Infectious Diseases and Clinical Research Meta-Analysis of Risk Factors for Development of Liver Cirrhosis in Chronic Hepatitis B Patients. *Glob. J. Infect. Dis. Clin. Res.* 4, 4–9.
- Cai, J., Cai, Y. an, Ma, Q., Chang, F. an, Xu, L., 2017. Association of p53 codon 72 polymorphism with susceptibility to hepatocellular carcinoma in a Chinese population from northeast Sichuan. *Biomed. Reports* 6, 217–222. <https://doi.org/10.3892/br.2017.840>
- Cainelli, F., Kew, M.C., 2012. Hepatocellular carcinoma in developing countries : Prevention , diagnosis and treatment. *World J. Gastroenterol.* 4, 99–104. <https://doi.org/10.4254/wjh.v4.i3.99>
- CDC, 2016. Viral Hepatitis - Hepatitis B Information [WWW Document]. URL <https://www.cdc.gov/hepatitis/hbv/hbvfaq.htm#treatment>. Diakses pada: 10 Januari 2018
- Chan, C., Thurnherr, T., Wang, J., Gallart-Palau, X., Sze, S.K., Rozen, S., Lee, C.G., 2016. Global re-wiring of p53 transcription regulation by the hepatitis B

- virus X protein. *Mol. Oncol.* 10, 1183–1195. <https://doi.org/10.1016/j.molonc.2016.05.006>
- Chang, J.J., Lewin, S.R., 2007. Immunopathogenesis of hepatitis B virus infection. *Immunol. Cell Biol.* 85, 16–23. <https://doi.org/10.1038/sj.icb.7100009>
- Chen, G.G., Li, M.Y., Ho, R.L.K., Chak, E.C.W., Lau, W.Y., Lai, P.B.S., 2005. Identification of hepatitis B virus X gene mutation in Hong Kong patients with hepatocellular carcinoma. *J. Clin. Virol.* 34, 7–12. <https://doi.org/10.1016/j.jcv.2005.01.006>
- Chen, Y.C., Hsu, P.Y., Hsiao, C.C., Lin, M.C., 2019. Epigenetics: A Potential Mechanism Involved in the Pathogenesis of Various Adverse Consequences of Obstructive Sleep Apnea. *Int. J. Mol. Sci.* 20, 2937. <https://doi.org/10.3390/ijms20122937>
- Cheng, K., Yang, N., Mahato, R.I., 2009. TGF-beta1 gene silencing for treating liver fibrosis. *Mol. Pharm.* 6, 772–9. <https://doi.org/10.1021/mp9000469>
- Cheong, J.Y., Cho, S.W., Hwang, I.L., Yoon, S.K., Lee, J.H., Park, C.S., Lee, J.E., Hahm, K.B., Kim, J.H., 2006. Association between chronic hepatitis B virus infection and interleukin-10, tumor necrosis factor-alpha gene promoter polymorphisms. *J. Gastroenterol. Hepatol.* 21, 1163–1169. <https://doi.org/10.1111/j.1440-1746.2006.04304.x>
- Chou, H.T., Chen, C.H., Tsai, C.H., Tsai, F.J., 2004. Association between transforming growth factor- β 1 gene C-509T and T869C polymorphisms and rheumatic heart disease. *Am. Heart J.* 148, 181–186. <https://doi.org/10.1016/j.ahj.2004.03.032>
- Chu, C., Hussain, M., Lok, F., 2002. Quantitative Serum HBV DNA levels During Different Stages of Chronic Hepatitis B Infection. *Hepatology* 36, 1408–1415.
- Cooper, a, 2003. The earliest steps in hepatitis B virus infection. *Biochim. Biophys. Acta - Biomembr.* 1614, 89–96. [https://doi.org/10.1016/S0005-2736\(03\)00166-4](https://doi.org/10.1016/S0005-2736(03)00166-4)
- Croagh, C.M., 2014. Natural history of chronic hepatitis B: Phases in a complex relationship. *World J. Gastroenterol.* 20, 10395–10404. <https://doi.org/10.3748/wjg.v20.i30.10395>
- D'Souza, R., Foster, G.R., 2004. Diagnosis and treatment of chronic hepatitis B. *J. R. Soc. Med.* 97, 318–321. <https://doi.org/10.1258/jrsm.97.7.318>
- Departemen Kesehatan Republik Indonesia, 2016. Sebagian Besar Kematian Akibat Hepatitis Virus Berhubungan dengan Hepatitis B dan C Kronis [WWW Document]. <http://www.depkes.go.id/article/view/16042700001/sebagian-besar-kematian-akibat-hepatitis-virus-berhubungan-dengan-hepatitis-b-dan-c-kronis.html>. Diakses pada: 25 Juli 2017
- Di Como, C.J., Gaiddon, C., Prives, C., 1999. p73 function is inhibited by tumor-derived p53 mutants in mammalian cells. *Mol. Cell. Biol.* 19, 1438–49. <https://doi.org/10.1128/MCB.19.2.1438>
- Dondeti, M.F., El-maadawy, E.A., Talaat, R.M., 2016. Hepatitis-related

- hepatocellular carcinoma : Insights into cytokine gene polymorphisms. *World J. Gastroenterol.* 22, 6800–6816. <https://doi.org/10.3748/wjg.v22.i30.6800>
- Dong, Z.Z., Yao, D.F., Yao, M., Qiu, L.W., Zong, L., Wu, W., Wu, X.H., Yao, D.B., Meng, X.Y., 2008. Clinical impact of plasma TGF- β 1 and circulating TGF- β 1 mRNA in diagnosis of hepatocellular carcinoma. *Hepatobiliary Pancreat. Dis. Int.* 7, 288–295.
- Doo, E.C., Ghany, M.G., 2010. Hepatitis B Virology for Clinicians. *Clin. Liver Dis.* 14, 397–408. <https://doi.org/10.1016/j.cld.2010.05.001>
- Dooley, S., Ten Dijke, P., 2012. TGF- β in progression of liver disease. *Cell Tissue Res.* 347, 245–256. <https://doi.org/10.1007/s00441-011-1246-y>
- Driessler, F., Venstrom, K., Sabat, R., Asadullah, K., Area, B., 2004. Molecular mechanisms of interleukin-10-mediated inhibition of NF- κ B activity : a role for p50 64–73. <https://doi.org/10.1046/j.1365-2249.2004.02342.x>
- EASL, 2017. EASL 2017 Clinical Practice Guidelines on the management of hepatitis B virus infection. *J. Hepatol.* 67, 370–398. <https://doi.org/10.1016/j.jhep.2017.03.021>
- El-serag, H.B., 2011. Hepatocellular Carcinoma. *N. Engl. J. Med.* 365, 1118–27.
- El Far, M.A., Atwa, M.A., Yahya, R.S., El Basuni, M.A., 2006. Evaluation of serum levels of p53 in hepatocellular carcinoma in Egypt. *Clin. Chem. Lab. Med.* 44, 653–656. <https://doi.org/10.1515/CCLM.2006.091>
- Elmore, L.W., Hancock, A.R., Chang, S.-F., Wang, X.W., Chang, S., Callahan, C.P., Geller, D.A., Will, H., Harris, C.C., 1997. Hepatitis B virus X protein and p53 tumor suppressor interactions in the modulation of apoptosis. *Proc. Natl. Acad. Sci. USA* 94, 14707–14712. <https://doi.org/10.1073/pnas.94.26.14707>
- Eskandari, E., Metanat, M., Pahlevani, E., Nakhzari-Khodakheir, T., 2017. Association between TGF β 1 polymorphisms and chronic hepatitis B infection in an Iranian population. *Rev. Soc. Bras. Med. Trop.* 50, 301–308. <https://doi.org/10.1590/0037-8682-0266-2016>
- Eskander, E.F., Abd-Rabou, A.A., Yahya, S.M.M., El Sherbini, A., Mohamed, M.S., Shaker, O.G., 2014. p53 codon 72 single base substitution in viral hepatitis C and hepatocarcinoma incidences. *Indian J. Clin. Biochem.* 29, 3–7. <https://doi.org/10.1007/s12291-013-0317-0>
- European Centre for Disease Prevention and Control, 2016. Hepatitis B. Stockholm.
- Falletti, E., Fabris, C., Toniutto, P., Fontanini, E., Cussigh, A., Bitetto, D., Fornasiere, E., Avellini, C., Minisini, R., Pirisi, M., 2008. TGF-Beta1 genotypes in cirrhosis: Relationship with the occurrence of liver cancer. *Cytokine* 44, 256–261. <https://doi.org/10.1016/j.cyto.2008.08.008>
- Fan, W., Shi, B., Wei, H., 2011. Comparison of hepatitis B X gene mutation between patients with hepatocellular carcinoma and patients with chronic hepatitis B. *Virus Genes* 42, 162–170. <https://doi.org/10.1007/s11262-010-0557-5>

