

Tobacco in Australia

Facts & Issues

Relevant news and research

3.3 Smoking and cancer

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Research:

Alqithami, SM, Machwe, A, & Orren, DK. (2024). Cigarette Smoke-Induced Epithelial-to-Mesenchymal Transition: Insights into Cellular Mechanisms and Signaling Pathways. *Cells*, 13(17). Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/39273025>

Asgharian, B, Price, O, Wasdo, S, Li, C, Peters, KO, Haskins, RM et al. (2024). The fate of an inhaled cigarette puff in the human respiratory tract. *Inhal Toxicol*, 1-13. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/38909354>

Jiang, Y, & Li, H. (2024). The effect of smoking on tumor immunoediting: Friend or foe? *Tob Induc Dis*, 22. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/38887597>

Mohr, T, Probst, E, Idel, C, Plotze-Martin, K, Fleckner, J, Rades, D et al. (2024). Different Influence Pattern of Conventional and Alternative Sources of Smoking on Adhesion Molecules and Cytokine Secretion in THP-1 Monocytes. *Anticancer Res*, 44(4), 1455-1464 Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/38537980>

Lee, T, George, CD, Jiang, C, Asgari, MM, Nijsten, T, Pardo, LM, & Choquet, H. (2024). Association between lifetime smoking and cutaneous squamous cell carcinoma: A 2-sample Mendelian randomization study. *JAAD Int*, 14, 69-76. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/38274396>

Nakayama, J, & Yamamoto, Y. (2023). Cancer-prone Phenotypes and Gene Expression Heterogeneity at Single-cell Resolution in Cigarette-smoking Lungs. *Cancer Res Commun*, 3(11), 2280-2291. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/37910161>

Seo, YS, Park, JM, Kim, JH, & Lee, MY. (2023). Cigarette Smoke-Induced Reactive Oxygen Species Formation: A Concise Review. *Antioxidants (Basel)*, 12(9). Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/37760035>

Yang, P. (2023). From Womb to Tomb: In Utero Exposure to Tobacco Smoke and Adult Cancers. *Mayo Clin Proc*, 98(8), 1116-1117. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/37536799>

Phua, ZJ, MacInnis, RJ, Hodge, AM, Lynch, BM, Hopper, JL, Smith-Warner, SA et al. (2023). Pre-diagnostic cigarette smoking and risk of second primary cancer: The Melbourne Collaborative Cohort Study. *Cancer Epidemiol*, 85, 102406. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/37390701>

Boo, HJ, Min, HY, Hwang, SJ, Lee, HJ, Lee, JW, Oh, SRet al. (2023). The tobacco-specific carcinogen NNK induces pulmonary tumorigenesis via nAChR/Src/STAT3-mediated activation of the renin-angiotensin system and IGF-1R signaling. *Exp Mol Med*. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/37258578>

Khan, AB, Patel, R, McDonald, MF, Goethe, E, English, C, Gadot, R et al. (2023). Integrated clinical genomic analysis reveals xenobiotic metabolic genes are downregulated in meningiomas of current smokers. *J Neurooncol*. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/37318677>

Alisoltani, A, Qiu, X, Jaroszewski, L, Sedova, M, Iyer, M, & Godzik, A. (2023). Gender differences in smoking-induced changes in the tumor immune microenvironment. *Arch Biochem Biophys*, 739, 109579. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/36933758>

Tran, TXM, Kim, S, Song, H, & Park, B. (2022). Longitudinal Changes in Smoking Habits in Women and Subsequent Risk of Cancer. *Am J Prev Med*. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/36050198>

The global burden of cancer attributable to risk factors, 2010-19: a systematic analysis for the Global Burden of Disease Study 2019. (2022). *Lancet*, 400(10352), 563-591. Retrieved from <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9395583/>

Patel, AV, Deubler, E, Teras, LR, Colditz, GA, Lichtman, CJ, Cance, WG, & Clarke, CA. (2022). Key risk factors for the relative and absolute 5-year risk of cancer to enhance cancer screening and prevention. *Cancer*, 128(19), 3502-3515. doi:<https://doi.org/10.1002/cncr.34396>

Jao, NC, Martinez-Cardoso, A, Vahora, M, & Tan, MM. (2022). The role of smoking history in longitudinal changes in C-reactive protein between Black and White older adults in the US. *Prev Med Rep*, 28, 101885. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/35836347>

Oswald, LB, Brownstein, NC, Whiting, J, Hoogland, AI, Saravia, S, Kirtane, K et al. (2022). Smoking Is Related to Worse Cancer-related Symptom Burden. *Oncologist*, 27(2), e176-e184. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/35641215>

Levin, MG, Nakao, T, Zekavat, SM, Koyama, S, Bick, AG, Niroula, A et al. (2022). Genetics of smoking and risk of clonal hematopoiesis. *Sci Rep*, 12(1), 7248. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/35508625>

Fuchs, HE, O'Connell, K, Du, M, Navarro, SL, Brasky, TM, & Kantor, ED. (2021). Vitamin B12 Supplementation and Vitamin B12 Blood Serum Levels: Evaluation of Effect Modification by Gender and Smoking Status. *Nutr Cancer*, 1-11. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/34817305>

Gudenkauf, FJ, & Thrift, AP. (2021). Preventable causes of cancer in Texas by race/ethnicity: tobacco smoking. *Epidemiol Health*, e2021046. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/34265892>

Astori, E, Garavaglia, ML, Colombo, G, Landoni, L, Portinaro, NM, Milzani, A, & Dalle Donne, I. (2021). Antioxidants in Smokers. *Nutr Res Rev*, 1-77. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/33926594>

Mohanapriya, S, Maheswaran, T, Ganapathy, N, Yoithaprabhunath, TR, Dineshshankar, J, Ilayaraja, V et al. (2021). Evaluation of DNA damage in tobacco associated human buccal cells using comet assay. *Med Pharm Rep*, 94(2), 214-219. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/34013193>

Kadam, S, Vandana, M, Patwardhan, S, & Kaushik, KS. (2021). Looking beyond the smokescreen: can the oral microbiome be a tool or target in the management of tobacco-associated oral cancer? *Ecancermedicalscience*, 15, 1179. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/33777172>

Nakhaee, S, Amirabadizadeh, A, Ataei, M, Ataei, H, Zardast, M, Shariatmadari, MR et al (2021). Comparison of serum concentrations of essential and toxic elements between cigarette smokers and non-smokers. *Environ Sci Pollut Res Int*. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/33721162>

King, B, Borland, R, Morphett, K, Gartner, C, Fielding, K, O'Connor, RJ et al (2021). 'It's all the other stuff!' How smokers understand (and misunderstand) chemicals in cigarettes and cigarette smoke. *Public Underst Sci*, 963662521991351. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/33627027>

Baiju, N, Sandanger, TM, Saetrom, P, & Nost, TH. (2021). Gene expression in blood reflects smoking exposure among cancer-free women in the Norwegian Women and Cancer (NOWAC) postgenome cohort. *Sci Rep*, 11(1), 680. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/33436844>

Ballesteros, S, Barguilla, I, Marcos, R, & Hernandez, A. (2021). Nanoceria, alone or in combination with cigarette-smoke condensate, induce transforming and epigenetic cancer-like features in vitro. *Nanomedicine (Lond)*. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/33501851>

