

REFERENSI

- Alcaraz, A., Medina, R., Maroto, P., Climent, M. Á., Castellano, D., & Carles, J. (2012). Castration-resistant prostate cancer: Where are we going? *Actas Urológicas Españolas (English Edition)*, 36(6), 367–374. <https://doi.org/10.1016/j.acuroe.2011.10.001>
- Baisden, B. L., Kahane, H., & Epstein, J. I. (1999). Perineural Invasion, Mucinous Fibroplasia, and Glomerulations. *The American Journal of Surgical Pathology*, 23(8), 918. <https://doi.org/10.1097/00000478-199908000-00009>
- Bankhead, P., Loughrey, M. B., Fernández, J. A., Dombrowski, Y., McArt, D. G., Dunne, P. D., McQuaid, S., Gray, R. T., Murray, L. J., Coleman, H. G., James, J. A., Salto-Tellez, M., & Hamilton, P. W. (2017). QuPath: Open source software for digital pathology image analysis. *Scientific Reports*, 7(1), 16878. <https://doi.org/10.1038/s41598-017-17204-5>
- Bostwick, D. G., Burke, H. B., Djakiew, D., Euling, S., Ho, S., Landolph, J., Morrison, H., Sonawane, B., Shifflett, T., Waters, D. J., & Timms, B. (2004). Human prostate cancer risk factors. *Cancer*, 101(S10), 2371–2490. <https://doi.org/10.1002/cncr.20408>
- Bray, F., Laversanne, M., Sung, H., Ferlay, J., Siegel, R. L., Soerjomataram, I., & Jemal, A. (2024). Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA: A Cancer Journal for Clinicians*, 74(3), 229–263. <https://doi.org/10.3322/caac.21834>
- Bronte, V., & Zanovello, P. (2005). Regulation of immune responses by L-arginine metabolism. *Nature Reviews Immunology*, 5(8), 641–654. <https://doi.org/10.1038/nri1668>
- Cancer Genome Atlas Research Network. (2015). The Molecular Taxonomy of Primary Prostate Cancer. *Cell*, 163(4), 1011–1025. <https://doi.org/10.1016/j.cell.2015.10.025>
- Chen, D. S., & Mellman, I. (2017). Elements of cancer immunity and the cancer–immune set point. *Nature*, 541(7637), 321–330. <https://doi.org/10.1038/nature21349>
- Daskivich, T. J., Fan, K.-H., Koyama, T., Albertsen, P. C., Goodman, M., Hamilton, A. S., Hoffman, R. M., Stanford, J. L., Stroup, A. M., Litwin, M. S., & Penson, D. F. (2015). Prediction of Long-term Other-cause Mortality in Men With Early-stage Prostate Cancer: Results From the Prostate Cancer Outcomes Study. *Urology*, 85(1), 92–100. <https://doi.org/10.1016/j.urology.2014.07.003>
- Elgün, S., Keskinöge, A., Yilmaz, E., Baltacı, S., & Bedük, Y. (1999). Evaluation of Serum Arginase Activity in Benign Prostatic Hypertrophy and Prostatic Cancer. *International Urology and Nephrology*, 31(1), 95–99. <https://doi.org/10.1023/A:1007132109061>
- Eng, T. Y., Thomas, C. R., & Herman, T. S. (2002). Primary radiation therapy for localized prostate cancer. *Urologic Oncology: Seminars and Original Investigations*, 7(6), 239–257. [https://doi.org/10.1016/S1078-1439\(02\)00198-9](https://doi.org/10.1016/S1078-1439(02)00198-9)
- Epstein, J. I. (2004). Diagnosis and reporting of limited adenocarcinoma of the prostate on needle biopsy. *Modern Pathology*, 17(3), 307–315. <https://doi.org/10.1038/modpathol.3800050>
- Epstein, J. I., Allsbrook, W. C., Amin, M. B., & Egevad, L. L. (2005). The 2005 International Society of Urological Pathology (ISUP) Consensus Conference on Gleason Grading of Prostatic Carcinoma. *American Journal of Surgical Pathology*, 29(9), 1228–1242. <https://doi.org/10.1097/01.pas.0000173646.99337.b1>

