Submolecular Dysregulation Due to Deuterium Accumulation Is the Cause of Cancer

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Complete References

1. Horgan, J. (n.d.). The cancer industry: Hype vs. Reality. Scientific American Blog Network. Retrieved November 6, 2022, from https://blogs.scientificamerican.com/cross-check/the-cancer-industry-hype-vs-reality/

2. Somlyai, G., Jancsó, G., Jákli, G., et al. (1993). Naturally occurring deuterium is essential for the normal growth rate of cells. FEBS Letters, 317(1–2), 1–4. https://doi.org/10.1016/0014-5793(93)81479-j

3. Boveri T. (1914). Zur frage der entstehung maligner tumoren. Gustav Fischer

4. Nurk, S., Koren, S., Rhie, A., et al. (2022). The complete sequence of a human genome. Science (New York, N.Y.), 376(6588), 44–53. https://doi.org/10.1126/science.abj6987

5. The Human Genome Project. (n.d.). Genome.gov. Retrieved November 6, 2022, from https://www.genome.gov/human-genome-project

6. Kettering, M. S. (2022, February 3). The mystery of metastasis: Can a tumor's genetic mutations predict whether and where cancer will spread? Memorial Sloan Kettering Cancer Center; Memorial Sloan Kettering. https://www.mskcc.org/news/mystery-metastasis-can-tumor-s-genetic-mutations-predict-whether-and-where-cancer-will-spread

7. Anandakrishnan, R., Varghese, R. T., Kinney, N. A, et al. (2019). Estimating the number of genetic mutations (hits) required for carcinogenesis based on the distribution of somatic mutations. *PLoS Computational Biology*, 15(3), e1006881. https://doi.org/10.1371/journal.pcbi.1006881

8. Jacobs, K., Yeager, M., Zhou, W. et al. Detectable clonal mosaicism and its relationship to aging and cancer. *Nat Genet* 44, 651–658 (2012). https://doi.org/10.1038/ng.2270

9. Monti, N., Verna, R., Piombarolo, A., et al. (2022). Paradoxical behavior of oncogenes undermines the Somatic Mutation Theory. *Biomolecules,* 12(5), 662. https://doi.org/10.3390/biom12050662

10. de Magalhães, J. P. (2022). Every gene can (and possibly will) be associated with cancer. *Trends in Genetics*: TIG, 38(3), 216–217. https://doi.org/10.1016/j.tig.2021.09.005

11. Cosmic. (2020, April 7). Mutational signatures (v3.3 - June 2022). COSMIC | Mutational Signatures. Retrieved November 6, 2022, from https://cancer.sanger.ac.uk/signatures/

12. Alexandrov, L. B., Kim, J., Haradhvala, N. J….PCAWG Mutational Signatures Working Group, Getz, G., … PCAWG Consortium (2020). The repertoire of mutational signatures in human cancer. *Nature*, 578(7793), 94–101. https://doi.org/10.1038/s41586-020-1943-3

13. v Stadler, Z. K., Thom, P., Robson, M. E., et al. (2010). Genome-wide association studies of cancer. *Journal of Clinical Oncology*: Official Journal of the American Society of Clinical Oncology, 28(27), 4255–4267. https://doi.org/10.1200/JCO.2009.25.7816

14. Pandey, N., Lanke, V., Vinod, P. K. (2020). Network-based metabolic characterization of renal cell carcinoma. *Scientific Reports*, 10(1), 5955. https://doi.org/10.1038/s41598-020-62853-8

15. Boros, L. G., Somlyai, G., & Davalaar Dorfsman, P. (n.d.). Mitochondrial deuterium depletion restrains prokaryote proliferation and virus hosting cellular events thus may alleviate the use of biologics. Onb.It. Retrieved November 6, 2022, from https://cdn.onb.it/2020/02/Boros.pdf

16. Perona, R., & Serrano, R. (1988). Increased pH and tumorigenicity of fibroblasts expressing a yeast proton pump. Nature, 334(6181), 438–440. https://doi.org/10.1038/334438a0

17. https://www.mdpi.com/journal/molecules/special_issues/Medicinal_Biochemistry_Deuterium

18. Kou, F., Wu, L., Ren, X., & Yang, L. (2020). Chromosome abnormalities: New insights into their clinical significance in cancer. Molecular Therapy Oncolytics, 17, 562–570. https://doi.org/10.1016/j.omto.2020.05.010

19. Knouse, K. A., Davoli, T., Elledge, S. J., & Amon, A. (2017). Aneuploidy in cancer: Seq-ing answers to old questions. Annual Review of Cancer Biology, 1(1), 335–354. https://doi.org/10.1146/annurev-cancerbio-042616-072231

20. Balasubramanian, B., Pogozelski, W. K., & Tullius, T. D. (1998). DNA strand breaking by the hydroxyl radical is governed by the accessible surface areas of the hydrogen atoms of the DNA backbone. Proceedings of the National Academy of Sciences of the United States of America, 95(17), 9738–9743. https://doi.org/10.1073/pnas.95.17.9738

21. Ingle, S., Azad, R. N., Jain, S. S., & Tullius, T. D. (2014). Chemical probing of RNA with the hydroxyl radical at single-atom resolution. Nucleic Acids Research, 42(20), 12758–12767. https://doi.org/10.1093/nar/gku934

22. Gabor Jancso and W. Alexander Van Hook. (1974). Condensed phase isotope effects. Chemical Reviews. 74 (6), 689-750 DOI: 10.1021/cr60292a004

