

References

- Ahmed, S., Bradshaw, A.-D., Gera, S., Dewan, M., & Xu, R. (2017). The TGF- β /Smad4 Signaling Pathway in Pancreatic Carcinogenesis and Its Clinical Significance. *Journal of Clinical Medicine*, 6(1), 5. <https://doi.org/10.3390/jcm6010005>
- American Cancer Society. (2024). *Pancreatic Cancer Risk Factors*. [Www.cancer.org. https://www.cancer.org/cancer/types/pancreatic-cancer/causes-risks-prevention/risk-factors.html](https://www.cancer.org/cancer/types/pancreatic-cancer/causes-risks-prevention/risk-factors.html)
- Barbiero, M., Cirillo, L., Sapthaswaran Veerapathiran, Coates, C., Ruffilli, C., & Pines, J. (2022). Cell cycle-dependent binding between Cyclin B1 and Cdk1 revealed by time-resolved fluorescence correlation spectroscopy. *Open Biology*, 12(6). <https://doi.org/10.1098/rsob.220057>
- Barnum, K. J., & O'Connell, M. J. (2014). Cell Cycle Regulation by Checkpoints. *Methods in Molecular Biology*, 1170, 29–40. https://doi.org/10.1007/978-1-4939-0888-2_2
- Baslan, T., Morris, J. P., Zhao, Z., Reyes, J., Ho, Y.-J., Tsanov, K. M., Bermeo, J., Tian, S., Zhang, S., Askan, G., Yavas, A., Lecomte, N., Erakky, A., Varghese, A. M., Zhang, A., Kendall, J., Ghiban, E., Chorbadjiev, L., Wu, J., & Dimitrova, N. (2022). Ordered and deterministic cancer genome evolution after p53 loss. *Nature*, 608(7924), 795–802. <https://doi.org/10.1038/s41586-022-05082-5>
- Beishline, K., & Azizkhan-Clifford, J. (2014). Interplay Between the Cell Cycle and Double-Strand Break Response in Mammalian Cells. *Methods in Molecular Biology*, 41–59. https://doi.org/10.1007/978-1-4939-0888-2_3
- Bogumil, D., Stram, D., Preston, D. L., Pandol, S. J., Wu, A. H., McKean-Cowdin, R., Conti, D. V., & Veronica Wendy Setiawan. (2023). Excess pancreatic cancer risk due to smoking and modifying effect of quitting smoking: The Multiethnic Cohort Study. *Cancer Causes & Control*, 35(3), 541–548. <https://doi.org/10.1007/s10552-023-01811-x>

- Bretones, G., Delgado, M. D., & León, J. (2015). Myc and cell cycle control. *Biochimica et Biophysica Acta (BBA) - Gene Regulatory Mechanisms*, 1849(5), 506–516. <https://doi.org/10.1016/j.bbagr.2014.03.013>
- Chang, H. H. Y., Pannunzio, N. R., Adachi, N., & Lieber, M. R. (2017). Non-homologous DNA end joining and alternative pathways to double-strand break repair. *Nature Reviews Molecular Cell Biology*, 18(8), 495–506. <https://doi.org/10.1038/nrm.2017.48>
- Dai, Y., & Grant, S. (2010). New Insights into Checkpoint Kinase 1 in the DNA Damage Response Signaling Network. *Clinical Cancer Research*, 16(2), 376–383. <https://doi.org/10.1158/1078-0432.ccr-09-1029>
- Fang, Y.-T., Yang, W.-W., Niu, Y.-R., & Sun, Y.-K. (2023). Recent advances in targeted therapy for pancreatic adenocarcinoma. *World Journal of Gastrointestinal Oncology*, 15(4), 571–595. <https://doi.org/10.4251/wjgo.v15.i4.571>
- Ferlay, J., Ervik, M., Lam, F., Laversanne, M., Colombet, M., Mery, L., Piñeros, M., Znaor, A., Soerjomataram, I., & Bray, F. (2024). *Global Cancer Observatory: Cancer Today*. Lyon, France: International Agency for Research on Cancer. <https://gco.iarc.who.int/today>
- Guiducci, G., & Stojic, L. (2021). Long Noncoding RNAs at the Crossroads of Cell Cycle and Genome Integrity. *Trends in Genetics*, 37(6), 528–546. <https://doi.org/10.1016/j.tig.2021.01.006>
- Hanahan, D., & Weinberg, Robert A. (2011). Hallmarks of cancer: the next Generation. *Cell*, 144(5), 646–674. <https://doi.org/10.1016/j.cell.2011.02.013>
- Haydock, M. M., Sigdel, S., & Pacioles, T. (2018). Gemcitabine-induced skin necrosis. *SAGE Open Medical Case Reports*, 6, 2050313X1880926. <https://doi.org/10.1177/2050313x18809268>
- Hudson, D. F., Amor, D. J., Boys, A., Butler, K., Williams, L., Zhang, T., & Kalitsis, P. (2016). Loss of RMI2 Increases Genome Instability and Causes a Bloom-Like Syndrome. *PLOS Genetics*, 12(12), e1006483. <https://doi.org/10.1371/journal.pgen.1006483>