Hopkins, RJ, Duan, F, Gamble, GD, Chiles, C, Cavadino, A, Billings, P et al (2021). Chr15q25 genetic variant (rs16969968) independently confers risk of lung cancer, COPD and smoking intensity in a prospective study of high-risk smokers. *Thorax*. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/33419953>

Laytragoon Lewin, N, Karlsson, JE, Robinsson, D, Fagerberg, M, Kentsson, M, Sayardoust, S et al (2021). Influence of single nucleotide polymorphisms among cigarette smoking and non-smoking patients with coronary artery disease, urinary bladder cancer and lung cancer. *PLoS One*, 16(1), e0243084. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/33507988>

Qi, F, Xu, Z, Zhang, H, Wang, R, Wang, Y, Jia, X et al (2021). Predicting the mortality of smoking attributable to cancer in Qingdao, China: A time-series analysis. *PLoS One*, 16(1), e0245769. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/33493221>

Shakeri, MT, Nezami, H, Nakhaee, S, Aaseth, J , & Mehrpour, O. (2021). Assessing Heavy Metal Burden Among Cigarette Smokers and Non-smoking Individuals in Iran: Cluster Analysis and Principal Component Analysis. *Biol Trace Elem Res*. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/33469740>

Al Bataineh, MT, Dash, NR, Elkhazendar, M, Alnusairat, DMH, Darwish, IMI, Al-Hajjaj, M S, & Hamid, Q. (2020). Revealing oral microbiota composition and functionality associated with heavy cigarette smoking. *J Transl Med*, 18(1), 421. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/33167991>

Prakash, AR, Nahar, P, Ashtekar, M, Natarajan, S, Singh, R, & Kulkarni, G. (2020). Detection of Salivary Alkaline Phosphatase Levels in Smokers, Diabetic Patients, Potentially Malignant Diseases and Oral Malignant Tumours. *J Pharm Bioallied Sci*, 12(Suppl 1), S430-S435. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/33149500>

Hua, Q, Liu, Y, Li, M, Chen, Y, Diao, Q, Zeng, H, & Jiang, Y. (2020). Tobacco-related exposure upregulates circ_0035266 to exacerbate inflammatory responses in human bronchial epithelial cells. *Toxicol Sci*. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/33107911>

Masjedi, MR, Dobaradaran, S, Keshmiri, S, Taghizadeh, F, Arfaeinia, H, Fanaei, F et al (2020). Use of toenail-bounded heavy metals to characterize occupational exposure and oxidative stress in workers of waterpipe/cigarette cafes. *Environ Geochem Health*. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/33098497>

King, C, Mulugeta, A, Nabi, F, Walton, R, Zhou, A, & Hypponen, E. (2020). Mendelian randomization case-control PheWAS in UK Biobank shows evidence of causality for smoking intensity in 28 distinct clinical conditions. *EClinicalMedicine*, 26, 100488. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/33089118>

Almutairi, M, Rouabchia, M, Sahab Almutairi, M, Al-Zahrani, M, Al-Numair, NS, Mohammad Alhadeq, A et al. (2020). Correlation between genetic variation in thymine DNA glycosylase and smoking behavior. *Gene*, 766, 145092. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/32916247>

Chen, Z, Wen, W, Cai, Q, Long, J, Wang, Y, Lin, W et al. (2020). From tobacco smoking to cancer mutational signature: a mediation analysis strategy to explore the role of epigenetic changes. *BMC Cancer*, 20(1), 880. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/32928150>

Reigle, J, Secic, D, Biesiada, J, Wetzel, C, Shamsaei, B, Chu, J et al. (2020). Tobacco smoking induces metabolic reprogramming of renal cell carcinoma. *J Clin Invest*. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/32970633>

Banday, AR, Papenberg, BW, & Prokunina-Olsson, L. (2020). When the Smoke Clears m(6)A from a Y Chromosome-Linked lncRNA, Men Get an Increased Risk of Cancer. *Cancer Res*, 80(13), 2718-2719. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/32616506>

Liu, YN, Guan, Y, Shen, J, Jia, YL, Zhou, JC, Sun, Y et al (2020). Shp2 positively regulates cigarette smoke-induced epithelial mesenchymal transition by mediating MMP-9 production. *Respir Res*, 21(1), 161. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/32586329>

Sarlak, S, Lalou, C, Amoedo, ND, & Rossignol, R. (2019). Metabolic reprogramming by tobacco-specific nitrosamines (TSNAs) in cancer. *Semin Cell Dev Biol*. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/31385764>

Vainshelboim, B, Chen, Z, Lima, RM, & Myers, J. (2019). Cardiorespiratory Fitness, Smoking Status, and Risk of Incidence and Mortality From Cancer: Findings From the Veterans Exercise Testing Study. *J Phys Act Health*, 16(12), 1098-1104. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/31385764>

Ahmadi-Motamayel, F, Falsafi, P, Abolsamadi, H, Goodarzi, MT, & Poorolajal, J. (2019). Salivary antioxidants and oxidative stress markers in male smokers. *Comb Chem High Throughput Screen*. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/31385764>

Song, M, & Giovannucci, E. (2019). Preventable incidence of carcinoma associated with adiposity, alcohol and physical inactivity according to smoking status in the United States. *Int J Cancer*. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/31369145>

Anukriti, Dhasmana, A., Uniyal, S., Somvanshi, P., Bhardwaj, U., Gupta, M., . . . Kesari, K. K. (2019). Investigation of Precise Molecular Mechanistic Action of Tobacco-Associated Carcinogen 'NNK

Induced Carcinogenesis: A System Biology Approach. *Genes (Basel)*, 10(8). Available from: <https://www.ncbi.nlm.nih.gov/pubmed/31357510>

Robsahm, TE, Heir, T, Sandvik, L, Prestgaard, E, Tretli, S, Eriksson, JE, & Falk, RS. (2019). Changes in midlife fitness, body mass index, and smoking influence cancer incidence and mortality: A prospective cohort study in men. *Cancer Med.* Available from: <https://www.ncbi.nlm.nih.gov/pubmed/31270954>

Pezzuto, A, Citarella, F, Croghan, I, & Tonini, G. (2019). The effects of cigarette smoking extracts on cell cycle and tumor spread: novel evidence. *Future Sci OA*, 5(5), FSO394. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/31205749>

Schuller, HM. (2019). The Neuro-Psychological Axis of Smoking-Associated Cancer. *J Immunol Sci*, 3(2), 1-5. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/31245796>

Aedo, G, Miranda, M, Chavez, MN, Allende, ML, & Egana, JT. (2019). A Reliable Preclinical Model to Study the Impact of Cigarette Smoke in Development and Disease. *Curr Protoc Toxicol*, e78. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/31058471>

Hartono, RK, Hamid, SA, & Hafizurrachman, M. (2019). Do the Number of Cigarettes Smokes per Day Contribute to the Incident of Malignant Cancer? *Asian Pac J Cancer Prev*, 20(5), 1403-1408. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/31127899>

Hydes, TJ, Burton, R, Inskip, H, Bellis, MA, & Sheron, N. (2019). A comparison of gender-linked population cancer risks between alcohol and tobacco: how many cigarettes are there in a bottle of wine? *BMC Public Health*, 19(1), 316. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/30917803>

