

## REFERENCES

- Alberts, B., Johnson, A., Lewis, J., Morgan, D., Raff, M., Roberts, K., & Walter, P. (2015). *Molecular Biology of the Cell* (6th ed.). Garland Science.
- Armstrong, L. (2014). *Epigenetics*. Garland Science, Taylor & Francis Group.
- Atezolizumab Combo Approved for PD-L1–positive TNBC. (2019). *Cancer Discovery*, 9(5), OF2–OF2.
- Balmana, J., Diez, O., & Castiglione, M. (2009). BRCA in breast cancer: ESMO Clinical Recommendations. *Annals of Oncology*, 20(Supplement 4), iv19–iv20.
- Barroso-Sousa, R., & Metzger-Filho, O. (2016). Differences between invasive lobular and invasive ductal carcinoma of the breast: results and therapeutic implications. *Therapeutic Advances in Medical Oncology*, 8(4), 261–266.
- Bonneterre, J., Bosq, J., Jamme, P., Valent, A., Gilles, E. M., Zukiwski, A. A., Fuqua, S. A. W., Lange, C. A., & O’Shaughnessy, J. (2016). Tumour and cellular distribution of activated forms of PR in breast cancers: a novel immunohistochemical analysis of a large clinical cohort. *ESMO Open*, 1(4), e000072.
- Bray, F., Ferlay, J., Soerjomataram, I., Siegel, R. L., Torre, L. A., & Jemal, A. (2018). Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA: A Cancer Journal for Clinicians*, 68(6), 394–424.
- Brewer, H. R., Jones, M. E., Schoemaker, M. J., Ashworth, A., & Swerdlow, A. J. (2017). Family history and risk of breast cancer: an analysis accounting for family structure. *Breast Cancer Research and Treatment*, 165(1), 193–200.
- Bruneau, B. G. (2010). Epigenetic Regulation of the Cardiovascular System. *Circulation Research*, 107(3), 324–326.
- Caldwell, C. C., Kojima, H., Lukashev, D., Armstrong, J., Farber, M., Apasov, S. G., & Sitkovsky, M. V. (2001). Differential Effects of Physiologically Relevant Hypoxic Conditions on T Lymphocyte Development and Effector Functions. *The Journal of Immunology*, 167(11), 6140–6149.
- Camuzi, D., de Amorim, Í., Ribeiro Pinto, L., Oliveira Trivilin, L., Mencialha, A., & Soares Lima, S. (2019). Regulation Is in the Air: The Relationship between Hypoxia and Epigenetics in Cancer. *Cells*, 8(4), 300.
- Chakraborty, A. A., Laukka, T., Myllykoski, M., Ringel, A. E., Booker, M. A., Tolstorukov, M. Y., Meng, Y. J., Meier, S. R., Jennings, R. B., Creech, A. L., Herbert, Z. T., McBrayer, S. K., Olenchock, B. A., Jaffe, J. D., Haigis, M. C., Beroukhim, R., Signoretti, S., Koivunen, P., & Kaelin, W. G. (2019). Histone demethylase KDM6A directly senses oxygen to control chromatin and cell fate. *Science*, 363(6432), 1217–1222.
- Chavez, K. J., Garimella, S. V., & Lipkowitz, S. (2011). Triple negative breast cancer cell lines: One tool in the search for better treatment of triple negative breast cancer. *Breast Disease*, 32(1–2), 35–48.

- Chen, M., Pockaj, B., Andreozzi, M., Barrett, M. T., Krishna, S., Eaton, S., Niu, R., & Anderson, K. S. (2018). JAK2 and PD-L1 Amplification Enhance the Dynamic Expression of PD-L1 in Triple-negative Breast Cancer. *Clinical Breast Cancer, 18*(5), e1205–e1215.
- Collaborative Group on Hormonal Factors in Breast Cancer. (2012). Menarche, menopause, and breast cancer risk: individual participant meta-analysis, including 118 964 women with breast cancer from 117 epidemiological studies. *The Lancet Oncology, 13*(11), 1141–1151.
- Cui, J., Shen, Y., & Li, R. (2013). Estrogen synthesis and signaling pathways during aging: from periphery to brain. *Trends in Molecular Medicine, 19*(3), 197–209.
