References

Abu-Sbeih, H., Ali, F. S., Qiao, W., Lu, Y., Patel, S., Diab, A., & Wang, Y. (2019). Immune checkpoint inhibitor-induced colitis as a predictor of survival in metastatic melanoma. *Cancer Immunology, Immunotherapy*, *68*(4), 553–561. https://doi.org/10.1007/s00262-019-02303-1

American Cancer Society. (2024). *Cancer facts & figures 2024*. Www.cancer.org; American Cancer Society. https://www.cancer.org/research/cancer-facts-statistics/all-cancer-facts-figures/2024-cancer-facts-figures.html

André Wendindondé Nana, Wu, S., Yang, Y., Yu Tang Chin, Tsai Mu Cheng, Ho, Y., Li, W., Yu Min Liao, Yi Ru Chen, Ya Jung Shih, Yun Ru Liu, Pedersen, J. Z., Incerpi, S., Aleck Hercbergs, Liu, L. F., Whang-Peng, J., Davis, P. J., & Hung Yun Lin. (2018). Nano-Diamino-Tetrac (NDAT) enhances resveratrol-induced antiproliferation by action on the RRM2 pathway in colorectal cancers. *Hormones and Cancer*, *9*(5), 349–360. https://doi.org/10.1007/s12672-018-0334-9

Arnold, M., Morgan, E., Rumgay, H., Mafra, A., Singh, D., Laversanne, M., Vignat, J., Gralow, J. R., Cardoso, F., Siesling, S., & Soerjomataram, I. (2022). Current and future burden of breast cancer: Global statistics for 2020 and 2040. *The Breast*, *66*(66). https://doi.org/10.1016/j.breast.2022.08.010

Bai, X., Sun, P., Wang, X., Long, C., Liao, S., Dang, S., Zhuang, S., Du, Y., Zhang, X., Li, N., He, K., & Zhang, Z. (2023). Structure and dynamics of the EGFR/HER2 heterodimer. *Cell Discovery*, *9*(1). https://doi.org/10.1038/s41421-023-00523-5

Barroso, L., Viegas, C., Vieira, J., Ferreira-Pêgo, C., Costa, J., & Fonte, P. (2021). Lipid-based carriers for food ingredients delivery. *Journal of Food Engineering*, *295*, 110451. https://doi.org/10.1016/j.jfoodeng.2020.110451

Cai, S., Sun, Z., Sun, P.-H., Gao, X., Ji, K., Tian, X., Ji, J., Hao, C., Soliman, F., Liu, C., Al-Sarireh, B., Griffiths, P., Hiscox, S., Jiang, W., & Ye, L. (2021). Reduced kinase D-interacting substrate of 220 kDa (Kidins220) in pancreatic cancer promotes EGFR/ERK signalling and disease progression. *International Journal of Oncology*, *58*(6). https://doi.org/10.3892/ijo.2021.5214

Carnero, A., & Paramio, J. M. (2014). The PTEN/PI3K/AKT pathway in vivo, cancer mouse models. *Frontiers in oncology, 4*, 252.

Cha, J.-H., Chan, L.-C., Li, C.-W., Hsu, J. L., & Hung, M.-C. (2019). Mechanisms controlling PD-L1 expression in cancer. *Molecular Cell*, *76*(3), 359–370. https://doi.org/10.1016/j.molcel.2019.09.030

Chae, W.-J., & Bothwell, A. L. M. (2018). Canonical and non-canonical wnt signaling in immune cells. *Trends in Immunology*, *39*(10), 830–847. https://doi.org/10.1016/j.it.2018.08.006

Chang, T.-C., Chin, Y.-T., Nana, A. W., Wang, S.-H., Liao, Y.-M., Chen, Y.-R., Shih, Y.-J., Changou, C. A., Yang, Y.-C. S., Wang, K., Whang-Peng, J., Wang, L.-S., Stain, S. C., Shih, A., Lin, H.-Y., Wu, C.-H., & Davis, P. J. (2018). Enhancement by nano-diamino-tetrac of antiproliferative action of gefitinib on colorectal cancer cells: Mediation by EGFR sialylation and PI3K activation. *Hormones and Cancer*, *9*(6), 420–432. https://doi.org/10.1007/s12672-018-0341-x

Chen, M., Sharma, A., Lin, Y., Wu, Y., He, Q., Gu, Y., Xu, Z. P., Monteiro, M., & Gu, W. (2019). Insluin and epithelial growth factor (EGF) promote programmed death ligand 1(PD-L1) production and transport in colon cancer stem cells. *BMC Cancer*, *19*(1). https://doi.org/10.1186/s12885-019-5364-3

Chen, N., Fang, W., Lin, Z., Peng, P., Wang, J., Zhan, J., Hong, S., Huang, J., Liu, L., Sheng, J., Zhou, T., Chen, Y., Zhang, H., & Zhang, L. (2017). KRAS mutation-induced upregulation of PD-L1 mediates immune escape in human lung adenocarcinoma. *Cancer Immunology, Immunotherapy: CII*, *66*(9), 1175–1187. https://doi.org/10.1007/s00262-017-2005-z