- Jackman, M., Marcozzi, C., Barbiero, M., Pardo, M., Yu, L., Tyson, A. L., Choudhary, J. S., & Pines, J. (2020). Cyclin B1-Cdk1 facilitates MAD1 release from the nuclear pore to ensure a robust spindle checkpoint. *Journal of Cell Biology*, 219(6). <https://doi.org/10.1083/jcb.201907082>
- Jain, A., & Bhardwaj, V. (2021). Therapeutic resistance in pancreatic ductal adenocarcinoma: Current challenges and future opportunities. *World Journal of Gastroenterology*, 27(39), 6527–6550. <https://doi.org/10.3748/wjg.v27.i39.6527>
- Lai, E., Ziranu, P., Spanu, D., Dubois, M., Pretta, A., Tolu, S., Camera, S., Liscia, N., Mariani, S., Persano, M., Migliari, M., Donisi, C., Demurtas, L., Pusceddu, V., Puzzoni, M., & Scartozzi, M. (2021). BRCA-mutant pancreatic ductal adenocarcinoma. *British Journal of Cancer*, 125(10), 1321–1332. <https://doi.org/10.1038/s41416-021-01469-9>
- Lambert, A., Gavaille, C., & Conroy, T. (2017). Current status on the place of FOLFIRINOX in metastatic pancreatic cancer and future directions. *Therapeutic Advances in Gastroenterology*, 10(8), 631–645. <https://doi.org/10.1177/1756283x17713879>
- Lee, K. Y., & Dutta, A. (2021). Chk1 promotes non-homologous end joining in G1 through direct phosphorylation of ASF1A. *Cell Reports*, 34(4), 108680. <https://doi.org/10.1016/j.celrep.2020.108680>
- Li, Y., He, X., Zhang, X., Xu, Y., Chen, W., Liu, X., & Xu, X. (2021). RMI2 is a prognostic biomarker and promotes tumor growth in hepatocellular carcinoma. *Clinical and Experimental Medicine*. <https://doi.org/10.1007/s10238-021-00742-8>
- Liben, M., & Warren, A. (2023). DELAYED STEROID THERAPY IN GEMCITABINE-INDUCED PNEUMONITIS. *CHEST*, 164(4), A3339. <https://doi.org/10.1016/j.chest.2023.07.2179>
- Lin, Y. C., & Prasanth, S. G. (2021). Replication initiation: Implications in genome integrity. *DNA repair*, 103, 103131. <https://doi.org/10.1016/j.dnarep.2021.103131>
- Liu, J., Nie, S., Gao, M., Jiang, Y., Wan, Y., Ma, X., Zhou, S., & Cheng, W. (2019). Identification of EPHX2 and RMI2 as two novel key genes in cervical squamous cell carcinoma by an integrated