- Cyprian, F. S., Akhtar, S., Gatalica, Z., & Vranic, S. (2019). Targeted immunotherapy with a checkpoint inhibitor in combination with chemotherapy: A new clinical paradigm in the treatment of triple-negative breast cancer. *Bosnian Journal of Basic Medical Sciences, 19*(3), 227–233.
- Dahlén, E., Veitonmäki, N., & Norlén, P. (2018). Bispecific antibodies in cancer immunotherapy. *Therapeutic Advances in Vaccines and Immunotherapy, 6*(1), 3–17.
- Dai, X., Li, T., Bai, Z., Yang, Y., Liu, X., Zhan, J., & Shi, B. (2015). Breast cancer intrinsic subtype classification, clinical use and future trends. *American Journal of Cancer Research, 5*(10), 2929–2943.
- de Saint Basile, G., Sepulveda, F. E., Maschalidi, S., & Fischer, A. (2015). Cytotoxic granule secretion by lymphocytes and its link to immune homeostasis. *F1000Research, 4*(930).
- Dong, Y., Sun, Q., & Zhang, X. (2016). PD-1 and its ligands are important immune checkpoints in cancer. *Oncotarget, 8*(2), 2171–2186.
- Dunn, G. P., Old, L. J., & Schreiber, R. D. (2004). The Immunobiology of Cancer Immunosurveillance and Immunoediting. *Immunity, 21*(2), 137–148.
- Dunn, J., & Rao, S. (2017). Epigenetics and immunotherapy: The current state of play. *Molecular Immunology, 87*, 227–239.
- Eckschlager, T., Plch, J., Stiborova, M., & Hrabeta, J. (2017). Histone Deacetylase Inhibitors as Anticancer Drugs. *International Journal of Molecular Sciences, 18*(7), 1414.
- Eliyatkın, N., Yalcin, E., Zengel, B., Aktaş, S., & Vardar, E. (2015). Molecular Classification of Breast Carcinoma: From Traditional, Old-Fashioned Way to A New Age, and A New Way. *Journal of Breast Health, 11*(2), 59–66.
- FDA Approves Second CAR T-cell Therapy. (2017). *Cancer Discovery, 8*(1), 5–6.
- Forget, M.-A., Haymaker, C., Hess, K. R., Meng, Y. J., Creasy, C., Karpinets, T., Fulbright, O. J., Roszik, J., Woodman, S. E., Kim, Y. U., Sakellariou-Thompson, D., Bhatta, A., Wahl, A., Flores, E., Thorsen, S. T., Tavera, R. J., Ramachandran, R., Gonzalez, A. M., Toth, C. L., ... Bernatchez, C. (2018). Prospective Analysis of Adoptive TIL Therapy in Patients with Metastatic Melanoma: Response, Impact of Anti-CTLA4, and Biomarkers to Predict Clinical Outcome. *Clinical Cancer Research, 24*(18), 4416–4428.
- Guiu, S., Michiels, S., André, F., Cortes, J., Denkert, C., Di Leo, A., Hennessy, B. T., Sorlie, T., Sotiriou, C., Turner, N., Van de Vijver, M., Viale, G., Loi, S., & Reis-Filho, J. S. (2012). Molecular subclasses of breast cancer: how do we define them? The IMPAKT 2012 Working Group Statement. *Annals of Oncology, 23*(12), 2997–3006.
- Harbeck, N., & Gnant, M. (2017). Breast cancer. *The Lancet, 389*(10074), 1134–1150.
- Hudis, C. A. (2007). Trastuzumab — Mechanism of Action and Use in Clinical Practice. *New England Journal of Medicine, 357*(1), 39–51.

- Iqbal, N., & Iqbal, N. (2014). Human Epidermal Growth Factor Receptor 2 (HER2) in Cancers: Overexpression and Therapeutic Implications. *Molecular Biology International*, 2014(Article ID 852748), 1–9.
- Ivashkiv, L. B. (2018). IFN $\gamma$ : signalling, epigenetics and roles in immunity, metabolism, disease and cancer immunotherapy. *Nature Reviews Immunology*, 18(9), 545–558.
