

Daftar pustaka

- Agnihotri, S.A., Mallikarjuna, N.N., Aminabhavi, T.M., 2004. Recent advances on chitosan-based micro- and nanoparticles in drug delivery B. *J. Control. Release* 100: 5–28.
- Anwar, S., S.J, H., Aryandono, T., Haryana, S.M., 2017. micro-RNA : biogenesis, fungsi, dan perannya dalam proses karsinogenesis dan penatalaksanaan kanker. Gadjah Mada University Press, Yogyakarta.
- Bajan, S., Hutvagner, G., 2020. RNA-Based Therapeutics : From Antisense Oligonucleotides to miRNAs. *Cells* 137: 1–27.
- Balogh, J., Victor III, D., Gordon, S., Li, X., Ghobrial, R.M., Monsour Jr, P.H., 2016. Hepatocellular carcinoma : a review. *J. Hepatocell. Carcinoma* 3: 41–53.
- Beg, M.S., Brenner, A.J., Sachdev, J., Borad, M., Kang, Y.-K., Stoudemire, J., et.al., 2017b. Phase I study of MRX34, a liposomal miR-34a mimic, administered twice weekly in patients with advanced solid tumors. *Invest New Drugs* 35(2): 180–188.
- Calvisi, D.F., Ladu, S., Gorden, A., Farina, M., Conner, E.A., Lee, J.U.S., et.al., 2006. Ubiquitous Activation of. *Gastroenterology* 130: 1117–1128.
- Carballal-santos, B., Aaldering, L.J., Ritzefeld, M., Pereira, S., Sewald, N., Moerschbacher, M., 2015. Physicochemical and biological characterization of chitosan- microRNA nanocomplexes for gene delivery to MCF-7 breast cancer cells. *Nat. Publ. Gr.* 5: 1–15.
- Chiao, P.J., Ling, J., 2011. Kras , Pten , NF-kB , and inflammation : Dangerous Liaisons. *Cancer Discov.* 1: 103–106.
- Cho, C.W., 2012. MicroRNAs as therapeutic targets and their potential applications in cancer therapy. *Expert Opin. Ther. Targets* 16: 747–759.
- Chou, C., Shrestha, S., Yang, C., Chang, N., 2018. miRTarBase update 2018 : a resource for experimentally validated microRNA-target interactions. *Nucleic Acids Res.* 46: 296–302.
- Chow, P.K.H., Gandhi, M., Tan, S., Khin, M.W., Khasbazar, A., Ong, J., et.al., 2020. SIRveNIB : Selective Internal Radiation Therapy Versus Sorafenib in Asia-Pacific Patients With Hepatocellular Carcinoma. *J. Clin. Oncol.* 36: 1913-1921.



- COM, J., I, H., As, S., Ra, G., CRA, L., J, K., 2019. Risk Factors for Hepatocellular Carcinoma and Its Mortality Rate : A Multicenter Study in Indonesia Abstract. *Arch. Cancer Res.* 7 (1): 1–7.
- Csaba, N., Köping-höggård, M., Alonso, M.J., 2009. Ionically crosslinked chitosan / tripolyphosphate nanoparticles for oligonucleotide and plasmid DNA delivery. *Int. J. Pharm.* 382: 205–214.
- D, L., SW, C., MJ, F., BB, K., 2009. Hep G2 is a hepatoblastoma-derived cell line. *Hum. Pathol.* 40(10): 1512–1515.
- Dhiman, G., Srivastava, N., Goyal, M., Rakha, E., Khaiboullina, S.F., Rizvanov, A.A., Baranwal, M., 2019. Metadherin : A Therapeutic Target in Multiple Cancers. *Front. Oncol.* 9: 1–8.
- Dietrich, P., Freese, K., Mahli, A., Thasler, W.E., 2018. Combined effects of PLK1 and RAS in hepatocellular carcinoma reveal rigosertib as promising novel therapeutic “ dual-hit ” option. *Oncotarget* 9: 3605–3618.
- Dietrich, P., Koch, A., Fritz, V., Hartmann, A., Bosserhoff, A.K., Hellerbrand, C., 2017. Wild type Kirsten rat sarcoma is a novel microRNA- 622-regulated therapeutic target for hepatocellular carcinoma and contributes to sorafenib resistance. *Gut* 67: 1328–1341.
- Dizaj, S.M., Jafari, S., Khosroushahi, A.Y., 2014. A sight on the current nanoparticle-based gene delivery vectors. *Nanoscale Res. Lett.* 9: 1–9.
- Dutta, R., Mahato, R.I., 2017. Recent Advances in Hepatocellular Carcinoma Therapy. *Pharmacol. Ther.* 173: 106–117.
- Emdad, L., Das, S., Hu, B., 2016. AEG-1 / MTDH / LYRIC : A Promiscuous Protein Partner Critical in Cancer , Obesity , and CNS Diseases, *Advances in Cancer Research.*
- Fan, R., Chen, P., Zhao, D., 2011. Cooperation of deregulated Notch signaling and Ras pathway in human hepatocarcinogenesis. *J. Mol. Histol.* 42: 473–481.
- Forner, A., Reig, M., Bruix, J., 2018. Hepatocellular carcinoma. *Lancet* 391: 1301–1314.
- Freier, T., Shan, H., Kazazian, K., Shoichet, M.S., 2005. Controlling cell adhesion and degradation of chitosan films by N -acetylation. *Biomaterials* 26: 5872–5878.