- Fatimawali, Kepel, B., 2014. Analisis Mutasi Gen Protein X Virus HBV pada Penderita Hepatitis B Akut di Manado. *J. LPPM Bid. Sains dan Teknol.* 1, 47–55.
- Freed-Pastor, W.A., Prives, C., 2012. Mutant p53: One name, many proteins. *Genes Dev.* 26, 1268–1286. <https://doi.org/10.1101/gad.190678.112>
- Gama, S., Chachá, F., Gomes-gouvêa, M.S., Ferreira, C., Villanova, M.G., Souza, F.F., Teixeira, A.C., Dinis, A., Renato, J., Pinho, R., Lourdes, A. De, Martinelli, C., 2017. Basal core promoter and precore mutations among hepatitis B virus circulating in Brazil and its association with severe forms of hepatic diseases 112, 626–631. <https://doi.org/10.1590/0074-02760160540>
- Geng, M., Xin, X., Bi, L., Zhou, L., Liu, X., 2015. 2015 Advances in Hepatitis B virus Molecular mechanism of hepatitis B virus X protein function in hepatocarcinogenesis. *World J. Gastroenterol.* 21, 10732–10738. <https://doi.org/10.3748/wjg.v21.i38.10732>
- Ghabeshi, S., Sharifi, Z., Hosseini, S.M., Mahmoodian, M., 2013. Correlation Between Viral Load of HBV in Chronic Hepatitis B Patients and Precore and Basal Core Promoter Mutations. *Hepat. Mon.* 13, 1–5. <https://doi.org/10.5812/hepatmon.7415>
- Goldstein, S.T., Zhou, F., Hadler, S.C., Bell, B.P., Mast, E.E., Margolis, H.S., 2005. A mathematical model to estimate global hepatitis B disease burden and vaccination impact. *Int. J. Epidemiol.* 34, 1329–1339. <https://doi.org/10.1093/ije/dyi206>
- Gouas, D.A., Villar, S., Ortiz-Cuaran, S., Legros, P., Ferro, G., Kirk, G.D., Lesi, O.A., Mendy, M., Bah, E., Friesen, M.D., Groopman, J., Chemin, I., Hainaut, P., 2012. TP53 R249S mutation, genetic variations in HBX and risk of hepatocellular carcinoma in The Gambia. *Carcinogenesis* 33, 1219–1224. <https://doi.org/10.1093/carcin/bgs135>
- Greenblatt, M.S., Bennett, W.P., Hollstein, M., Harris, C.C., 1994. Mutations in the p53 tumor suppressor gene: Clues to cancer etiology and molecular pathogenesis. *Cancer Res.* 54, 4855–4878. [https://doi.org/10.1016/0169-5002\(94\)92083-4](https://doi.org/10.1016/0169-5002(94)92083-4)
- Grochola, L.F., Zeron-Medina, J., Meriaux, S., Bond, G.L., 2010. Single-nucleotide polymorphisms in the p53 signaling pathway. *Cold Spring Harb. Perspect. Biol.* 2, 1–18. <https://doi.org/10.1101/cshperspect.a001032>
- Guerrieri, F., Belloni, L., Pediconi, N., Levrero, M., 2013. Molecular mechanisms of HBV-associated hepatocarcinogenesis. *Semin. Liver Dis.* 33, 147–156. <https://doi.org/10.1055/s-0033-1345721>
- Guo, Y., Zang, C., Li, Y., Yuan, L., Liu, Q., Zhang, L., Li, S., 2013. Association Between TGF- B1 Polymorphisms and Hepatocellular Carcinoma Risk : A Meta-Analysis. *Genet. Test. Mol. Biomarkers* 17, 814–820. <https://doi.org/10.1089/gtmb.2013.0268>
- Hamid, A.S., Tesfamariam, I.G., Zhang, Y., Zhang, Z.G., 2013. Aflatoxin B1-induced hepatocellular carcinoma in developing countries : Geographical

- distribution , mechanism of action and prevention (Review). *Oncol. Lett.* 5, 1087–1092. <https://doi.org/10.3892/ol.2013.1169>
- Hann, H.W., Wan, S., Myers, R.E., Hann, R.S., Xing, J., Chen, B., Yang, H., 2012. Comprehensive Analysis of Common Serum Liver Enzymes as Prospective Predictors of Hepatocellular Carcinoma in HBV Patients. *PLoS One* 7, 6–15. <https://doi.org/10.1371/journal.pone.0047687>
- Harkisoen, S., Arends, J.E., Hoek, J.A.R. Van Den, Whelan, J., Erpecum, K.J. Van, Boland, G.J., Hoepelman, A.I.M., 2014. Historic and current hepatitis B viral DNA and quantitative HBsAg level are not associated with cirrhosis in non-Asian women with chronic hepatitis B. *Int. J. Infect. Dis.* 29, 133–138. <https://doi.org/10.1016/j.ijid.2014.08.005>
- Hassan, M.M., Botrus, G., Abdel-wahab, R., Wolff, R.A., Li, D., Rashid, A., Lenzi, R., Hassabo, H.M., Abaza, Y., Ahmed, S., 2018. Estrogen Replacement Reduces Risk and Increases Survival Times of Women With Hepatocellular Carcinoma. *Clin Gastroenterol Hepatol* 15, 1791–1799. <https://doi.org/10.1016/j.cgh.2017.05.036>. Estrogen
- Hayati, L., Delvia, S., 2018. Hubungan Polimorfisme Gen p53 Codon 72 dengan Kejadian Kanker Serviks di Rumah Sakit Dr. Mohammad Hoesin Palembang. *Sriwij. J. Med.* 1, 209–216.
- He, Y., Huang, C., Sun, X., Long, X. ran, Lv, X. wen, Li, J., 2012. MicroRNA-146a modulates TGF-beta1-induced hepatic stellate cell proliferation by targeting SMAD4. *Cell. Signal.* 24, 1923–1930. <https://doi.org/10.1016/j.cellsig.2012.06.003>
- Heidari, Z., Moudi, B., Mahmoudzadeh Sagheb, H., Moudi, M., 2016. Association of TNF- α Gene Polymorphisms with Production of Protein and Susceptibility to Chronic Hepatitis B Infection in the South East Iranian Population. *Hepat. Mon.* 16, 1–11. <https://doi.org/10.5812/hepatmon.41984>
- Hochman, J. a, Balistreri, W.F., 2003. Chronic Viral Hepatitis : Always Be Current! *Pediatr. Rev.* 24, 399–410. <https://doi.org/10.1542/pir.24-12-399>
- Hosseini, R.A., Azimzadeh, P., Mohebbi, S., Hosseini, S., Romani, S., Khanyaghma, M., 2014. Lack of Association Between Transforming Growth Factor Beta 1 -509C/T and +915G/C Polymorphisms and Chronic Hepatitis B in Iranian Patients. *Hepat. Mon.* 14, 301–308.
- Hu, Q., Lou, G.-G., Liu, Y.-C., Qian, L., Lv, B.-D., 2014. The Tumor Necrosis Factor- α -308 and -238 Polymorphisms and Risk of.pdf. *Curr. Ther. Res.* 76, 70–75.
- Hu, S., Zhao, L., Yang, J., Hu, M., 2014. The association between polymorphism of P53 Codon72 Arg/Pro and hepatocellular carcinoma susceptibility: Evidence from a meta-analysis of 15 studies with 3,704 cases. *Tumor Biol.* 35, 3647–3656. <https://doi.org/10.1007/s13277-013-1483-7>
- Hussain, S.P., Schwank, J., Staib, F., Wang, X.W., Harris, C.C., 2007. TP53 mutations and hepatocellular carcinoma: Insights into the etiology and pathogenesis of liver cancer. *Oncogene* 26, 2166–2176.