- Jen, E. Y., Xu, Q., Schetter, A., Przepiorka, D., Shen, Y. L., Roscoe, D., Sridhara, R., Deisseroth, A., Philip, R., Farrell, A. T., & Pazdur, R. (2019). FDA Approval: Blinatumomab for Patients with B-cell Precursor Acute Lymphoblastic Leukemia in Morphologic Remission with Minimal Residual Disease. *Clinical Cancer Research*, 25(2), 473–477.
- Kapil, U., Bhadoria, A., Sareen, N., Singh, P., & Dwivedi, S. (2014). Reproductive factors and risk of breast cancer: A Review. *Indian Journal of Cancer*, 51(4), 571–576.
- Kim, P. K. M., Armstrong, M., Liu, Y., Yan, P., Bucher, B., Zuckerbraun, B. S., Gambotto, A., Billiar, T. R., & Yim, J. H. (2004). IRF-1 expression induces apoptosis and inhibits tumor growth in mouse mammary cancer cells in vitro and in vivo. *Oncogene*, 23(5), 1125–1135.
- Knipstein, J., & Gore, L. (2011). Entinostat for treatment of solid tumors and hematologic malignancies. *Expert Opinion on Investigational Drugs*, 20(10), 1455–1467.
- Krah, S., Kolmar, H., Becker, S., & Zielonka, S. (2018). Engineering IgG-Like Bispecific Antibodies—An Overview. *Antibodies*, 7(3), 28.
- Krishnamurthy, A., & Jimeno, A. (2018). Bispecific antibodies for cancer therapy: A review. *Pharmacology & Therapeutics*, 185, 122–134.
- Larsen, M. J., Thomassen, M., Gerdes, A.-M., & Kruse, T. A. (2014). Hereditary Breast Cancer: Clinical, Pathological and Molecular Characteristics. *Breast Cancer: Basic and Clinical Research*, 8, 145–155.
- Li, Y., & Seto, E. (2016). HDACs and HDAC Inhibitors in Cancer Development and Therapy. *Cold Spring Harbor Perspectives in Medicine*, 6(10), a026831.
- Liu, D., Zhao, J., Song, Y., Luo, X., & Yang, T. (2019). Clinical trial update on bispecific antibodies, antibody-drug conjugates, and antibody-containing regimens for acute lymphoblastic leukemia. *Journal of Hematology & Oncology*, 12(1).
- Liu, M., & Guo, F. (2018). Recent updates on cancer immunotherapy. *Precision Clinical Medicine*, 1(2), 65–74.
- Lukashev, D., Klebanov, B., Kojima, H., Grinberg, A., Ohta, A., Berenfeld, L., Wenger, R. H., Ohta, A., & Sitkovsky, M. (2006). Cutting Edge: Hypoxia-Inducible Factor 1 $\alpha$  and Its Activation-Inducible Short Isoform I.1 Negatively Regulate Functions of CD4 $^{+}$  and CD8 $^{+}$  T Lymphocytes. *The Journal of Immunology*, 177(8), 4962–4965.
- Maimela, N. R., Liu, S., & Zhang, Y. (2019). Fates of CD8 $^{+}$  T cells in Tumor Microenvironment. *Computational and Structural Biotechnology Journal*, 17(1), 1–13.
- Martinez, M., & Moon, E. K. (2019). CAR T Cells for Solid Tumors: New Strategies for Finding, Infiltrating, and Surviving in the Tumor Microenvironment. *Frontiers in Immunology*, 10(128).
- Martinez-Garcia, E., & Licht, J. D. (2010). Deregulation of H3K27 methylation in cancer. *Nature Genetics*, 42(2), 100–101.
- McGuire, A., Brown, J., Malone, C., McLaughlin, R., & Kerin, M. (2015). Effects of Age on the Detection and Management of Breast Cancer. *Cancers*, 7(2), 908–929.