- bioinformatic analysis. *Journal of cellular physiology*, 234(11), 21260–21273.
<https://doi.org/10.1002/jcp.28731>
- Liu, Y., & West, S. C. (2008). More complexity to the Bloom's syndrome complex. *Genes & development*, 22(20), 2737–2742. <https://doi.org/10.1101/gad.1732808>
- Lu, S., Ahmed, T., Du, P., & Wang, Y. (2017). Genomic Variations in Pancreatic Cancer and Potential Opportunities for Development of New Approaches for Diagnosis and Treatment. *International Journal of Molecular Sciences*, 18(6), 1201.
<https://doi.org/10.3390/ijms18061201>
- Luo, J. (2021). KRAS mutation in pancreatic cancer. *Seminars in Oncology*, 48(1), 10–18.
<https://doi.org/10.1053/j.seminoncol.2021.02.003>
- Luo, W., Wang, D., Chen, H., Ye, L., Qiu, J., Liu, Y., Wang, R., Weng, G., Liu, T., Su, D., Tao, J., Ding, C., Li, Y., & Zhang, T. (2023). Epidemiology of pancreatic cancer: New version, new vision. *Chinese Journal of Cancer Research*, 35(5), 438–450.
<https://doi.org/10.21147/j.issn.1000-9604.2023.05.03>
- Montalto, F. I., & De Amicis, F. (2020). Cyclin D1 in Cancer: A Molecular Connection for Cell Cycle Control, Adhesion and Invasion in Tumor and Stroma. *Cells*, 9(12), 2648.
<https://doi.org/10.3390/cells9122648>
- Moore, M. J., Goldstein, D., Hamm, J., Figer, A., Hecht, J. R., Gallinger, S., Au, H. J., Murawa, P., Walde, D., Wolff, R. A., Campos, D., Lim, R., Ding, K., Clark, G., Voskoglou-Nomikos, T., Ptasynski, M., & Parulekar, W. (2007). Erlotinib Plus Gemcitabine Compared With Gemcitabine Alone in Patients With Advanced Pancreatic Cancer: A Phase III Trial of the National Cancer Institute of Canada Clinical Trials Group. *Journal of Clinical Oncology*, 25(15), 1960–1966.
<https://doi.org/10.1200/jco.2006.07.9525>
- Morton, J. P., Timpson, P., Karim, S. A., Ridgway, R. A., Athineos, D., Doyle, B., Jamieson, N. B., Oien, K. A., Lowy, A. M., Brunton, V. G., Frame, M. C., Evans, T. R. J., & Sansom, O. J. (2010). Mutant p53 drives metastasis and overcomes growth arrest/senescence in pancreatic cancer.

- Proceedings of the National Academy of Sciences of the United States of America*, 107(1), 246–251. <https://doi.org/10.1073/pnas.0908428107>
- Mukund, A., Afridi, M. A., Karolak, A., Park, M. A., Permuth, J. B., & Rasool, G. (2024). Pancreatic Ductal Adenocarcinoma (PDAC): A Review of Recent Advancements Enabled by Artificial Intelligence. *Cancers*, 16(12), 2240. <https://doi.org/10.3390/cancers16122240>
- Murakawa, M., Kawahara, S., Takahashi, D., Yuto Kamioka, Yamamoto, N., Kobayashi, S., Ueno, M., Morimoto, M., Sho Sawazaki, Takahashi, H., Takashi Ohshima, Yukawa, N., Rino, Y., & Morinaga, S. (2023). Risk factors for early recurrence in patients with pancreatic ductal adenocarcinoma who underwent curative resection. *World Journal of Surgical Oncology*, 21(1). <https://doi.org/10.1186/s12957-023-03141-3>
- National Cancer Institute. (2011). <https://www.cancer.gov/publications/dictionaries/cancer-terms/def/genomic-instability>.
Www.cancer.gov.
<https://www.cancer.gov/publications/dictionaries/cancer-terms/def/genomic-instability>
- National Cancer Institute. (2023). *Cancer of the Pancreas - Cancer Stat Facts*. SEER; National Cancer Institute. <https://seer.cancer.gov/statfacts/html/pancreas.html>
- Nguyen, D.-D., Kim, E. Y., Sang, P. B., & Chai, W. (2020). Roles of OB-Fold Proteins in Replication Stress. *Frontiers in Cell and Developmental Biology*, 8. <https://doi.org/10.3389/fcell.2020.574466>
- Patil, M., Pabla, N., & Dong, Z. (2013). Checkpoint kinase 1 in DNA damage response and cell cycle regulation. *Cellular and Molecular Life Sciences*, 70(21), 4009–4021. <https://doi.org/10.1007/s00018-013-1307-3>
- Pellarin, I., Dall'Acqua, A., Favero, A., Segatto, I., Rossi, V., Crestan, N., Karimbayli, J., Belletti, B., & Baldassarre, G. (2025). Cyclin-dependent protein kinases and cell cycle regulation in biology and disease. *Signal Transduction and Targeted Therapy*, 10(1). <https://doi.org/10.1038/s41392-024-02080-z>