<https://doi.org/10.1038/sj.onc.1210279>

- Hytiroglou, P., Snover, D.C., Alves, V., Balabaud, C., Bhathal, P.S., Bioulac-Sage, P., Crawford, J.M., Dhillon, A.P., Ferrell, L., Guido, M., Nakanuma, Y., Paradis, V., Quaglia, A., Theise, N.D., Thung, S.N., Tsui, W.M.S., Van Leeuwen, D.J., 2012. Beyond “cirrhosis.” *Am. J. Clin. Pathol.* 137, 5–9. <https://doi.org/10.1309/AJCP2T2OHTAPBTMP>
- Iavarone, M., Trabut, J.-B., Delpuech, O., Carnot, F., Colombo, M., Kremsdorf, D., Br  chot, C., Thiers, V., 2003. Characterisation of hepatitis B virus X protein mutants in tumour and non-tumour liver cells using laser capture microdissection. *J. Hepatol.* 39, 253–261. [https://doi.org/10.1016/S0168-8278\(03\)00217-4](https://doi.org/10.1016/S0168-8278(03)00217-4)
- Inan, N., Tabak, F., 2015. Hepatitis B Virus : Biology and Life Cycle. *Viral Hepat. J.* 21, 1–7. <https://doi.org/10.4274/vhd.36036>
- Jamil, K., Jayaraman, A., Ahmad, J., Joshi, S., Yerra, S.K., 2016. TNF-alpha -308G/A and -238G/A polymorphisms and its protein network associated with type 2 diabetes mellitus. *Saudi J. Biol. Sci.* 1–9. <https://doi.org/10.1016/j.sjbs.2016.05.012>
- Jang, J.W., Chun, J.Y., Park, Y.M., Shin, S.K., Yoo, W., Kim, S.O., Hong, S.P., 2012. Mutational complex genotype of the hepatitis B virus X/precure regions as a novel predictive marker for hepatocellular carcinoma. *Cancer Sci.* 103, 296–304. <https://doi.org/10.1111/j.1349-7006.2011.02170.x>
- Jeng, J., Tsai, J., Chuang, L., Ho, M., Lin, Z., Hsieh, M., 2007. Tumor Necrosis Factor- A 308 . 2 Polymorphism Is Associated with Advanced Hepatic Fibrosis and Higher Risk for heparocellular Carcinoma. *Neoplasia* 9, 987–992. <https://doi.org/10.1593/neo.07781>
- Jeng, K.-S., Sheen, I.-S., Chen, B.-F., Wu, J.-Y., 2000. Is the p53 Gene Mutation of Prognostic Value in Hepatocellular Carcinoma After Resection? *Arch. Surg.* 135, 1329–1333.
- Karimi-googheri, M., Daneshvar, H., Nosratabadi, R., Zare-bidaki, M., Hassanshahi, G., Ebrahim, M., Arababadi, M.K., Kennedy, D., 2014. Important Roles Played by TGF- b in Hepatitis B Infection. *J. Med. Virol.* 86, 102–108. <https://doi.org/10.1002/jmv>
- Keum, W., Parkt, C., Lee, J., Khil, L., Kang, I., Kim, S., Jung, J., Oh, S., Wo, H., Lee, J., Kim, Y., Yoon, Y., Choi, J., Ha, J., 1997. Primers Determine the Sensitivity of PCR-mediated Hepatitis B Virus DNA Detection and Pretreatment of PCR Mixture with 8-Methoxypsoralen Eliminates False-positive Results. *Mol. Cells* 7, 244–250.
- Kew, M.C., 2013. Aflatoxins as a Cause of Hepatocellular Carcinoma. *J. Gastrointestin Liver Dis* 22, 305–310.
- Kgatle, M.M., Kalla, A.A., Spearman, C.W., Hairwadzi, H.N., 2017. The Role of HBx-mediated Transcriptional Activities and Epigenetic Alterations in Hepatitis B Virusinduced Hepatocellular Carcinoma. *J. Emerg. Dis. Virol.* 3, 1–10. <https://doi.org/10.16966/2473-1846.126>

- Khan, F., Shams, S., Qureshi, I.D., Israr, M., Khan, H., 2011. Hepatitis B virus infection among different sex and age groups in Pakistani Punjab. *Viol. J.* 8, 225. <https://doi.org/10.1186/1743-422X-8-225>
- Kim, H.-J., Park, J.-H., Jee, Y., Lee, S.-A., Kim, H., Song, B.-C., Yang, S., Lee, M., Yoon, J.-H., Kim, Y.J., Lee, H.-S., Hwang, E.-S., Kook, Y.-H., Kim, B.-J., 2008. Hepatitis B Virus X Mutations Occurring Naturally Associated With Clinical Severity of Liver Disease Among Korean Patients With Chronic Genotype C Infection. *J. Med. Virol.* 80, 1337–1343. <https://doi.org/10.1002/jmv>
- Kim, H., Lee, S., Kim, B., Kim, H., Lee, S., Kim, B., 2016. X region mutations of hepatitis B virus related to clinical severity. *World J. Gastroenterol.* 22, 5467–5478. <https://doi.org/10.3748/wjg.v22.i24.5467>
- Kim, Y.J., Lee, H.-S., Im, J.P., Min, B.-H., Kim, H.-D., Jeong, J.B., Yoon, J.-H., Kim, C.Y., Kim, M.S., Kim, J.Y., Jung, J.H., Kim, L.H., Park, B.L., Shin, H.D., 2003. Association of Transforming Growth Factor-Beta1 Gene Polymorphism with a Hepatocellular Carcinoma Risk in Patients with Chronic Hepatitis B Virus Infection. *Exp. Mol. Med.* 35, 196–202.
- Koike, K., 2009. Hepatitis B virus X gene is implicated in liver carcinogenesis. *Cancer Lett.* 286, 60–68. <https://doi.org/10.1016/j.canlet.2009.04.010>
- Korah, T.E.M., Abd Elfatah Badr, E., Mohamed Emara, M., Ahmed Samy Kohla, M., Gamal Saad Michael, G., 2016. Relation between sex hormones and hepatocellular carcinoma. *Andrologia* 48, 948–955. <https://doi.org/10.1111/and.12536>
- Kusumobroto, H.O., 2015. Sirosis Hati, in: Tjokroprawiro, A., Setiawan, P.B., Effendi, C., Santoso, D., Soegiarto, G. (Eds.), *Buku Ajar Ilmu Penyakit Dalam*. Airlangga University Press, Surabaya, pp. 292–298.
- Kwun, H.J., Jang, K.L., 2004. Natural variants of hepatitis B virus X protein have differential effects on the expression of cyclin-dependent kinase inhibitor p21 gene. *Nucleic Acids Res.* 32, 2202–2213. <https://doi.org/10.1093/nar/gkh553>
- Lamontagne, R.J., Bagga, S., Bouchard, M.J., 2016. Hepatitis B virus molecular biology and pathogenesis. *Hepatoma Res.* 2, 163–86. <https://doi.org/10.20517/2394-5079.2016.05>
- Lara-Pezzi, E., Majano, P.L., Gomez-Gonzalo, M., Garcia-Monzon, C., Moreno-Otero, R., Levrero, M., Lopez-CABRERA, M., 1998. The Hepatitis B Virus X Protein Up-regulates Tumor Necrosis Factor-Alpha Gene Expression in Hepatocytes. *Hepatology* 28, 1013–1021.
- Ledesma, M.M.G.L., Galdame, O., Bouzas, B., Tadey, L., Livellara, B., Giuliano, S., Viaut, M., Paz, S., Fainboim, H., Gadano, A., Campos, R., Flichman, D., 2011. Characterization of the basal core promoter and precore regions in anti-HBe-positive inactive carriers of hepatitis B virus. *Int. J. Infect. Dis.* 15, 314–320. <https://doi.org/10.1016/j.ijid.2010.12.009>
- Lee, J., Han, K., Lee, J.M., Park, J.H., Kim, H., 2011. Impact of Hepatitis B Virus (HBV) X Gene Mutations on Hepatocellular Carcinoma Development in