- Epstein, J. I., Egevad, L., Humphrey, P. A., & Montironi, R. (2014). Best Practices Recommendations in the Application of Immunohistochemistry in the Prostate. *American Journal of Surgical Pathology*, 38(8), e6–e19. <https://doi.org/10.1097/PAS.0000000000000238>
- Epstein, J. I., Zelefsky, M. J., Sjoberg, D. D., Nelson, J. B., Egevad, L., Magi-Galluzzi, C., Vickers, A. J., Parwani, A. V., Reuter, V. E., Fine, S. W., Eastham, J. A., Wiklund, P., Han, M., Reddy, C. A., Ciezki, J. P., Nyberg, T., & Klein, E. A. (2016). A Contemporary Prostate Cancer Grading System: A Validated Alternative to the Gleason Score. *European Urology*, 69(3), 428–435. <https://doi.org/10.1016/j.eururo.2015.06.046>
- Fernando, A., Tokell, M., Ishak, Y., Love, J., Klammer, M., & Koh, M. (2023). Mental health needs in cancer – a call for change. *Future Healthcare Journal*, 10(2), 112–116. <https://doi.org/10.7861/fhj.2023-0059>
- Ferry, P. :, Rainy, S., Danarto, U., Hakim, L., Mirsa, S., Agus, W., Hamid, R., Hudaya, S., Ismy, J., Soerohardjo, I., Widjanarko, S., Yudianana, W., Shidqy, E. M., & Kloping, Y. P. (2022). *PANDUAN PENANGANAN KANKER PROSTAT*.
- Gajewski, T. F., Woo, S.-R., Zha, Y., Spaapen, R., Zheng, Y., Corrales, L., & Spranger, S. (2013). Cancer immunotherapy strategies based on overcoming barriers within the tumor microenvironment. *Current Opinion in Immunology*, 25(2), 268–276. <https://doi.org/10.1016/j.coi.2013.02.009>
- Galon, J., Costes, A., Sanchez-Cabo, F., Kirilovsky, A., Mlecnik, B., Lagorce-Pagès, C., Tosolini, M., Camus, M., Berger, A., Wind, P., Zinzindohoué, F., Bruneval, P., Cugnenc, P.-H., Trajanoski, Z., Fridman, W.-H., & Pagès, F. (2006). Type, Density, and Location of Immune Cells Within Human Colorectal Tumors Predict Clinical Outcome. *Science*, 313(5795), 1960–1964. <https://doi.org/10.1126/science.1129139>
- Gandaglia, G., Abdollah, F., Schiffmann, J., Trudeau, V., Shariat, S. F., Kim, S. P., Perrotte, P., Montorsi, F., Briganti, A., Trinh, Q., Karakiewicz, P. I., & Sun, M. (2014). Distribution of metastatic sites in patients with prostate cancer: A population-based analysis. *The Prostate*, 74(2), 210–216. <https://doi.org/10.1002/pros.22742>
- Gann, P. H. (2002). Risk factors for prostate cancer. *Reviews in urology*, 4 Suppl 5(Suppl 5), S3–S10.
- Gannon, P. O., Godin-Ethier, J., Hassler, M., Delvoye, N., Aversa, M., Poisson, A. O., Péant, B., Fahmy, M. A., Saad, F., Lapointe, R., & Mes-Masson, A. M. (2010). Androgen-regulated expression of arginase 1, arginase 2 and interleukin-8 in human prostate cancer. *PLoS ONE*, 5(8). <https://doi.org/10.1371/journal.pone.0012107>
- Geiger, R., Rieckmann, J. C., Wolf, T., Basso, C., Feng, Y., Fuhrer, T., Kogadeeva, M., Picotti, P., Meissner, F., Mann, M., Zamboni, N., Sallusto, F., & Lanzavecchia, A. (2016). L-Arginine Modulates T Cell Metabolism and Enhances Survival and Anti-tumor Activity. *Cell*, 167(3), 829–842.e13. <https://doi.org/10.1016/j.cell.2016.09.031>
- Giraldo, N. A., Becht, E., Remark, R., Damotte, D., Sautès-Fridman, C., & Fridman, W. H. (2014). The immune contexture of primary and metastatic human tumours. *Current Opinion in Immunology*, 27, 8–15. <https://doi.org/10.1016/j.coi.2014.01.001>
- Giri, V. N., Knudsen, K. E., Kelly, W. K., Cheng, H. H., Cooney, K. A., Cookson, M. S., Dahut, W., Weissman, S., Soule, H. R., Petrylak, D. P., Dicker, A. P., AlDubayan, S. H., Toland, A. E., Pritchard, C. C., Pettaway, C. A., Daly, M. B., Mohler, J. L., Parsons, J. K., Carroll, P. R., ... Gomella, L. G. (2020). Implementation of Germline Testing for Prostate Cancer:

- Philadelphia Prostate Cancer Consensus Conference 2019. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*, 38(24), 2798–2811. <https://doi.org/10.1200/JCO.20.00046>
- Grzywa, T. M., Sosnowska, A., Matryba, P., Rydzynska, Z., Jasinski, M., Nowis, D., & Golab, J. (2020). Myeloid Cell-Derived Arginase in Cancer Immune Response. Dalam *Frontiers in Immunology* (Vol. 11). Frontiers Media S.A. <https://doi.org/10.3389/fimmu.2020.00938>
- Habibi, A., Risqiyani, S. Z., & Putri, D. A. S. (2021). Potensi Chimeric Antigen Receptor T Cell (CAR-T Cell) dengan Target Prostate-Specific Membrane Antigen (PSMA) Termodifikasi CRISPR/Cas9 sebagai Terapi Kanker Prostat. *JIMKI: Jurnal Ilmiah Mahasiswa Kedokteran Indonesia*, 9(1), 23–37. <https://doi.org/10.53366/jimki.v9i1.321>
- Hara, M., Torisu, K., Tomita, K., Kawai, Y., Tsuruya, K., Nakano, T., & Kitazono, T. (2020). Arginase 2 is a mediator of ischemia–reperfusion injury in the kidney through regulation of nitrosative stress. *Kidney International*, 98(3), 673–685. <https://doi.org/10.1016/j.kint.2020.03.032>
- Hendry, S., Salgado, R., Gevaert, T., Russell, P. A., John, T., Thapa, B., Christie, M., van de Vijver, K., Estrada, M. V., Gonzalez-Ericsson, P. I., Sanders, M., Solomon, B., Solinas, C., Van den Eynden, G. G. G. M., Allory, Y., Preusser, M., Hainfellner, J., Pruneri, G., Vingiani, A., ... Fox, S. B. (2017). Assessing Tumor-infiltrating Lymphocytes in Solid Tumors: A Practical Review for Pathologists and Proposal for a Standardized Method From the International Immunooncology Biomarkers Working Group: Part 1: Assessing the Host Immune Response, TILs in Invasive Breast Carcinoma and Ductal Carcinoma In Situ, Metastatic Tumor Deposits and Areas for Further Research. *Advances in Anatomic Pathology*, 24(5), 235–251. <https://doi.org/10.1097/PAP.0000000000000162>
- Hsueh, E. C., Knebel, S. M., Lo, W.-H., Leung, Y.-C., Ning, P., Cheng, M., & Hsueh, C.-T. (2012). *Deprivation of arginine by recombinant human arginase in prostate cancer cells*. <http://www.jhonline.org/content/5/1/17>
- Humphrey, P. A. (2007). Diagnosis of adenocarcinoma in prostate needle biopsy tissue. *Journal of Clinical Pathology*, 60(1), 35–42. <https://doi.org/10.1136/jcp.2005.036442>
- Ino, K., Yamamoto, E., Shibata, K., Kajiyama, H., Yoshida, N., Terauchi, M., Nawa, A., Nagasaka, T., Takikawa, O., & Kikkawa, F. (2008). Inverse Correlation between Tumoral Indoleamine 2,3-Dioxygenase Expression and Tumor-Infiltrating Lymphocytes in Endometrial Cancer: Its Association with Disease Progression and Survival. *Clinical Cancer Research*, 14(8), 2310–2317. <https://doi.org/10.1158/1078-0432.CCR-07-4144>
- Jenkinson, C. P., Grody, W. W., & Cederbaum, S. D. (1996). Comparative properties of arginases. *Comparative Biochemistry and Physiology Part B: Biochemistry and Molecular Biology*, 114(1), 107–132. [https://doi.org/10.1016/0305-0491\(95\)02138-8](https://doi.org/10.1016/0305-0491(95)02138-8)
- Kumar, V., Randhawa, P., Bilodeau, R., Mercola, D., McClelland, M., Agrawal, A., Nguyen, J., Castro, P., Ittmann, M. M., & Rahmatpanah, F. (2022). Spatial Profiling of the Prostate Cancer Tumor Microenvironment Reveals Multiple Differences in Gene Expression and Correlation with Recurrence Risk. *Cancers*, 14(19), 4923. <https://doi.org/10.3390/cancers14194923>
- Larasati, P. ajeng ayu. (2019). KORELASI ANTARA EKSPRESI Her-2 DAN Ki-67 DENGAN GLEASON GRADE GROUP PADA ADENOKARSINOMA ASINAR PROSTAT. *Jurnal Kedokteran Raflesia*, 5(1), 39–52. <https://doi.org/10.33369/juke.v5i1.9125>

- Lee, C. H., Akin-Olugbade, O., & Kirschenbaum, A. (2011). Overview of Prostate Anatomy, Histology, and Pathology. Dalam *Endocrinology and Metabolism Clinics of North America* (Vol. 40, Nomor 3, hlm. 565–575). <https://doi.org/10.1016/j.ecl.2011.05.012>
- Li, J., Zheng, Y., Chen, C., Lin, Z., Pan, J., Liang, Y., Jiang, F., Jiang, M., Zhou, X., & Zhong, W. (2024). Arginase 2 is a Diagnostic and Prognostic Marker for Prostate Cancer and Is Associated with Metabolism. *Alternative therapies in health and medicine*, 30(9), 102–111.
- Li, Y., Yang, R., Henzler, C. M., Ho, Y., Passow, C., Auch, B., Carreira, S., Nava Rodrigues, D., Bertan, C., Hwang, T. H., Quigley, D. A., Dang, H. X., Morrissey, C., Fraser, M., Plymate, S. R., Maher, C. A., Feng, F. Y., de Bono, J. S., & Dehm, S. M. (2020). Diverse AR Gene Rearrangements Mediate Resistance to Androgen Receptor Inhibitors in Metastatic Prostate Cancer. *Clinical cancer research : an official journal of the American Association for Cancer Research*, 26(8), 1965–1976. <https://doi.org/10.1158/1078-0432.CCR-19-3023>
- Lindez, A.-A. M., Dunand-Sauthier, I., Conti, M., Gobet, F., Núñez, N., Hannich, J. T., Riezman, H., Geiger, R., Piersigilli, A., Hahn, K., Lemeille, S., Becher, B., De Smedt, T., Hugues, S., & Reith, W. (2019). Mitochondrial arginase-2 is a cell-autonomous regulator of CD8+ T cell function and antitumor efficacy. *JCI Insight*, 4(24). <https://doi.org/10.1172/jci.insight.132975>
- Loughrey, M. B., Bankhead, P., Coleman, H. G., Hagan, R. S., Craig, S., McCorry, A. M. B., Gray, R. T., McQuaid, S., Dunne, P. D., Hamilton, P. W., James, J. A., & Salto-Tellez, M. (2018). Validation of the systematic scoring of immunohistochemically stained tumour tissue microarrays using QuPath digital image analysis. *Histopathology*, 73(2), 327–338. <https://doi.org/10.1111/his.13516>
- Magi-Galluzzi, C. (2018). Prostate cancer: diagnostic criteria and role of immunohistochemistry. *Modern Pathology*, 31, 12–21. <https://doi.org/10.1038/modpathol.2017.139>
- Matos, A., Carvalho, M., Bicho, M., & Ribeiro, R. (2021). Arginine and arginases modulate metabolism, tumor microenvironment and prostate cancer progression. Dalam *Nutrients* (Vol. 13, Nomor 12). MDPI. <https://doi.org/10.3390/nu13124503>
- Morriss, N. J., Conley, G. M., Ospina, S. M., Meehan, W. P., Qiu, J., & Mannix, R. (2020). Automated Quantification of Immunohistochemical Staining of Large Animal Brain Tissue Using QuPath Software. *Neuroscience*, 429, 235–244. <https://doi.org/10.1016/j.neuroscience.2020.01.006>
- Mumenthaler, S. M., Rozengurt, N., Livesay, J. C., Sabaghian, A., Cederbaum, S. D., & Grody, W. W. (2008). Disruption of arginase II alters prostate tumor formation in TRAMP mice. *Prostate*, 68(14), 1561–1569. <https://doi.org/10.1002/pros.20816>
- Mumenthaler, S. M., Yu, H., Tze, S., Cederbaum, S. D., Pegg, A. E., Seligson, D. B., & Grody, W. W. (2008). Expression of arginase II in prostate cancer. *International journal of oncology*, 32(2), 357–365.
- Munder, M. (2005). Arginase I is constitutively expressed in human granulocytes and participates in fungicidal activity. *Blood*, 105(6), 2549–2556. <https://doi.org/10.1182/blood-2004-07-2521>
- Nakayama, M., Bennett, C. J., Hicks, J. L., Epstein, J. I., Platz, E. A., Nelson, W. G., & De Marzo, A. M. (2003). Hypermethylation of the human glutathione S-transferase-pi gene (GSTP1) CpG island is present in a subset of proliferative inflammatory atrophy lesions