Gao, W., Lu, Y., Wang, F., Sun, J., Bian, J., Wu, H., 2019. miRNA-217 inhibits proliferation of hepatocellular carcinoma cells by regulating KLF5. *Eur. Rev. Med. Pharmacol. Sci.* 23: 7874–7883.

Gao, Z., Zhang, L., Sun, Y., 2012. Nanotechnology applied to overcome tumor drug resistance. *J. Control. Release* 162: 45–55.

Gaur, S., Wen, Y., Song, J.H., Parikh, N.U., Lingegowda, S., Shi, Y., et.al., 2015. Chitosan nanoparticle-mediated delivery of miRNA-34a decreases prostate tumor growth in the bone and its expression induces non-canonical autophagy. *Oncotarget* 6: 29161–29177.

Ghadi, A., 2014. Synthesis and optimization of chitosan nanoparticles: Potential applications in nanomedicine and biomedical engineering. *Casp. J. Int. Med.* 5: 156–161.

Grammatikakis, I., Gorospe, M., Abdelmohsen, K., 2013. Modulation of Cancer Traits by Tumor Suppressor microRNAs. *Int. J. Mol. Sci.* 14: 1822–1842.

Hagemann, T., Lawrence, T., Mcneish, I., Charles, K.A., Kulbe, H., Thompson, R.G., et.al., 2008. macrophages by targeting NF- κ B. *J. Exp. Med.* 205: 1261–1268.

He, R., Yang, L., Lin, Xiaomiao, Chen, X., Lin, Xinggu, Wei, F., Liang, X., Wu, Y., et.al., 2015. MiR-30a-5p suppresses cell growth and enhances apoptosis of hepatocellular carcinoma cells via targeting AEG-1. *Int. J. Clin. Exp. Pathol.* 8: 15632–15641.

Huan, L., Liang, L., He, X., 2016. Role of microRNAs in inflammation-associated liver cancer. *Cancer Biol. Med.* 13: 408–424.

Huang, M., Fong, C., Khor, E., Lim, L., 2005. Transfection efficiency of chitosan vectors : Effect of polymer molecular weight and degree of deacetylation. *J. Control. Release* 106: 391–406.

Huang, S., He, X., 2011. The role of microRNAs in liver cancer progression. *Br. J. Cancer* 104: 235–240.

Jin'en, W., Juntao, D., Jing, Y., Xiaola, G., Yadong, Z., 2018. MicroRNA Roles in the Nuclear Factor Kappa B Signaling Pathway in Cancer. *Front. Immunol.* 9: 546–555.