- Melstrom, L. G., Salabat, M. R., Ding, X.-Z., Strouch, M. J., Grippo, P. J., Mirzoeva, S., Pelling, J. C., & Bentrem, D. J. (2011). Apigenin Down-Regulates the Hypoxia Response Genes: HIF-1 $\alpha$ , GLUT-1, and VEGF in Human Pancreatic Cancer Cells. *Journal of Surgical Research*, *167*(2), 173–181.
- Miller, K. M., Tjeertes, J. V., Coates, J., Legube, G., Polo, S. E., Britton, S., & Jackson, S. P. (2010). Human HDAC1 and HDAC2 function in the DNA-damage response to promote DNA nonhomologous end-joining. *Nature Structural & Molecular Biology*, *17*(9), 1144–1151.
- Minn, A. J., Gupta, G. P., Siegel, P. M., Bos, P. D., Shu, W., Giri, D. D., Viale, A., Olshen, A. B., Gerald, W. L., & Massagué, J. (2005). Genes that mediate breast cancer metastasis to lung. *Nature*, *436*(7050), 518–524.
- Morera, L., Lübbert, M., & Jung, M. (2016). Targeting histone methyltransferases and demethylases in clinical trials for cancer therapy. *Clinical Epigenetics*, *8*(1).
- Negishi, H., Fujita, Y., Yanai, H., Sakaguchi, S., Ouyang, X., Shinohara, M., Takayanagi, H., Ohba, Y., Taniguchi, T., & Honda, K. (2006). Evidence for licensing of IFN- $\gamma$ -induced IFN regulatory factor 1 transcription factor by MyD88 in Toll-like receptor-dependent gene induction program. *Proceedings of the National Academy of Sciences*, *103*(41), 15136–15141.
- Nichol, J. N., Dupéré-Richer, D., Ezponda, T., Licht, J. D., & Miller, W. H. (2016). H3K27 Methylation: A Focal Point of Epigenetic Dereglulation in Cancer. *Advances in Cancer Research*, *131*, 59–95.
- Nowicki, T. S., Hu-Lieskovan, S., & Ribas, A. (2018). Mechanisms of Resistance to PD-1 and PD-L1 Blockade. *The Cancer Journal*, *24*(1), 47–53.
- Palazón, A., Aragonés, J., Morales-Kastresana, A., de Landázuri, M. O., & Melero, I. (2011). Molecular Pathways: Hypoxia Response in Immune Cells Fighting or Promoting Cancer. *Clinical Cancer Research*, *18*(5), 1207–1213.
- Pan, M.-R., Hsu, M.-C., Chen, L.-T., & Hung, W.-C. (2018). Orchestration of H3K27 methylation: mechanisms and therapeutic implication. *Cellular and Molecular Life Sciences*, *75*(2), 209–223.
- Park, W., Heo, Y.-J., & Han, D. K. (2018). New opportunities for nanoparticles in cancer immunotherapy. *Biomaterials Research*, *22*, 24.
- Petrova, V., Annicchiarico-Petruzzelli, M., Melino, G., & Amelio, I. (2018). The hypoxic tumour microenvironment. *Oncogenesis*, *7*(1), 10.
- Restifo, N. P., Smyth, M. J., & Snyder, A. (2016). Acquired resistance to immunotherapy and future challenges. *Nature Reviews Cancer*, *16*(2), 121–126. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6330026/>
- Roy, R., Chun, J., & Powell, S. N. (2012). BRCA1 and BRCA2: different roles in a common pathway of genome protection. *Nature Reviews Cancer*, *12*(1), 68–78.
- Sasidharan Nair, V., & Elkord, E. (2017). Immune checkpoint inhibitors in cancer therapy: a focus on T-regulatory cells. *Immunology and Cell Biology*, *96*(1), 21–33.
- Schadendorf, D., Hodi, F. S., Robert, C., Weber, J. S., Margolin, K., Hamid, O., Patt, D., Chen, T.-T., Berman, D. M., & Wolchok, J. D. (2015). Pooled Analysis of Long-Term Survival Data From Phase II and Phase III Trials of Ipilimumab in Unresectable or Metastatic Melanoma. *Journal of Clinical Oncology*, *33*(17), 1889–1894.