- but not in normal or hyperplastic epithelium of the prostate: a detailed study using laser-capture microdissection. *The American journal of pathology*, 163(3), 923–933.
[https://doi.org/10.1016/s0002-9440\(10\)63452-9](https://doi.org/10.1016/s0002-9440(10)63452-9)
- Niu, F., Yu, Y., Li, Z., Ren, Y., Li, Z., Ye, Q., Liu, P., Ji, C., Qian, L., & Xiong, Y. (2022). Arginase: An emerging and promising therapeutic target for cancer treatment. Dalam *Biomedicine and Pharmacotherapy* (Vol. 149). Elsevier Masson s.r.l.
<https://doi.org/10.1016/j.biopha.2022.112840>
- Ohuri, M., Scardino, P. T., Lapin, S. L., Seale-Hawkins, C., Link, J., & Wheeler, T. M. (1993). The Mechanisms and Prognostic Significance of Seminal Vesicle Involvement by Prostate Cancer. *The American Journal of Surgical Pathology*, 17(12), 1252–1261.
<https://doi.org/10.1097/00000478-199312000-00006>
- Omura, A., Kimura, T., Maniwa, T., Watabe, T., Honma, K., Shintani, Y., & Okami, J. (2025). Quantification of the immunohistochemical staining of fibroblast activation protein in intrathoracic solitary fibrous tumors using QuPath. *Surgery Today*, 55(9), 1269–1273.
<https://doi.org/10.1007/s00595-025-03024-y>
- Peng, Y., Jiang, Y., Eisengart, L., Healy, M. A., Straus, F. H., & Yang, X. J. (2011). Segmentation of prostatic glands in histology images. *2011 IEEE International Symposium on Biomedical Imaging: From Nano to Macro*, 2091–2094.
<https://doi.org/10.1109/ISBI.2011.5872824>
- Rahardjo, H. E., Ückert, S., Tsikas, D., Hedlund, P., Bannowsky, A., Kuczyk, M. A., & Kedia, G. T. (2019). Arginase enzymes in the human prostate: A molecular biological and immunohistochemical approach. *Andrologia*, 51(9). <https://doi.org/10.1111/and.13349>
- Rickman, D. S., Beltran, H., Demichelis, F., & Rubin, M. A. (2017). Biology and evolution of poorly differentiated neuroendocrine tumors. *Nature medicine*, 23(6), 1–10.
<https://doi.org/10.1038/nm.4341>
- Robinson, D., Van Allen, E. M., Wu, Y.-M., Schultz, N., Lonigro, R. J., Mosquera, J.-M., Montgomery, B., Taplin, M.-E., Pritchard, C. C., Attard, G., Beltran, H., Abida, W., Bradley, R. K., Vinson, J., Cao, X., Vats, P., Kunju, L. P., Hussain, M., Feng, F. Y., ... Chinnaiyan, A. M. (2015). Integrative Clinical Genomics of Advanced Prostate Cancer. *Cell*, 162(2), 454. <https://doi.org/10.1016/j.cell.2015.06.053>
- Roerden, M., & Spranger, S. (2025). Cancer immune evasion, immunoediting and intratumour heterogeneity. *Nature Reviews Immunology*, 25(5), 353–369.
<https://doi.org/10.1038/s41577-024-01111-8>
- Rosenberg, S. A., Restifo, N. P., Yang, J. C., Morgan, R. A., & Dudley, M. E. (2008). Adoptive cell transfer: a clinical path to effective cancer immunotherapy. *Nature Reviews Cancer*, 8(4), 299–308. <https://doi.org/10.1038/nrc2355>
- Satriano, J. (2004). Arginine pathways and the inflammatory response: Interregulation of nitric oxide and polyamines: Review article. *Amino Acids*, 26(4).
<https://doi.org/10.1007/s00726-004-0078-4>
- Sauter, G., Steurer, S., Clauditz, T. S., Krech, T., Wittmer, C., Lutz, F., Lennartz, M., Janssen, T., Hakimi, N., Simon, R., von Petersdorff-Campen, M., Jacobsen, F., von Loga, K., Wilczak, W., Minner, S., Tsourlakis, M. C., Chirico, V., Haese, A., Heinzer, H., ... Schlomm, T. (2016). Clinical Utility of Quantitative Gleason Grading in Prostate Biopsies and Prostatectomy Specimens. *European Urology*, 69(4), 592–598.
<https://doi.org/10.1016/j.eururo.2015.10.029>