Jisha, K.D.M.S., 2017. Chitosan nanoparticles preparation and applications. *Environ. Chem. Lett.*

- Jun, L., Yang, G., Zhisu, L., 2019. Biomedicine & Pharmacotherapy The utility of serum exosomal microRNAs in hepatocellular carcinoma. *Biomed. Pharmacother.* 111: 1221–1227.
- Jung, H. Il, Ahn, T., Bae, S.H., Chung, J.C., Kim, H., Chin, S., Jeong, D., 2015. Astrocyte elevated gene-1 overexpression in hepatocellular carcinoma : an independent prognostic factor. *Ann. Surg. Treat. Res. Astrocyte* 88: 77–85.
- Kaban, K., Salva, E., Akbuga, J., 2016. In Vitro Dose Studies on Chitosan Nanoplexes for microRNA Delivery in Breast Cancer Cells. *Nucleic Acid Ther.* 1–11.
- Kanda, T., Goto, T., Hirotsu, Y., Moriyama, M., 2019. Molecular Mechanisms Driving Progression of Liver Cirrhosis towards Hepatocellular Carcinoma in Chronic Hepatitis B and C Infections : A Review. *Int. J. Mol. Sci.* 20.
- Karimi, M., Avci, P., Ahi, M., Gazori, T., Hamblin, R.M., 2016. Evaluation of Chitosan-Tripolyphosphate Nanoparticles as a p- shRNA Delivery Vector: Formulation, Optimization and Cellular Uptake Study. *J. Nanopharmaceutical Drug Deliv.* 1: 266–278.
- Karin, M., Greten, F.R., 2005. NF- κ B: linking inflammation and immunity to cancer development and progression. *Nat. Rev. Immunol.* 5: 749–759.
- Karmakar, S., Kaushik, G., Nimmakayala, R., Rachagani, S., 2019. MicroRNA regulation of K-Ras in pancreatic cancer and opportunities for therapeutic intervention. *Semin. Cancer Biol.* 54: 63–71.
- Katas, H., Alpar, H.O., 2006. Development and characterisation of chitosan nanoparticles for siRNA delivery. *J. Control. Release* 115: 216–225.
- Khan, A.Q., Kuttikrishnan, S., Siveen, K.S., Prabhu, K.S., Shanmugakonar, M., Naemi, H.A.A., Haris, M., et.al., 2019. RAS-mediated oncogenic signaling pathways in human malignancies. *Semin. Cancer Biol.* 54: 1–13.
- Kim, M., Slack, F.J., 2014. MicroRNA-mediated regulation of KRAS in cancer. *J. Hematol. Oncol.* 2014 7: 1–4.
- Lam, J.K.W., Chow, M.Y.T., Zhang, Y., Leung, S.W.S., 2015. siRNA Versus miRNA as Therapeutics for Gene Silencing. *Mol. Ther. Nucleic Acids* 4: 1–20.

- Li, Q., Wang, M., Wang, N., Wang, J., Qi, L., Mao, P., 2018. Biomedicine & Pharmacotherapy Downregulation of microRNA-216b contributes to glioma cell growth and migration by promoting AEG-1-mediated signaling. *Biomed. Pharmacother.* 104: 420–426.
- Li, Wen-fang, Dai, H., Ou, Q., Zuo, G., Liu, C., 2015a. Overexpression of microRNA-30a-5p inhibits liver cancer cell proliferation and induces apoptosis by targeting MTDH / PTEN / AKT pathway. *Tumor Biol.*
- Li, Wen-fang, Ou, Q., Dai, H., Liu, C., 2015b. Lentiviral-Mediated Short Hairpin RNA Knockdown of MTDH Inhibits Cell Growth and Induces Apoptosis by Regulating the PTEN / AKT Pathway in Hepatocellular Carcinoma. *Int. J. Mol. Sci.* 16: 19419–19432.
- Li, Weijia, Zhou, J., Xu, Y., 2015. Study of the in vitro cytotoxicity testing of medical devices (Review). *Biomed. Reports* 3: 617–620.
- Liu, T., Zhang, L., Joo, D., Sun, S., 2017. NF- κ B signaling in inflammation. *Signal Transduct. Target. Ther.* 2.
- Luck, M.E., Muljo, S.A., Collins, C.B., Alerts, E., 2015. Prospects for Therapeutic Targeting of MicroRNAs in Human Immunological Diseases. *J. Immunol.* 194: 5047–5052.
- Maliawan, R.P., Veronica, S., Putu, N., Pande, A., Dewi, A., Wisnu, P., et.al., 2018. miRNA-124 loaded chitosan as novel therapy to induce neuroprotective and neurogenesis for improving brain revitalization after ischemic stroke. *Bali Med. J.* 7: 361–368.
- Mancino, A., Lawrence, T., 2019. NF κ B and tumor-associated macrophages. *Clin. Cancer Res.* 16: 784–789.
- Meng, X., Zhu, D., Yang, S., Wang, X., Xiong, Z., Zhang, Y., et.al., 2012. Cytoplasmic Metadherin (MTDH) Provides Survival. *J. Biol. Chem.* 287: 4485–4491.
- Mickey, B., Park, S., Zhao, D., Hatanpaa, K.J., Mickey, B.E., Saha, D., et.al., 2009. RIP1 activates PI3K-Akt via a dual mechanism involving NF- κ B-mediated inhibition of the mTOR-S6K-IRS1 negative feedback loop and down- regulation of PTEN RIP1 Activates PI3K-Akt via a Dual Mechanism Involving NF- K B – Mediated Inhibition of the mTOR-S6. *Cancer Res.* 69. d
- Mohammed, M.A., Syeda, J.T.M., Wasan, K.M., Wasan, E.K., 2017. An Overview of