- Schepisi, G., Cursano, M. C., Casadei, C., Menna, C., Altavilla, A., Lolli, C., Cerchione, C., Paganelli, G., Santini, D., Tonini, G., Martinelli, G., & De Giorgi, U. (2019). CAR-T cell therapy: a potential new strategy against prostate cancer. *Journal for ImmunoTherapy of Cancer*, *7*(258).

- Schmid, P., Rugo, H. S., Adams, S., Schneeweiss, A., Barrios, C. H., Iwata, H., Diéras, V., Henschel, V., Molinero, L., Chui, S. Y., Maiya, V., Husain, A., Winer, E. P., Loi, S., & Emens, L. A. (2020). Atezolizumab plus nab-paclitaxel as first-line treatment for unresectable, locally advanced or metastatic triple-negative breast cancer (IMpassion130): updated efficacy results from a randomised, double-blind, placebo-controlled, phase 3 trial. *The Lancet Oncology*, *21*(1), 44–59.
- Shao, Y., Cheng, Z., Li, X., Chernaya, V., Wang, H., & Yang, X. (2014). Immunosuppressive/anti-inflammatory cytokines directly and indirectly inhibit endothelial dysfunction- a novel mechanism for maintaining vascular function. *Journal of Hematology & Oncology*, *7*(80).
- Sharma, P., Hu-Lieskovan, S., Wargo, J. A., & Ribas, A. (2017). Primary, Adaptive, and Acquired Resistance to Cancer Immunotherapy. *Cell*, *168*(4), 707–723.
- Sharma, P. (2018). Update on the Treatment of Early-Stage Triple-Negative Breast Cancer. *Current Treatment Options in Oncology*, *19*(5).
- Siegel, D., Hussein, M., Belani, C., Robert, F., Galanis, E., Richon, V. M., Garcia-Vargas, J., Sanz-Rodriguez, C., & Rizvi, S. (2009). Vorinostat in solid and hematologic malignancies. *Journal of Hematology & Oncology*, *2*(31).
- Sinn, H.-P., & Kreipe, H. (2013). A Brief Overview of the WHO Classification of Breast Tumors, 4th Edition, Focusing on Issues and Updates from the 3rd Edition. *Breast Care*, *8*(2), 149–154.
- Slaney, C. Y., Wang, P., Darcy, P. K., & Kershaw, M. H. (2018). CARs versus BiTEs: A Comparison between T Cell–Redirection Strategies for Cancer Treatment. *Cancer Discovery*, *8*(8), 924–934.
- Smyth, M. J., Dunn, G. P., & Schreiber, R. D. (2006). Cancer Immunosurveillance and Immunoediting: The Roles of Immunity in Suppressing Tumor Development and Shaping Tumor Immunogenicity. *Advances in Immunology*, *90*, 1–50.
- Sporikova, Z., Koudelakova, V., Trojanec, R., & Hajduch, M. (2018). Genetic Markers in Triple-Negative Breast Cancer. *Clinical Breast Cancer*, *18*(5), e841–e850.
- Sun, W., Lv, S., Li, H., Cui, W., & Wang, L. (2018). Enhancing the Anticancer Efficacy of Immunotherapy through Combination with Histone Modification Inhibitors. *Genes*, *9*(12), 633.
- Sun, Y.-S., Zhao, Z., Yang, Z.-N., Xu, F., Lu, H.-J., Zhu, Z.-Y., Shi, W., Jiang, J., Yao, P.-P., & Zhu, H.-P. (2017). Risk Factors and Preventions of Breast Cancer. *International Journal of Biological Sciences*, *13*(11), 1387–1397.
- Tan, J., Yang, X., Zhuang, L., Jiang, X., Chen, W., Lee, P. L., Karuturi, R. K. M., Tan, P. B. O., Liu, E. T., & Yu, Q. (2007). Pharmacologic disruption of Polycomb-repressive complex 2-mediated gene repression selectively induces apoptosis in cancer cells. *Genes & Development*, *21*(9), 1050.
- Tokarew, N., Ogonek, J., Endres, S., von Bergwelt-Baildon, M., & Kobold, S. (2018). Teaching an old dog new tricks: next-generation CAR T cells. *British Journal of Cancer*, *120*(1), 26–37.