- Chronic HBV Infection. *Clin. Vaccine Immunol.* 18, 914–921. <https://doi.org/10.1128/CVI.00474-10>
- Lee, S., Kim, H., Won, Y., Seok, S., Na, Y., Shin, H., Inn, K., Kim, B., 2015. Male-specific hepatitis B virus large surface protein variant W4P potentiates tumorigenicity and induces gender disparity. *Mol. Cancer* 14, 1–10. <https://doi.org/10.1186/s12943-015-0303-7>
- Lee, U.E., Friedman, S.L., 2011. Mechanisms of hepatic fibrogenesis. *Best Pract. Res. Clin. Gastroenterol.* 25, 195–206. <https://doi.org/10.1016/j.bpg.2011.02.005>
- Lemeshow, S., Jr, D.W.H., Klar, J., Lwanga, S.K., 1990. Adequacy of Sample Size in Health Studies. John Wiley and Sons/World Health Organization.
- Li, W., Goto, K., Matsubara, Y., Ito, S., Muroyama, R., Li, Q., 2015. The Characteristic Changes in Hepatitis B Virus X Region for Hepatocellular Carcinoma : A Comprehensive Analysis Based on Global Data. *PLoS One* 10, 1–16. <https://doi.org/10.1371/journal.pone.0125555>
- Li, X., Liang, C., Parkman, V., Lv, Z., 2018. The association between TNF- α 238A/G and 308A/G polymorphisms and juvenile idiopathic arthritis. *Medicine (Baltimore)*. 97, 1–11.
- Liang, T.J., 2009. Hepatitis B: The Virus and Disease. *Hepatology* 49, S13–S21. <https://doi.org/10.1002/hep.22881.Hepatitis>
- Liaw, Y., Brunetto, M.R., Hadziyannis, S., 2010. Review The natural history of chronic HBV infection and geographical differences. *Antivir. Ther.* 33, 25–33. <https://doi.org/10.3851/IMP1621>
- Liaw, Y., Chu, C., 2009. Hepatitis B virus infection. *Lancet* 373, 582–592. [https://doi.org/10.1016/S0140-6736\(09\)60207-5](https://doi.org/10.1016/S0140-6736(09)60207-5)
- Liaw, Y.F., Sollano, J.D., 2006. Factors influencing liver disease progression in chronic hepatitis B. *Liver Int.* 26, 23–29. <https://doi.org/10.1111/j.1478-3231.2006.01372.x>
- Lin, X., Xu, X., Huang, Q., Liu, Y., Zheng, D., Chen, W., Lin, J., 2005. Biological impacts of “hot-spot” mutations of hepatitis B virus X proteins are genotype B and C differentiated. *World J. Gastroenterol.* 11, 4703–4708.
- Liu, C.-J., Chen, B.-F., Chen, P.-J., Lai, M.-Y., Huang, W.-L., Kao, J.-H., Chen, D.-S., 2006. Role of Hepatitis B Viral Load and Basal Core Promoter Mutation in Hepatocellular Carcinoma in Hepatitis B Carriers. *J. Infect. Dis.* 193, 1258–1265.
- Liu, S., Zhang, H., Gu, C., Yin, J., He, Y., Xie, J., Cao, G., 2009. Associations between hepatitis B virus mutations and the risk of hepatocellular carcinoma: a meta-analysis. *J. Natl. Cancer Inst.* 101, 1066–82. <https://doi.org/10.1093/jnci/djp180>
- Lizzano, R.A., Yang, B., Clippinger, A.J., Bouchard, M.J., 2012. The C-terminal region of the hepatitis B virus X protein is essential for its stability and function. *Virus Res.* 155, 231–239. <https://doi.org/10.1016/j.virusres.2010.10.013>

- Loggi, E., Vitale, G., Conti, F., Bernardi, M., Andreone, P., 2015. Chronic hepatitis B: Are we close to a cure? *Dig. Liver Dis.* 47, 836–841. <https://doi.org/10.1016/j.dld.2015.05.019>
- Lu, H.Z., Zhou, J.H., 2013. Hepatitis B virus X protein up-regulates tumor necrosis factor- α expression in cultured mesangial cells via ERKs and NF- κ B pathways. *Asian Pac. J. Trop. Biomed.* 3, 217–222. [https://doi.org/10.1016/S2221-1691\(13\)60053-2](https://doi.org/10.1016/S2221-1691(13)60053-2)
- Lu, X., 2011. Pathogenesis of Hepatitis B Virus (HBV) -Mediated Liver Injury 4.
- Lu, X., Block, T., 2004. Study of the early steps of the Hepatitis B Virus life cycle. *Int. J. Med. Sci.* 1, 21–33.
- Luedde, T., Schwabe, R.F., 2011. NF- κ B in the liver—linking injury, fibrosis and hepatocellular carcinoma. *Nat. Publ. Gr.* 8, 108–118. <https://doi.org/10.1038/nrgastro.2010.213>
- Lusida, M.I., Juniastuti, Yano, Y., 2016. Current hepatitis B virus infection situation in Indonesia and its genetic diversity. *World J. Gastroenterol.* 22, 7264–7274. <https://doi.org/10.3748/wjg.v22.i32.7264>
- Ma, J., Liu, Y.C., Fang, Y., Cao, Y., Liu, Z.L., 2015. TGF- β 1 polymorphism 509 C>T is associated with an increased risk for hepatocellular carcinoma in HCV-infected patients. *Genet. Mol. Res.* 14, 4461–4468. <https://doi.org/10.4238/2015.May.4.3>
- Maheshwari, S., Sarraj, A., Kramer, J., El-serag, H.B., 2007. Oral contraception and the risk of hepatocellular carcinoma. *J. Hepatol.* 47, 506–513. <https://doi.org/10.1016/j.jhep.2007.03.015>
- Martin, J., Dufour, J.F., 2008. Tumor suppressor and hepatocellular carcinoma. *World J. Gastroenterol.* 14, 1720–1733. <https://doi.org/10.3748/wjg.14.1720>
- Martins, G.R., Gelaleti, G.B., Moschetta, M.G., Maschio-Signorini, L.B., De Campos Zuccari, D.A.P., 2016. Proinflammatory and Anti-Inflammatory Cytokines Mediated by NF- κ B Factor as Prognostic Markers in Mammary Tumors. *Mediators Inflamm.* 2016. <https://doi.org/10.1155/2016/9512743>
- Mathar, N.R.S., 2011. Hubungan Polimorfisme Gen Tumor Necrosis Factor Alpha (TNF-Alpha) Dengan Akne Vulgaris Ringan Di Makassar [WWW Document]. URL <http://med.unhas.ac.id/ikkk/?p=273>. Diakses pada 7 November 2017.
- Mathew, S., Abdel-Hafiz, H., Raza, A., Fatima, K., Qadri, I., 2016. Host nucleotide polymorphism in hepatitis B virus associated hepatocellular carcinoma. *World J. Hepatol.* 8, 485–498. <https://doi.org/10.4254/wjh.v8.i10.485>
- Matsuzaki, K., Murata, M., Yoshida, K., Sekimoto, G., Uemura, Y., Sakaida, N., Kaibori, M., Kamiyama, Y., Nishizawa, M., Fujisawa, J., Okazaki, K., Seki, T., 2007. Chronic inflammation associated with hepatitis C virus infection perturbs hepatic transforming growth factor β signaling, promoting cirrhosis and hepatocellular carcinoma. *Hepatology* 46, 48–57. <https://doi.org/10.1002/hep.21672>
- McGlynn, K.A., London, W.T., 2011. The Global Epidemiology of Hepatocellular

