

REFERENCES

- Anderson, A. C., Joller, N., & Kuchroo, V. K. (2016). Lag-3, Tim-3, and TIGIT co-inhibitory receptors with specialized functions in immune regulation. *Immunity*, 44(5), 989. <https://doi.org/10.1016/j.immuni.2016.05.001>
- Baldanzi G. (2022). Immune Checkpoint Receptors Signaling in T Cells. *International journal of molecular sciences*, 23(7), 3529. <https://doi.org/10.3390/ijms23073529>
- Balke-Want, H., Keerthi, V., Cadinanos-Garai, A., Fowler, C., Gkitsas, N., Brown, A. K., Tunuguntla, R., & Feldman, S. A. (2023). Non-viral chimeric antigen receptor (CAR) T cells going viral. *Immuno-Oncology and Technology*, 18. <https://doi.org/10.1016/j.iotech.2023.100375>
- Bonifant, C. L., Jackson, H. J., Brentjens, R. J., & Curran, K. J. (2016). Toxicity and management in CAR T-cell therapy. *Molecular Therapy-Oncolytics*, 3. <https://doi.org/10.1038/mto.2016.11>
- Bozso, S. J., Kang, J. J. H., & Nagendran, J. (2020). The role of competing mechanisms on Lck regulation. *Immunologic research*, 68(5), 289–295. <https://doi.org/10.1007/s12026-020-09148-2>
- Chang, V. T., Fernandes, R. A., Ganzinger, K. A., Lee, S. F., Siebold, C., McColl, J., Jönsson, P., Palayret, M., Harlos, K., Coles, C. H., Jones, E. Y., Lui, Y., Huang, E., Gilbert, R. J., Klenerman, D., Aricescu, A. R., & Davis, S. J. (2016). Initiation of T cell signaling by CD45 segregation at 'close contacts'. *Nature Immunology*, 17(5), 574-582. <https://doi.org/10.1038/ni.3392>
- Chen, B. J., Dashnamoorthy, R., Galera, P., Makarenko, V., Chang, H., Ghosh, S., & Evens, A. M. (2019). The immune checkpoint molecules PD-1, PD-L1, TIM-3 and LAG-3 in diffuse large B-cell lymphoma. *Oncotarget*, 10(21), 2030-2040. <https://doi.org/10.18632/oncotarget.26771>
- Chen, N., Morello, A., Tano, Z., & Adusumilli, P. S. (2017). CAR T-cell intrinsic PD-1 checkpoint blockade: A two-in-one approach for solid tumor immunotherapy. *Oncoimmunology*, 6(2). <https://doi.org/10.1080/2162402X.2016.1273302>
- Clark, R. A. (2015). Resident memory T cells in human health and disease. *Science translational medicine*, 7(269), 269rv1-269rv1. <https://doi.org/10.1126/scitranslmed.3010641>
- Cordoba, P., Choudhuri, K., Zhang, H., Bridge, M., Basat, A. B., & Dustin, M. L. (2013). The large ectodomains of CD45 and CD148 regulate their segregation from and inhibition of ligated T-cell receptor. *Blood*, 121(21), 4295-4302. <https://doi.org/10.1182/blood-2012-07-442251>
- Courtney, A. H., Shvets, A. A., Lu, W., Griffante, G., Mollenauer, M., Horkova, V., Lo, L., Yu, S., Stepanek, O., Chakraborty, A. K., & Weiss, A. (2019). CD45 functions as a signaling gatekeeper in T cells. *Science Signaling*, 12(604). <https://doi.org/10.1126/scisignal.aaw8151>
- Doroshov, D. B., Bhalla, S., Beasley, M. B., Sholl, L. M., Kerr, K. M., Gnjatic, S., ... & Hirsch, F. R. (2021). PD-L1 as a biomarker of response to immune-checkpoint inhibitors. *Nature reviews Clinical oncology*, 18(6), 345-362. <https://doi.org/10.1038/s41571-021-00473-5>