Cheng, T.-M., Chang, W.-J., Chu, H.-Y., De Luca, R., Pedersen, J. Z., Incerpi, S., Li, Z.-L., Shih, Y.-J., Lin, H.-Y., Wang, K., & Whang-Peng, J. (2021). Nano-Strategies targeting the integrin αvβ3 network for cancer therapy. *Cells*, *10*(7), 1684. https://doi.org/10.3390/cells10071684

Chin, Y.-T., He, Z.-R., Chen, C.-L., Chu, H.-C., Ho, Y., Su, P.-Y., Yang, Wang, K., Shih, Y.-J., Chen, Y.-R., Pedersen, J. Z., Incerpi, S., Nana, A. W., Tang, H.-Y., Lin, H.-Y., Mousa, S. A., Davis, P. J., & Whang-Peng, J. (2019). Tetrac and NDAT induce anti-proliferation via integrin αvβ3 in colorectal cancers with different K-RAS status. *Frontiers in Endocrinology*, *10*. https://doi.org/10.3389/fendo.2019.00130

Davis, P. J., Glinsky, G. V., Lin, H.-Y., Leith, J. T., Hercbergs, A., Tang, H.-Y., Ashur-Fabian, O., Incerpi, S., & Mousa, S. A. (2015). Cancer cell gene expression modulated from plasma membrane integrin αvβ3 by thyroid hormone and nanoparticulate tetrac. *Frontiers in Endocrinology*, *5*. https://doi.org/10.3389/fendo.2014.00240

Davis, P. J., & Mousa, S. A. (2016). Tetraiodothyroacetic acid at integrin αvβ3: A model of pharmaceutical anti-angiogenesis. *Elsevier EBooks*, 133–146. https://doi.org/10.1016/b978-0-12-802576-5.00009-7

Davis, P. J., Mousa, S. A., & Lin, H.-Y. (2018). Tetraiodothyroacetic acid (tetrac), integrin αvβ3 and disabling of immune checkpoint defense. *Future Medicinal Chemistry*, *10*(14), 1637–1639. https://doi.org/10.4155/fmc-2018-0123

Doi, T., Ishikawa, T., Okayama, T., Oka, K., Mizushima, K., Yasuda, T., Sakamoto, N., Katada, K., Kamada, K., Uchiyama, K., Handa, O., Takagi, T., Naito, Y., & Itoh, Y. (2017). The JAK/STAT pathway is involved in the upregulation of PD-L1 expression in pancreatic cancer cell lines. *Oncology Reports*, *37*(3), 1545–1554. https://doi.org/10.3892/or.2017.5399

Feng, M., Xiong, G., Cao, Z., Yang, G., Zheng, S., Song, X., You, L., Zheng, L., Zhang, T., & Zhao, Y. (2017). PD-1/PD-L1 and immunotherapy for pancreatic cancer. *Cancer Letters*, *407*, 57–65. https://doi.org/10.1016/j.canlet.2017.08.006

Fessler, J., Matson, V., & Gajewski, T. F. (2019). Exploring the emerging role of the microbiome in cancer immunotherapy. *Journal for ImmunoTherapy of Cancer*, *7*(1). https://doi.org/10.1186/s40425-019-0574-4

Fitzgerald, T. L., Lertpiriyapong, K., Cocco, L., Martelli, A. M., Libra, M., Candido, S., Montalto, G., Cervello, M., Steelman, L., Abrams, S. L., & McCubrey, J. A. (2015). Roles of EGFR and KRAS and their downstream signaling pathways in pancreatic cancer and pancreatic cancer stem cells. *Advances in Biological Regulation*, *59*, 65–81. https://doi.org/10.1016/j.jbior.2015.06.003

Gao, Y., Zhao, H., Wang, P., Wang, J., & Zou, L. (2018). The roles of SOCS3 and STAT3 in bacterial infection and inflammatory diseases. *Scandinavian Journal of Immunology*, *88*(6). https://doi.org/10.1111/sji.12727

Gao, Z., Chen, J.-F., Li, X.-G., Shi, Y.-H., Tang, Z., Liu, W.-R., Zhang, X., Huang, A., Luo, X.-M., Gao, Q., Shi, G.-M., Ke, A.-W., Zhou, J., Fan, J., Fu, X.-T., & Ding, Z.-B. (2022). KRAS acting through ERK signaling stabilizes PD-L1 via inhibiting autophagy pathway in intrahepatic cholangiocarcinoma. *Cancer Cell International*, *22*(1). https://doi.org/10.1186/s12935-022-02550-w

Grapa, C. M., Mocan, T., Gonciar, D., Zdrehus, C., Mosteanu, O., Pop, T., & Mocan, L. (2019). Epidermal growth factor receptor and its role in pancreatic cancer treatment mediated by nanoparticles. *International Journal of Nanomedicine*, *Volume 14*, 9693–9706. https://doi.org/10.2147/ijn.s226628

