

## DAFTAR PUSTAKA

- Abcam, 2007. T47D (Human ductal breast epithelial tumor cell line) Whole Cell Lysate (ab14899) <http://www.abcam.com/index.html?datasheet=14899>, diakses tgl 26 Agustus 2015.
- Ahern, T.P., Pedersen, L., Tarp, M., Cronin-Fenton, D.P., Garne, J.P., Silliman, R.A., Sørensen, H.T., Lash, T.L., 2011. Statin prescriptions and breast cancer recurrence risk: a Danish nationwide prospective cohort study. *J. Natl. Cancer Inst.* 103(19):1461-1468.
- Alberts, B., Johnson, A., Lewis, J., Raff, M., Roberts, K., Walter, P., 2008. *Molecular Biology of The Cell*. Fifth Edition. Garland Science, New York.
- Arur, S., Uche, U.E., Rezaul, K., Fong, M., Scranton, V., Cowan, A.E., Mohler, W., Han, D.K., 2003. Annexin I is an endogenous ligand that mediates apoptotic cell engulfment. *Dev. Cell.* 4(4):587-598.
- Barros, A.L.S., Aguiar, J.S., Araújo, L.C.C., Peixoto, C.A., de Medeiros, P.L., Catanho, M.T.J.A., da Silva, T.G., 2014. Synergistic anticancer effects of valproic acid, atorvastatin and pioglitazone in human malignant and murine cells. *Afr. J. Pharm. Pharmacol.* 8(2):31-39.
- Blais, L., Desgagné, A., LeLorier, J., 2000. 3-Hydroxy-3-Methylglutaryl Coenzyme A Reductase Inhibitors and the Risk of Cancer : A Nested Case-Control Study. *Arch. Intern. Med.* 160(15):2363-2368.
- Blanco-Colio, L.M., Villa, A., Ortego, M., Hernández- Presa, M.A., Pascual, A., Plaza, J.J., Egido, J., 2002. 3-Hydroxy-3-methyl-glutaryl coenzyme A reductase inhibitors, atorvastatin and simvastatin, induce apoptosis of vascular smooth muscle cells by down-regulation of Bcl-2 expression and Rho A prenylation. *Atherosclerosis* 161: 17-26.
- Borgquist, S., Jögi, A., Pontén, F., Rydén, L., Brennan, D., Jirstrom, K., 2008. Prognostic impact of tumour-specific HMG-CoA reductase expression in primary breast cancer. *Breast Cancer Res.* 10(5):79.
- Boyle, P., Levin, B., 2008. *World Cancer Report 2008*. WHO Press, Lyon.
- Burdall, S.E., Hanby, A.M., Lansdown, M.R., Speirs, V., 2003. Breast cancer cell lines: friend or foe?. *Breast Cancer Res.* 5(2):89-95.
- Campbell, M.J., Esserman, L.J., Zhou, Y., Shoemaker, M., Lobo, M., Borman, E., Baehner, F., Kumar, A.S., Adduci, K., Marx, C., Petricoin, E.F., Liotta, L.A., Winters, M., Benz, S., Benz, C.C., 2006. Breast cancer growth prevention by statins. *Cancer Res.* 66(17):8707-8714.

- Cancer Chemoprevention Research Center (CCRC). 2014. *Prosedur Tetap Uji Sitotoksitas metode MTT*. Fakultas Farmasi UGM, Yogyakarta.
- Cao, S.G., Valerie, H.L., Wu, X.H., Sim, K.Y., Tan, B.H.K., Pereira, J.T., Goh, S.H. 1998. Novel cytotoxic polyprenylated xanthenes from *garcinia gaudichaudii*. *Tetrahedron* 54: 10915-10924.
- Cardwell, C.R., Hicks, B.M., Hughes, C., Murray, L.J., 2015. Statin use after diagnosis of breast cancer and survival: a population-based cohort study. *Epidemiology* 26(1):68-78.
- Chan, K.K., Oza, A.M., Siu, L.L., 2003. The statins as anticancer agents. *Clin. Cancer Res.* 9:10-19.