- Ehrke-Schulz, E., Schiwon, M., Leitner, T., Dávid, S., Bergmann, T., Liu, J., & Ehrhardt, A. (2017). CRISPR/Cas9 delivery with one single adenoviral vector devoid of all viral genes. *Scientific reports*, 7(1), 17113. <https://doi.org/10.1038/s41598-017-17180-w>
- Elmas, E., Saljoughian, N., Pereira, S. F., Tullius, B. P., Sorathia, K., Nakkula, R. J., Lee, D. A., & Kararoudi, M. N. (2022). CRISPR Gene Editing of Human Primary NK and T Cells for Cancer Immunotherapy. *Frontiers in Oncology*, 12. <https://doi.org/10.3389/fonc.2022.834002>
- Emens, L. A., Ascierto, P. A., Darcy, P. K., Demaria, S., Eggermont, A. M. M., Redmond, W. L., Seliger, B., & Marincola, F. M. (2017). Cancer immunotherapy: Opportunities and challenges in the rapidly evolving clinical landscape. *European journal of cancer (Oxford, England : 1990)*, 81, 116–129. <https://doi.org/10.1016/j.ejca.2017.01.035>
- Feucht, J., Sun, J., Eyquem, J., Ho, Y., Zhao, Z., Leibold, J., Dobrin, A., Cabriolu, A., Hamieh, M., & Sadelain, M. (2018). Calibration of CAR activation potential directs alternative T cell fates and therapeutic potency. *Nature Medicine*, 25(1), 82-88. <https://doi.org/10.1038/s41591-018-0290-5>
- Gajewski, T. F., Schreiber, H., & Fu, Y. X. (2013). Innate and adaptive immune cells in the tumor microenvironment. *Nature immunology*, 14(10), 1014–1022. <https://doi.org/10.1038/ni.2703>
- Guerriero, J. L. (2019). Macrophages: their untold story in T cell activation and function. *International Review of Cell and Molecular Biology*, 342, 73-93. <https://doi.org/10.1016/bs.ircmb.2018.07.001>
- Graham, D. B., & Root, D. E. (2015). Resources for the design of CRISPR gene editing experiments. *Genome biology*, 16, 260. <https://doi.org/10.1186/s13059-015-0823-x>
- Hartmann, J., Bondanza, A., & Buchholz, C. J. (2017). Clinical development of CAR T cells—Challenges and opportunities in translating innovative treatment concepts. *EMBO Molecular Medicine*, 9(9), 1183-1197. <https://doi.org/10.15252/emmm.201607485>
- Hryhorowicz, M., Lipiński, D., Zeyland, J., & Słomski, R. (2017). CRISPR/Cas9 Immune System as a Tool for Genome Engineering. *Archivum immunologiae et therapiae experimentalis*, 65(3), 233–240. <https://doi.org/10.1007/s00005-016-0427-5>
- Ishibashi, A., Saga, K., Hisatomi, Y., Li, Y., Kaneda, Y., & Nimura, K. (2020). A simple method using CRISPR-Cas9 to knock-out genes in murine cancerous cell lines. *Scientific Reports*, 10(1), 1-10. <https://doi.org/10.1038/s41598-020-79303-0>
- Jayaraman, J., Mellody, M. P., Hou, A. J., Desai, R. P., Fung, A. W., Pham, A. H. T., Chen, Y. Y., & Zhao, W. (2020). CAR-T design: Elements and their synergistic function. *EBioMedicine*, 58, 102931. <https://doi.org/10.1016/j.ebiom.2020.102931>
- Jiang, F., & Doudna, J. A. (2017). CRISPR–Cas9 Structures and Mechanisms. <https://doi.org/10.1146/annurev-biophys-062215-010822>