- Vanhaecke, T., Papeleu, P., Elaut, G., & Rogiers, V. (2004). Trichostatin A - like Hydroxamate Histone Deacetylase Inhibitors as Therapeutic Agents: Toxicological Point of View. *Current Medicinal Chemistry*, *11*(12), 1629–1643.
- von Burstin, J., Eser, S., Paul, M. C., Seidler, B., Brandl, M., Messer, M., von Werder, A., Schmidt, A., Mages, J., Pagel, P., Schnieke, A., Schmid, R. M., Schneider, G., & Saur, D. (2009). E-Cadherin Regulates Metastasis of Pancreatic Cancer In Vivo and Is Suppressed by a SNAIL/HDAC1/HDAC2 Repressor Complex. *Gastroenterology*, *137*(1), 361-371.e5.
- Wang, J., & Zhou, P. (2017). New Approaches in CAR-T Cell Immunotherapy for Breast Cancer. *Advances in Experimental Medicine and Biology*, *1026*, 371–381.

- Wang, X., & Lin, Y. (2008). Tumor necrosis factor and cancer, buddies or foes? *Acta Pharmacologica Sinica*, *29*(11), 1275–1288.
- Wapenaar, H., & Dekker, F. J. (2016). Histone acetyltransferases: challenges in targeting bi-substrate enzymes. *Clinical Epigenetics*, *8*(59).
- Xu, W. S., Parmigiani, R. B., & Marks, P. A. (2007). Histone deacetylase inhibitors: molecular mechanisms of action. *Oncogene*, *26*(37), 5541–5552.
- Xu, X., Sun, Q., Liang, X., Chen, Z., Zhang, X., Zhou, X., Li, M., Tu, H., Liu, Y., Tu, S., & Li, Y. (2019). Mechanisms of Relapse After CD19 CAR T-Cell Therapy for Acute Lymphoblastic Leukemia and Its Prevention and Treatment Strategies. *Frontiers in Immunology*, *10*.
- Yamaguchi, T., Cubizolles, F., Zhang, Y., Reichert, N., Kohler, H., Seiser, C., & Matthias, P. (2010). Histone deacetylases 1 and 2 act in concert to promote the G1-to-S progression. *Genes & Development*, *24*(5), 455–469.
- Yao, H., He, G., Yan, S., Chen, C., Song, L., Rosol, T. J., & Deng, X. (2016). Triple-negative breast cancer: is there a treatment on the horizon? *Oncotarget*, *8*(1), 1913–1924.
- Zang, X. (2018). 2018 Nobel Prize in medicine awarded to cancer immunotherapy: Immune checkpoint blockade – A personal account. *Genes & Diseases*, *5*(4), 302–303.
- Zavras, P., Wang, Y., Gandhi, A., Lontos, K., & Delgoffe, G. (2019). Evaluating tisagenlecleucel and its potential in the treatment of relapsed or refractory diffuse large B cell lymphoma: evidence to date. *OncoTargets and Therapy*, *Volume 12*, 4543–4554.
- Zhang, J., & Wang, L. (2019). The Emerging World of TCR-T Cell Trials Against Cancer: A Systematic Review. *Technology in Cancer Research & Treatment*, *18*, 1533033819831068.
- Zhang, J., & Zhong, Q. (2014). Histone deacetylase inhibitors and cell death. *Cellular and Molecular Life Sciences*, *71*(20), 3885–3901.
- Zhang, R., Erler, J., & Langowski, J. (2017). Histone Acetylation Regulates Chromatin Accessibility: Role of H4K16 in Inter-nucleosome Interaction. *Biophysical Journal*, *112*(3), 450–459.
- Zhang, T., Zhang, Z., Dong, Q., Xiong, J., & Zhu, B. (2020). Histone H3K27 acetylation is dispensable for enhancer activity in mouse embryonic stem cells. *Genome Biology*, *21*(1).
- Ziello, J. E., Jovin, I. S., & Huang, Y. (2007). Hypoxia-Inducible Factor (HIF)-1 regulatory pathway and its potential for therapeutic intervention in malignancy and ischemia. *The Yale Journal of Biology and Medicine*, *80*(2), 51–60.