Gu, X., & Minko, T. (2024). Targeted nanoparticle-based diagnostic and treatment options for pancreatic cancer. *Cancers*, *16*(8), 1589–1589. https://doi.org/10.3390/cancers16081589

Gu, Y., Yang, D., Zou, J., & Ma, W. (2010). Systematic interpretation of comutated genes in large-scale cancer mutation profiles. *Molecular Cancer Therapeutics*, *9*(8), 2186–2195. http://dx.doi.org/10.1158/1535-7163.MCT-10-0022

Halbrook, C. J., Lyssiotis, C. A., Magliano, M. P. di, & Maitra, A. (2023). Pancreatic cancer: Advances and challenges. *Cell*, *186*(8), 1729–1754. https://doi.org/10.1016/j.cell.2023.02.014

Heckl, S. M., Mau, F., Anke Senftleben, Daunke, T., Beckinger, S., Samir Abdullazade, Schreiber, S., Christoph Röcken, Sebens, S., & Heiner Schäfer. (2021). Programmed death-ligand 1 (PD-L1) expression is induced by insulin in pancreatic ductal adenocarcinoma cells pointing to its role in immune checkpoint control. *Medical Sciences*, *9*(3), 48–48. https://doi.org/10.3390/medsci9030048

Ho, Y., Li, Z.-L., Shih, Y.-J., Chen, Y.-R., Wang, K., Whang-Peng, J., Lin, H.-Y., & Davis, P. J. (2020). Integrin αvβ3 in the mediating effects of dihydrotestosterone and resveratrol on breast cancer cell proliferation. *International Journal of Molecular Sciences*, *21*(8), 2906–2906. https://doi.org/10.3390/ijms21082906

Hu, Z. I., & O'Reilly, E. M. (2024). Therapeutic developments in pancreatic cancer. *Nature Reviews Gastroenterology & Hepatology*, *21*(1), 7–24. https://doi.org/10.1038/s41575-023-00840-w

Huang, L., Hu, B., Ni, J., Wu, J., Jiang, W., Chen, C., Yang, L., Zeng, Y., Wan, R., Hu, G., & Wang, X. (2016). Transcriptional repression of SOCS3 mediated by IL-6/STAT3 signaling via DNMT1 promotes pancreatic cancer growth and metastasis. *Journal of Experimental & Clinical Cancer Research*, *35*(1). https://doi.org/10.1186/s13046-016-0301-7

Huang, T.-Y., Chang, T.-C., Chin, Y.-T., Pan, Y.-S., Chang, W.-J., Liu, F.-C., Hastuti, E. D., Chiu, S.-J., Wang, S.-H., Changou, C. A., Li, Z.-L., Chen, Y.-R., Chu, H.-R., Shih, Y.-J., Cheng, R. H., Wu, A., Lin, H.-Y., Wang, K., Whang-Peng, J., & Mousa, S. A. (2020). NDAT targets PI3K-mediated PD-L1 upregulation to reduce proliferation in gefitinib-resistant colorectal cancer. *Cells*, *9*(8), 1830–1830. https://doi.org/10.3390/cells9081830

Iacovelli, R., Nolè, F., Verri, E., Renne, G., Paglino, C., Santoni, M., Cossu Rocca, M., Giglione, P., Aurilio, G., Cullurà, D., Cascinu, S., & Porta, C. (2015). Prognostic role of PD-L1 expression in renal cell carcinoma. A systematic review and meta-analysis. *Targeted Oncology*, *11*(2), 143–148. https://doi.org/10.1007/s11523-015-0392-7

Javadrashid, D., Baghbanzadeh, A., Derakhshani, A., Leone, P., Silvestris, N., Racanelli, V., Solimando, A. G., & Baradaran, B. (2021). Pancreatic cancer signaling pathways, genetic alterations, and tumor microenvironment: The barriers affecting the method of treatment. *Biomedicines*, *9*(4), 373. https://doi.org/10.3390/biomedicines9040373

Karandish, F., & Mallik, S. (2016). Biomarkers and targeted therapy in pancreatic cancer. *Biomarkers in Cancer*, *8s1*, BIC.S34414. https://doi.org/10.4137/bic.s34414

Kim, K., Wu, H. G., & Jeon, S. R. (2015). Epidermal growth factor-induced cell death and radiosensitization in epidermal growth factor receptor-overexpressing cancer cell lines. *PubMed*, *35*(1), 245–253.