McCambridge, J, & Morris, S. (2019). Comparing alcohol with tobacco indicates that it is time to move beyond tobacco exceptionalism. *Eur J Public Health*, 29(2), 200-201. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/30893438>

Adjei Boakye, E, Buchanan, P, Hinyard, L, Osazuwa-Peters, N, Simpson, MC, Schootman, M, & Piccirillo, JF. Trends in the risk and burden of second primary malignancy among survivors of smoking-related cancers in the United States. *Int J Cancer*, 2019. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/30613963>

Gallaway, MS, Henley, SJ, Steele, CB, Momin, B, Thomas, CC, Jamal, A et al. Surveillance for Cancers Associated with Tobacco Use - United States, 2010-2014. *MMWR Surveill Summ*, 2018, 67(12), 1-42. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6220819/pdf/ss6712a1.pdf>

Singhavi, H, Ahluwalia, JS, Stepanov, I, Gupta, PC, Gota, V, Chaturvedi, P, & Khariwala, SS. Tobacco carcinogen research to aid understanding of cancer risk and influence policy. *Laryngoscope Investig Otolaryngol*, 2018, 3(5), 372-376. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6209619/pdf/LIO2-3-372.pdf>

Mons, U, Gredner, T, Behrens, G, Stock, C, & Brenner, H. Cancers Due to Smoking and High Alcohol Consumption. *Dtsch Arztebl Int*, 2018, 115(35-36), 571-577. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/30236215>

Sanders NT, Dutson DJ, Durrant JW, Lewis JB, Wilcox SH, et al. Cigarette smoke extract (cse) induces rage-mediated inflammation in the ca9-22 gingival carcinoma epithelial cell line. *Arch Oral Biol*, 2017; 80:95-100. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/28399471>

Lugo A, Bosetti C, Peveri G, Rota M, Bagnardi V, et al. Dose-response relationship between cigarette smoking and site-specific cancer risk: Protocol for a systematic review with an original design combining umbrella and traditional reviews. *BMJ Open*, 2017; 7(10):e018930. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/29092902>

Little MP and Hendry JH. Mathematical models of tissue stem and transit target cell divisions and the risk of radiation- or smoking-associated cancer. *PLoS Comput Biol*, 2017; 13(2):e1005391. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/28196079>

El-Aarag SA, Mahmoud A, Hashem MH, Abd Elkader H, Hemeida AE, et al. In silico identification of potential key regulatory factors in smoking-induced lung cancer. *BMC Med Genomics*, 2017; 10(1):40. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/28592245>

Understanding how smoking increases cancer risk. *Cancer Discov*, 2017; 7(1):OF2. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/27913392>

Zheng Y, Li X, Jiang Y, Xu Y, Song B, et al. Promoter hypermethylation of wnt inhibitory factor-1 in patients with lung cancer: A systematic meta-analysis. *Medicine (Baltimore)*, 2016; 95(49):e5433. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/27930522>

Siegel LR, Miller KD, and Jemal A. Cancer statistics, 2016. *CA: A Cancer Journal for Clinicians*, 2016; 66(1):7–30. Available from: <http://onlinelibrary.wiley.com/doi/10.3322/caac.21332/full>

Shi B, Gao H, Zhang T, and Cui Q. Analysis of plasma microRNA expression profiles revealed different cancer susceptibility in healthy young adult smokers and middle-aged smokers. *Oncotarget*, 2016. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/26943588>

Reddy AV, Killampalli LK, Prakash AR, Naag S, Sreenath G, et al. Analysis of lipid profile in cancer patients, smokers, and nonsmokers. *Dent Res J (Isfahan)*, 2016; 13(6):494-9. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/28182070>

Ordonez-Mena JM, Schottker B, Mons U, Jenab M, Freisling H, et al. Quantification of the smoking-associated cancer risk with rate advancement periods: Meta-analysis of individual participant data from cohorts of the chances consortium. *BMC Med*, 2016; 14(1):62. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/27044418>

Loeb LA. Tobacco causes human cancers-a concept founded on epidemiology and an insightful experiment now requires translation worldwide. *Cancer Res*, 2016; 76(4):765-6. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/26880808>

Little MP, Hendry JH, and Puskin JS. Lack of correlation between stem-cell proliferation and radiation- or smoking-associated cancer risk. *PLoS ONE*, 2016; 11(3):e0150335. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/27031507>

Kristina SA, Endarti D, and Thavorncharoensap M. Burden of cancer attributable to tobacco smoking in member countries of the association of southeast asian nations (asean), 2012. *Cancer Epidemiol*, 2016; 44:84-90. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/27513722>

Alexandrov LB, Ju YS, Haase K, Van Loo P, Martincorena I, et al. Mutational signatures associated with tobacco smoking in human cancer. *Science*, 2016; 354(6312):618-22. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/27811275>

Tabuchi T, Ozaki K, Ioka A, and Miyashiro I. Joint and independent effect of alcohol and tobacco use on the risk of subsequent cancer incidence among cancer survivors: A cohort study using cancer registries. *Journal international du cancer*, 2015. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/25904109>

Soder B, Andersson LC, Meurman JH, and Soder PO. Unique database study linking gingival inflammation and smoking in carcinogenesis. *Philos Trans R Soc Lond B Biol Sci*, 2015; 370(1661). Available from: <http://www.ncbi.nlm.nih.gov/pubmed/25533098>

Pandeya N, Wilson LF, Bain CJ, Martin KL, Webb PM, et al. Cancers in australia in 2010 attributable to tobacco smoke. *Aust N Z J Public Health*, 2015; 39(5):464-70. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/26437733>

Leon ME, Peruga A, McNeill A, Kralikova E, Guha N, et al. European code against cancer, 4th edition: Tobacco and cancer. *Cancer Epidemiol*, 2015. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/26272517>

Howdon D and Jones AM. A discrete latent factor model for smoking, cancer and mortality. *Econ Hum Biol*, 2015; 18:57-73. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/25898078>

Gilhodes J, Belot A, Bouvier AM, Remontet L, Delafosse P, et al. Incidence of major smoking-related cancers: Trends among adults aged 20-44 in france from 1982 to 2012. *Cancer Epidemiol*, 2015. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/26209939>

Chen ZM, Peto R, Iona A, Guo Y, Chen YP, et al. Emerging tobacco-related cancer risks in china: A nationwide, prospective study of 0.5 million adults. *Cancer*, 2015; 121 Suppl 17:3097-106. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/26331816>

Xue J, Yang S, and Seng S. Mechanisms of cancer induction by tobacco-specific nnk and nnn. *Cancers (Basel)*, 2014; 6(2):1138-56. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/24830349>

Wang A, Kubo J, Luo J, Desai M, Hedlin H, et al. Active and passive smoking in relation to lung cancer incidence in the women's health initiative observational study prospective cohort. *Ann Oncol*, 2014. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/25316260>

Sobus SL and Warren GW. The biologic effects of cigarette smoke on cancer cells. *Cancer*, 2014. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/25043526>

Schaal C and Chellappan SP. Nicotine-mediated cell proliferation and tumor progression in smoking-related cancers. *Mol Cancer Res*, 2014; 12(1):14-23. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/24398389>

McBride D. Smoking and animal-based diets are leading lifestyle cancer risk factors in new study. *ONS Connect*, 2014; 29(1):40. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/24669538>