- Chen, C.L., Huang, S.S., Huang, J.S., 2008. Cholesterol modulates cellular TGF- $\beta$  responsiveness by altering TGF- $\beta$  binding to TGF- $\beta$  receptors. *J. Cell. Physiol.* 215: 223–233.
- Clendening, J.W., Pandya, A., Boutrosa, P.C., Ghamrasni, S.E., Khosravia, F., Trentina, G.A., Martirosyana, A., Hakem, A., Hakem, R., Jurisica, I., Penna, L.Z., 2010. Dysregulation of the mevalonate pathway promotes transformation. *Proc. Natl. Acad. Sci. USA* 107(34):15051–15056.
- Coqueret, O., 2002. Linking cyclins to transcriptional control. *Gene* 299(1-2):35-55.
- Cornelissen, M., Philipp'e, J., Sitter, S.D., De Ridde, L., 2002. Annexin V expression in apoptotic peripheral blood lymphocytes: An electron microscopic evaluation. *Apoptosis* 7: 41–47.
- Crawford, K.W., Bowen, W.D., 2002. Sigma-2 receptor agonists activate a novel apoptosis pathway and potentiate antineoplastic drugs in breast tumor cell lines. *Cancer Res.* 62(1):313-22.
- Crescencio, M.E., Rodríguez, E., Páez, A., Masso, F.A., Montaña, L.F., López-Marure, R., 2009. Statins inhibit the proliferation and induce cell death of human papilloma virus positive and negative cervical cancer cells. *Int. J. Biomed. Sci.* 5(4):411-420.
- DeClue, J.E., Vass, W.C., Papageorge, A.G., Lowy, D.R., Willumsen, B.M., 1991. Inhibition of cell growth by lovastatin is independent of ras function. *Cancer Res.* 51(2):712-717.
- Demchenko, A.P., 2012. The change of cellular membranes on apoptosis: fluorescence detection. *Exp. Oncol.* 34(3):263-268.
- Endo, A., 2004. The origin of the statins. *Atheroscler. Suppl.* 5(3):125-130.

- Eray, M., Matto, M., Kaartinen, M., Anderson, L.C., Pelkonen, J., 2001. Flow cytometric analysis of apoptotic subpopulations with a combination of annexin V-FITC, propidium iodide, and SYTO 17. *Cytometry* 43: 134-142.
- Gallelli, L., Falcone, D., Scaramuzzino, M., Pelaia, G., D'Agostino, B., Mesuraca, M., Terracciano, R., Spaziano, G., Maselli, R., Navarra, M., Savino, R., 2014. Effects of simvastatin on cell viability and proinflammatory pathways in lung adenocarcinoma cells exposed to hydrogen peroxide. *BMC. Pharmacol. Toxicol.* 15:67.
- Gazzerro, P., Proto, M.C., Gangemi, G., Malfitano, A.M., Ciaglia, E., Pisanti, S., Santoro, A., Laezza, C., Bifulco, M., 2012. Pharmacological actions of statins: A critical appraisal in the management of cancer. *Pharmacol. Rev.* 64(1):102-46.
- Ghosh-Choudhury, N., Mandal, C.C., Ghosh-Choudhury, N., Ghosh-Choudhury, G., 2010. Simvastatin induces derepression of PTEN expression via NFkappaB to inhibit breast cancer cell growth. *Cell. Signal.* 22(5):749-58.
- Givan, A.L., 2011. Flow cytometry : an introduction. *Methods Mol. Biol.* 699:1-29.
- Gopalan, A., Yu, W., Sanders, B.G., Kline, K., 2013. Simvastatin inhibition of mevalonate pathway induces apoptosis in human breast cancer cells via activation of JNK/CHOP/DR5 signaling pathway. *Cancer Lett.* 329(1):9-16.
- Graaf, M.R., Beiderbeck, A.B., Egberts, A.C.G., Richel, D.J., Guchelaar H.J., 2004. The risk of cancer in users of statins. *J. Clin. Oncol.* 22(12):2388-2394.