- Petsalaki, E., & Zachos, G. (2020). DNA damage response proteins regulating mitotic cell division: double agents preserving genome stability. *The FEBS Journal*, 287(9), 1700–1721. <https://doi.org/10.1111/febs.15240>
- Principe, D. R., Underwood, P. W., Korc, M., Trevino, J. G., Munshi, H. G., & Rana, A. (2021). The Current Treatment Paradigm for Pancreatic Ductal Adenocarcinoma and Barriers to Therapeutic Efficacy. *Frontiers in Oncology*, 11. <https://doi.org/10.3389/fonc.2021.688377>
- Prabahar, A., Zamora, R., Barclay, D., Yin, J., Ramamoorthy, M., Bagheri, A., Johnson, S. A., Badylak, S., Yoram Vodovotz, & Jiang, P. (2024). Unraveling the complex relationship between mRNA and protein abundances: a machine learning-based approach for imputing protein levels from RNA-seq data. *NAR Genomics and Bioinformatics*, 6(1). <https://doi.org/10.1093/nargab/lqae019>
- Ren, S., Qian, L.-C., Cao, Y.-Y., Daniels, M. J., Song, L.-N., Tian, Y., & Wang, Z.-Q. (2024). Computed tomography-based radiomics diagnostic approach for differential diagnosis between early- and late-stage pancreatic ductal adenocarcinoma. *World Journal of Gastrointestinal Oncology*, 16(4), 1256–1267. <https://doi.org/10.4251/wjgo.v16.i4.1256>
- Reyngold, M., O'Reilly, E. M., Varghese, A. M., Fiasconaro, M., Zinovoy, M., Romesser, P. B., Wu, A., Hajj, C., Cuaron, J. J., Tuli, R., Hilal, L., Khalil, D., Park, W., Yorke, E. D., Zhang, Z., Yu, K. H., & Crane, C. H. (2021). Association of Ablative Radiation Therapy With Survival Among Patients With Inoperable Pancreatic Cancer. *JAMA Oncology*, 7(5), 735. <https://doi.org/10.1001/jamaoncol.2021.0057>
- RM12 RecQ mediated genome instability 2 [Homo sapiens (human)] - Gene - NCBI*. (2025). Nih.gov. <https://www.ncbi.nlm.nih.gov/gene/116028>
- Sarantis, P., Koustas, E., Papadimitropoulou, A., Papavassiliou, A. G., & Karamouzis, M. V. (2020). Pancreatic ductal adenocarcinoma: Treatment hurdles, tumor microenvironment and immunotherapy. *World Journal of Gastrointestinal Oncology*, 12(2), 173–181. <https://doi.org/10.4251/wjgo.v12.i2.173>