Jacobs EJ, Newton CC, Carter BD, Feskanich D, Freedman ND, et al. What proportion of cancer deaths in the contemporary united states is attributable to cigarette smoking? *Ann Epidemiol*, 2014. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/25487970>

Everatt R, Kuzmickiene I, Virviciute D, and Tamosiunas A. Cigarette smoking, educational level and total and site-specific cancer: A cohort study in men in lithuania. *Eur J Cancer Prev*, 2014; 23(6):579-86. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/24589745>

Caffrey MK. 50th anniversary report: Even more known about smoking, cancer connections. *Am J Manag Care*, 2014; 20(5 Spec No.):SP157-9. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/25618631>

Balogh EP, Dresler C, Fleury ME, Gritz ER, Kean TJ, et al. Reducing tobacco-related cancer incidence and mortality: Summary of an institute of medicine workshop. *Oncologist*, 2014; 19(1):21-31. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/24304712>

Report links smoking to poor cancer outcomes. *Cancer Discov*, 2014; 4(3):263-4. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/24596186>

Lortet-Tieulent J, Renteria E, Sharp L, Weiderpass E, Comber H, et al. Convergence of decreasing male and increasing female incidence rates in major tobacco-related cancers in europe in 1988-2010. *Eur J Cancer*, 2013. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/24269041>

Edwards B, Noone A, Mariotto A, Simard E, Boscoe F, et al. Annual report to the nation on the status of cancer, 1975-2010, featuring prevalence of comorbidity and impact on survival among persons with lung, colorectal, breast, or prostate cancer. *Cancer*, 2013; [Epub ahead of print]. Available from: <http://onlinelibrary.wiley.com/doi/10.1002/cncr.28509/full>

3.3.1 Carcinogens in cigarette smoke

Korenjak, M, Temiz, NA, Keita, S, Chavanel, B, Renard, C, Sirand, C et al. (2024). Human cancer genomes harbor the mutational signature of tobacco-specific nitrosamines NNN and NNK. *bioRxiv*. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/38979250>

Lin, W. (2024). Understanding the mediation effects of cigarettes per day on time to first cigarette and carcinogen biomarkers: National Health and Nutrition Examination Survey 2015-2016. *Tob Induc Dis*, 22. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/38860151>

Li, X, Ye, Z, Wang, J, Lin, P, Zhang, X, Xie, S, & Chen, C. (2024). Intake of tobacco nitrosamines of smokers in various provinces of China and their cancer risk: A meta-analysis. *J Environ Sci (China)*, 141, 249-260. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/38408825>

Hikisz, P, & Jacenik, D. (2023). The Tobacco Smoke Component, Acrolein, as a Major Culprit in Lung Diseases and Respiratory Cancers: Molecular Mechanisms of Acrolein Cytotoxic Activity. *Cells*, 12(6). Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/36980220>

Kim, B, Rhie, M, Park, S, Kim, HS, & Kwon, JA. (2023). Nonlinear Associations between Blood Cadmium Concentration and Thyroid Hormones According to Smoking Status in Korean Adults: The Korea National Health and Nutrition Examination Survey (KNHANES). *Toxics*, 11(2). Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/36851004>

Kim, J, Song, H, Lee, J, Kim, YJ, Chung, HS, Yu, JM et al. (2023). Smoking and passive smoking increases mortality through mediation effect of cadmium exposure in the United States. *Sci Rep*, 13(1), 3878. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/36890267>

Mingard, C, Battey, JND, Takhayev, V, Blatter, K, Hurlimann, V, Sierro, N et al. (2023). Dissection of Cancer Mutational Signatures with Individual Components of Cigarette Smoking. *Chem Res Toxicol*. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/36976926>

Peluso, M, Munnia, A, Russo, V, Galli, A, Pala, V, Schouw, YTV et al. (2022). Cruciferous Vegetable Intake and Bulky DNA Damage within Non-Smokers and Former Smokers in the Gen-Air Study (EPIC Cohort). *Nutrients*, 14(12). Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/35745207>

Jamal, QMS, & Alharbi, AH. (2021). Molecular docking and dynamics studies of cigarette smoke carcinogens interacting with acetylcholinesterase and butyrylcholinesterase enzymes of the central nervous system. *Environ Sci Pollut Res Int*. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/34382170>

Gearhart-Serna, LM, Tacam, M, Jr, Slotkin, TA, & Devi, GR. (2021). Analysis of polycyclic aromatic hydrocarbon intake in the US adult population from NHANES 2005-2014 identifies vulnerable subpopulations, suggests interaction between tobacco smoke exposure and sociodemographic factors. *Environ Res*, 201, 111614. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/34216610>

Peterson, LA, Oram, MK, Flavin, M, Seabloom, D, Smith, WE, O'Sullivan, MG et al (2021). Coexposure to Inhaled Aldehydes or Carbon Dioxide Enhances the Carcinogenic Properties of the Tobacco-Specific Nitrosamine 4-Methylnitrosamino-1-(3-pyridyl)-1-butanone in the A/J Mouse Lung. *Chem Res Toxicol*. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/33629582>

Weng MW, Lee HW, Park SH, Hu Y, Wang HT, et al. Aldehydes are the predominant forces inducing DNA damage and inhibiting DNA repair in tobacco smoke carcinogenesis. *Proc Natl Acad Sci U S A*, 2018. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/29915082>

Hirata N, Yamada S, Sekino Y, and Kanda Y. Tobacco nitrosamine nnk increases aldh-positive cells via ros-wnt signaling pathway in a549 human lung cancer cells. *J Toxicol Sci*, 2017; 42(2):193-204. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/28321046>

3.3.2 Genotoxic effects of cigarette smoke

Guedes Pinto, T, Magalhaes, FAC, Renno, ACM, & Ribeiro, DA. (2024). Does waterpipe smoke induce genotoxicity (DNA damage) in mammalian cells in vivo? A systematic review. *Toxicol Mech Methods*, 1-10. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/39370712>

Ma, Q, Shen, Y, Guo, W, Feng, K, Huang, T, & Cai, Y. (2024). Machine Learning Reveals Impacts of Smoking on Gene Profiles of Different Cell Types in Lung. *Life (Basel)*, 14(4). Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/38672772>

Picchio, V, Ferrero, G, Cozzolino, C, Pardini, B, Floris, E, Tarallo, S et al. (2023). Effect of traditional or heat-not-burn cigarette smoking on circulating miRNAs in healthy subjects. *Eur J Clin Invest*, e14140. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/38050790>

Adler, N, Bahcheli, AT, Cheng, KCL, Al-Zahrani, KN, Slobodyanyuk, M, Pellegrina, D et al. (2023). Mutational processes of tobacco smoking and APOBEC activity generate protein-truncating

mutations in cancer genomes. *Sci Adv*, 9(44), eadh3083. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/37922356>

Liu, Y, Lu, L, Yang, H, Wu, X, Luo, X, Shen, J et al. (2023). Dysregulation of immunity by cigarette smoking promotes inflammation and cancer: A review. *Environ Pollut*, 339, 122730. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/37838314>

Strulovici-Barel, Y, Rostami, MR, Kaner, RJ., Mezey, JG, & Crystal, RG. (2023). Serial Sampling of the Small Airway Epithelium to Identify Persistent Smoking-dysregulated Genes. *Am J Respir Crit Care Med*. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/37531632>