- Herrero-Martin, G., Lopez-Rivas, A., 2008. Statins activate a mitochondrial-operated pathway of apoptosis in breast tumor cells by a mechanism regulated by ErbB2 and dependent on the prenylation of proteins. *FEBS Lett.* 582(17):2589-2594.
- Hirai, A., Nakamura, S., Noguchi, Y., Yasuda, T., Kitagawa, M., Tatsuno, I., Oeda, T., Tahara, K., Terano, T., Narumiya, S., Kohn, L.D., Saito, Y., 1997. Geranylgeranylated rho small GTPase(s) are essential for the degradation of p27<sup>Kip1</sup> and facilitate the progression from G1 to S phase in growth-stimulated rat FRTL-5 cells. *J. Biol. Chem.* 272(1):13-16.
- Holliday, D.L., and Speirs, V., 2011. Choosing the right cell line for breast cancer research. *Breast Cancer Res.* 13(4): 215.

- Hoque, A., Chen, H., Xu, X.C., 2008. Statin induces apoptosis and cell growth arrest in prostate cancer cells. *Cancer Epidemiol. Biomarkers Prev.* 17(1):88-94.
- Horiguchi, A., Sumitomo, M., Asakuma, J., Asano, T., Asano, T., Hayakawa, M., 2004. 3-hydroxy-3-methylglutaryl-coenzyme a reductase inhibitor, fluvastatin, as a novel agent for prophylaxis of renal cancer metastasis. *Clin. Cancer Res.* 10(24):8648-8655.
- Huang, X., Ma, J., Xu, J., Su, Q., Zhao, J., 2015. Simvastatin induces growth inhibition and apoptosis in HepG2 and Huh7 hepatocellular carcinoma cells via upregulation of Notch1 expression. *Mol. Med. Rep.* 11(3):2334-2340.
- Jemal, A., Bray, F., Center, M.M., Ferlay, J., Ward, E., Forman, D., 2011. Global Cancer Statistics. *CA. Cancer J. Clin.* 61:69-90.
- Kastan, M. B., Skapek, S. X., 2001. *Molecular Biology of Cancer : The Cell Cycle in Cancer Principle & Practice of Oncology*. Ed 6<sup>th</sup>. pp. 91-102. Philadelphia.
- Kato, J., Matsushime, H., Hiebert, S.W., Ewen, M.E., Sherr, C.J., 1993. Direct binding of cyclin D to the retinoblastoma gene product (pRb) and pRb phosphorylation by the cyclin D-dependent kinase CDK4. *Genes Dev.* 7(3):331-342.
- Kementrian Kesehatan Republik Indonesia., 2015. *Stop Kanker*. Pusat Data dan Informasi. Kementrian Kesehatan RI. Diakses : 14 Juli 2015.
- Kim, Y.S., Seol, C.H., Jung, J.W., Oh, S.J., Hwang, K.E., Kim, H.J., Jeong, E.T., Kim, H.R., 2015. Synergistic effect of sulindac and simvastatin on apoptosis in lung cancer A549 cells through AKT-Dependent downregulation of survivin. *Cancer Res. Treat.* 47(1):90-100.
- Klawitter, J., Shokati, T., Moll, V., Christians, U., Klawitter, J., 2010. Effects of lovastatin on breast cancer cells: a proteo-metabonomic study. *Breast Cancer Res.* 12(2):1-20.
- Knudsen, K.E., Diehl, J.A., Haiman, C.A., Knudsen, E.S., 2006. Cyclin D1: polymorphism, aberrant splicing and cancer risk. *Oncogene* 25(11):1620-1608.
- Koyuturk, M., Ersoz, M., Altioek, N., 2007. Simvastatin induces apoptosis in human breast cancer cells: p53 and estrogen receptor independent pathway requiring signalling through JNK. *Cancer Lett.* 250(2):220-228.
- Kubatka, P., Zihlavniková, K., Kajo, K., Péc, M., Stollárová, N., Bojková, B., Kassayová, M., Orendás, P., Antineoplastic effects of simvastatin in experimental breast cancer. *Klin. Onkol.* 24(1):41-5.

