

## DAFTAR PUSTAKA

- Abramowitz, M. & Stegun, I. A., 1970, *Handbook of Mathematical Functions with Formulas, Graphs, and Mathematical Tables*, McGraw-Hill, USA.
- Andreeff, M. (ed.), 2015, *Targeted Therapy of Acute Myeloid Leukemia: Current Cancer Research*, Springer-Verlag, New York.
- Akagi, T., Ogawa, S., Dugas, M., dkk, 2009, Frequent Genomic Abnormalities in Acute Myeloid Leukemia/Myelodysplastic Syndrome with Normal Karyotype, *Haematologica* vol. 94: 213 – 223. doi:10.3324/haematol.13024.
- Arkun, Y., 2016, Dynamic Modeling and Analysis of the Cross-Talk Between Insulin-AKT and MAPK/ERK Signaling Pathways, *PloS ONE*, vol. 11, no. 3: e0149684. doi:10.1371/journal.pone.0149684.
- Bakta, I. M., 2006, *Hematologi Klinis Ringkas*, Penerbit Buku Kedokteran EGC :Jakarta Hlm:120 – 148.
- Bartholdy, B., Christopeit, M., Will, B., Mo, Y., dkk, 2014, HSC Commitment-associated epigenetic signature is prognostic in acute Myeloid Leukemia, *The Journal of Clinical Investigation*, vol. 124, no. 3, March 2014.
- Beagle, B. & Fruman, D. A., 2015, The PI3K-AKT-mTOR Signaling Network in AML, dalam *Targeted Therapy of Acute Myeloid Leukemia*, Andreeff, M. Ed. USA: Springer, 335 – 362.
- Behar, M., Barken, D., Wener, S. L., Hoffmann, A., 2013, The Dynamics of Signaling as a Pharmacological Target, *Cell*, vol. 155, no. 2.
- Besse, A., Clapp, G. D., Bernard, S., dkk, 2018, Stability Analysis of a Model of Interaction Between the Immune System and Cancer Cell in Chronic Myelogenous Leukemia, *Bull. Math. Biol.*, vol. 80, no. 5: 1084 – 1110.

- Bozzone, D., 2009, *The biology of Cancer : Leukemia*, Chelsea House Pub. New York.
- Brandts, C. H., Sargin, B., Rode, M., dkk, 2005, Constitutive Activation of Akt by Flt3 Internal Tandem Duplications is Necessary for Increased Survival, Prplifera-tion, and Myeloid Tansformation, *Cancer Res*, vol. 65, no. 21: 9643 – 9650.
- Buonomo, B., 2015, A Note on the Direction of the Transcritical Bifurcation in Epi-demic Models, *Nonlinear Analysis:Modelling and Control*, vol. 20, no. 1: 38 - 55.
- Carneiro, B. A., Kaplan, J. B. , Altman, J. K., dkk, 2015. Targeting mTOR Sig-nalling Pathways and Related Negative Feedback Loops for The Treatment of Acute Myeloid Leukemia, *Cancer Biology and Therapy* 16:5; 648 – 656, DOI 10.1080/15384047.2015.1026510
- Chavez C. C. & Song, B., 2004, Dynamical Model of Tuberculosis and Their Appli-cations, *Math. Biosci. Eng.*, vol.1, no. 2: 361 – 404.
- Chen, J., Odenika, O., Rowley, J. D., 2010, Leukemogenesis : More Than Mutant Genes, *Nat. Rev. Cancer*, vol.10, no. 1: 23 – 36, doi:10.1038/nrc2765.
- Chitnis, N., Hyman, J. M., and Cushing, J. M., 2008, Determining important para-meters in the spread of malaria through the sensitivity analisys of a mathematical model,*Bull. Math. Biol*, vol. 70, no. 5: 1272 – 1296.
- Clapp, G. D. & Levy, D., 2015, A Review of MAtheMatical MOdels for Lymphoma and Leukemia,*Drug Discovery Today: Disease Models*, Vol. 16: 1 – 6.
- Cucuianu, A. and Precup, R., 2010, A Hypothetical Mathematical Model of Acute Myeloid Leukemia Pathogenesis, *Computational and Mathematical Methods in Medicine* vol.11, no. 1: 49 – 65