- Jung, Y., Wen, L., Altman, A., & Ley, K. (2021). CD45 pre-exclusion from the tips of T cell microvilli prior to antigen recognition. *Nature Communications*, 12(1), 1-16. <https://doi.org/10.1038/s41467-021-23792-8>
- Kalinin, R. S., Ukrainskaya, V. M., Chumakov, S. P., Moysenovich, A. M., Tereshchuk, V. M., Volkov, D. V., Pershin, D. S., Maksimov, E. G., Zhang, H., Maschan, M. A., Rubtsov, Y. P., & Stepanov, A. V. (2021). Engineered Removal of PD-1 From the Surface of CD19 CAR-T Cells Results in Increased Activation and Diminished Survival. *Frontiers in Molecular Biosciences*, 8, 745286. <https://doi.org/10.3389/fmolb.2021.745286>
- Kumar, B. V., Connors, T. J., & Farber, D. L. (2018). Human T cell development, localization, and function throughout life. *Immunity*, 48(2), 202-213. <https://doi.org/10.1016/j.immuni.2018.01.007>
- Li, B., Chan, H. L., & Chen, P. (2019). Immune checkpoint inhibitors: basics and challenges. *Current medicinal chemistry*, 26(17), 3009-3025. <https://doi.org/10.2174/0929867324666170804143706>
- Li, J., Zhou, W., Li, D., Huang, Y., Yang, X., Jiang, L., Hu, X., Yang, J., Fu, M., Zhang, M., Wang, F., Li, J., Zhang, Y., Yang, Y., Yan, F., Gao, H., & Wang, W. (2023). Co-infusion of CAR T cells with aAPCs expressing chemokines and costimulatory ligands enhances the anti-tumor efficacy in mice. *Cancer Letters*, 568, 216287. <https://doi.org/10.1016/j.canlet.2023.216287>
- Liu, L., Wang, A., Liu, X., Han, S., Sun, Y., Zhang, J., Guo, L., & Zhang, Y. (2022). Blocking TIGIT/CD155 signalling reverses CD8+ T cell exhaustion and enhances the antitumor activity in cervical cancer. *Journal of translational medicine*, 20(1), 280. <https://doi.org/10.1186/s12967-022-03480-x>
- Liu, X., Zhang, Y., Cheng, C., Cheng, A. W., Zhang, X., Li, N., Xia, C., Wei, X., Liu, X., & Wang, H. (2017). CRISPR-Cas9-mediated multiplex gene editing in CAR-T cells. *Cell research*, 27(1), 154–157. <https://doi.org/10.1038/cr.2016.142>
- Ma, Y., Zhang, L., & Huang, X. (2014). Genome modification by CRISPR/Cas9. *The FEBS journal*, 281(23), 5186–5193. <https://doi.org/10.1111/febs.13110>
- Mahoney, K. M., Freeman, G. J., & McDermott, D. F. (2015). The next immune-checkpoint inhibitors: PD-1/PD-L1 blockade in melanoma. *Clinical therapeutics*, 37(4), 764-782. <https://doi.org/10.1016/j.clinthera.2015.02.018>
- Majzner, R. G., & Mackall, C. L. (2019). Clinical lessons learned from the first leg of the CAR T cell journey. *Nature medicine*, 25(9), 1341–1355. <https://doi.org/10.1038/s41591-019-0564-6>
- Marofi, F., Motavalli, R., Safonov, V. A., Thangavelu, L., Yumashev, A. V., Alexander, M., Shomali, N., Chartrand, M. S., Pathak, Y., Jarahian, M., Izadi, S., Hassanzadeh, A., Shirafkan, N., Tahmasebi, S., & Khiavi, F. M. (2021). CAR T cells in solid tumors: challenges and opportunities. *Stem cell research & therapy*, 12(1), 81. <https://doi.org/10.1186/s13287-020-02128-1>

- McGowan, E., Lin, Q., Ma, G., Yin, H., Chen, S., & Lin, Y. (2019). PD-1 disrupted CAR-T cells in the treatment of solid tumors: Promises and challenges. *Biomedicine & Pharmacotherapy*, 121, 109625. <https://doi.org/10.1016/j.biopha.2019.109625>