- Carcinoma, Present and Future. *Clin. Liver Dis.* 15, 223–245. <https://doi.org/10.1016/j.cld.2011.03.006>.The
- Mcglynn, K.A., Sahasrabudhe, V. V, Campbell, P.T., Graubard, B.I., Chen, J., Schwartz, L.M., Petrick, J.L., 2015. Reproductive factors , exogenous hormone use and risk of hepatocellular carcinoma among US women : results from the Liver Cancer Pooling Project. *Br. J. Cancer* 112, 1266–1272. <https://doi.org/10.1038/bjc.2015.58>
- Mekaroonkamol, P., Staros, E.B., 2014. Hepatitis B Test [WWW Document]. Medscape. URL <https://emedicine.medscape.com/article/2109144-overview#a2>. Diakses pada 13 Maret 2017
- Mittal, S., El-Serag, H.B., 2014. Epidemiology of HCC: Consider the Population. *J. Clin. Gastroenterol.* 47, 1–10. <https://doi.org/10.1097/MCG.0b013e3182872f29>.Epidemiology
- Mohy, A., Fouad, A., 2014. Role of transforming growth factor- β 1 in serum and -509 C>T promoter gene polymorphism in development of liver cirrhosis in Egyptian patients. *Meta Gene* 2, 631–637. <https://doi.org/10.1016/j.mgene.2014.08.002>
- Montella, M., D’Arena, G., Crispo, A., Capunzo, M., Nocerino, F., Grimaldi, M., Barbieri, A., D’Ursi, A.M., Tecce, M.F., Amore, A., Galdiero, M., Ciliberto, G., Giudice, A., 2015. Role of Sex Hormones in the Development and Progression of Hepatitis B Virus-Associated Hepatocellular Carcinoma. *Int. J. Endocrinol.* 1–9. <https://doi.org/10.1155/2015/854530>
- Murata, M., Matsuzaki, K., Yoshida, K., Sekimoto, G., Tahashi, Y., Mori, S., Uemura, Y., Sakaida, N., Fujisawa, J., Seki, T., Kobayashi, K., Yokote, K., Koike, K., Okazaki, K., 2009. Hepatitis B virus X protein shifts human hepatic transforming growth factor (TGF)- β signaling from tumor suppression to oncogenesis in early chronic hepatitis B. *Hepatology* 49, 1203–1217. <https://doi.org/10.1002/hep.22765>
- Nature, 2014a. SNP [WWW Document]. URL <http://www.nature.com/scitable/definition/single-nucleotide-polymorphism-snp-295>. Diakses pada 3 Oktober 2017
- Nature, 2014b. Polymerase Chain Reaction/PCR [WWW Document]. URL <http://www.nature.com/scitable/definition/polymerase-chain-reaction-pcr-110>. Diakses pada 3 Oktober 2017.
- Nawar, E.A., Mabul-fadl, A., El-Din Hassanin, B., Abd El Haie, O.M., EL-Tokhy, M., 2011. Clinical value of transforming growth factor beta as a marker of Fibrosis in adolescents with Chronic Liver Diseases. *J. Am. Sci.* 77, 464–471.
- NCBI, 2016. Restriction Fragment Length Polymorphism (RFLP) [WWW Document]. URL <https://www.ncbi.nlm.nih.gov/probe/docs/techrflp/>. Diakses pada 28 Desember 2016.
- NIH, 2017. Mutations and Health [WWW Document]. URL <https://ghr.nlm.nih.gov/primer/mutationsanddisorders.pdf>. Diakses pada 3 Oktober 2017.

- Niro, G.A., Fontana, R., Gioffreda, D., Valvano, M.R., Lacobellis, A., Facciorusso, D., Andriulli, A., 2005. Tumor necrosis factor gene polymorphisms and clearance or progression of hepatitis B virus infection. *Liver Int.* 25, 1175–1181. <https://doi.org/10.1111/j.1478-3231.2005.01166.x>
- Nurhajjah, S., Ratnaningrum, S.D., Mundhofir, F.E.P., Faradz, S.M., 2014. Polimorfisme Gen TNF- α -308 G>A pada Penderita Sindrom Down. *MKA* 37, 44–49.
- Nwokediuko, S., 2010. Risk Factors For Hepatitis B Virus Transmission In Nigerians : A Case-Control Study. *Internet J. Gastroenterol.* 10, 1–5.
- Osiowy, C., Giles, E., Tanaka, Y., Mizokami, M., Minuk, G.Y., 2006. Molecular Evolution of Hepatitis B Virus over 25 Years. *J. Virol.* 80, 10307–10314. <https://doi.org/10.1128/JVI.00996-06>
- Ota, M., Fukushima, H., Kulski, J.K., Inoko, H., 2007. Single nucleotide polymorphism detection by polymerase chain reaction-restriction fragment length polymorphism. *Nature* 2, 2857–2864. <https://doi.org/10.1038/nprot.2007.407>
- Ozaki, I., Hamajima, H., Matsushashi, S., Mizuta, T., 2011. Regulation of TGF- β 1-induced pro-apoptotic signaling by growth factor receptors and extracellular matrix receptor integrins in the liver. *Front. Physiol.* 2 OCT, 1–8. <https://doi.org/10.3389/fphys.2011.00078>
- Ozaki, T., Nakagawara, A., 2011. Role of p53 in cell death and human cancers. *Cancers (Basel)*. 3, 994–1013. <https://doi.org/10.3390/cancers3010994>
- Panek, M., Pietras, T., Fabijan, A., Ziolo, J., Wieteska, Ł., Małachowska, B., Fendler, W., Szemraj, J., Kuna, P., 2014. Identification and association of the single nucleotide polymorphisms, C-509T, C+466T and T+869C, of the TGF- β 1 gene in patients with asthma and their influence on the mRNA expression level of TGF- β 1. *Int. J. Mol. Med.* 34, 975–986. <https://doi.org/10.3892/ijmm.2014.1894>
- Papastergiou, V., Lombardi, R., Macdonald, D., Tsochatzis, E.A., 2015. Global Epidemiology of Hepatitis B Virus (HBV) Infection. *Curr. Hepatol. Rep.* 14, 171–178. <https://doi.org/10.1007/s11901-015-0269-3>
- Pawlotsky, J., 2003. Hepatitis B virus (HBV) DNA assays (methods and practical use) and viral kinetics. *J. Hepatol.* 39, S31–S35. [https://doi.org/10.1016/S0168-8278\(03\)00136-3](https://doi.org/10.1016/S0168-8278(03)00136-3)
- Perhimpunan Peneliti Hati Indonesia, 2013. Artikel Umum: Sirosis Hati [WWW Document]. URL <http://pphi-online.org/alpha/?p=570>. Diakses pada 2 Januari 2018.
- Petersen, J., Lutgehetmann, M., Volz, T., Dandri, M., 2007. What is the Role of cccDNA in Chronic HBV Infection ? Impact on HBV Therapy 9–13.
- Poh, Z., Goh, B.G., Chang, P.J., Tan, C., 2015. Rates of cirrhosis and hepatocellular carcinoma in chronic hepatitis B and the role of surveillance : a 10-year follow-up of 673 patients. *Eur. J. Gastroenterol. Hepatol.* 27, 638–643. <https://doi.org/10.1097/MEG.0000000000000341>

- Pontoriero, A.C., Trinks, J., Hulaniuk, M.L., Caputo, M., Fortuny, L., Pratz, L.B., Frías, A., Torres, O., Nuñez, F., Gadano, A., Argibay, P., Corach, D., Flichman, D., 2015. Influence of ethnicity on the distribution of genetic polymorphisms associated with risk of chronic liver disease in South American populations. *BMC Genet.* 16, 1–8. <https://doi.org/10.1186/s12863-015-0255-3>
- Popowicz, G.M., Czarna, A., Holak, T. a, 2008. Structure of the human Mdmx protein bound to the p53 tumor suppressor transactivation domain. *Cell Cycle* 7, 2441–2443. <https://doi.org/10.4161/cc.6365>
- Pray, L.A., 2008. Discovery of DNA Structure and Function: Watson and Crick [WWW Document]. *Nat. Educ.* URL <https://www.nature.com/scitable/topicpage/discovery-of-dna-structure-and-function-watson-397/>. Diakses pada 7 Juni 2019
- Prokai, L., Prokai-Tatrai, K., Pa'1 Perje'si, Simpkins, J.W., 2006. Mechanistic Insights into the Direct Antioxidant Effects of Estrogens '. *Drug Dev. Res.* 66, 118–125. <https://doi.org/10.1002/ddr>
- Qi, P., Chen, Y., Wang, H., Fang, M., Ji, Q., Zhao, Y., Sun, X., Liu, Y., Gao, C., 2009. -509C>T polymorphism in the TGF-beta1 gene promoter, impact on the hepatocellular carcinoma risk in Chinese patients with chronic hepatitis B virus infection. *Cancer Immunol. Immunother.* 58, 1433–40. <https://doi.org/10.1007/s00262-009-0660-4>
- Qingzhong Wang, Roy, B., Turecki, G., Shelton, R.C., Dwivedi, Y., 2018. A complex epigenetic switching is critical for TNF- α upregulation in prefrontal cortex of suicide subjects. *Am J Psychiatry* 175, 262–274. <https://doi.org/10.1016/j.physbeh.2017.03.040>
- Radwan, M.I., Pasha, H.F., Mohamed, R.H., Hussien, H.I.M., 2012. Cytokine Influence of transforming growth factor- b 1 and tumor necrosis factor- a genes polymorphisms on the development of cirrhosis and hepatocellular carcinoma in chronic hepatitis C patients. *Cytokine* 60, 271–276. <https://doi.org/10.1016/j.cyto.2012.05.010>
- Raina, P., Sikka, R., Kaur, R., Sokhi, J., Matharoo, K., Singh, V., Bhanwer, A.J.S., 2015. Association of Transforming Growth Factor Beta-1 (TGF- β 1) Genetic Variation with Type 2 Diabetes and End Stage Renal Disease in Two Large Population Samples from North India. *OMICS* 19, 306–17. <https://doi.org/10.1089/omi.2015.0005>
- Rawat, S., Clippinger, A.J., Bouchard, M.J., 2012. Modulation of apoptotic signaling by the Hepatitis B Virus X protein. *Viruses* 4, 2945–2972. <https://doi.org/10.3390/v4112945>
- Rehermann, B., 2013. Pathogenesis of chronic viral hepatitis : differential roles of T cells and NK cells. *Nat. Med.* 19, 859–868. <https://doi.org/10.1038/nm.3251>
- Reiling, E., Lyssenko, V., Boer, J.M.A., Imholz, S., Verschuren, W.M.M., Isomaa, B., Tuomi, T., Groop, L., Dollé, M.E.T., 2012. Codon 72 polymorphism (rs1042522) of TP53 is associated with changes in diastolic blood pressure over time. *Eur. J. Hum. Genet.* 20, 696–700.