Nguyen, D.D., Chang, S., 2018. Development of novel therapeutic agents by inhibition of oncogenic microRNAs. *Int. J. Mol. Sci.* 19: 1–17.

Nussinov, R., Tsai, C., Jang, H., 2019. Seminars in Cancer Biology Is Nanoclustering essential for all oncogenic KRas pathways ? Can it explain why wild-type KRas can inhibit its oncogenic variant ? *Semin. Cancer Biol.* 54: 114–120.

Palomba, G., Colombino, M., Contu, A., Massidda, B., Baldino, G., Pazzola, A., et.al., 2012. Prevalence of KRAS , BRAF , and PIK3CA somatic mutations in patients with colorectal carcinoma may vary in the same population : clues from Sardinia. *J. Transl. Med.* 10: 1.

Parikh, N.D., 2019. Treatment for Advanced Hepatocellular Carcinoma : Current Standard and the Future. *Clin. Liver Dis.* 13.

Pawar, A., Prabhu, P., 2019. Nanosoldiers : A promising strategy to combat triple negative breast cancer. *Biomed. Pharmacother.* 110: 319–341.

Pereira, D.M., Rodrigues, P.M., Borralho, P.M., Rodrigues, C.M.P., 2013. Delivering the promise of miRNA cancer therapeutics. *Drug Discov. Today* 18: 282–289.

Piasecka, D., Braun, M., Kordek, R., Sadej, R., Romanska, H., 2018. MicroRNAs in regulation of triple-negative breast cancer progression. *J. Cancer Res. Clin. Oncol.* 144: 1401–1411.

Rai, V., Abdo, J., Alsuwaidan, A.N., Agrawal, S., 2018. Cellular and molecular targets for the immunotherapy of hepatocellular carcinoma. *Mol. Cell. Biochem.* 437: 13–36.

Rampino, A., Borgogna, M., Blasi, P., Bellich, B., Cesàro, A., 2013. Chitosan nanoparticles : Preparation , size evolution and stability. *Int. J. Pharm.* 455: 219–228.

Reid, G., Kao, S.C., Pavlakis, N., Brahmhatt, H., MacDiarmid, J., Clarke, S., et.al., 2016. Clinical development of TargomiRs, a miRNA mimic-based treatment for patients with recurrent thoracic cancer. *Epigenomics* 8: 1079–1085.

Rennie, W., Kanoria, S., Liu, C., Mallick, B., Long, D., Wolenc, A., et.al., 2016b.