Kiyatkin, A., van Alderwerelt van Rosenburgh, I. K., Klein, D. E., & Lemmon, M. A. (2020). Kinetics of receptor tyrosine kinase activation define ERK signaling dynamics. *Science Signaling*, *13*(645), eaaz5267. https://doi.org/10.1126/scisignal.aaz5267

Kleeff, J., Korc, M., Apte, M., La Vecchia, C., Johnson, C. D., Biankin, A. V., Neale, R. E., Tempero, M., Tuveson, D. A., Hruban, R. H., & Neoptolemos, J. P. (2016). Pancreatic cancer. *Nature Reviews Disease Primers*, *2*(1). https://doi.org/10.1038/nrdp.2016.22

Koji Miyabayashi, Hideaki Ijichi, Dai Mohri, Tada, M., Yamamoto, K., Yoshinari Asaoka, Tsuneo Ikenoue, Tateishi, K., Nakai, Y., Hiroyuki Isayama, Morishita, Y., Masao Omata, Moses, H. L., & Koike, K. (2013). Erlotinib prolongs survival in pancreatic cancer by blocking gemcitabine-induced MAPK signals. *Cancer Research*, *73*(7), 2221–2234. https://doi.org/10.1158/0008-5472.can-12-1453

Lake, D., Corrêa, S. A. L., & Müller, J. (2016). Negative feedback regulation of the ERK1/2 MAPK pathway. *Cellular and Molecular Life Sciences*, *73*(23), 4397–4413. https://doi.org/10.1007/s00018-016-2297-8

Lavoie, H., Gagnon, J., & Therrien, M. (2020). ERK signalling: a master regulator of cell behaviour, life and fate. *Nature Reviews Molecular Cell Biology*, *21*(10), 607–632.

Lee, Y.-S., Chin, Y.-T., Shih, Y.-J., Nana, A. W., Chen, Y.-R., Wu, H.-C., Yang, Lin, H.-Y., & Davis, P. J. (2018). Thyroid hormone promotes β-Catenin activation and cell proliferation in colorectal cancer. *Hormones and Cancer*, *9*(3), 156–165. https://doi.org/10.1007/s12672-018-0324-y

Lee, Y.-S., Chin, Y.-T., Yang, Y.-C. S. H., Wei, P.-L., Wu, H.-C., Shih, A., Lu, Y.-T., Pedersen, J. Z., Incerpi, S., Liu, L. F., Lin, H.-Y., & Davis, P. J. (2016). The combination of tetraiodothyroacetic acid and cetuximab inhibits cell proliferation in colorectal cancers with different K-ras status. *Steroids*, *111*, 63–70. https://doi.org/10.1016/j.steroids.2016.03.006

Lei, Y., He, J., & Tang, Y. (2023). Long non-coding RNA and the tumor microenvironment: Prospects for clinical applications in breast cancer. *Critical Reviews in Oncology/Hematology*, *190*, 104102–104102. https://doi.org/10.1016/j.critrevonc.2023.104102

Levantini, E., Maroni, G., Del Re, M., & Tenen, D. G. (2022). EGFR signaling pathway as therapeutic target in human cancers. *Seminars in Cancer Biology*, *85*. https://doi.org/10.1016/j.semcancer.2022.04.002

Li, X., Lian, Z., Wang, S., Xing, L., & Yu, J. (2018). Interactions between EGFR and PD-1/PD-L1 pathway: Implications for treatment of NSCLC. *Cancer Letters*, *418*, 1–9. https://doi.org/10.1016/j.canlet.2018.01.005

Li, X., Ma, Q., Xu, Q., Liu, H., Lei, J., Duan, W., Bhat, K., Wang, F., Wu, E., & Wang, Z. (2012). SDF-1/CXCR4 signaling induces pancreatic cancer cell invasion and epithelial–mesenchymal transition in vitro through non-canonical activation of Hedgehog pathway. *Cancer Letters*, *322*(2), 169–176. https://doi.org/10.1016/j.canlet.2012.02.035

Li, X., Wu, C., Chen, N., Gu, H., Yen, A., Cao, L., Wang, E., & Wang, L. (2016). PI3K/Akt/mTOR signaling pathway and targeted therapy for glioblastoma. *Oncotarget*, *7*(22). https://doi.org/10.18632/oncotarget.7961

Lin, H., Chin, Y., Yang, Lai, H., Whang-Peng, J., Liu, L. F., Tang, H., & Davis, P. J. (2016). Thyroid hormone, cancer, and apoptosis. *Comprehensive Physiology*, 1221–1237. https://doi.org/10.1002/cphy.c150035

Lin, H.-Y., Chen, Y.-R., Li, Z.-L., Shih, Y.-J., Davis, P., Whang-Peng, J., & Wang, K. (2019). Thyroid hormone, PD-L1, and cancer. *Journal of Cancer Research and Practice*, *6*(4), 162. https://doi.org/10.4103/jcrp.jcrp_26_19

Lin, S., Yu Tang Chin, Ho, Y., Szu Yi Chou, Yang, Y., André Wendindondé Nana, Su, K.-W., Yee Tong Lim, Wang, K., Lee, S. Y., Ya Jung Shih, Yi Ru Chen, Whang-Peng, J., Davis, P. J., Hung Yun Lin, & Fu, E. (2018). Nano-diamino-tetrac (NDAT) inhibits PD-L1 expression which is essential for proliferation in oral cancer cells. *Food and Chemical Toxicology*, *120*, 1–11. https://doi.org/10.1016/j.fct.2018.06.058