<https://doi.org/10.1038/ejhg.2011.240>

- Ringehan, M., McKeating, J.A., Protzer, U., 2017. Viral hepatitis and liver cancer. *Philos. Trans. R. Soc. B Biol. Sci.* 372, 20160274. <https://doi.org/10.1098/rstb.2016.0274>
- Riyanti, E., Oewen, R.R., Haroen, E.R., Maskoen, A.M., Satari, M.H., Kedokteran, B., Anak, G., Kedokteran, F., Universitas, G., Oral, B.B., Kedokteran, F., Universitas, G., 2018. Metoda Pemeriksaan Polymerase Chain Reaction Restriction Fragment Length Polymorphism pada Deteksi Genotip Polimorfisme C-509t Gen Transforming Growth Factor Beta 1 Penderita, in: *Prosiding Pertemuan Ilmiah Nasional V IDGAI*. pp. 1–10.
- Rodwell, V.W., Bender, D., Botham, K., Kennely, P., Murray, R., Gross, P.L., Jacob, M., Mayes, P.A., Rand, M.L., Varghese, J., 2015. *Harper Illustrated Biochemistry*, 30th ed. The McGraw Hill Education, New York.
- Romanque, P., Piguet, A., Dufour, J.-F., 2008. Targeting vessels to treat hepatocellular carcinoma. *Clin. Sci.* 14, 467–477. <https://doi.org/10.1042/CS20070310>
- Salarnia, F., Besharat, S., Zhand, S., Javid, N., Khodabakhshi, B., Moradi, A., 2017. Mutations in hepatitis-B X-gene region: Chronic hepatitis-B versus cirrhosis. *J. Clin. Diagnostic Res.* 11, OC31–OC34. <https://doi.org/10.7860/JCDR/2017/22570.9498>
- Santarpia, M., González-Cao, M., Viteri, S., Karachaliou, N., Altavilla, G., Rosell, R., 2015. Programmed cell death protein-1/programmed cell death ligand-1 pathway inhibition and predictive biomarkers: understanding transforming growth factor-beta role. *Transl. lung cancer Res.* 4, 728–42. <https://doi.org/10.3978/j.issn.2218-6751.2015.12.04>
- Saxena, R., Chawla, Y.K., Verma, I., Kaur, J., 2014. IFN- γ (+874) and not TNF- α (-308) is associated with HBV-HCC risk in India. *Mol. Cell. Biochem.* 385, 297–307. <https://doi.org/10.1007/s11010-013-1838-9>
- Schon, H., Weiskirchen, R., 2014. Immunomodulatory effects of transforming growth factor- β in the liver. *Hepatobiliary Surg. Nutr.* 3, 386–406. <https://doi.org/10.3978/j.issn.2304-3881.2014.11.06>
- Schuppan, D., Afdhal, N.H., 2008. Liver cirrhosis. *Lancet (London, England)* 371, 838–51. [https://doi.org/10.1016/S0140-6736\(08\)60383-9](https://doi.org/10.1016/S0140-6736(08)60383-9)
- Setiawan, P.B., 2015. Karsinoma Hepatoseluler, in: Tjokroprawiro, A., Setiawan, P.B., Effendi, C., Santoso, D., Soegiarto, G. (Eds.), *Buku Ajar Ilmu Penyakit Dalam*. Airlangga University Press, Surabaya, pp. 312–316.
- Setiawan, P.B., Thamrin, H., 2015. Hepatitis B Kronis, in: Tjokroprawiro, A., Setiawan, P.B., Effendi, C., Santoso, D., Soegiarto, G. (Eds.), *Buku Ajar Ilmu Penyakit Dalam*. Airlangga University Press, Surabaya, pp. 278–286.
- Sghaier, I., Zidi, S., Mouelhi, L., Dabbech, R., Ghazouani, E., Brochot, E., Stayoussef, M., Yacoubi-Loueslati, B., 2015. The relationship between TNF alpha gene polymorphisms (-238/-308), TNF RII VNTR (p75) and outcomes of hepatitis B virus infection in Tunisian population. *Gene* 568, 140–145.

<https://doi.org/10.1016/j.gene.2015.05.029>

- Shah, S.M., Singh, S.P., 2007. Hepatitis B Virus Serology : Use and Interpretation [WWW Document]. *Hepat. B Annu.* URL <http://www.hepatitisbannual.org/downloadpdf.asp?issn=0972-9747;year=2007;volume=4;issue=1;spage=39;epage=54;auiast=Shah;type=2>. Diakses pada 27 Februari 2018
- Shahnazari, P., Sayehmiri, K., Minucheher, Z., Parhizkar, A., Poustchi, H., Montazeri, G., Mohamadkhani, A., 2014. The increased level of serum p53 in hepatitis B-associated liver cirrhosis. *Iran. J. Med. Sci.* 39, 446–451.
- Shimizu, I., Kohno, N., Tamaki, K., Shono, M., Huang, H., He, J., Yao, D., 2007. Female hepatology : Favorable role of estrogen in chronic liver disease with hepatitis B virus infection. *World J. Gastroenterol.* 13, 4295–4305.
- Shin, S.P., Kim, N.K., Kim, J.H., Lee, J.H., Kim, J.O., Cho, S.H., Park, H., 2015. Association between hepatocellular carcinoma and tumor necrosis factor alpha polymorphisms in South Korea. *World J. Gastroenterol.* 21, 13064–13072. <https://doi.org/10.3748/wjg.v21.i46.13064>
- Shukla, R., Yue, J., Siouda, M., Gheit, T., Hantz, O., Merle, P., Zoulim, F., Krutovskikh, V., Tommasino, M., Sylla, B.S., 2011. Proinflammatory cytokine TNF- α increases the stability of hepatitis B virus X protein through NF- κ B signaling. *Carcinogenesis* 32, 978–985. <https://doi.org/10.1093/carcin/bgr057>
- Somi, M.H., Najafi, L., Noori, B.N., Alizadeh, A.H., Aghah, M.R., Shavakhi, A., Ehsani, M.J., Aghazadeh, R., Masoodi, M., Amini, S., Baladast, M., Zali, M.R., 2006. Tumor necrosis factor- α gene promoter polymorphism in Iranian patients with chronic hepatitis B. *Indian J Gastroenterol* 25, 14–15.
- Song, L.H., Duy, D.N., Binh, V.Q., Luty, A.J.F., Kremsner, P.G., Bock, C.T., 2005. Low frequency of mutations in the X gene, core promoter and precore region of hepatitis B virus infected Vietnamese. *J. Viral Hepat.* 12, 160–167. <https://doi.org/10.1111/j.1365-2893.2005.00560.x>
- Su, C., 2016. Survivin in survival of hepatocellular carcinoma. *Cancer Lett.* 379, 184–190. <https://doi.org/10.1016/j.canlet.2015.06.016>
- Su, I.-J., Wang, L.H.-C., Hsieh, W.-C., Wu, H.-C., Teng, C.-F., Tsai, H.-W., Huang, W., 2014. The emerging role of hepatitis B virus Pre-S2 deletion mutant proteins in HBV tumorigenesis. *J. Biomed. Sci.* 21, 98. <https://doi.org/10.1186/s12929-014-0098-7>
- Sugauchi, F., Mizokami, M., Orito, E., Ohno, T., Kato, H., Suzuki, S., Kimura, Y., Ueda, R., Butterworth, L.A., Cooksley, W.G.E., 2001. A novel variant genotype C of hepatitis B virus identified in isolates from Australian Aborigines: Complete genome sequence and phylogenetic relatedness. *J. Gen. Virol.* 82, 883–892. <https://doi.org/10.1099/0022-1317-82-4-883>
- Sukocheva, O.A., 2018. Estrogen, estrogen receptors, and hepatocellular carcinoma: Are we there yet? *World J. Gastroenterol.* 24, 1–4. <https://doi.org/10.3748/wjg.v24.i1.1>