- Dohner, H., Weisdorf D. J., Bloomfield, C. D., 2015, Acute Myeloid Leukemia, *New England Journal of Medicine* 373 (12): 1136 - 1152. doi: 10.1056/NEJMr1406184.
- Dohner, H., Estey, E., Grimwade, D., 2017, Diagnosis and Management of AML in AdultsL 2017 ELN Recommendations From an International Expert Panel, *Blood*, vol. 129, no. 4: 424 - 447.
- Faduola, P., Hakim, A., Mansnerus, J., dkk, 2013, Acute Myeloid leukemia: Therapy past, present, dan future, *Translation Biomedicine*, vol. 4 No.2:1, doi:10.3823/440
- Foley, C. and Makey, M. C., 2009, Dynamic Hematological Diseases : A Review, *J Mathematical Biology* Vol. 58(1-2): 285–322
- Forsythe, A., Brandt, P. S., Dolph, M., dkk , 2018, Systematic Review of Helath State Utility Values for Acute Myeloid Leukemia, *ClinicoEconomics and Outcomes Research*, vol. 2018, no. 10, 83 –92.
- Fransecky, L., Mochmann, L. H., and Baldus, C. D., 2015, Outlook on PI3K/AKT/mTOR inhibition in Acute Leukemia. *Molecular and Cellular Therapies* vol.3, no. 2.
- Gantmacher, F., 1959, *Applications of the Theory of Matrices*, New York: Interscience.
- Garcia, M. L. & Bear, M. R., 2017, FLT3 Inhibitors in Acute Myeloid Leukemia: Current Status and Future Directions, *Mol Cancer Ther.* 2017, vol. 16, no. 6: 991 – 1001.
- Garcia, J. S., Percival, M. E., 2017, Midostourin for the Treatment of Adult Patients with Newly Diagnosed Acute Myleoid Leukemia that is FLT3 Mutation Positif, *Drug of Today*. 2017, vol. 53, no. 10: 531 – 543.

- Grafone T., Palmisano M., Nici C., Storti S., 2012, An Overview on The Role of FLT3 Tyrosine Kinase Receptor in Acute Myeloid Leukemia: Biology and Treatment, *Oncology Reviews*, vol. 6:e8.
- Grimwade D., Ivey A., and Huntly B. J. P, 2016, Molecular landscape of acute myeloid leukemia in younger adults and its clinical relevance, *Blood*, vol. 127, no. 1, DOI 10.1182/blood-2015-07-604496.
- Hatakeyama, M., Kimura, S., Naka, T., dkk, 2003, A Computational Model on The Modulation of Mitogen Activated Protein Kinase (MAPK) and AKT Pathways in Hergulin Induced ErbB Signalling, *Biochem J*, vol. 373: 451 – 463.
- Hatzimichael, E., Georgiou, G., Benetatos, L., and Briasoulis, E., 2013, Gene Mutations and Molecularly Targeted Therapies in Acute Myeloid Leukemia, *Am J. Blood Res*, vol. 3: 29 – 51.
- Herschbein, L. & Liesveld, L., 2018, Dueling for dual inhibition: Means to enhance effectiveness of PI3K/AKT/mTOR inhibitors in AML, *Boold Review*, vol. 32, no. 3:235 - 248.
- Horne, G. A., Kinstrie, R., Copland, M., 2015, Novel drug therapies in myeloid leukemia, *Pharm. Pt. Anal.*, vol. 4, no. 3: 187 – 205.
- Horton, S. J & Huntly, B. J. P., 2012, Recent advances in acute myeloid leukemia stem cell biology, *Haematologica*, vol. 97: 966-974; doi:10.3324/haematol.2011.054734
- Ingalls, B. P., 2013, *Mathematical Modelling in System Biology: An Introduction*, MIT Press, Cambridge.
- Jane-Bain, B., 2014, *Hematologi: Kurikulum Inti*, EGC, Jakarta.
- Kadia, T. M., Ravandi, F., Cortes, J., and Kantarjian, H., 2016, New drugs in acute myeloid leukemia, *Annals of Oncology*, vol. 27: 770 – 778, doi:10.1093/annonc/mdw015.