- Sfanos, K. S., Yegnasubramanian, S., Nelson, W. G., & De Marzo, A. M. (2018). The inflammatory microenvironment and microbiome in prostate cancer development. *Nature reviews. Urology*, 15(1), 11–24. <https://doi.org/10.1038/nrurol.2017.167>
- Shah, R. B., Zhou, M., LeBlanc, M., Snyder, M., & Rubin, M. A. (2002). Comparison of the Basal Cell-Specific Markers, 34 β E12 and p63, in the Diagnosis of Prostate Cancer. *The American Journal of Surgical Pathology*, 26(9), 1161–1168. <https://doi.org/10.1097/00000478-200209000-00006>
- Smith, G. L., Lopez-Olivo, M. A., Advani, P. G., Ning, M. S., Geng, Y., Giordano, S. H., & Volk, R. J. (2019). Financial Burdens of Cancer Treatment: A Systematic Review of Risk Factors and Outcomes. *Journal of the National Comprehensive Cancer Network*, 17(10), 1184–1192. <https://doi.org/10.6004/jnccn.2019.7305>
- Soda, K. (2011). The mechanisms by which polyamines accelerate tumor spread. *Journal of Experimental & Clinical Cancer Research*, 30(1), 95. <https://doi.org/10.1186/1756-9966-30-95>
- Stamey, T. A., Yemoto, C. M., Neal, J. E. M. c, Sigal, B. M., & Johnstone, I. M. (2000). Prostate cancer is highly predictable: a prognostic equation based on all morphological variables in radical prostatectomy specimens. *Journal of Urology*, 163(4), 1155–1160. [https://doi.org/10.1016/S0022-5347\(05\)67713-0](https://doi.org/10.1016/S0022-5347(05)67713-0)
- Suh, J. H., Park, J.-W., Lee, C., & Moon, K. C. (2012). ERG Immunohistochemistry and Clinicopathologic Characteristics in Korean Prostate Adenocarcinoma Patients. *Korean Journal of Pathology*, 46(5), 423. <https://doi.org/10.4132/KoreanJPathol.2012.46.5.423>
- Taheri, F., Ochoa, J. B., Faghiri, Z., Culotta, K., Park, H.-J., Lan, M. S., Zea, A. H., & Ochoa, A. C. (2001). l-Arginine Regulates the Expression of the T-Cell Receptor ζ Chain (CD3 ζ) in Jurkat Cells. *Clinical Cancer Research*, 7(3), 958s–965s.
- Taylor, B. S., Schultz, N., Hieronymus, H., Gopalan, A., Xiao, Y., Carver, B. S., Arora, V. K., Kaushik, P., Cerami, E., Reva, B., Antipin, Y., Mitsiades, N., Landers, T., Dolgalev, I., Major, J. E., Wilson, M., Socci, N. D., Lash, A. E., Heguy, A., ... Gerald, W. L. (2010). Integrative genomic profiling of human prostate cancer. *Cancer cell*, 18(1), 11–22. <https://doi.org/10.1016/j.ccr.2010.05.026>
- Thorson, P., & Humphrey, P. A. (2000). Minimal Adenocarcinoma in Prostate Needle Biopsy Tissue. *American Journal of Clinical Pathology*, 114(6), 896–909. <https://doi.org/10.1309/KVPX-C1EM-142L-1M6W>
- Tomlins, S. A., Rhodes, D. R., Perner, S., Dhanasekaran, S. M., Mehra, R., Sun, X.-W., Varambally, S., Cao, X., Tchinda, J., Kuefer, R., Lee, C., Montie, J. E., Shah, R. B., Pienta, K. J., Rubin, M. A., & Chinnaiyan, A. M. (2005). Recurrent fusion of TMPRSS2 and ETS transcription factor genes in prostate cancer. *Science (New York, N.Y.)*, 310(5748), 644–648. <https://doi.org/10.1126/science.1117679>
- Varma, M., Lee, M. W., Tamboli, P., Zarbo, R. J., Jimenez, R. E., Salles, P. G. O., & Amin, M. B. (2002). Morphologic Criteria for the Diagnosis of Prostatic Adenocarcinoma in Needle Biopsy Specimens. *Archives of Pathology & Laboratory Medicine*, 126(5), 554–561. <https://doi.org/10.5858/2002-126-0554-MCFTDO>
- Vilaça, M., Correia Pinto, J., Magalhães, H., Reis, F., & Mesquita, A. (2023). Tumor-Infiltrating Lymphocytes in Localized Prostate Cancer: Do They Play an Important Role? *Cureus*. <https://doi.org/10.7759/cureus.34007>