- Robertson, C.L., Srivastava, J., Rajasekaran, D., Gredler, R., Akiel, M.A., Jariwala, N., et.al., 2015. The role of AEG-1 in the development of liver cancer. *Hepatology* 2: 303–312.
- Rupaimoole, R., Slack, F.J., 2017. MicroRNA therapeutics: Towards a new era for the management of cancer and other diseases. *Nat. Rev. Drug Discov.* 16: 203–221.
- Santos-carballal, B., 2018. Chitosan in Non-Viral Gene Delivery : Role of Structure , Characterization Methods , and Insights in Cancer and Rare Diseases Therapies. *Polymers (Basel)*. 10: 1–51.
- Serna-blasco, R., Sanz-álvarez, M., Aguilera, Ó., García-foncillas, J., 2019. Targeting the RAS-dependent chemoresistance : The Warburg connection. *Semin. Cancer Biol.* 54: 80–90.
- Shi, L., Middleton, J., Jeon, Y., Magee, P., Veneziano, D., Laganà, A., et.al., 2018. KRAS induces lung tumorigenesis through microRNAs modulation. *Cell Death Dis.*
- Sia, D., Villanueva, A., Friedman, S.L., Llovet, J.M., 2017. Liver Cancer Cell of Origin, Molecular Class, and Effects on Patient Prognosis. *Gastroenterology* 152: 745–761.
- Sidhu, K., Kapoor, N.R., Pandey, V., Kumar, V., 2015. The “ macro ” world of microRNAs in hepatocellular carcinoma. *Front. Oncol.* 5: 1–8.
- Simanshu, D.K., Nissley, D. V, McCormick, F., 2017. RAS Proteins and Their Regulators in Human Disease. *Cell* 170: 17–33.
- Srdic-rajic, T., Zuvela, M., 2017. Targeted therapy and personalized medicine in hepatocellular carcinoma : drug resistance , mechanisms , and treatment strategies. *J. Hepatocell. Carcinoma* 4: 93–103.
- Stotz, M., Gerger, A., Haybaeck, J., Kiesslich, T., Bullock, M.D., Pichler, M., 2015. Molecular Targeted Therapies in Hepatocellular Carcinoma : Past , Present and Future. *Anticancer Res.* 5744: 5737–5744.
- Tang, J., Ahmad, A., Sarkar, F.H., 2012. The Role of MicroRNAs in Breast Cancer Migration , Invasion and Metastasis. *Int. J. Mol. Sci.* 12: 13414–13437.
- Thillai, K., Ross, P., Sarker, D., Thillai, K., Ross, P., Sarker, D., 2016. Molecularly targeted

- Vasudevan, K.M., Gurumurthy, S., Rangnekar, V.M., 2004. Suppression of PTEN Expression by NF- κ B Prevents Apoptosis. *Mol. Cell. Biol.* 24: 1007–1021.
- Villanueva, A., 2019. Hepatocellular Carcinoma. *N. Engl. J. Med.* 380: 1450–1462.
- Visalli, M., Bartolotta, M., Polito, F., Oteri, R., Barbera, A., Arrigo, R., et.al., 2018. miRNA expression profiling regulates necroptotic cell death in hepatocellular carcinoma. *Int. J. Oncol.* 53: 771–780.
- Waller, L.P., Deshpande, V., Pyrsopoulos, N., Waller, L.P., Deshpande, V., Pyrsopoulos, N., 2015. Hepatocellular carcinoma : A comprehensive review. *World J. Gastroenterol.* 7: 2648–2663.
- Wang, L., Yue, Y., Wang, X., Jin, H., 2015. Function and clinical potential of microRNAs in hepatocellular carcinoma (Review). *Oncol. Lett.* 10: 3345–3353.
- Wang, T., Larcher, M.L., Ma, L., Veedu, N.R., 2018. Systematic Screening of Commonly Used Commercial Transfection Reagents towards Efficient Transfection. *Molecules* 23: 1–15.
- Xu, W., Deng, B., Lin, P., Liu, C., Li, B., Huang, Q., et.al., 2019. Ribosome profiling analysis identified a KRAS-interacting microprotein that represses oncogenic signaling in hepatocellular carcinoma cells. *Sci. China Life Sci.* 62: 1–14.
- Xu, X., Tao, Y., Shan, L., Chen, R., Jiang, H., Qian, Z., et.al., 2018. The Role of MicroRNAs in Hepatocellular Carcinoma. *J. Cancer* 9: 3557–3569.
- Yan, C., Huo, X., Wang, S., Feng, Y., Gong, Z., 2015. Stimulation of hepatocarcinogenesis by neutrophils upon induction of oncogenic kras expression in transgenic zebrafish. *J. Hepatol.* 63: 420–428.
- Yang, C., Yin, M., Xu, G., Lin, W., Chen, J., Zhang, Y., 2019. Biodegradable Polymers as a Noncoding miRNA Nanocarrier for Multiple Targeting Therapy of Human Hepatocellular Carcinoma. *Adv. Healthc. Mater.* 8 (8).
- Yang, F., Zhang, W., Shen, Y.A.N., Guan, X., 2015. Identification of dysregulated