- Sumbul, A.T., Akkız, H., Bayram, S., Bekar, A., Akgo, E., Sandıkcı, M., 2012. p53 codon 72 polymorphism is associated with susceptibility to hepatocellular carcinoma in the Turkish population : a case – control study. *Mol Biol Rep* 39, 1639–1647. <https://doi.org/10.1007/s11033-011-0903-2>
- Suneetha, P.V., Sarin, S.K., Goyal, A., Kumar, G.T., Shukla, D.K., Hissar, S., 2006. Association between vitamin D receptor , CCR5 , TNF- α and TNF- β gene polymorphisms and HBV infection and severity of liver disease. *J. Hepatol.* 44, 856–863. <https://doi.org/10.1016/j.jhep.2006.01.028>
- Suryohudoyo, P., Suryohudoyo, S.U., 2015. Pengantar Bioteknologi. Airlangga University Press, Surabaya.
- Suryohudoyo, P., Suryohudoyo, S.U., 2013. Pengantar Biologi Molekuler. Airlangga University Press, Surabaya.
- Talaat, R.M., Dondeti, M.F., El-shenawy, S.Z., Khamiss, O.A., 2013. Transforming Growth Factor-Beta 1 Gene Polymorphism (T29C) in Egyptian Patients with Hepatitis B Virus Infection : A Preliminary Study. *Hepat. Res. Treat.* 2013, 1–7.
- Tarigan, A.P., Syafiuddin, T., Yunus, F., Suradi, 2015. Association of Tumor Necrosis Factor Alpha and Lymphotoxin Alpha Gene Polymorphisms with the Presence of Chronic Obstructive Pulmonary Disease. *Acta Medica Indones. - Indones. J. Intern. Med.* 47, 283–290.
- Tavakolpour, S., Sali, S., 2016. Tumor Necrosis Factor- α -308 G / A Polymorphisms and Risk of Hepatocellular Carcinoma : A Meta-Analysis. *Hepat. Mon.* 16, 1–11. <https://doi.org/10.5812/hepatmon.33537.Review>
- Tetrian, D., Mailana, W., Kurnia, I., Syaifudin, M., 2015. Preliminary Study on the Single Nucleotide Polymorphism (SNP) of XRCC1 Gene Identification to Improve the Outcomes of Radiotherapy for Cervical Cancer. *Biosaintifika* 7, 79–86. <https://doi.org/10.15294/biosaintifika.v7i2.3949>
- Thomas, M., Kalita, a, Labrecque, S., Pim, D., Banks, L., Matlashewski, G., 1999. Two polymorphic variants of wild-type p53 differ biochemically and biologically. *Mol. Cell. Biol.* 19, 1092–1100. <https://doi.org/10.1128/MCB.19.2.1092>
- Thursz, M., Yee, L., 2011. Understanding the host genetics of chronic hepatitis B and C. *Semin. Liver Dis.* 31, 115–127.
- Tong, S., 2012. Hepatitis B Virus, A Sex Hormone-Responsive Virus. *Gastroenterology* 142, 696–699. <https://doi.org/10.1053/j.gastro.2012.02.036>
- Tseng, T.A.I.C., Liu, C.J.E.N., Yang, H.C., Su, T.H., Wang, C.C.H.I., 2012. High Levels of Hepatitis B Surface Antigen Increase Risk of Hepatocellular Carcinoma in Patients With Low HBV Load. *Gastroenterology* 142, 1140–1149. <https://doi.org/10.1053/j.gastro.2012.02.007>
- Urban, S., Schulze, A., Dandri, M., Petersen, J., 2010. The replication cycle of hepatitis B virus. *J. Hepatol.* 52, 282–284.
- Utama, A., Siburian, M.D., Fanany, I., Intan, M.D.B., Dhenni, R., Kurniasih, T.S., Lelosutan, S.A.R., Achwan, W.A., Zubir, N., Arnelis, Lukito, B., Yusuf, I.,

- Lesmana, L.A., Sulaiman, A., 2012. Hepatitis B virus pre-S2 start codon mutations in Indonesian liver disease patients. *World J. Gastroenterol.* 18, 5418–5426. <https://doi.org/10.3748/wjg.v18.i38.5418>
- Vázquez-Huerta, D.I., Alvarez-Rodríguez, B.A., Topete-Reyes, J.F., Muñoz-Valle, J.F., Parra-Michel, R., Fuentes-Ramírez, F., Salazar-López, M.A., Valle, Y., Reyes-Castillo, Z., Cruz-González, A., Brennan-Bourdon, L.M., Torres-Carrillo, N., 2014. Tumor necrosis factor alpha -238 G/A and -308 G/A polymorphisms and soluble TNF- α levels in chronic kidney disease: Correlation with clinical variables. *Int. J. Clin. Exp. Med.* 7, 2111–2119.
- Vuolo, V. Di, Buonaguro, L., Izzo, F., Losito, S., Botti, G., Buonaguro, F.M., Tornesello, M.L., 2011. TP 53 and MDM2 gene polymorphisms and risk of hepatocellular carcinoma among Italian patients. *Infect. Agent. Cancer* 6, 1–6.
- Wahyuni, R.M., Utsumi, T., Juniastuti, Yano, Y., Murti, I.S., Amin, M., Yamani, L.N., Istimagfiroh, A., Purwono, P.B., Soetjpto, Lusida, M.I., Hayashi, Y., 2019. Analysis of hepatitis B virus genotype and gene mutation in patients with advanced liver disease in East Kalimantan, Indonesia. *Biomed. reports* 10, 303–310. <https://doi.org/10.3892/br.2019.1202>
- Wang, B., Wang, J., Zheng, Y., Zhou, S., Zheng, J., Wang, F., Ma, X., Zeng, Z., and the HBV study Consortium, 2010. A study of TNF-alpha-238 and -308 polymorphisms with different outcomes of persistent hepatitis B virus infection in China. *Pathology* 42, 674–80. <https://doi.org/10.3109/00313025.2010.523696>
- Wang, S.H., Yeh, S.H., Lin, W.H., Yeh, K.H., Yuan, Q., Xia, N.S., Chen, D.S., Chen, P.J., 2012. Estrogen Receptor _ Represses Transcription of HBV Genes via Interaction With Hepatocyte Nuclear Factor 4_. *Gastroenterology* 142, 989-998.e4. <https://doi.org/10.1053/j.gastro.2011.12.045>
- Wang, Y., Zeng, L., Chen, W., 2016. HBV X gene point mutations are associated with the risk of hepatocellular carcinoma: A systematic review and meta-analysis. *Mol. Clin. Oncol.* 4, 1045–1051. <https://doi.org/10.3892/mco.2016.847>
- Wang, Z., Gou, W., Liu, M., Sang, W., Chu, H., Zhang, W., 2015. Expression of P53 and HSP70 in Chronic Hepatitis, Liver Cirrhosis, and Early and Advanced Hepatocellular Carcinoma Tissues and Their Diagnostic Value in Hepatocellular Carcinoma: An Immunohistochemical Study. *Med. Sci. Monit.* 21, 3209–3215. <https://doi.org/10.12659/MSM.895592>
- Wei, F., Zheng, Q., Li, M., Wu, M., 2017. The association between hepatitis B mutants and hepatocellular carcinoma. *Med. (United States)* 96, 1–8. <https://doi.org/10.1097/MD.00000000000006835>
- Wei, Y., Liu, F., Li, B., Chen, X., Ma, Y., Yan, L., Wen, T., Xu, M., Wang, W., Yang, J., 2011. Polymorphisms of tumor necrosis factor-alpha and hepatocellular carcinoma risk: A HuGE systematic review and meta-analysis. *Dig. Dis. Sci.* 56, 2227–2236. <https://doi.org/10.1007/s10620-011-1617-y>
- Wen, J., Song, C., Jiang, D., Jin, T., Dai, J., Zhu, L., 2015. Hepatitis B virus genotype, mutations, human leukocyte antigen polymorphisms and their