Liu, J., Zhang, J., Gao, Y., Jiang, Y., Guan, Z., Xie, Y., Hu, J., & Chen, J. (2023). Barrier permeation and improved nanomedicine delivery in tumor microenvironments. *Cancer Letters*, *562*, 216166–216166. https://doi.org/10.1016/j.canlet.2023.216166

Lu, S.-W., Pan, H.-C., Hsu, Y.-H., Chang, K.-C., Wu, L.-W., Chen, W.-Y., & Chang, M.-S. (2020). IL-20 antagonist suppresses PD-L1 expression and prolongs survival in pancreatic cancer models. *Nature Communications*, *11*(1). https://doi.org/10.1038/s41467-020-18244-8

Ludmila Danilova, Won Jin Ho, Zhu, Q., Vithayathil, T., Ana De Jesus-Acosta, Azad, N. S., Laheru, D. A., Fertig, E. J., Anders, R. A., Jaffee, E. M., & Yarchoan, M. (2019). Programmed cell death ligand-1 (PD-L1) and CD8 expression profiling identify an immunologic subtype of pancreatic ductal adenocarcinomas with favorable survival. *Cancer Immunology Research*, *7*(6), 886–895. https://doi.org/10.1158/2326-6066.cir-18-0822

Luo, G., Fan, Z., Gong, Y., Jin, K., Yang, C., Cheng, H., Huang, D., Ni, Q., Liu, C., & Yu, X. (2019). Characteristics and outcomes of pancreatic cancer by histological subtypes. *Pancreas*, *48*(6), 817–822. https://doi.org/10.1097/mpa.0000000000001338

Ma, Y.-C., Li, C., Gao, F., Xu, Y., Jiang, Z.-B., Liu, J.-X., & Jin, L.-Y. (2013). Epigallocatechin gallate inhibits the growth of human lung cancer by directly targeting the EGFR signaling pathway. *Oncology Reports*, *31*(3), 1343–1349. https://doi.org/10.3892/or.2013.2933

Mace, T. A., Shakya, R., Pitarresi, J. R., Swanson, B. J., McQuinn, C., Loftus, S., Nordquist, E., Zobeida Cruz-Monserrate, Yu, L., Young, G. S., Zhong, X., Zimmers, T. A., Ostrowski, M. C., Ludwig, T., Bloomston, M., Tanios Bekaii-Saab, & Lesinski, G. B. (2016). IL-6 and PD-L1 antibody blockade combination therapy reduces tumour progression in murine models of pancreatic cancer. *Gut*, *67*(2), 320–332. https://doi.org/10.1136/gutjnl-2016-311585

Margetis, N., Kouloukoussa, M., Pavlou, K., Vrakas, S., & Mariolois-Sapsakos, T. (2017). K-ras mutations as the earliest driving force in a subset of colorectal carcinomas. *In Vivo*, *31*(4), 527–542. https://doi.org/10.21873/invivo.11091

Means, A. L. (2014). Cell of origin and mouse models for pancreatic cancer. *Pathobiology of Human Disease*, 2274–2283. https://doi.org/10.1016/b978-0-12-386456-7.04906-6

Meyers, N., Gérard, C., Lemaigre, F. P., & Jacquemin, P. (2020). Differential impact of the ERBB receptors EGFR and ERBB2 on the initiation of precursor lesions of pancreatic ductal adenocarcinoma. *Scientific Reports*, *10*(1). https://doi.org/10.1038/s41598-020-62106-8

Mizrahi, J. D., Surana, R., Valle, J. W., & Shroff, R. T. (2020). Pancreatic cancer. *The Lancet*, *395*(10242), 2008–2020. https://doi.org/10.1016/S0140-6736(20)30974-0

Mucileanu, A., Chira, R., & Mircea, P. A. (2021). PD-1/PD-L1 expression in pancreatic cancer and its implication in novel therapies. *Medicine and Pharmacy Reports*, *94*(4). 402. https://doi.org/10.15386/mpr-2116

Neoptolemos, J. P., Kleeff, J., Michl, P., Costello, E., Greenhalf, W., & Palmer, D. H. (2018). Therapeutic developments in pancreatic cancer: Current and future perspectives. *Nature Reviews Gastroenterology & Hepatology*, *15*(6), 333–348. https://doi.org/10.1038/s41575-018-0005-x