Almushawwah, S, Almutairi, MH, Alamri, AM, & Semlali, A. (2023). A Significant Increasing Risk Association between Cigarette Smoking and XPA and XPC Genes Polymorphisms. *Genes (Basel)*, 14(7). Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/37510255>

Liam, CK, Yew, CY, Pang, YK, Wong, CK, Poh, ME, Tan, JL et al. (2023). Common driver mutations and programmed death-ligand 1 expression in advanced non-small cell lung cancer in smokers and never smokers. *BMC Cancer*, 23(1), 659. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/37452277>

Vellichirammal, NN, Albahrani, A, & Guda, C. (2022). Fusion gene recurrence in non-small cell lung cancers and its association with cigarette smoke exposure. *Transl Lung Cancer Res*, 11(10), 2022-2039. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/36386463>

Ferrer, JLM, & Garcia, RL. (2022). Antioxidant Systems, lncRNAs, and Tunneling Nanotubes in Cell Death Rescue from Cigarette Smoke Exposure. *Cells*, 11(15). Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/35892574>

Thomas, AJ, Nair, BJ, Oommen, S, Syamkumar, V, & Raman, RK. (2021). Comparative Evaluation of Genotoxicity in Tobacco Users versus Nontobacco Users. *J Pharm Bioallied Sci*, 13(Suppl 2), S960-S964. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/35017907>

Wang, R, Li, S, Wen, W, & Zhang, J. (2021). Multi-Omics Analysis of the Effects of Smoking on Human Tumors. *Front Mol Biosci*, 8, 704910. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/34796198>

Farkas, G, Kocsis, ZS, Szekely, G, Dobozi, M, Kenessey, I, Polgar, C, & Juranyi, Z. (2021). Smoking, chromosomal aberrations, and cancer incidence in healthy subjects. *Mutat Res*, 867, 503373. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/34266629>

Caliri, AW, Tommasi, S, & Besaratinia, A. (2021). Relationships among smoking, oxidative stress, inflammation, macromolecular damage, and cancer. *Mutat Res*, 787, 108365. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/34083039>

Cao, C, Tian, B, Geng, X, Zhou, H, Xu, Z, Lai, T et al (2021). IL-17-Mediated Inflammation Promotes Cigarette Smoke-Induced Genomic Instability. *Cells*, 10(5). Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/34065904>

Patino-Garcia, A, Guruceaga, E, Segura, V, Sanchez Bayona, R, Andueza, MP, Tamayo Uria, I et al (2021). Whole exome sequencing characterization of individuals presenting extreme phenotypes of high and low risk of developing tobacco-induced lung adenocarcinoma. *Transl Lung Cancer Res*, 10(3), 1327-1337. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/33889513>

Jamal, QMS, Alharbi, AH, Dhasmana, A, Anukriti, Albejaidi, F , & Sajid, M. (2021). Deciphering the Influence of Cigarette Smoke Carcinogens on CNS Associated Biomolecules: A Computational Synergistic Approach. *CNS Neurol Disord Drug Targets*. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/33687903>

Almutairi, MH, Almutairi, BO, Alrubie, TM, Alharbi, SN, Parine, NR, Alrefaei, AF et al (2021). Association between tobacco substance usage and a missense mutation in the tumor suppressor gene P53 in the Saudi Arabian population. *PLoS One*, 16(1), e0245133. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/33481818>

Bline, AP, Dearfield, KL, DeMarini, DM, Marchetti, F, Yauk, CL, Escher, J, & Workshop, P. (2020). Heritable hazards of smoking: Applying the "clean sheet" framework to further science and policy. *Environ Mol Mutagen*. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/33064321>

Dhasmana, A, Dhasmana, A, H, HY, Farasani, A, Habibullah, M, Alshammary, FL et al (2020). Tobacco Smoke Carcinogens Induce DNA Repair Machinery Function Loss: Protection by Carbon Nanotubes. *Asian Pac J Cancer Prev*, 21(10), 3099-3108. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/33112573>

Lu, L, Liang, Q, Shen, S, Feng, L, Jin, L, & Liang, ZF. (2020). Tobacco Smoke Plays an Important Role in Initiation and Development of Lung Cancer by Promoting the Characteristics of Cancer Stem Cells. *Cancer Manag Res*, 12, 9735-9739. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/33116833>

Chen, LH, Shen, TC, Li, CH, Chiu, KL, Hsiao, YC, Wang, YC et al. (2020). The Significant Interaction of Excision Repair Cross-complementing Group 1 Genotypes and Smoking to Lung Cancer Risk. *Cancer Genomics Proteomics*, 17(5), 571-577. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/32859635>

Guan, Q, Zhang, J, Guo, Y, Xia, J, Zhang, J, Xie, J et al. (2020). The Effects of Age, Cigarette Smoking, Sex, and Race on the Qualitative Characteristics of Lung Transcriptome. *Biomed Res Int*, 2020, 6418460. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/32802863>

3.3.2.1 DNA is the main target of genotoxic carcinogens

Alshehri, E, Al-Dogmi, AM, Al-Hazani, TMI, Alwaili, MA, Safhi, FA, Alneghery, LM et al. (2023). Patterns of mutations in nine cancer-related genes and PAF development among smoking male patients diagnosed with bladder cancer. *Tumour Biol*, 45(1), 1-14. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/36806529>

Dong, YM, Li, M, He, QE, Tong, YF, Gao, HZ, Zhang, YZ (2020). Epigenome-Wide Tobacco-Related Methylation Signature Identification and Their Multilevel Regulatory Network Inference for Lung Adenocarcinoma. *Biomed Res Int*, 2020, 2471915. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/32420331>

3.3.2.2 Activation of carcinogens to form DNA adducts

Folesani, G, Galetti, M, Ranzieri, S, Petronini, PG, La Monica, S, Corradi, M, & Cavallo, D. (2022). Interaction between occupational radon exposure and tobacco smoke: a systematic review. *Expert Rev Respir Med*, 16(7), 787-800. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/35912519>

Chen, KM, Sun, YW, Krebs, NM, Sun, D, Krzeminski, J, Reinhart, L et al. (2022). Detection of DNA Adducts Derived from the Tobacco Carcinogens, Benzo[a]pyrene and Dibenz[def,p]chrysene in Human Oral Buccal Cells. *Carcinogenesis*. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/35749296>

Jokipii Krueger, CC, Park, SL, Madugundu, G, Patel, Y, Le Marchand, L, Stram, DO, & Tretyakova, N. (2021). Ethnic differences in excretion of butadiene-DNA adducts by current smokers. *Carcinogenesis*. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/33693566>

Munnia A, Giese RW, Polvani S, Galli A, Cellai F, et al. Bulky DNA adducts, tobacco smoking, genetic susceptibility, and lung cancer risk. *Adv Clin Chem*, 2017; 81:231-77. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/28629590>

Ma Y and Li MD. Establishment of a strong link between smoking and cancer pathogenesis through DNA methylation analysis. *Sci Rep*, 2017; 7(1):1811. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/28500316>

Brenner DR, Fanidi A, Grankvist K, Muller DC, Brennan P, et al. Inflammatory cytokines and lung cancer risk in 3 prospective studies. *Am J Epidemiol*, 2017; 185(2):86-95. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/27998891>

3.3.2.3 Conversion of DNA adducts to mutations

Li, J. L., Jain, N., Tamayo, L. I., Tong, L., Jasmine, F., Kibriya, M. G., . . . Pierce, B. L. (2024). The association of cigarette smoking with DNA methylation and gene expression in human tissue samples. *Am J Hum Genet*.