- Kritchevsky, S.B., Kritchevsky, D., 1992. Serum cholesterol and cancer risk: an epidemiologic perspective. *Annu. Rev. Nutr.* 12:391-416.
- Kumar, V., Abbas, A.K., Fausto, N., 2005. *Robbins and Contran Pathology Basic of Disease*, 7th Ed. Elsvier saunders, Pennsylvania.
- Larsson, O., Carlberg, M., 1992. Requirement for isoprenoid-dependent post translational modifications in the cell cycle progression of human breast-cancer cells. *Int. J. Oncol.* (4):489-493.
- Lee, J., Hong, E.M., Jang, J.A., Park, S.W., Koh, D.H., Choi, M.H., Jang, H.J., Kae, S.H., 2016. Simvastatin induces apoptosis and suppresses insulin-like growth factor 1 receptor in bile duct cancer cells. *Gut Liver* 10(2):310-317.
- Lee, S.J., Hwang, J.W., Yim, H., Yim, H.J., Woo, S.U., Suh, S.J., Hyun, J.J., Jung, S.W., Koo, J.S., Kim, J.H., Seo, Y.S., Yeon, J.E., Lee, S.W., Byun, K.S., Um, S.H., 2014. Synergistic effect of simvastatin plus NS398 on inhibition of proliferation and survival in hepatocellular carcinoma cell line. *J. Gastroenterol. Hepatol.* 29(6):1299-307.
- Lee, S.K., Kim, Y.C., Song, S.B., Young, B.S., Kim, S., 2010. Stabilization and translocation of p53 to mitochondria is linked to Bax translocation to mitochondria in simvastatin-induced apoptosis. *Biochem. Biophys. Res. Commun.* 391(4):1592-1597.
- Leemans, C.R., Braakhuis, B.J., Brakenhoff, R.H., 2011. The molecular biology of head and neck cancer. *Nat. Rev. Cancer* 11(1):9-22.
- Li, Y., Fu, J., Yuan, X., Hu, C., 2014. Simvastatin inhibits the proliferation of A549 lung cancer cells through oxidative stress and up-regulation of SOD2. *Pharmazie.* 69(8):610-614.
- Liang, Y.W., Chang, C.C., Hung, C.M., Chen, T.Y., Huang, T.Y., Hsu, Y.C., 2013. Preclinical Activity of Simvastatin Induces Cell Cycle Arrest in G1 via Blockade of Cyclin D-Cdk4 Expression in Non-Small Cell Lung Cancer (NSCLC). *Int. J. Mol. Sci.* 14(3):5806-5816..
- Mandal, C.C., Ghosh-Choudhury, N., Yoneda, T., Choudhury, G.G., Ghosh-Choudhury, N., 2011. Simvastatin prevents skeletal metastasis of breast cancer by an antagonistic interplay between p53 and CD44. *J. Biol. Chem.* 286(13):11314-11327.
- McDonald, M., Hearts, R.P., Lowenthal, S.W., 2008. *The Burden of Cancer*. Pfizer Medical Division, USA.
- Medina, P.J., Fausel, C., 2008. *Cancer treatment and chemotherapy* in: Dippiro J.T., Talbert, R.L., Yee, G.C., Matzke, G.R., Wells, B.G., dan

- Posey, L.M., eds. *Pharmacotherapy: A Patophysiologic Approach*. 7th Ed. McGraw-hill Publishing Company. New York.
- Moffat, A.C., Osselton, M.D., Widdop, B., 2004. *Clarke's Analysis Of Drug and Poisons*. 3<sup>rd</sup> Ed. Phamaceutical Press., London.
- Munawar, M., Hartono, B., Rifqi S., 2013. LDL Cholesterol Goal Attainment in Hypercholesterolemia: CEPHEUS Indonesian Survey. *Acta. Cardiol. Sin.* 29(1):71-81.
- Musgrove, E.A., 2006. Cyclins: roles in mitogenic signaling and oncogenic transformation. *Growth Factors* 24(1):13-19.