- Miliotou, A. N., & Papadopoulou, L. C. (2018). CAR T-cell Therapy: A New Era in Cancer Immunotherapy. *Current pharmaceutical biotechnology*, 19(1), 5–18. <https://doi.org/10.2174/1389201019666180418095526>
- Mucida, D., Husain, M. M., Muroi, S., Van Wijk, F., Shinnakasu, R., Naoe, Y., ... & Cheroutre, H. (2013). Transcriptional reprogramming of mature CD4+ helper T cells generates distinct MHC class II–restricted cytotoxic T lymphocytes. *Nature immunology*, 14(3), 281–289. <https://doi.org/10.1038/ni.2523>
- Mueller, S. N., & Mackay, L. K. (2016). Tissue-resident memory T cells: local specialists in immune defence. *Nature Reviews Immunology*, 16(2), 79–89. <https://doi.org/10.1038/nri.2015.3>
- Pauken, K. E., Godec, J., Odorizzi, P. M., Brown, K. E., Yates, K. B., Ngiow, S. F., Burke, K. P., Maleri, S., Grande, S. M., Francisco, L. M., Ali, A., Imam, S., Freeman, G. J., Haining, W. N., Wherry, E. J., & Sharpe, A. H. (2020). The PD-1 Pathway Regulates Development and Function of Memory CD8+ T Cells following Respiratory Viral Infection. *Cell Reports*, 31(13), 107827. <https://doi.org/10.1016/j.celrep.2020.107827>
- Pennock, N. D., White, J. T., Cross, E. W., Cheney, E. E., Tamburini, B. A., & Kedl, R. M. (2013). T cell responses: naive to memory and everything in between. *Advances in physiology education*, 37(4), 273–283. <https://doi.org/10.1152/advan.00066.2013>
- Picardo, S. L., Doi, J., & Hansen, A. R. (2019). Structure and Optimization of Checkpoint Inhibitors. *Cancers*, 12(1). <https://doi.org/10.3390/cancers12010038>
- Poltorak, M. P., Graef, P., Tschulik, C., Wagner, M., Cletiu, V., Dreher, S., Borjan, B., Fraessle, S. P., Effenberger, M., Turk, M., Busch, D. H., Plitzko, J., Kugler, D. G., Ragan, S., Schmidt, T., Stemberger, C., & Germeroth, L. (2020). Expamers: A new technology to control T cell activation. *Scientific Reports*, 10(1), 1–15. <https://doi.org/10.1038/s41598-020-74595-8>
- Rezalotfi, A., Fritz, L., Förster, R., & Bošnjak, B. (2022). Challenges of CRISPR-Based Gene Editing in Primary T Cells. *International Journal of Molecular Sciences*, 23(3). <https://doi.org/10.3390/ijms23031689>
- Rheinländer, A., Schraven, B., & Bommhardt, U. (2018). CD45 in human physiology and clinical medicine. *Immunology Letters*, 196, 22–32. <https://doi.org/10.1016/j.imlet.2018.01.009>
- Ribas, A., & Wolchok, J. D. (2018). Cancer immunotherapy using checkpoint blockade. *Science*. <https://doi.org/aar4060>
- Rodrigo, S., Senasinghe, K. & Quazi, S. Molecular and therapeutic effect of CRISPR in treating cancer. *Med Oncol* 40, 81 (2023). <https://doi.org/10.1007/s12032-022-01930-6>

- Rupp, L. J., Schumann, K., Roybal, K. T., Gate, R. E., Ye, C. J., Lim, W. A., & Marson, A. (2017). CRISPR/Cas9-mediated PD-1 disruption enhances anti-tumor efficacy of human chimeric antigen receptor T cells. *Scientific Reports*, 7(1), 1-10. <https://doi.org/10.1038/s41598-017-00462-8>