Moreira, AL, & Sabari, JK. (2023). Seeing Beyond the Smoke: Reclassifying Lung Cancer by Smoking-Related Mutational Signatures. *J Thorac Oncol*, 18(4), 396-398. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/36990571>

Huang, A. T., & Tang, W. (2023). Smoking-Related DNA Alkylation Events Are Mapped at Single-Nucleotide Resolution. *ACS Cent Sci*, 9(3), 346-348. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/36968536>

Bhutani, P Murray, MT, Sommer, CW, Wilson, KA, & Wetmore, SD. (2021). Structural Rationalization for the Nonmutagenic and Mutagenic Bypass of the Tobacco-Derived O4-4-(3-Pyridyl)-4-oxobut-1-yl-thymine Lesion by Human Polymerase eta: A Multiscale Computational Study. *Chemical Research in Toxicology*. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/33856186>

Kruger, M, Metzger, C, Al-Nawas, B, Kammerer, PW, & Brieger, J. (2020). Cigarette smoke modulates binding of the transcription factor MZF1 to the VEGF promoter and regulates VEGF expression in dependence of genetic variation SNP 405. *J Oral Pathol Med*. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/32449233>

3.3.3 Non-genotoxic effects of cigarette smoke

Pospiech, E, Rudnicka, J, Noroozi, R, Pisarek-Pacek, A, Wysocka, B, Masny, A et al. (2024). DNA methylation at AHRR as a master predictor of smoke exposure and a biomarker for sleep and exercise. *Clin Epigenetics*, 16(1), 147. Retreived from <https://www.ncbi.nlm.nih.gov/pubmed/39425209>

Schmidt, S. (2024). Epigenetic Biomarker: Improving Estimates of Fetal Exposure to Cigarette Smoke. *Environ Health Perspect*, 132(9), 94002. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/39315750>

Jang, HJ, Min, HY, Kang, YP, Boo, HJ, Kim, J, Ahn, JH et al. (2024). Tobacco-induced hyperglycemia promotes lung cancer progression via cancer cell-macrophage interaction through paracrine IGF2/IR/NPM1-driven PD-L1 expression. *Nat Commun*, 15(1), 4909. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/38851766>

Li, JL, Jain, N, Tamayo, LI, Tong, L, Jasmine, F, Kibriya, MG et al. (2024). The association of cigarette smoking with DNA methylation and gene expression in human tissue samples. *Am J Hum Genet*. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/38490207>

Hoang, TT, Lee, Y, McCartney, DL, Kersten, ETG, Page, CM, Hulls, PM et al. (2024). Comprehensive evaluation of smoking exposures and their interactions on DNA methylation. *EBioMedicine*, 100, 104956. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/38199042>

Joshi, J, Pandit, A, & Shah, F. (2023). Nicotine mediated epithelial modulations: An in-vitro evidence. *J Oral Biol Craniofac Res*, 13(6), 796-800. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/38111634>

van Dongen, J, Willemsen, G, Consortium, B, de Geus, EJC, Boomsma, DI, & Neale, MC. (2023). Effects of smoking on genome-wide DNA methylation profiles: A study of discordant and concordant monozygotic twin pairs. *Elife*, 12. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/37643467>

Domingo-Relloso, A, Joehanes, R, Rodriguez-Hernandez, Z, Lahousse, L, Haack, K, Fallin, MD et al. (2023). Smoking, blood DNA methylation sites and lung cancer risk. *Environ Pollut*, 334, 122153. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/37442331>

Henke, K, Balcerzak, I, Czepil, E, Bem, A, Piskorska, E, Olszewska-Slonina, D et al. (2023). 30-Min Exposure to Tobacco Smoke Influences Airway Ion Transport-An In Vitro Study. *Curr Oncol*, 30(7), 7007-7018. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/37504368>

Karabegovic, I, Maas, SCE, Shuai, Y, Ikram, MA, Stricker, B, Aerts, J et al. (2023). Smoking-related dysregulation of plasma circulating microRNAs: the Rotterdam study. *Hum Genomics*, 17(1), 61. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/37430296>

Shang, J, Nie, X, Qi, Y, Zhou, J, & Qi, Y. (2023). Short-term smoking cessation leads to a universal decrease in whole blood genomic DNA methylation in patients with a smoking history. *World J Surg Oncol*, 21(1), 227. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/37496025>

Zhou, Y, Zhou, X, Sun, J, Wang, L, Zhao, J, Chen, J et al. (2023). Exploring the cross-cancer effect of smoking and its fingerprints in blood DNA methylation on multiple cancers: A Mendelian randomization study. *Int J Cancer*. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/37449541>

Dugue, PA, Yu, C, Hodge, AM, Wong, EM, Joo, JE, Jung, CH et al . (2023). Methylation scores for smoking, alcohol consumption, and body mass index and risk of seven types of cancer. *Int J Cancer*. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/36919377>

Shapiro, H, Goldenberg, K, Ratiner, K, & Elinav, E. (2022). Smoking-induced microbial dysbiosis in health and disease. *Clin Sci (Lond)*, 136(18), 1371-1387. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/36156126>

Lei, MK, Gibbons, FX, Gerrard, M, Beach, SRH, Dawes, K, & Philibert, R. (2022). Digital methylation assessments of alcohol and cigarette consumption account for common variance in accelerated epigenetic ageing. *Epigenetics*, 1-15. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/35866695>

Mishra, MK, Gupta, S, Shivangi, & Sehgal, S. (2022). Assessing long non-coding RNAs in tobacco-associated oral cancer. *Curr Cancer Drug Targets*. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/35747968>

Klopack, ET, Carroll, JE, Cole, SW, Seeman, TE, & Crimmins, EM. (2022). Lifetime exposure to smoking, epigenetic aging, and morbidity and mortality in older adults. *Clin Epigenetics*, 14(1), 72. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/35643537>

Almutairi, BO, Almutairi, MH, Alrefaei, AF, Ali, D, Alkahtani, S, & Alarifi, S. (2022). Cigarette Smoke Regulates the Expression of EYA4 via Alteration of DNA Methylation Status. *Biomed Res Int*, 2022, 5032172. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/35607307>

Joglekar, R, Grenier, C, Hoyo, C, Hoffman, K& Murphy, SK. (2022). Maternal tobacco smoke exposure is associated with increased DNA methylation at human metastable epialleles in infant cord blood. *Environ Epigenet*, 8(1), dvac005. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/35355955>

Besaratinia, A, Caceres, A, & Tommasi, S. (2022). DNA Hydroxymethylation in Smoking-Associated Cancers. *Int J Mol Sci*, 23(5). Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/35269796>

Huang, X, Wu, B, Zhang, F, Chen, F, Zhang, Y, Guo, H, & Zhang, H. (2022). Epigenetic Biomarkers Screening of Non-Coding RNA and DNA Methylation Based on Peripheral Blood Monocytes in Smokers. *Front Genet*, 13, 766553. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/35269796>

Watkins, SH, Iles-Caven, Y, Pembrey, M, Golding, J, & Suderman, M. (2022). Grandmaternal smoking during pregnancy is associated with differential DNA methylation in peripheral blood of their grandchildren. *Eur J Hum Genet*. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/35347270>