- Karabekmez, R., 2013, *Modeling of Cancer Signaling*, UWSpace, Canada.
- Kayser, S. & Levis, M., 2018, Advanced in Targeted Therapy for Acute Myeloid Leukemia. *Br J. Haematol*, vol. 180, no. 4:484 – 500.
- Keener, J. & Sneyd, J., 1998, *Mathematical Physiology* 8, Springer-Verlag, New York.
- Khalil, H. K., 2002, *Nonlinear Systems*, Prentice-Hall Inc., USA.
- Klipp, E., Liebermeister, W., Wierling, C., dkk, 2009. *Systems Biology: A Textbook*. Weinheim: Wiley-VCH
- Koh, G., Teong, H. F. C., Clement, M. V., Hsu, D., and Thiagarajan, P. S., 2006, A decomposition approach to parameter estimation in pathway modeling : a case study of the Akt and MAPK pathways and their crosstalk. *Bioinformatic*, vol. 22, no. 14: e271 - e280.
- Kornblau, S. M., Singh, N., Qiu, Y. H., dkk, 2010, High Phosphorylated FOXO3a is an Adverse Prognostic Factor in Acute Myeloid Leukemia, *Clin Cancer Res.*, vol. 16, no. 6: 1865 – 1875.
- Kosasih, A. S., Setiawan, L., Hartini, S., dkk, 2011, Immunophenotyping in the Diagnosis and Classification of Acute Leukimia: Dharmais Cancer Hospital Experience, *Ind. Journal of Cancer*, vol. 5, no. 1: 3 – 8.
- Kouchkovsky, I. D, Abdul-Hay M., 2016, Acute Myeloid Leukemia: A Comprehensive Review and 2016 Update, *Blood Cancer Journal*, vol. 2016, no. 6, e441; doi:10.1038/bcj.2016.50.
- Kuznetsov, Y. A, 1998, *Element of Applied Bifurcation Theory*. Springer Verlag New York, Inc.
- Layek, G.C., 2015, *An Introduction to Dynamical Systems and Chaos*, Springer, New Dehli.

- Leskovac, V., 2003, *Comprehensive Enzyme Kinetics*, Kluwer Academic Publishers, New York.
- Levis, M., 2017, Midostourin Approved for FLT3-mutated AML. *Blood*, vol. 129, no. 26:3403 – 3406.
- Lindblad, O., Cordero, E., Puissant, A., dkk, 2016, Aberant Activation of The Pi-  
k/mTOR Pathway Promotes Resistance to Sorafenib in AML ,*Oncogene*, 1 - 13.
- Lynch, S. 2014, *Dynamical System with Applications Using MATLAB*, Birkhauser, London
- MacLean, A. L., Lo, C. C., Stumpf, M. P. H., 2013, Population dynamics of normal and leukaemia stem cells in the haematopoietic stem cell niche show distinct regimes where leukaemia will be controlled. *J. R. Soc. Interface*, vol.10: 20120968, <http://dx.doi.org/10.1098/rsif.2012.0968>
- Mackey, M. C., Ou, C., Pujo-Menjouet, L., Wu, J., 2006, Periodic Oscilation of Blood Cell Population in Cronic Myelogenous Leukemia,*SIAM J. Math Anal.*, vol. 38, no. 1: 166 – 187.
- Martelli, M. P., Sportoletti, P., Tiacci, E., Martelli, M. F., and Falini, B., 2013, Mutation Lanscape of AML with normal Cytogenetics: Biolgical and Clinical Implications, *Blood Review*, vol. 27: 13 – 22.
- Martinez-Climent, J. A., Fontan, L., dkk., Lymphoma stem cells: enough evidence to support their existence?, *Haematologica*,2010, 95:293-302. doi:10.3324/haematol.2009.013318.
- Nanda, S., Depillis, L., Radunskaya, 2013, B Cell Cronic Lymphocytic Leukemia- A Model with Immune Response,*Discrete and Continuous Dynamical Systems Series B*, vol. 18, no. 4: 1053 – 1076.
- National Comprehensive Cancer Network (NCCN). NCCN Guidelines Version 1. 2016 Acute Myeloid Leukemia. National Comprehensive Cancer Network.