- Neal, P., McLeod, M., Odunsi, Y., Pierpoint, S., Inchausti, K., 2008. *Rediscovering Biology* [online textbook] [cited 2013 August5]; Unit8:[13screen]. Available from URL [http : //www.learner.org/ courses / biology / textbook / cancer/cancer\\_2.html](http://www.learner.org/courses/biology/textbook/cancer/cancer_2.html).
- Nurani, L.H., Widyarini, S., Mursyidi, A., 2015. Uji sitotoksik dan uji kombinasi fraksi etil asetat ekstrak etanol akar pasak bumi (*Eurycoma longifolia* Jack.) dan doksorubisin pada sel limfosit. *J. Trop. Pharm. Chem.* 3(2):138-147.
- Pollard, T.D., Earnshaw, W.C., 2008. *Cell Biology*. Elsevier Inc., Philadelphia.
- Rao, S., Lowe, M., Herliczek, T.W., Keyomarsi, K., 1998. Lovastatin mediated G1 arrest in normal and tumor breast cells is through inhibition of CDK2 activity and redistribution of p21 and p27, independent of p53. *Oncogene* 17(18):2393-402.
- Rao, S.K., Prasad, T., Mohanta, G.P., Manna, P.K., 2011. An overview of statins as hypolipidemic drugs. *Int. J. Pharm. Sci. Drug Res.* 3(3): 178-183.
- Raynal, P., Pollard, H.B., 1994. Annexins : the problem of assessing the biological role for a gene family of multifunctional calcium- and phospholipid-binding proteins. *Biochim. Biophys. Acta* 1197(1):63-93.
- Relja, B., Meder, F., Wilhelm, K., Henrich, D., Marzi, I., Lehnert, M., 2010. Simvastatin inhibits cell growth and induces apoptosis and G0/G1 cell cycle arrest in hepatic cancer cells. *Int. J. Mol. Med.* 26(5):735-741.
- Reutelingsperger, C.P., Hornstra, G., Hemker, H.C., 1985. Isolation and partial purification of a novel anticoagulant from arteries of human umbilical cord. *Eur. J. Biochem.* 151(3):625-629.
- Rode, H.D., Eisel, D., Frost, I., 2004. *Apoptosis, Cell Death and Cell Proliferation Manual*, 3<sup>rd</sup> ed. Roche Applied Science, Scotland.
- Rugo, H.S., 2006. *Cancer in Current Medical Diagnosis and Treatment*. 45<sup>th</sup> Edition. Publishing Company, New York, USA.



- S´anchez, C.A., Rodr´ıguez, E., Varela, E., Zapata, E., P´aez, A., Mass´o, F.A., Monta, L.F., L´opez-Marure, R., 2008. Statin-Induced inhibition of MCF-7 breast cancer cell proliferation is related to cell cycle arrest and apoptotic and necrotic cell death mediated by an enhanced oxidative stress. *Cancer Invest.* 26:698–707.
- Sadeghi-Aliabadi, H., Minaiyan, M., Dabestan, A., 2010. Cytotoxic evaluation of doxorubicin in combination with simvastatin against human cancer cells. *Res. Pharm. Sci.* 5(2):127-133.
- Schafer, J.M., Lee, E.S., O'Regan, R.M., Yao, K., Jordan, V.C., 2000. Rapid development of tamoxifen-stimulated mutant p53 breast tumor (T4D7) in athymic mice. *Clin. Cancer Res.* 6(11):4373-4380.
- Schointuch, M.N., Gilliam, T.P., Stine, J.E., Han, X., Zhou, C., Gehrig, P.A., Kim, K., Bae-Jump, V.L., 2014. Simvastatin, an HMG-CoA reductase inhibitor, exhibits anti-metastatic and anti-tumorigenic effects in endometrial cancer. *Gynecol. Oncol.* 134(2):346-355.
- Sewester, C.S., Dombeck, C., Olin, B.R., Kastrup, E.K., Hebel, S.K., 2004. *Drugs facts and comparisons*. Lippincott Co. St. Louis.