Neoptolemos, J. P., Palmer, D. H., Ghaneh, P., Psarelli, E. E., Valle, J. W., Halloran, C. M., Faluyi, O., O'Reilly, D. A., Cunningham, D., Wadsley, J., Darby, S., Meyer, T., Gillmore, R., Anthoney, A., Lind, P., Glimelius, B., Falk, S., Izbicki, J. R., Middleton, G. W., & Cummins, S. (2017). Comparison of adjuvant gemcitabine and capecitabine with gemcitabine monotherapy in patients with resected pancreatic cancer (ESPAC-4): A multicentre, open-label, randomised, phase 3 trial. *The Lancet*, *389*(10073), 1011–1024. https://doi.org/10.1016/s0140-6736(16)32409-6

Oliveira-Cunha, M., Newman, W. G., & Siriwardena, A. K. (2011). Epidermal growth factor receptor in pancreatic cancer. *Cancers*, *3*(2), 1513–1526. https://doi.org/10.3390/cancers3021513

Park, H., Bang, J.-H., Nam, A.-R., Park, J. E., Jin, M. H., Bang, Y.-J., & Oh, D.-Y. (2019). Prognostic implications of soluble programmed death-ligand 1 and its dynamics during chemotherapy in unresectable pancreatic cancer. *Scientific Reports*, *9*(1). https://doi.org/10.1038/s41598-019-47330-1

Park, W., Chawla, A., & O'Reilly, E. M. (2021). Pancreatic cancer. *JAMA*, *326*(9), 851–862. https://doi.org/10.1001/jama.2021.13027

Pearson, H. B., Li, J., Meniel, V. S., Fennell, C. M., Waring, P., Montgomery, K. G., Rebello, R. J., Macpherson, A. A., Koushyar, S., Furic, L., Cullinane, C., Clarkson, R. W., Smalley, M. J., Simpson, K. J., Phesse, T. J., Shepherd, P. R., Humbert, P. O., Sansom, O. J., & Phillips, W. A. (2018). Identification of pik3ca mutation as a genetic driver of prostate cancer that cooperates with pten loss to accelerate progression and castration-resistant growth. *Cancer Discovery*, *8*(6), 764–779. https://doi.org/10.1158/2159-8290.cd-17-0867

Peer, D., Karp, J., Hong, S., Farokhzad, O., Margalit, R., & Langer, R. (2020). *Nanocarriers as an emerging platform for cancer therapy* (1st ed., pp. 61–91).

Poh, A. R., & Ernst, M. (2023). Functional roles of SRC signaling in pancreatic cancer: Recent insights provide novel therapeutic opportunities. *Oncogene*, 1–16. https://doi.org/10.1038/s41388-023-02701-x

Pramanik, K., Makena, M., Bhowmick, K., & Pandey, M. (2018). Advancement of NF-κB signaling pathway: A novel target in pancreatic cancer. *International Journal of Molecular Sciences*, *19*(12), 3890. https://doi.org/10.3390/ijms19123890

Qin, T., Zeng, Y., Qin, G., Xu, F., Lu, J., Fang, W., Xue, C., Zhan, J., Zhang, X., Zheng, Q., Peng, R., Yuan, Z., Zhang, L., & Wang, S. (2015). High PD-L1 expression was associated with poor prognosis in 870 Chinese patients with breast cancer. *Oncotarget*, *6*(32). https://doi.org/10.18632/oncotarget.5583

Qin, Y., Han, S., Yu, Y., Qi, D., Ran, M., Yang, M., Liu, Y., Li, Y., Lu, L., Liu, Y., & Li, Y. (2024). Lenvatinib in hepatocellular carcinoma: Resistance mechanisms and strategies for improved efficacy. *Liver International*, *44*(8), 1808–1831. https://doi.org/10.1111/liv.15953

Ruan, Z., Liang, M., Shang, L., Lai, M., Deng, X., & Su, X. (2021). Shikonin-mediated PD-L1 degradation suppresses immune evasion in pancreatic cancer by inhibiting NF-κB/STAT3 and NF-κB/CSN5 signaling pathways. *Pancreatology*, *21*(3), 630–641. https://doi.org/10.1016/j.pan.2021.01.023

Rubio, K., Romero-Olmedo, A. J., Sarvari, P., Swaminathan, G., Ranvir, V. P., Rogel-Ayala, D. G., ... & Barreto, G. (2023). Non-canonical integrin signaling activates EGFR and RAS-MAPK-ERK signaling in small cell lung cancer. *Theranostics, 13*(8), 2384.