- Weis-Banke, S. E., Lisle, T. L., Perez-Penco, M., Schina, A., Hübbe, M. L., Siersbæk, M., Holmström, M. O., Jørgensen, M. A., Marie Svane, I., Met, Ö., Ødum, N., Madsen, D. H., Donia, M., Grøntved, L., & Andersen, M. H. (2022). Arginase-2-specific cytotoxic T cells specifically recognize functional regulatory T cells. *Journal for ImmunoTherapy of Cancer*, 10(10). <https://doi.org/10.1136/jitc-2022-005326>
- Wheeler, T. M., Dillioglulil, Ö., Kattan, M. W., Arakawa, A., Soh, S., Suyama, K., Ohori, M., & Scardino, P. T. (1998). Clinical and pathological significance of the level and extent of capsular invasion in clinical stage T1–2 prostate cancer. *Human Pathology*, 29(8), 856–862. [https://doi.org/10.1016/S0046-8177\(98\)90457-9](https://doi.org/10.1016/S0046-8177(98)90457-9)
- Whiteside, T. L. (2008). The tumor microenvironment and its role in promoting tumor growth. *Oncogene*, 27(45), 5904–5912. <https://doi.org/10.1038/onc.2008.271>
- Yuan, Y. (2016). Spatial Heterogeneity in the Tumor Microenvironment. *Cold Spring Harbor Perspectives in Medicine*, 6(8), a026583. <https://doi.org/10.1101/cshperspect.a026583>
- Zea, A. H., Rodriguez, P. C., Culotta, K. S., Hernandez, C. P., DeSalvo, J., Ochoa, J. B., Park, H.-J., Zabaleta, J., & Ochoa, A. C. (2004). l-Arginine modulates CD3ζ expression and T cell function in activated human T lymphocytes. *Cellular Immunology*, 232(1–2), 21–31. <https://doi.org/10.1016/j.cellimm.2005.01.004>



KEMENTERIAN PENDIDIKAN, KEBUDAYAAN, RISET DAN TEKNOLOGI
UNIVERSITAS HASANUDDIN FAKULTAS KEDOKTERAN
KOMITE ETIK PENELITIAN UNIVERSITAS HASANUDDIN
RSPTN UNIVERSITAS HASANUDDIN
RSUP Dr. WAHIDIN SUDIROHUSODO MAKASSAR
Sekretariat : Lantai 2 Gedung Laboratorium Terpadu
JL.PERINTIS KEMERDEKAAN KAMPUS TAMALANREA KM.10 MAKASSAR 90245.



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REKOMENDASI PERSETUJUAN ETIK

Nomor : 817A/UN4.6.4.5.31/ PP36/ 2025

Tanggal: 20 Oktober 2025

Dengan ini Menyatakan bahwa Protokol dan Dokumen yang Berhubungan Dengan Protokol berikut ini telah mendapatkan Persetujuan Etik :

No Protokol	UH25090679	No Sponsor	
Peneliti Utama	dr. Arif Budiman Kaharuddin	Sponsor	
Judul Peneliti	HUBUNGAN EKSPRESI ARGINASE 2 DENGAN INFILTRASI LIMFOSIT TUMOR PADA ADENOKARSINOMA PROSTAT		
No Versi Protokol	1	Tanggal Versi	8 September 2025
No Versi PSP		Tanggal Versi	
Tempat Penelitian	RS Universitas Hasanuddin Makassar		
Jenis Review	☐ Exempted ☒ Expedited ☐ Fullboard Tanggal	Masa Berlaku 20 Oktober 2025 sampai 20 Oktober 2026	Frekuensi review lanjutan
Ketua KEP Universitas Hasanuddin	Prof. dr. Muh Nasrum Massi, PhD, SpMK, Subsp. Bakt(K)	Tanda tangan	
Sekretaris KEP Universitas Hasanuddin	Prof.dr. Firdaus Hamid, PhD, SpMK(K)	Tanda tangan	

Kewajiban Peneliti Utama:

- Menyerahkan Amandemen Protokol untuk persetujuan sebelum di implementasikan
- Menyerahkan Laporan SAE ke Komisi Etik dalam 24 Jam dan dilengkapi dalam 7 hari dan Lapor SUSAR dalam 72 Jam setelah Peneliti Utama menerima laporan
- Menyerahkan Laporan Kemajuan (progress report) setiap 6 bulan untuk penelitian resiko tinggi dan setiap setahun untuk penelitian resiko rendah
- Menyerahkan laporan akhir setelah Penelitian berakhir
- Melaporkan penyimpangan dari prokol yang disetujui (protocol deviation / violation)
- Mematuhi semua peraturan yang ditentukan

Nonparametric Correlations

Correlations

			Mean_HScore	Mean_TILs
Spearman's rho	Mean_HScore	Correlation Coefficient	1.000	.048
		Sig. (2-tailed)	.	.630
		N	105	105
	Mean_TILs	Correlation Coefficient	.048	1.000
		Sig. (2-tailed)	.630	.
		N	105	105

Spearman's rho Correlations

 **Highly Positive** : (None)

 **Positive** : (Mean_HScore <---> Mean_TILs)

 **No Linear Correlation** : (None)

 **Negative** : (None)

 **Highly Negative** : (None)

Note: Curated Help is calculated based on actual cell values, not the formatted values.