- Sławińska-Brych, A., Zdzisińska, B., Kandefer-Szerszeń, M., 2014. Fluvastatin inhibits growth and alters the malignant phenotype of the C6 glioma cell line. *Pharmacol. Rep.* 66(1):121-129.
- Soma, M.R., Corsini, A., Paoletti, R., 1992. Cholesterol and mevalonic acid modulation in cell metabolism and multiplication. *Toxicol. Lett.* 64:1-15.
- Suffness, M., Pezzuto, J.M., 1991. *Assays Related to Cancer Drug Discovery Methods in Plant Biochemistry ; Assays for Bioactivity*. Academic Press, London.
- Thurnher, M., Gruenbacher, G., Nussbaumer, O., 2013. Regulation of mevalonate metabolism in cancer and immune cells. *Biochim. Biophys. Acta* 1831(6):1009-1015.
- Van-Engeland, M., Nieland, L.J., Ramaekers, F.C., Schutte, B., Reutelingsperger, C.P., 1998. Annexin V-affinity assay: a review on an apoptosis detection system based on phosphatidylserine exposure. *Cytometry* 31(1):1-9.
- Verma, S.P., Goldin, B.R., Lin, P.S., 1998. The Inhibition of the Estrogenic Effects of Pesticides dan Enviromental Chemicals by Curcumin and Isoflavonoids. *Envir. Health Presp.* 106(12) : 807-812.
- Vermes, I., Clemens, C., Steffens-Nakken, H., Reutelingsperger, C., 1995. A novel assay for apoptosis flow cytometric detection of phosphatidylserine early apoptotic cells using fluorescein labelled expression on Annexin V. *J. Immunol. Methods* 184(1):39-51.

- Vermes, I., Haanen, C., Reutelingsperger, C., 2000. Flow cytometry of apoptotic cell death. *J. Immunol. Methods* 243(1-2):167-90.
- Vermeulen, K., Van Bockstaele, D.R., Berneman, Z.N., 2003. The cell cycle: a review of regulation, deregulation and therapeutic targets in cancer. *Cell Prolif.* 36(3):131-149.
- Wang, T., Seah, S., Loh, X., Chan, C.W., Hartman, M., Goh, B.C., Lee, S.C., 2016. Simvastatin-induced breast cancer cell death and deactivation of PI3K/Akt and MAPK/ERK signalling are reversed by metabolic products of the mevalonate pathway. *Oncotarget* 7(3):2532-2544.
- Weinberg, R.A., 1995. The retinoblastoma protein and cell cycle control. *Cell* 81(3):323-330.
- Wong, R.S.Y., 2011. Apoptosis in cancer: from pathogenesis to treatment. *J. Exp. Clin. Cancer Res.* 30(1): 87.
- Wong, W.W., Dimitroulakos, J., Minden, M.D., Penn, L.Z., 2002. HMG-CoA reductase inhibitors and the malignant cell: the statin family of drugs as triggers of tumor-specific apoptosis. *Leukemia* 16(4):508-519.
- World Health Organization, 2015. *World Health Statistic New*. WHO Press, Geneva
- Wu, M., Ding, H.F., Fisher, D.E., 2001. *Apoptosis: molecular mechanisms*. In : encyclopedia of life sciences. Nature Publishing Group, London. United Kingdom.
- Yu, X., Luo, Y., Zhou, Y., Zhang, Q., Wang, J., Wei, N., Mi, M., Zhu, J., Wang, B., Chang, H., Tang, Y., 2008. BRCA1 overexpression sensitizes cancer cells to lovastatin via regulation of cyclin D1-CDK4-p21WAF1/CIP1 pathway: analyses using a breast cancer cell line and tumoral xenograft model. *Int. J. Oncol.* 33(3):555-563.
- Zampieri, L., Bianchi, P., Ruff, P., Arbuthnot, P., 2002. Differential modulation by estradiol of P-glycoprotein drug resistance protein expression in cultured MCF7 and T47D breast cancer cells. *Anticancer Res.* 22(4):2253-2259.