National Comprehensive Cancer Network (NCCN). NCCN Guidelines for Patients  
Acute Myeloid Leukemia (Version 1.2018) Feb 5; National Comprehensive Cancer  
Network.

Nguyen, H. P., Hang, D. T., Ly, Q. T., dkk, 2015, Targeting PI3K/AKT/mTOR sig-  
naling in Acute Myeloid Leukemia. *Vietnam Journal of Science*, vol. 2, no. 2: 11 –  
16.

Nho, R. S. & Hergert, P., 2014, FoxO3a and Disease Progression. *World J. Biol.  
Chem.*, vol. 5, no. 3: 346 – 354.

Nordigarden, A., 2013, *The FLT3 Tyrosine Kinase in Leukemia: Deciphe-  
ring The Downstream Signaling Events and Drug-Escape Mechanisms*. Di-  
sertasi, Linkoping University, Swedia. Dapat diakses melalui [http://www.diva-  
portal.org/smash/get/diva2:602086/FULLTEXT01.pdf](http://www.diva-portal.org/smash/get/diva2:602086/FULLTEXT01.pdf)

Nurmalasari, S. S., Widjajanto, P. H., Mulatsih, S., Purwanto, I., 2012, Leukemia  
Myeloblastik Akut: Luaran Terapi di RSUP DR. Sardjito, Yogyakarta, 2004 –  
2008, *Indonesian Jour. of Cancer*, vol. 6: 49 – 52.

Nurnberg, B. & Beer-Hammer, S., 2019, Function, Regulation and Biological Roles  
of PI3K $\gamma$  Variants, *Biomolecules*, vol. 9, no. 427.

Ozbay, H., Bonnet, C., Benjelloun, H., Clairambault, J., 2012, Stability Analysis of  
Cell Dynamics in Leukemia. *Mat. Model. Nat. Phenom.*, vol. 7, no. 1: 203 – 234.

Pandolfi, A., Barreyro, L., Steidl, U., 2013, Concise Review: Preleukemic Stem  
Cell: Molecular Biology and Clinical Implications of the Precursors to le-  
ukemia Stem Cells. *Stem Cell Translational Medicine*, vol. 2: 143 – 150.  
<http://dx.doi.org/10.5966/sctm.2012-0109>.

Park, S., Chapuis, N., Tamburini, J., dkk., Role of the PI3K/AKT and mTOR signa-  
ling pathways in acute myeloid leukemia, *Haematologica*, vol. 95, no. 5: 819- 828.  
doi:10.3324/haematol.2009.013797.