Sasada, T., Azuma, K., Ohtake, J., & Fujimoto, Y. (2016). Immune responses to epidermal growth factor receptor (EGFR) and their application for cancer treatment. *Frontiers in Pharmacology*, *7*. https://doi.org/10.3389/fphar.2016.00405

Schmohl, K. A., Mueller, A. M., Dohmann, M., Spellerberg, R., Urnauer, S., Schwenk, N., Ziegler, S. I., Bartenstein, P., Nelson, P. J., & Spitzweg, C. (2019). Integrin αvβ3-Mediated effects of thyroid hormones on mesenchymal stem cells in tumor angiogenesis. *Thyroid*, *29*(12), 1843–1857. https://doi.org/10.1089/thy.2019.0413

Sharma, N., Arya, G., Kumari, R., Gupta, N., & Nimesh, S. (2019). Evaluation of anticancer activity of silver nanoparticles on the A549 human lung carcinoma cell lines through alamar blue assay. *BIO-PROTOCOL*, *9*(1). https://doi.org/10.21769/bioprotoc.3131

Shen, W., Tao, G., Zhang, Y., Cai, B., Sun, J., & Tian, Z. (2017). TGF-β in pancreatic cancer initiation and progression: two sides of the same coin. *Cell & Bioscience*, *7*(1). https://doi.org/10.1186/s13578-017-0168-0

Shi, M., Hou, J., Shao, S., Liang, W., Wang, S., Yang, Y., Guo, Z., & Pan, F. (2023). Short-Term starvation weakens the efficacy of cell cycle specific chemotherapy drugs through G1 arrest. *International Journal of Molecular Sciences*, *24*(3), 2498–2498. https://doi.org/10.3390/ijms24032498

Siegel, R. L., Giaquinto, A. N., & Jemal, A. (2024). Cancer statistics, 2024. *CA: A Cancer Journal for Clinicians*, *74*(1), 12–49. https://doi.org/10.3322/caac.21820

Song, M.-K., Park, B.-B., & Uhm, J. (2019). Understanding immune evasion and therapeutic targeting associated with PD-1/PD-L1 pathway in diffuse large b-cell lymphoma. *International Journal of Molecular Sciences*, *20*(6), 1326. https://doi.org/10.3390/ijms20061326

Spada, M., Piras, C., Diana, G., Vera Piera Leoni, Daniela Virginia Frau, Serreli, G., Simbula, G., Loi, R., Noto, A., Murgia, F., Caria, P., & Atzori, L. (2023). Glutamine starvation affects cell cycle, oxidative homeostasis and metabolism in colorectal cancer cells. *Antioxidants*, *12*(3), 683–683. https://doi.org/10.3390/antiox12030683

Stutvoet, T. S., Kol, A., Vries, E. G., Bruyn, M., Fehrmann, R. S., Terwisscha van Scheltinga, A. G., & Jong, S. (2019). MAPK pathway activity plays a key role in PD-L1 expression of lung adenocarcinoma cells. *The Journal of Pathology*, *249*(1), 52–64. https://doi.org/10.1002/path.5280

Tahara, H., Matsuda, S., Yamamoto, Y., Yoshizawa, H., Fujita, M., Katsuoka, Y., & Kasahara, T. (2017). High-content image analysis (HCIA) assay has the highest correlation with direct counting cell suspension compared to the ATP, WST-8 and Alamar blue assays for measurement of cytotoxicity. *Journal of Pharmacological and Toxicological Methods*, *88*, 92–99. https://doi.org/10.1016/j.vascn.2017.08.003

Togashi, Y., Hayashi, H., Terashima, M., de Velasco, M. A., Sakai, K., Fujita, Y., Tomida, S., Nakagawa, K., & Nishio, K. (2015). Inhibition of β-Catenin enhances the anticancer effect of irreversible EGFR-TKI in EGFR-mutated non–small-cell lung cancer with a T790M mutation. *Journal of Thoracic Oncology*, *10*(1), 93–101. https://doi.org/10.1097/jto.0000000000000353

Torres, C., Linares, A., Alejandre, M. J., Palomino-Morales, R. J., Delgado, J. R., & Perales, S. (2016). Interplay between gemcitabine and erlotinib over pancreatic adenocarcinoma cells. *Pancreas*, *45*(2), 269–280. https://doi.org/10.1097/mpa.0000000000000452

Trembath, D. G. (2016). Molecular testing for glioblastoma. *Elsevier EBooks*, 339–347. https://doi.org/10.1016/b978-0-12-800886-7.00026-1

Valsecchi, M. E., McDonald, M., Brody, J. R., Hyslop, T., Freydin, B., Yeo, C. J., Solomides, C., Peiper, S. C., & Witkiewicz, A. K. (2011). Epidermal growth factor receptor and insulinlike growth factor 1 receptor expression predict poor survival in pancreatic ductal adenocarcinoma. *Cancer*, *118*(14), 3484–3493. https://doi.org/10.1002/cncr.26661

Viegas, C., Patrício, A. B., Prata, J., Fonseca, L., Macedo, A. S., Duarte, S. O. D., & Fonte, P. (2023). Advances in pancreatic cancer treatment by nano-based drug delivery systems. *Pharmaceutics*, *15*(9), 2363. https://doi.org/10.3390/pharmaceutics15092363

Wee, P., & Wang, Z. (2017). Epidermal growth factor receptor cell proliferation signaling pathways. *Cancers*, *9*(12), 52.