- Roche, P. A., & Furuta, K. (2015). The ins and outs of MHC class II-mediated antigen processing and presentation. *Nature Reviews Immunology*, 15(4), 203-216. <https://doi.org/10.1038/nri3818>
- Ross, S. H., & Cantrell, D. A. (2018). Signaling and Function of Interleukin-2 in T Lymphocytes. *Annual Review of Immunology*, 36, 411. <https://doi.org/10.1146/annurev-immunol-042617-053352>
- Schenkel, J. M., & Masopust, D. (2014). Tissue-resident memory T cells. *Immunity*, 41(6), 886-897. <http://dx.doi.org/10.1016/j.immuni.2014.12.007>
- Schoutrop, E., Poiret, T., El-Serafi, I., Zhao, Y., He, R., Moter, A., Henriksson, J., Hassan, M., Magalhaes, I., & Mattsson, J. (2023). Tuned activation of MSLN-CAR T cells induces superior antitumor responses in ovarian cancer models. *Journal for immunotherapy of cancer*, 11(2), e005691. <https://doi.org/10.1136/jitc-2022-005691>
- Song, W., & Zhang, M. (2020). Use of CAR-T cell therapy, PD-1 blockade, and their combination for the treatment of hematological malignancies. *Clinical Immunology*, 214, 108382. <https://doi.org/10.1016/j.clim.2020.108382>
- Srivastava, S., & Riddell, S. R. (2015). Engineering CAR-T Cells: Design Concepts. *Trends in Immunology*, 36(8), 494. <https://doi.org/10.1016/j.it.2015.06.004>
- Sterner, R. C., & Sterner, R. M. (2021). CAR-T cell therapy: Current limitations and potential strategies. *Blood Cancer Journal*, 11(4), 1-11. <https://doi.org/10.1038/s41408-021-00459-7>
- Su, S., Hu, B., Shao, J., Shen, B., Du, J., Du, Y., Zhou, J., Yu, L., Zhang, L., Chen, F., Sha, H., Cheng, L., Meng, F., Zou, Z., Huang, X., & Liu, B. (2016). CRISPR-Cas9 mediated efficient PD-1 disruption on human primary T cells from cancer patients. *Scientific Reports*, 6(1), 1-14. <https://doi.org/10.1038/srep20070>
- Sung, H., Ferlay, J., Siegel, R. L., Laversanne, M., Soerjomataram, I., Jemal, A., & Bray, F. (2021). Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA: a cancer journal for clinicians*, 71(3), 209-249. <https://doi.org/10.3322/caac.21660>
- Tanaka, A., & Sakaguchi, S. (2017). Regulatory T cells in cancer immunotherapy. *Cell research*, 27(1), 109-118. <https://doi.org/10.1038/cr.2016.151>
- Tang, J., Yu, J. X., Hubbard-Lucey, V. M., Neftelinov, S. T., Hodge, J. P., & Lin, Y. (2018). Trial watch: the clinical trial landscape for PD1/PDL1 immune checkpoint inhibitors. *Nature reviews Drug discovery*, (12), 854-856. <https://doi.org/10.1038/nrd.2018.209>

- Volkov, D. V., Stepanova, V. M., Rubtsov, Y. P., Stepanov, A. V., & Gabibov, A. G. (2023). Protein Tyrosine Phosphatase CD45 As an Immunity Regulator and a Potential Effector of CAR-T therapy. *Acta Naturae*, 15(3), 17-26. <https://doi.org/10.32607/actanaturae.25438>
- Wang, Q., Bardhan, K., Boussiotis, V. A., & Patsoukis, N. (2021). The PD-1 Interactome. *Advanced Biology*, 5(9), 2100758. <https://doi.org/10.1002/adbi.202100758>