- Yang, L., Tian, Y., Leong, W.S., Song, H., Yang, W., Wang, M., et.al., 2018. Efficient and tumor-specific knockdown of MTDH gene attenuates paclitaxel resistance of breast cancer cells both in vivo and in vitro. *Breast Cancer Res.* 20: 1–13.
- Ye, H., Zhang, C., Wang, B., Tan, X., Zhang, W., Teng, Y., et.al., 2014. Synergistic function of Kras mutation and HBx in initiation and progression of hepatocellular carcinoma in mice. *Oncogene* 33: 5133–5138.
- Yin, Z., Ren, W., 2019. MicroRNA-217 acts as a tumor suppressor and correlates with the chemoresistance of cervical carcinoma to cisplatin. *Oncol. Targets. Ther.* 12: 759–771.
- Yoo, B.K., Emdad, L., Su, Z., Villanueva, A., Chiang, D.Y., Mukhopadhyay, N.D., et.al., 2009. Astrocyte elevated gene-1 regulates hepatocellular carcinoma development and progression. *J. Clin. Invest.* 119: 465–477.
- Yoon, S.M., Ryoo, B.-Y., Lee, S.J., Kim, J.H., Shin, J.H., An, J.H., et.al., 2018. Efficacy and Safety of Transarterial Chemoembolization Plus External Beam Radiotherapy vs Sorafenib in Hepatocellular Carcinoma With Macroscopic Vascular Invasion: A Randomized Clinical Trial. *JAMA Oncol.* 4: 661–669.
- Ysrafil, 2019. Efek Sitotoksisitas Sediaan Nanopartikel Kitosan Berbasis MikroRNA Terhadap Kultur Sel Line Kanker Ovarium SCOV3.
- Zhang, H., Zhao, X., Liu, S., Li, J., Wen, Z., Li, M., 2010. Molecular and Cellular Endocrinology 17 ⁴: E 2 promotes cell proliferation in endometriosis by decreasing PTEN via NFkB-dependent pathway. *Mol. Cell. Endocrinol.* 317: 31–43.
- Zhang, M., Li, M., Li, N., Zhang, Z., Liu, N., 2017. miR-217 suppresses proliferation , migration , and invasion promoting apoptosis via targeting MTDH in hepatocellular carcinoma. *Oncol. Rep.* 37: 1772–1778.
- Zhao, W., Yu, S., Lu, Z., Ma, Y., Gu, Y., Ā, J.C., 2010. The miR-217 microRNA functions as a potential tumor suppressor in pancreatic ductal adenocarcinoma by targeting KRAS. *Carcinogenesis* 31: 1726–1733.
- Zhou, K., Luo, X., Wang, Y., Cao, D., Sun, G., 2017. MicroRNA-30a suppresses tumor

progression by blocking Ras / Raf / MEK / ERK signaling pathway in hepatocellular carcinoma. *Biomed. Pharmacother.* 93: 1025–1032.

Zhou, Z., Deng, H., Yan, W., Huang, H., Deng, Y., 2012. Expression of Metadherin / AEG-1 Gene Is Positively Related to Orientation Chemotaxis and Adhesion of Human Hepatocellular Carcinoma Cell Lines of Different Metastatic Potentials *. *J. Huazong Univ. Sci. Technol.* 32: 353–357.

Zhu, H.D., Liao, J.Z., He, X.X., Li, P.Y., 2015. The emerging role of astrocyte-elevated gene-1 in hepatocellular carcinoma (Review). *Oncol. Rep.* 34: 539–546.

Zhu, X., Sun, H., 2019. Emerging agents and regimens for hepatocellular carcinoma. *J. Hematol. Oncol.* 12: 1–10.