Wharry, C. E., Haines, K. M., Carroll, R. G., & May, M. J. (2009). Constitutive noncanonical NFκB signaling in pancreatic cancer cells. *Cancer Biology & Therapy*, *8*(16), 1567–1576. https://doi.org/10.4161/cbt.8.16.8961

Wilson, H. M. (2014). SOCS proteins in macrophage polarization and function. *Frontiers in immunology, 5*, 357.

Wood, L. D., Canto, M. I., Jaffee, E. M., & Simeone, D. M. (2022). Pancreatic cancer: Pathogenesis, screening, diagnosis and treatment. *Gastroenterology*, *163*(2). https://doi.org/10.1053/j.gastro.2022.03.056

Wu, M., Huang, Q., Xie, Y., Wu, X., Ma, H., Zhang, Y., & Xia, Y. (2022). Improvement of the anticancer efficacy of PD-1/PD-L1 blockade via combination therapy and PD-L1 regulation. *Journal of Hematology & Oncology*, *15*(1). https://doi.org/10.1186/s13045-022-01242-2

Wu, S.-J., Arivajiagane Arundhathi, Wang, H.-C., Chen, C.-Y., Cheng, T.-M., Yuan, S.-S. F., & Wang, Y.-M. (2021). Migration and invasion of NSCLC suppressed by the downregulation of Src/focal adhesion kinase using single, double and tetra domain anti- CEACAM6 antibodies. *Translational Oncology*, *14*(7), 101057–101057. https://doi.org/10.1016/j.tranon.2021.101057

Xu, Z., Zhang, Y., Jiang, J., Yang, Y., Shi, R., Hao, B., Zhang, Z., Huang, Z., Kim, J. W., & Zhang, G. (2010). Epidermal growth factor induces HCCR expression via PI3K/Akt/mTOR signaling in PANC-1 pancreatic cancer cells. *BMC Cancer*, *10*(1). https://doi.org/10.1186/1471-2407-10-161

Yan, R., Li, J., Zhou, Y., Yao, L., Sun, R., Xu, Y., Ge, Y., & An, G. (2020). Inhibition of DCLK1 down-regulates PD-L1 expression through Hippo pathway in human pancreatic cancer. *Life Sciences*, *241*, 117150. https://doi.org/10.1016/j.lfs.2019.117150

Yang, Y.-C. S. H., Ko, P.-J., Pan, Y.-S., Lin, H.-Y., Whang-Peng, J., Davis, P. J., & Wang, K. (2021). Role of thyroid hormone-integrin αvβ3-signal and therapeutic strategies in colorectal cancers. *Journal of Biomedical Science*, *28*(1). https://doi.org/10.1186/s12929-021-00719-5

Yin, H., Pu, N., Chen, Q., Zhang, J., Zhao, G., Xu, X., Wang, D., Kuang, T., Jin, D., Lou, W., & Wu, W. (2021). Gut-derived lipopolysaccharide remodels tumoral microenvironment and synergizes with PD-L1 checkpoint blockade via TLR4/MyD88/AKT/NF-κB pathway in pancreatic cancer. *Cell Death and Disease*, *12*(11). https://doi.org/10.1038/s41419-021-04293-4

Zang, M., Zhang, Y., Zhang, B., Hu, L., Li, J., Fan, Z., Wang, H., Su, L., Zhu, Z., Li, C., Yan, C., Gu, Q., Liu, B., & Yan, M. (2015). CEACAM6 promotes tumor angiogenesis and vasculogenic mimicry in gastric cancer via FAK signaling. *Biochimica et Biophysica Acta (BBA) - Molecular Basis of Disease*, *1852*(5), 1020–1028. https://doi.org/10.1016/j.bbadis.2015.02.005

Zhang, N., Zeng, Y., Du, W., Zhu, J., Shen, D., Liu, Z., & Huang, J. (2016). The EGFR pathway is involved in the regulation of PD-L1 expression via the IL-6/JAK/STAT3 signaling pathway in EGFR-mutated non-small cell lung cancer. *International Journal of Oncology*, *49*(4), 1360–1368. https://doi.org/10.3892/ijo.2016.3632

Zhang, W., Pang, Q., Yan, C., Wang, Q., Yang, J., Yu, S., Liu, X., Yuan, Z., Wang, P., & Xiao, Z. (2017). Induction of PD-L1 expression by epidermal growth factor receptor–mediated signaling in esophageal squamous cell carcinoma. *OncoTargets and Therapy*, *Volume 10*, 763–771. https://doi.org/10.2147/ott.s118982

Zhao, Q., Chen, S., Zhu, Z., Yu, L., Ren, Y., Jiang, M., Weng, J., & Li, B. (2018). miR-21 promotes EGF-induced pancreatic cancer cell proliferation by targeting Spry2. *Cell Death & Disease*, *9*(12), 1–16. https://doi.org/10.1038/s41419-018-1182-9

Zhu, H., Li, T., Du, Y., & Li, M. (2018). Pancreatic cancer: Challenges and opportunities. *BMC Medicine*, *16*(1). https://doi.org/10.1186/s12916-018-1215-3