Ji, X, Lin, L, Fan, J, Li, Y, Wei, Y, Shen, S et al. (2021). Epigenome-wide three-way interaction study identifies a complex pattern between TRIM27, KIAA0226, and smoking associated with overall survival of early-stage NSCLC. *Mol Oncol*. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/34932879>

Mao, Y, Huang, P, Wang, Y, Wang, M, Li, MD, & Yang, Z. (2021). Genome-wide methylation and expression analyses reveal the epigenetic landscape of immune-related diseases for tobacco smoking. *Clin Epigenetics*, 13(1), 215. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/34886889>

Bouzigon, E, & Barouki, R. (2021). [Tobacco and DNA methylation: the case for epigenetic alterations]. *Rev Prat*, 71(7), 727-728. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/34792907>

Langdon, RJ, Yousefi, P, Relton, CL, & Suderman, MJ. (2021). Epigenetic modelling of former, current and never smokers. *Clin Epigenetics*, 13(1), 206. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/34789321>

Luo, R, Zhang, H, Mukherjee, N, Karmaus, W, Patil, V, Arshad, H, & Mzayek, F. (2021). Association of grandmaternal smoking during pregnancy with DNA methylation of grandchildren: the Isle of Wight study. *Epigenomics*, 13(18), 1473-1483. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/34596434>

Amador, C, Zeng, Y, Barber, M, Walker, RM, Campbell, A, McIntosh, AM et al. (2021). Genome-wide methylation data improves dissection of the effect of smoking on body mass index. *PLoS Genet*, 17(9), e1009750. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/34499657>

Cruz, CRV, Ferrer, J LM, & Garcia, RL. (2021). Concomitant and decoupled effects of cigarette smoke and SCAL1 upregulation on oncogenic phenotypes and ROS detoxification in lung adenocarcinoma cells. *Sci Rep*, 11(1), 18345. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/34526564>

Bravo-Gutierrez, OA, Falfan-Valencia, R, Ramirez-Venegas, A, Sansores, RH, Hernandez-Zenteno, R J., Hernandez-Perez, A et al. (2021). Hypomethylation of AHRR (cg05575921) Is Related to Smoking Status in the Mexican Mestizo Population. *Genes (Basel)*, 12(8). Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/34440450>

Jin, SW, Im, JS, Park, JH, Kim, HG, Lee, GH, Kim, SJ et al. (2021). Effects of tobacco compound 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) on the expression of epigenetically regulated genes in lung carcinogenesis. *J Toxicol Environ Health A*, 1-16. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/34459362>

Liu, X, Chen, J, Li, J, Zeng, Z, Jiang, X, Gao, Y et al. (2021). Comprehensive analysis reveals common DNA methylation patterns of tobacco-associated cancers: A pan-cancer analysis. *Gene*, 804, 145900. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/34400279>

Su, SF, Ho, H, Li, JH Wu, MF, Wang, HC, Yeh, HY et al. (2021). DNA methylome and transcriptome landscapes of cancer-associated fibroblasts reveal a smoking-associated malignancy index. *J Clin Invest*. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/34228648>

Di Vincenzo, S, Sangiorgi, C, Ferraro, M, Buscetta, M, Cipollina, C, & Pace, E. (2021). Cigarette smoke extract reduces FOXO3a promoting tumor progression and cell migration in lung cancer. *Toxicology*, 454, 152751. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/33693566>

Jung, J, Lee, YJ, Kim, CH, & Ahn, S. (2021). Landscape of epigenetically regulated lncRNAs and DNA methylation in smokers with lung adenocarcinoma. *PLoS One*, 16(3), e0247928. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/33684161>

Sun, YQ, Richmond, RC, Suderman, M, Min, JL, Battram, T, Flatberg, A et al (2021). Assessing the role of genome-wide DNA methylation between smoking and risk of lung cancer using repeated measurements: the HUNT study. *Int J Epidemiol*. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/33729499>

Christiansen, C, Castillo-Fernandez, JE, Domingo-Relloso, A, Zhao, W, El-Sayed Moustafa, JS, Tsai, P C et al (2021). Novel DNA methylation signatures of tobacco smoking with trans-ethnic effects. *Clin Epigenetics*, 13(1), 36. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/33593402>

Cheng, C, Wu, Y, Xiao, T, Xue, J, Sun, J, Xia, H et al (2021). METTL3-mediated m(6)A modification of ZBTB4 mRNA is involved in the smoking-induced EMT in cancer of the lung. *Mol Ther Nucleic Acids*, 23, 487-500. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/33510938>

Ji, X, Lin, L, Shen, S, Dong, X, Chen, C, Li, Y et al (2020). Epigenetic-smoking interaction reveals histologically heterogeneous effects of TRIM27 DNA methylation on overall survival among early-stage NSCLC patients. *Mol Oncol*, 14(11), 2759-2774. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/33448640>

Dugue, PA, Hodge, AM, Wong, EM, Joo, JE, Jung, CH, Hopper, JL et al. (2020). Methylation marks of prenatal exposure to maternal smoking and risk of cancer in adulthood. *Int J Epidemiol*. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/33169152>

Liu, CH, Chen, Z, Chen, K, Liao, FT, Chung, CE, Liu, X et al (2020). Lipopolysaccharide-mediated chronic inflammation promotes tobacco carcinogen-induced lung cancer and determines the efficacy of immunotherapy. *Cancer Res*. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/33122306>

Rousseaux, S, Seyve, E, Chuffart, F, Bourova-Flin, E, Benmerad, M, Charles, MA et al (2020). Immediate and durable effects of maternal tobacco consumption alter placental DNA methylation in enhancer and imprinted gene-containing regions. *BMC Med*, 18(1), 306. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/33023569>

Kupsco, A, Gonzalez, G, Baker, BH, Knox, JM, Zheng, Y, Wang, S et al . (2020). Associations of smoking and air pollution with peripheral blood RNA N(6)-methyladenosine in the Beijing truck driver air pollution study. *Environ Int*, 144, 106021. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/32791345>

Kankanamage, RNT, Ghosh, AB, Jiang, D, Gkika, KS, Keyes, TE, Achola, LA et al (2020). Metabolites of Tobacco- and E-Cigarette-related Nitrosamines Can Drive Cu²⁺-mediated DNA Oxidation. *Chem Res Toxicol*. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/32672941>

Markunas, CA, Semick, SA, Quach, BC, Tao, R, Deep-Soboslay, A, Carnes, MU et al (2020). Genome-wide DNA methylation differences in nucleus accumbens of smokers vs. nonsmokers. *Neuropsychopharmacology*. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/32731254>

Silva, CP, & Kamens, HM. (2020). Cigarette smoke-induced alterations in blood: A review of research on DNA methylation and gene expression. *Exp Clin Psychopharmacol*. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/32658533>

Lohan, SB, Buhring, K, Lauer, AC, Friedrich, A, Lademann, J, Buss, A et al (2020). Analysis of the Status of the Cutaneous Endogenous and Exogenous Antioxidative System of Smokers and the Short-Term Effect of Defined Smoking Thereon. *Antioxidants (Basel)*, 9(6). Available from: <https://www.ncbi.nlm.nih.gov/pubmed/32575569>