- Wang, Z., Li, N., Feng, K., Chen, M., Zhang, Y., Liu, Y., Yang, Q., Nie, J., Tang, N., Zhang, X., Cheng, C., Shen, L., He, J., Ye, X., Cao, W., Wang, H., & Han, W. (2021). Phase I study of CAR-T cells with PD-1 and TCR disruption in mesothelin-positive solid tumors. *Cellular & Molecular Immunology*, 18(9), 2188-2198. <https://doi.org/10.1038/s41423-021-00749-x>
- Weber, E. W., Maus, M. V., & Mackall, C. L. (2020). The Emerging Landscape of Immune Cell Therapies. *Cell*, 181(1), 46–62. <https://doi.org/10.1016/j.cell.2020.03.001>
- Wei, Y., Fan, J., Shan, X., Yin, D., Wang, L., Ye, W., & Zhao, W. (2022). TIGIT marks exhausted T cells and serves as a target for immune restoration in patients with chronic HBV infection. *American Journal of Translational Research*, 14(2), 942-954. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8902551/>
- Wolf, Y., Anderson, A. C., & Kuchroo, V. K. (2020). TIM3 comes of age as an inhibitory receptor. *Nature Reviews Immunology*, 20(3), 173-185. <https://doi.org/10.1038/s41577-019-0224-6>
- Xiao, Q., Zhang, X., Tu, L., Cao, J., Hinrichs, C. S., & Su, X. (2022). Size-dependent activation of CAR-T cells. *Science Immunology*. <https://doi.org/abl3995>
- Xu, J., Zhang, Q., Tian, K., Wang, H., Yin, H., & Zheng, J. (2018). Current status and future prospects of the strategy of combining CAR-T with PD-1 blockade for antitumor therapy (Review). *Molecular medicine reports*, 17(2), 2083–2088. <https://doi.org/10.3892/mmr.2017.8129>
- Yang, Z., Kim, H. J., Villasboas, J. C., Chen, P., Price-Troska, T., Jalali, S., Wilson, M., Novak, A. J., & Ansell, S. M. (2017). Expression of LAG-3 defines exhaustion of intratumoral PD-1+ T cells and correlates with poor outcome in follicular lymphoma. *Oncotarget*, 8(37), 61425-61439. <https://doi.org/10.18632/oncotarget.18251>
- Yudovich, D., Bäckström, A., Schmiderer, L., Žemaitis, K., Subramaniam, A., & Larsson, J. (2020). Combined lentiviral- and RNA-mediated CRISPR/Cas9 delivery for efficient and traceable gene editing in human hematopoietic stem and progenitor cells. *Scientific Reports*, 10(1), 1-11. <https://doi.org/10.1038/s41598-020-79724-x>
- Zak, K. M., Grudnik, P., Magiera, K., Dömling, A., Dubin, G., & Holak, T. A. (2017). Structural Biology of the Immune Checkpoint Receptor PD-1 and Its Ligands PD-L1/PD-L2. *Structure (London, England : 1993)*, 25(8), 1163–1174. <https://doi.org/10.1016/j.str.2017.06.011>

- Zhan, T., Rindtorff, N., Betge, J., Ebert, M. P., & Boutros, M. (2019). CRISPR/Cas9 for cancer research and therapy. *Seminars in Cancer Biology*, 55, 106-119. <https://doi.org/10.1016/j.semcancer.2018.04.001>
- Zhao, Z., Shi, L., Zhang, W., Han, J., Zhang, S., Fu, Z., & Cai, J. (2017). CRISPR knock out of programmed cell death protein 1 enhances anti-tumor activity of cytotoxic T lymphocytes. *Oncotarget*, 9(4), 5208-5215. <https://doi.org/10.18632/oncotarget.23730>
- Zolov, S. N., Rietberg, S. P., & Bonifant, C. L. (2018). Programmed cell death protein 1 activation preferentially inhibits CD28.CAR-T cells. *Cytotherapy*, 20(10), 1259–1266. <https://doi.org/10.1016/j.jcyt.2018.07.005>