- interactions in hepatocellular carcinoma : a multi-centre case- control study. *Nature* 5, 1–10. <https://doi.org/10.1038/srep16489>
- WHO, 2016. Hepatitis B Fact Sheet [WWW Document]. URL <http://www.who.int/mediacentre/factsheets/fs204/en/>. Diakses pada 27 Desember 2018.
- Wu, H., Santella, R., 2012. The Role of Aflatoxins in Hepatocellular Carcinoma. *Hepat. Mon.* 12, 1–9. <https://doi.org/10.5812/hepatmon.7238>
- Wu, S., Kanda, T., Nakamoto, S., Jiang, X.I.A., Nakamura, M., 2016. Cooperative effects of hepatitis B virus and TNF may play important roles in the activation of metabolic pathways through the activation of NF- κ B. *Int. J. Mol. Med.* 38, 475–481. <https://doi.org/10.3892/ijmm.2016.2643>
- Wungu, C.D.K., Amin, M., Kholili, U., Prabowo, G.I., Setiawan, P.B., Soetjipto, Handajani, R., 2018. The Analysis of Mutation Profile on Pre-S1 and Pre-S2 Region of Hepatitis B Virus in Chronic Liver Disease. *Malaysian J. Biochem. Mol. Biol.* 3, 85–92.
- Xiao, Q., Fu, B., Chen, P., Liu, Z.Z., Wang, W., Ye, Q., 2016. Three polymorphisms of tumor necrosis factor-alpha and hepatitis B virus related hepatocellular carcinoma. *Medicine (Baltimore)*. 95, 1–10.
- Xie, J., Zhang, Y., Zhang, Q., Han, Y., Yin, J., Pu, R., Shen, Q., Lu, W., Du, Y., 2013. Interaction of Signal Transducer and Activator of Transcription 3 Polymorphisms With Hepatitis B Virus Mutations in Hepatocellular Carcinoma. *Hepatology* 57, 2369–2377. <https://doi.org/10.1002/hep.26303>
- Xie, Y., Liu, S., Zhao, Y., Guo, Z., 2014. X protein mutations in hepatitis B virus DNA predict postoperative survival in hepatocellular carcinoma. *Tumor Biol.* 35, 10325–10331. <https://doi.org/10.1007/s13277-014-2331-0>
- Xu, H.-Z., Liu, Y.-P., Guleng, B., Ren, J.-L., 2014. Hepatitis B Virus-Related Hepatocellular Carcinoma: Pathogenic Mechanisms and Novel Therapeutic Interventions. *Gastrointest. Tumors* 1, 135–145. <https://doi.org/10.1159/000365307>
- Xu, H., Liu, Y.-P., Guleng, B., Ren, J.-L., 2014. Hepatitis B Virus-Related Hepatocellular Carcinoma : Pathogenic Mechanisms and Novel Therapeutic Interventions. *Gastrointest. Tumors* 1, 135–145. <https://doi.org/10.1159/000365307>
- Xu, R., Zhang, X., Zhang, W., Fang, Y., Zheng, S., Yu, X.F., 2007. Association of human APOBEC3 cytidine deaminases with the generation of hepatitis virus B x antigen mutants and hepatocellular carcinoma. *Hepatology* 46, 1810–1820. <https://doi.org/10.1002/hep.21893>
- Xu, X.-W., Lu, M.-H., Tan, D.-M., 2005. Association between tumour necrosis factor gene polymorphisms and the clinical types of patients with chronic hepatitis B virus infection. *Clin. Microbiol. Infect.* 11, 52–56. <https://doi.org/10.1111/j.1469-0691.2004.01029.x>
- Yan, H., Yang, Y., Zhang, L., Tang, G., Wang, Y., Xue, G., Zhou, W., Sun, S., 2015. Characterization of the Genotype and Integration Patterns of Hepatitis

- B Virus in Early- and Late-Onset Hepatocellular Carcinoma. *Hepatology* 61, 1821–1831. <https://doi.org/10.1002/hep.27722>
- Yang, P., Markowitz, G.J., Wang, X.-F., 2015. The hepatitis B virus-associated tumor microenvironment in hepatocellular carcinoma. *Natl. Sci. Rev.* 1, 396–412. <https://doi.org/10.1093/nsr/nwu038>.The
- Yano, Y., Azuma, T., Hayashi, Y., 2015a. Variations and mutations in the hepatitis B virus genome and their associations with clinical characteristics. *World J. Hepatol.* 7, 583–592. <https://doi.org/10.4254/wjh.v7.i3.583>
- Yano, Y., Utsumi, T., Lusida, M.I., Hayashi, Y., 2015b. Hepatitis B virus infection in Indonesia. *World J. Gastroenterol.* 21, 10714–10720. <https://doi.org/10.3748/wjg.v21.i38.10714>
- Yao, D.-F., Dong, Z.-Z., Yao, M., 2007. Specific molecular markers in hepatocellular carcinoma. *Hepatobiliary Pancreat. Dis. Int.* 6, 241–247. <https://doi.org/964> [pii]
- Yeh, S.H., Chen, P.J., 2010. Gender disparity of hepatocellular carcinoma: The roles of sex hormones. *Oncology* 78, 172–179. <https://doi.org/10.1159/000315247>
- Yi, Y.-S., Park, S.G., Byeon, S.M., Kwon, Y.-G., Jung, G., 2003. Hepatitis B virus X protein induces TNF- α expression via down-regulation of selenoprotein P in human hepatoma cell line , Hepatitis B virus X protein induces TNF- α expression via down-regulation of selenoprotein P in human hepatoma cell line , HepG2. *Biochim. Biophys. Acta* 1638, 249–256. [https://doi.org/10.1016/S0925-4439\(03\)00090-5](https://doi.org/10.1016/S0925-4439(03)00090-5)
- You, C.R., Lee, S.W., Jang, J.W., Yoon, S.K., 2014. Update on hepatitis B virus infection. *World J. Gastroenterol.* 20, 13293–13305. <https://doi.org/10.3748/wjg.v20.i37.13293>
- Yu, F., Chen, B.C., Fan, X.F., Li, G., Dong, P., Zheng, J., 2017. Epigenetically-Regulated MicroRNA-9-5p Suppresses the Activation of Hepatic Stellate Cells via TGFBR1 and TGFBR2. *Cell. Physiol. Biochem.* 43, 2242–2252. <https://doi.org/10.1159/000484303>
- Zakaria, M.K., Sankhyan, A., Ali, A., Fatima, K., Azhar, E., Qadri, I., 2014. Genetic Syndromes & Gene Therapy HBV / HCV Infection and Inflammation. *J. Genet. Syndr. Gene Ther.* 5, 1–11. <https://doi.org/10.4172/2157-7412.1000241>
- Zamor, P.J., deLemos, A.S., Russo, M.W., 2017. Viral hepatitis and hepatocellular carcinoma: Etiology and management. *J. Gastrointest. Oncol.* 8, 229–242. <https://doi.org/10.21037/jgo.2017.03.14>
- Zampino, R., Boemio, A., Sagnelli, C., Alessio, L., Adinolfi, L.E., Sagnelli, E., Coppola, N., 2015. 2015 Advances in Hepatitis B virus hepatitis B virus burden in developing countries. *World J. Gastroenterol.* 21, 11941–11953. <https://doi.org/10.3748/wjg.v21.i42.11941>
- Zeng, F., Guo, P., Huang, Y., Xin, W., Du, Z., Zhu, S., Deng, Y., 2016. Epidemiology of hepatitis B virus infection : results from a million residents

- in South China. *Nat. Publ. Gr.* 6, 1–11. <https://doi.org/10.1038/srep36186>
- Zeng, Z., 2014. Human genes involved in hepatitis B virus infection. *World J. Gastroenterol.* 20, 7696–7706. <https://doi.org/10.3748/wjg.v20.i24.7696>
- Zhang, Q., Yin, J., Zhang, Y., Deng, Y., Ji, X., Du, Y., Pu, R., Han, Y., Zhao, J., Han, X., 2013. HLA-DP Polymorphisms Affect the Outcomes of Chronic Hepatitis B Virus Infections, Possibly through Interacting with Viral Mutations. *J. Virol.* 87, 12176–12186. <https://doi.org/10.1128/JVI.02073-13>
- Zhang, Z.H., Wu, C.C., Chen, X.W., Li, X., Li, J., Lu, M.J., 2016. Genetic variation of hepatitis B virus and its significance for pathogenesis. *World J. Gastroenterol.* 22, 126–144. <https://doi.org/10.3748/wjg.v22.i1.126>