Nonparametric Correlations

Correlations

			Mean_HScore_Pola1	TILS Pola 1
Spearman's rho	Mean_HScore_Pola1	Correlation Coefficient	1.000	.016
		Sig. (2-tailed)	.	.869
		N	105	105
	TILS Pola 1	Correlation Coefficient	.016	1.000
		Sig. (2-tailed)	.869	.
		N	105	105

Spearman's rho Correlations

- Highly Positive** : (None)
- Positive** : (Mean_HScore_Pola1 <---> TILS Pola 1)
- No Linear Correlation** : (None)
- Negative** : (None)
- Highly Negative** : (None)

Note: Curated Help is calculated based on actual cell values, not the formatted values.

Nonparametric Correlations

Correlations			Mean_HScore_Pola2	TILS Pola 2
Spearman's rho	Mean_HScore_Pola2	Correlation Coefficient	1.000	-.118
		Sig. (2-tailed)	.	.251
		N	97	97
	TILS Pola 2	Correlation Coefficient	-.118	1.000
		Sig. (2-tailed)	.251	.
		N	97	105

Spearman's rho Correlations

- Highly Positive** : (None)
- Positive** : (None)
- No Linear Correlation** : (None)
- Negative** : (Mean_HScore_Pola2 <---> TILS Pola 2)
- Highly Negative** : (None)

Note: Curated Help is calculated based on actual cell values, not the formatted values.

Nonparametric Correlations

Correlations			Mean_HScore_Pola1	TILS Pola 1
Spearman's rho	Mean_HScore_Pola1	Correlation Coefficient	1.000	-.039
		Sig. (2-tailed)	.	.779
		N	54	54
	TILS Pola 1	Correlation Coefficient	-.039	1.000
		Sig. (2-tailed)	.779	.
		N	54	54

Spearman's rho Correlations

- Highly Positive** : (None)
- Positive** : (None)
- No Linear Correlation** : (None)
- Negative** : (Mean_HScore_Pola1 <----> TILS Pola 1)
- Highly Negative** : (None)

Note: Curated Help is calculated based on actual cell values, not the formatted values.

Nonparametric Correlations

Correlations

		TILS Pola 2	Mean_HScore_Pola2
Spearman's rho	TILS Pola 2	Correlation Coefficient	1.000
		Sig. (2-tailed)	.
		N	42
	Mean_HScore_Pola2	Correlation Coefficient	-.171
		Sig. (2-tailed)	.303
		N	38

Spearman's rho Correlations

- Highly Positive** : (None)
- Positive** : (None)
- No Linear Correlation** : (None)
- Negative** : (TILS Pola 2 <---> Mean_HScore_Pola2)
- Highly Negative** : (None)

Note: Curated Help is calculated based on actual cell values, not the formatted values.

NPar Tests

Kruskal-Wallis Test

Ranks			
	Kategori_TILs	N	Mean Rank
Mean_HScore	1.00	51	51.67
	2.00	53	54.85
	3.00	1	23.00
	Total	105	

Test Statistics^{a,b}

	Mean_HScore
Kruskal-Wallis H	1.263
df	2
Asymp. Sig.	.532

a. Kruskal Wallis Test

b. Grouping Variable:
Kategori_TILs

NPar Tests

Wilcoxon Signed Ranks Test

Ranks		N	Mean Rank	Sum of Ranks
Qupath Pola 1_3 - Qupath Pola 1_1	Negative Ranks	21 ^a	19.95	419.00
	Positive Ranks	32 ^b	31.63	1012.00
	Ties	0 ^c		
	Total	53		

a. Qupath Pola 1_3 < Qupath Pola 1_1

b. Qupath Pola 1_3 > Qupath Pola 1_1

c. Qupath Pola 1_3 = Qupath Pola 1_1

Test Statistics^a

	Qupath Pola 1_3 - Qupath Pola 1_1
Z	-2.625 ^b
Asymp. Sig. (2-tailed)	.009

a. Wilcoxon Signed Ranks Test

b. Based on negative ranks.