Tessema, M, Tassew, DD, Yingling, CM, Do, K, Picchi, MA, Wu, G et al (2020). Identification of novel epigenetic abnormalities as sputum biomarkers for lung cancer risk among smokers and COPD

patients. *Lung Cancer*, 146, 189-196. Available from:
<https://www.ncbi.nlm.nih.gov/pubmed/32559455>

Zeng, H, Kong, X, Zhang, H, Chen, Y, Cai, S, Luo, H, & Chen, P. (2020). Inhibiting DNA methylation alleviates cigarette smoke extract-induced dysregulation of Bcl-2 and endothelial apoptosis. *Tob Induc Dis*, 18, 51. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/32547354>

Takizawa, M, Nakano, M, Fukami, T, & Nakajima, M. (2020). Decrease in ADAR1 expression by exposure to cigarette smoke enhances susceptibility to oxidative stress. *Toxicol Lett*. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/32439581>

3.3.4 Loss of normal cell growth control mechanisms

Papapostolou, I, Ross-Kaschitza, D, Bochen, F, Peinelt, C, & Maldifassi, MC. (2023). Contribution of the alpha5 nAChR Subunit and alpha5SNP to Nicotine-Induced Proliferation and Migration of Human Cancer Cells. *Cells*, 12(15). Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/37566079>

Cao, ZZ, Ao, YJ, & Zhou, SH. (2021). The role of cancer stromal fibroblasts in mediating the effects of tobacco-induced cancer cell growth. *Cancer Cell Int*, 21(1), 707. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/34953503>

Rostami, MR, LeBlanc, MG, Strulovici-Barel, Y, Zuo, W, Mezey, JG, O'Beirne, SL et al. (2021). Smoking shifts human small airway epithelium club cells toward a lesser differentiated population. *NPJ Genom Med*, 6(1), 73. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/34497273>

Wang, Y, Ji, M, Zhu, M, Fan, J, Xie, J, Huang, Y et al. (2021). Genome-wide gene-smoking interaction study identified novel susceptibility loci for non-small cell lung cancer in Chinese populations. *Carcinogenesis*. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/34297049>

Jin, M, Li, G, Liu, W, Wu, X, Zhu, J, Zhao, D et al (2021). Cigarette smoking induces aberrant N(6)-methyladenosine of DAPK2 to promote non-small cell lung cancer progression by activating NF-kappaB pathway. *Cancer Lett*, 518, 214-229. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/34298122>

Lin, S, Mei, W, Lai, H, Li, X, Weng, H, Xiong, J et al (2021). Cigarette smoking promotes keratinocyte malignancy via generation of cancer stem-like cells. *J Cancer*, 12(4), 1085-1093. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/33442406>

Siegfried, JM, Njatcha, C, Farooqui, M, & Almotlak, AA. (2020). Prevention of tobacco carcinogen-induced lung tumor development by a novel STAT3 decoy inhibitor. *Cancer Prev Res (Phila)*. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/32655003>

Ma, B, Stepanov, I, & Hecht, SS. (2019). Recent Studies on DNA Adducts Resulting from Human Exposure to Tobacco Smoke. *Toxics*, 7(1). Available from: <https://www.ncbi.nlm.nih.gov/pubmed/30893918>

News reports:

No author listed. Comprehensive Report Says Tobacco Control Must Be Highest Priority in Cancer Control. American Cancer Society, 2018. Oct 18, 2018. Available from <http://pressroom.cancer.org/Ch2Blueprint>

Davis N. Four in 10 cancer cases could be prevented by lifestyle changes, in *The Guardian* 2018. Available from: <https://www.theguardian.com/society/2018/mar/23/four-in-10-cancer-cases-could-be-prevented-by-lifestyle-changes>.

Australian Institute of Health and Welfare. Participation in national cancer screening programs in 2015–2016. Australian Cancer Database (ACD), Canberra: AIWH 2018. Available from: <https://www.myhealthycommunities.gov.au/our-reports/cancer-screening/april-2018>.

Australian Institute of Health and Welfare. Incidence of selected cancers in 2009–2013. Australian Cancer Database (ACD), Canberra: AIWH 2018. Available from: <https://www.myhealthycommunities.gov.au/our-reports/cancer-incidence/april-2018>.

Australian Institute of Health and Welfare. Cancer in adolescents and young adults in australia. Canberra: AIHW 2018. Available from: <https://www.aihw.gov.au/reports/cancer/cancer-adolescents-young-adults/contents/table-of-contents>.

QIMR Berghofer Medical Research Institute. Guide to reduce your cancer risk. QIMR Berghofer Medical Research Institute, 2017. Available from: <http://www.qimrberghofer.edu.au/reduce-your-cancer-risk-guide/>.

No authors listed. Smoking and cancer, in *Action on Smoking and Health UK* 2017. Available from: <http://ash.org.uk/download/04-smoking-and-cancer/>

Miles J. Australian cancer rates: Research shows 40% of deaths avoidable. The Courier Mail, 2017. Available from: <http://www.news.com.au/national/queensland/australian-cancer-rates-research-shows-40-of-deaths-avoidable/news-story/70e93af922e33b92060caf8ae21a15e0>

Australian Institute of Health and Welfare and Australasian Association of Cancer Registries 2017. Cancer in australia: In brief 2017. Cancer series no. 102, Cat. no. CAN 101. Canberra: AIHW, 2017. Available from: <https://www.aihw.gov.au/reports/cancer/cancer-in-australia-in-brief-2017/contents/table-of-contents>.

Australian Institute of Health and Welfare. Burden of cancer in australia: Australian burden of disease study 2011. Australian Burden of Disease Study series no. 12, Cat. no. BOD 13 Canberra: AIHW, 2017. Available from: <https://www.aihw.gov.au/reports/burden-of-disease/burden-of-cancer-in-australia-australian-burden-of-disease-study-2011/contents/table-of-contents>.

Australian INstitute of Health and Welfare. Australian cancer incidence and mortality (acim) books. 2017. Last update: Viewed Available from: <https://www.aihw.gov.au/reports/cancer/acim-books/contents/acim-books>.

Radford T. Cancer rates up 12% in 20 years, say cancer research UK The Guardian, 2016. Available from: <https://www.theguardian.com/science/2016/feb/17/cancer-rates-up-12-in-20-years-say-cancer-research-uk>

No authors listed. Cancers linked to tobacco use make up 40% of all cancers diagnosed in the united states, in Medical News Today 2016. Available from:
<http://www.medicalnewstoday.com/releases/314073.php>.

No authors listed. Smoking kills, ok, but how much does it kill?, in MedPage Today 2016. Available from:
http://www.medpagetoday.com/HematologyOncology/LungCancer/61027?xid=nl_mpt_DHE_2016-10-27&eun=g220600d0r&pos=0.

Hewitt G. Asia's rising tobacco epidemic, in Yahoo News2014. Available from:
<http://news.yahoo.com/asias-rising-tobacco-epidemic-030055701.html>.

3.3.1 Carcinogens in cigarette smoke

3.3.2 Genotoxic effects of cigarette smoke

3.3.2.1 DNA is the main target of genotoxic carcinogens

3.3.2.2 Activation of carcinogens to form DNA adducts

3.3.2.3 Conversion of DNA adducts to mutations

3.3.3 Non-genotoxic effects of cigarette smoke

3.3.4 Loss of normal cell growth control mechanisms