- Perko, L., 2006, *Differential Equations and Dynamical Systems. Text in Applied Mathematics* 7. Springer-Verlag, New York.
- Polak, R. & Buitenhuis, 2012, The PI3K/PKB signaling Module as key Regulator of Hematopoiesis : Implications for Therapeutic Strategies in Leukemia. *Blood*, vol. 119, no. 4.
- Pu, T., Zhang, X., Liu, F., Wang, W., 2010, Coordination of the Nuclear and Cytoplasmic Activities of p53 in Response to DNA Damage, *Biophysical Journal*, vol. 99: 1696 – 1705.
- Price, N., Stevens, L., 1989, *Fundamentals of Enzymology*, Oxford University Press, USA.
- Reikvam, H., Tamborini, J., Skrede, S., dkk, 2014, Antileukemic Effect of PI3K-mTOR inhibitors in Acute Myeloid Leukemia-gene Expression Profiles Reveal CDC25B Expression as Determine of Pharmacological effect. *Brit. J. of Haematology*, vol. 164: 200 – 211.
- Rubinov, S. I. & Lebowitz, J. L., 1976, A Mathematical Model of The Acute Myeloblastic Leukemic State in Man, *Biophysical Journal*, vol. 16: 897 – 910.
- Santamaria, C. M., Chillon, M. C., Gracia-Sanz, R., dkk, 2009, High FOXO3a Expression is Associated with a Poorer Prognosis in AML with Normal Cytogenetics, *Leukemia Research* 33: 1706 - 1709.
- Sauro, H. M., 2011, *Enzyme Kinetics for Systems Biology* (Ambrosius Pub, Washington, 2011).
- Schiller, G. J., Tuttle, P., Desai, P., 2016, Allogeneic Hematopoietic Stem Cell Transplantation in FLT3-ITD Positive Acute Myelogenous Leukemia: The Role for FLT3 Tyrosine Kinase Inhibitors Post Transplantation, *Biol. Blood Marrows Transplant*, vol. 22: 982 – 990.



- Sharma, M. & Mohanty, S., 2013, Molecular Biomarkers in Cytogenetically Normal Acute Myeloid Leukemia: Hanessing the Targets, *J. Mol Biomarkers Diagnosis*, S8:009.Doi:10.4172/2155-9929.S8-009.
- Shen Y., Bai J., He A., 2016, Review Article; Role of mTOR signaling pathway in acute myeloid leukemia, *Int. J. Clin. Exp. Med*, vol. 9, no. 2: 637 – 647.
- Simanjourang, C., Kodim, N., Tehuteru, E., 2013, Perbedaan Kesintasan 5 tahun Pasien Leukemia Limfoblastik Akut dan Leukimia Mieloblastik Akut pada Anak di Rumah Sakit kanker Dharmais, Jakarta, 1997 – 2008. *Ind. Journal of Cancer*, vol. 7, no. 1: 15 – 21.
- Stiehl, T., Baran, N., Ho, A. D., Marchianiak-Czohcra, A., 2014, Selection and Therapy Resistance in Acute Myeloid Leukemia: MATHematical Modelling Explains Different Proliferation Pattern at Diagand Relapse. *Jour. Royal Soc. Interface*, vol. 11: 20140079.<http://dx.doi.org/10.1098/rsif.2014.0079>.
- Stiehl, T., Baran, N., Ho, A. D., Marchianiak-Czohcra, A., 2015, Cell Division Patterns in Acute Myeloid Leukemia Stem-like Cells Determine Clinical Course: A Model to Predict Patient Survival. *Cancer Res.*, vol. 75, no. 6: 940 – 949. doi: 10.1158/0009-5472.CAN-14-2508.
- Strogatz, S. H., 2001, *Nonlinear Dynamics and Chaos: With Applications to Physics, Biology, Chemistry, and Engineering*. Perseus Books Pub, LLC, Canada.
- Supriyadi, E., Wijayanto, P. H., Veerman, A. J. P., dkk, 2011, Immunophenotypic Pattern of Childhood Acute Leukemias in Indonesia. *Asian Pacific Journal of Cancer Prevention*, vol. 12: 3381 – 3387.
- Supriyadi, E., Purwanto, I., Widajanto, P. H., 2013, Terapi Leukimia Mieloblastik Akut Anak: Protokol Ara-C, Doxoubycine dan Etoposide (ADE) vs Modifikasi Nordic Society of Pediatric Hematology and Oncology)m-NPHO), *Sari Pediatri*, vol. 14, no. 6: 345 – 350.