NPar Tests

Kruskal-Wallis Test

Ranks			
	GRADE GROUP	N	Mean Rank
Mean_HScore	I	23	74.48
	II	11	68.27
	III	10	43.40
	IV	13	43.92
	V	48	43.67
	Total	105	
Mean_TILs	I	23	51.96
	II	11	47.00
	III	10	40.95
	IV	13	69.58
	V	48	52.90
	Total	105	

Test Statistics^{a,b}

	Mean_HScore	Mean_TILs
Kruskal-Wallis H	20.863	6.453
df	4	4
Asymp. Sig.	<.001	.168

a. Kruskal Wallis Test

b. Grouping Variable: GRADE GROUP

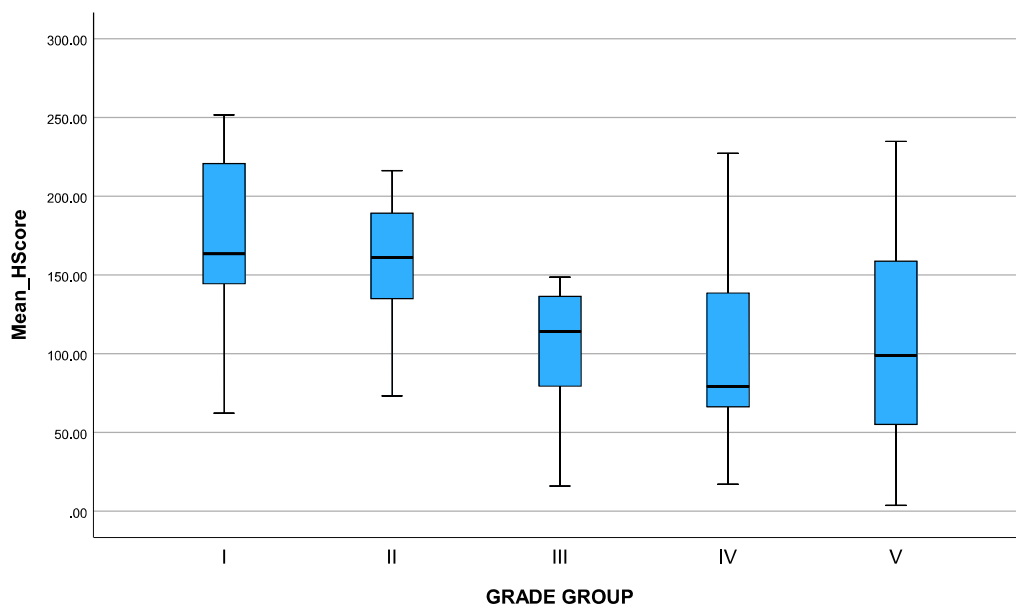
Explore

GRADE GROUP

Case Processing Summary

		Valid		Cases Missing		Total	
	GRADE GROUP	N	Percent	N	Percent	N	Percent
Mean_HScore	I	23	100.0%	0	0.0%	23	100.0%
	II	11	100.0%	0	0.0%	11	100.0%
	III	10	100.0%	0	0.0%	10	100.0%
	IV	13	100.0%	0	0.0%	13	100.0%
	V	48	100.0%	0	0.0%	48	100.0%

Mean_HScore



NPar Tests

Mann-Whitney Test

Ranks				
	GRADE GROUP	N	Mean Rank	Sum of Ranks
Mean_HScore	I	23	49.35	1135.00
	V	48	29.60	1421.00
	Total	71		

Test Statistics^a

	Mean_HScore
Mann-Whitney U	245.000
Wilcoxon W	1421.000
Z	-3.772
Asymp. Sig. (2-tailed)	<.001

a. Grouping Variable: GRADE GROUP

Nonparametric Correlations

Correlations

			IHC Pola 1	Mean_HScore_Pola1	IHC Pola 2
Spearman's rho	IHC Pola 1	Correlation Coefficient	1.000	.768***	.441***
		Sig. (2-tailed)	.	<.001	<.001
		N	105	105	105
	Mean_HScore_Pola1	Correlation Coefficient	.768***	1.000	.399***
		Sig. (2-tailed)	<.001	.	<.001
		N	105	105	105
	IHC Pola 2	Correlation Coefficient	.441***	.399***	1.000
		Sig. (2-tailed)	<.001	<.001	.
		N	105	105	105
	Mean_HScore_Pola2	Correlation Coefficient	.360***	.523***	.659***
		Sig. (2-tailed)	<.001	<.001	<.001
		N	97	97	97

Correlations

			Mean_HScore_Pola2
Spearman's rho	IHC Pola 1	Correlation Coefficient	.360***
		Sig. (2-tailed)	<.001
		N	97
	Mean_HScore_Pola1	Correlation Coefficient	.523***
		Sig. (2-tailed)	<.001
		N	97
	IHC Pola 2	Correlation Coefficient	.659***
		Sig. (2-tailed)	<.001
		N	97
	Mean_HScore_Pola2	Correlation Coefficient	1.000
		Sig. (2-tailed)	.
		N	97

***. Correlation is significant at the 0.001 level (2-tailed).

Spearman's rho Correlations

Highly Positive : (None)

Positive : (IHC Pola 1 <---> Mean_HScore_Pola1), (IHC Pola 1 <---> IHC Pola 2), (IHC Pola 1 <---> Mean_HScore_Pola2), (Mean_HScore_Pola1 <---> IHC Pola 2), (Mean_HScore_Pola1 <---> Mean_HScore_Pola2)

> Mean_HScore_Pola2), (IHC Pola 2 <---> Mean_HScore_Pola2)

 **No Linear Correlation** : (None)

 **Negative** : (None)

 **Highly Negative** : (None)

Note: Curated Help is calculated based on actual cell values, not the formatted values.