- Seshacharyulu, P., Baine, M. J., Soucek, J. J., Menning, M., Kaur, S., Yan, Y., Ouellette, M. M., Jain, M., Lin, C., & Batra, S. K. (2017). Biological determinants of radioresistance and their remediation in pancreatic cancer. *Biochimica et biophysica acta. Reviews on cancer*, 1868(1), 69–92. <https://doi.org/10.1016/j.bbcan.2017.02.003>
- Sharma, A., & Chari, S. T. (2018). Pancreatic cancer and diabetes mellitus. *Current treatment options in gastroenterology*, 16, 466-478. Chicago
- Singh, T. R., Ali, A. M., Busygina, V., Raynard, S., Fan, Q., Du, C. ., Andreassen, P. R., Sung, P., & Meetei, A. R. (2008). BLAP18/RMI2, a novel OB-fold-containing protein, is an essential component of the Bloom helicase-double Holliday junction dissolvosome. *Genes & Development*, 22(20), 2856–2868. <https://doi.org/10.1101/gad.1725108>
- Sun, G., Wu, Y., Li, J., Yang, M., Xu, H., Li, Y., Tong, P., Shao, R., Liu, Y., & Kong, X. (2025). Quercetin liposomes conjugated with hyaluronidase: An efficient drug delivery system to block pancreatic cancer. *Journal of Controlled Release*, 382, 113642. <https://doi.org/10.1016/j.jconrel.2025.113642>
- Tsuda, M., Fukuda, A., Kawai, M., Araki, O., & Seno, H. (2021). The role of the SWI/SNF chromatin remodeling complex in pancreatic ductal adenocarcinoma. *Cancer science*, 112(2), 490–497.
- Vermeulen, K., Van Bockstaele, D. R., & Berneman, Z. N. (2003). The cell cycle: a review of regulation, deregulation and therapeutic targets in cancer. *Cell Proliferation*, 36(3), 131–149. <https://doi.org/10.1046/j.1365-2184.2003.00266.x>
- Wang, H., Mannava, S., Grachtchouk, V., Zhuang, D., Soengas, M. S., Gudkov, A. V., Prochownik, E. V., & Nikiforov, M. A. (2008). c-Myc depletion inhibits proliferation of human tumor cells at various stages of the cell cycle. *Oncogene*, 27(13), 1905–1915. <https://doi.org/10.1038/sj.onc.1210823>
- Wijnen, R., Pecoraro, C., Carbone, D., Fiuji, H., Avan, A., Peters, G. J., Giovannetti, E., & Diana, P. (2021). Cyclin Dependent Kinase-1 (CDK-1) Inhibition as a Novel Therapeutic Strategy against

- Pancreatic Ductal Adenocarcinoma (PDAC). *Cancers*, 13(17), 4389.
<https://doi.org/10.3390/cancers13174389>
- Yang, V. W. (2012). The Cell Cycle. *Physiology of the Gastrointestinal Tract*, 1, 451–471.
<https://doi.org/10.1016/b978-0-12-382026-6.00015-4>
- Yasuda, S., Nagai, M., Nakamura, K., Matsuo, Y., & Sho, M. (2025). Role of radiotherapy in surgical approaches to pancreatic cancer treatment: A narrative review. *Annals of Gastroenterological Surgery*, 9(3), 418–428. <https://doi.org/10.1002/ags3.70012>
- Zhang, W., Liu, B., Wu, W., Li, L., Broom, B. M., Basourakos, S. P., Korentzelos, D., Luan, Y., Wang, J., Yang, G., Park, S., Azad, A. K., Cao, X., Kim, J., Corn, P. G., Logothetis, C. J., Aparicio, A. M., Chinnaiyan, A. M., Navone, N., Troncoso, P., ... Thompson, T. C. (2018). Targeting the MYCN-PARP-DNA Damage Response Pathway in Neuroendocrine Prostate Cancer. *Clinical cancer research : an official journal of the American Association for Cancer Research*, 24(3), 696–707. <https://doi.org/10.1158/1078-0432.CCR-17-1872>
- Zhan, W., Liu, Y., Gao, Y., Gong, R., Wang, W., Zhang, R., Wu, Y., Kang, T., & Wei, D. (2020). RMI2 plays crucial roles in growth and metastasis of lung cancer. *Signal Transduction and Targeted Therapy*, 5(1). <https://doi.org/10.1038/s41392-020-00295-4>
- Zhang, L., Hao, C., Han, B., Zeng, G., Han, L., Cao, C., Liu, H., Zhong, Z., Zhao, X., Wang, J., & Zhang, Q. (2022). RMI2 is a novel prognostic and predictive biomarker for breast cancer. *Cancer Medicine*, 12(7), 8331–8350. <https://doi.org/10.1002/cam4.5533>