- Takahashi, S., 2011, Downstream Molecular Pathways of FLT3 in the pathogenesis of Acute Myeloid Leukemia: Biology and Therapeutic Implications, *Journal of Hematology and Oncology*, vol. 4, no. 13.
- Tan, W. H., Popel, A. S., Mac-Gabhann, F., 2013, Computational Model of Gab  $\frac{1}{2}$  Dependent VEGFR2 Pathway to AKt Activation, *PLoS ONE*, vol. 8, no. 6:e67438. DOI:10.1371/journal.pone.0067438.
- Tayyab, M., Khan, M., Iqbal, Z., dkk, 2014, Distinct Gene Mutations, their Prognostic Relevance and Molecularly Targeted Therapies in Acute Myeloid Leukemia (AML), *J Cancer Sci. Ther.*, vol. 6, no. 9:337 – 349.
- Thol, F., Schlenk, F. S., Heuser, M., Ganser, A., 2015, How I treat refractory and early relapsed acute myeloid leukemia. *Blood*, vol. 126, no. 3:319–327.
- Tian, T. & Song, J., 2012, Mathematical Modelling of THE MAPK Kinase Pathway Using Proteomic Datasets. *Plos One*, vol. 7, no. 8:e42230.
- Tian, T. & Wu, F., 2013, Robustness Analysis of THE PI3K/AKT Cell Signaling Module, *Journal of Medical and Bioengineering*, vol. 2, no. 2: 93–97.
- Verhulst, F., 1996, *Nonlinear Differential Equations and Dynamical Systems*. Springer-Verlag, Germany.
- Wang, G., 2014. *Analysis of Complex Diseases*, CRC Press, Taylor & Francis Group
- Wang, G. & Li, T., 2014, Computer Aided Targeting of The PI3K/AKT/mTOR Pathway: Toxicity Reduction and Therapeutic Opportunities. *Int. J. Molecular Sciences*, vol. 15: 18856-18891; DOI:10.3390/ijms151018856.
- Warr, M. R., Pietras, E. M, Passegue, E., 2011, Mechanism Controlling Hematopoietic Stem Cell Functions During Normal Hematopoiesis and Hematological Malignancies, Advanced Reviews, *WIREs System Biology and Medicine*, John Wiley & Sons, Inc.

- Wee, K. B. & Aguda, B. D., 2006, Akt Versus p53 in a Network of Oncogenes and Tumor Suppressor Genes Regulating Cell Survival and Death. *Biophysics*, vol. 91: 857 – 865.
- Whichard, Z. L., Sarkar, C. A., Kimmel, M., Corey, S. J., 2010, Hematopoiesis and Its Disorder: A Systems Biology Approach. *Blood*, vol. 115, no. 12: 2339 - 2347. doi:10.1182/blood-2009-08-215798.
- Wiggins, S., 2003, *Introduction to Applied Nonlinear Dynamical Systems and Chaos*, Springer-Verlag, New York, Inc.
- Windiastruti, E., Nency, Y. M., Mulatsih, S., Sudarmanto, B., Ugrasena, I. D. G., 2018, *Buku Ajar Hematologi-Onkologi Anak*, IDAI, Salemba-Jakarta.
- Yan-Bin, Y., *Root of Polynomial*, Com S 477/577 Notes, 2017.
- Young, B., O'Dowd, G., Woodford, P., 2014, *Wheater's Functional Histology A text and Colour Atlas*, sixth ed. Churchill Livingstone, Elsevier, Chapt 3.
- Zhang, W., Ly, C., Ishizawa, J., dkk, 2018, Combination Targeting XPO1 and FLT3 Exerts Synergistic Anti Leukemia Effects Throught Induction of Differentiation and Apoptosis in FLT3 Mutated Acute Myeloid Leumekias: From Concept to Clinical Trial, *Haematologica*. 2018, 103 (10): 1642 – 1653.