23. Ladanie, A., Schmitt, A. M., Speich, B., Naudet, F., Agarwal, A., Pereira, T. V., Sclafani, F., Herbrand, A. K., Briel, M., Martin-Liberal, J., Schmid, T., Ewald, H., Ioannidis, J. P. A., Bucher, H. C., Kasenda, B., & Hemkens, L. G. (2020). Clinical trial evidence supporting US Food and Drug Administration approval of novel cancer therapies between 2000 and 2016. JAMA Network Open, 3(11), e2024406. https://doi.org/10.1001/jamanetworkopen.2020.24406

24. Boros, L. G., Somlyai, I., Kovács, B. Z., Puskás, L. G., Nagy, L. I., Dux, L., Farkas, G., & Somlyai, G. (2021). Deuterium Depletion Inhibits Cell Proliferation, RNA and Nuclear Membrane Turnover to Enhance Survival in Pancreatic Cancer. Cancer control: journal of the Moffitt Cancer Center, 28, 1073274821999655. https://doi.org/10.1177/1073274821999655

25. Kovács, A, Guller, I, Krempels, K, et al. Deuterium depletion may delay the progression of prostate cancer. J Cancer Ther. 2011;2:548–556. doi:10.4236/jct.2011.24075

26. Krempels, K., Somlyai I, Gyöngyi Z, Ember I, Balog K, Abonyi O, and Somlyai G. "A Retrospective Study of Survival in Breast Cancer Patients Undergoing Deuterium Depletion in Addition to Conventional Therapies." Journal of Cancer Research & Therapy 1, no. 8 (2013): 194–200. https://doi.org/10.14312/2052-4994.2013-29. 27. Cancer Immunotherapy Beyond 2020. (2021, February 19). https://www.youtube.com/watch?v=R5-aMqVKbj4

28. Boros, L. G. (2005). Metabolic targeted therapy of cancer: current tracer technologies and future drug design strategies in the old metabolic network. Metabolomics: Official Journal of the Metabolomic Society, 1(1), 11–15. https://doi.org/10.1007/s11306-005-1103-7

29. Nahmad, A. D., Reuveni, E., Goldschmidt, E., Tenne, T., Liberman, M., Horovitz-Fried, M., Khosravi, R., Kobo, H., Reinstein, E., Madi, A., Ben-David, U., & Barzel, A. (2022). Frequent aneuploidy in primary human T cells after CRISPR-Cas9 cleavage. Nature Biotechnology, 1–7. https://doi.org/10.1038/s41587-022-01377-0

30. CRISPR gene editing may cause permanent damage - study. The Jerusalem Post | JPost.com. (2022, July 24). Retrieved November 6, 2022, from https://www.jpost.com/health-andwellness/article-712930

31. Haines, I. E., & Gabor Miklos, G. L. (2020). Bevacizumab moonshots: An important outcome from the latest ovarian cancer mission. Journal of Clinical Oncology: Official Journal of the American Society of Clinical Oncology, 38(2), 171–172. https://doi.org/10.1200/JCO.19.01912

32. Abola, M. V., & Prasad, V. (2016, November 1). Industry funding of cancer patient advocacy organizations. Mayo Clinic Proceedings. Retrieved November 6, 2022, from https://www.mayoclinicproceedings.org/article/S0025-6196(16)30507-9/fulltext

33. Del Paggio JC, Berry JS, Hopman WM, et al. Evolution of the Randomized Clinical Trial in the Era of Precision Oncology. JAMA Oncol. 2021;7(5):728–734. doi:10.1001/jamaoncol.2021.0379

34. Gabor Miklos, G. L. (2005). The human cancer genome project--one more misstep in the war on cancer. Nature Biotechnology, 23(5), 535–537. https://doi.org/10.1038/nbt0505-535

35. Brücher, B. L., & Jamall, I. S. (2014). Epistemology of the origin of cancer: a new paradigm. BMC Cancer, 14(1), 331. https://doi.org/10.1186/1471-2407-14-331

36. Brücher, B. L. D. M., & Jamall, I. S. (2016). Somatic mutation theory - why it's wrong for most cancers. Cellular Physiology and Biochemistry: International Journal of Experimental Cellular Physiology, Biochemistry, and Pharmacology, 38(5), 1663–1680. https://doi.org/10.1159/000443106

37. Sonnenschein, C., & Soto, A. M. (2020). Over a century of cancer research: Inconvenient truths and promising leads. PLoS biology, 18(4), e3000670. https://doi.org/10.1371/journal.pbio.3000670

38. Fung J. (2020). The cancer code: a revolutionary new understanding of a medical mystery (First). Harper Wave an imprint of HarperCollins.

39. Nowell, P. C. (1976). The clonal evolution of tumor cell populations: Acquired genetic lability permits stepwise selection of variant sublines and underlies tumor progression. Science (New York, N.Y.), 194(4260), 23–28. https://doi.org/10.1126/science.959840

40. Greaves, M., & Maley, C. C. (2012). Clonal evolution in cancer. Nature, 481(7381), 306–313. https://doi.org/10.1038/nature10762

41. Galmarini C. M. (2020). Lessons from Hippocrates: Time to Change the Cancer Paradigm. International journal of chronic diseases, 2020, 4715426. https://doi.org/10.1155/2020/4715426

42. Gyawali, B., & Booth, C. M. (2022). Cancer treatments should benefit patients: a commonsense revolution in oncology. Nature medicine, 28(4), 617–620. https://doi.org/10.1038/s41591-021-01662-6

43. Szent-Györgyi, A. (1978). The living state and cancer. Ciba Foundation Symposium, 67, 3–18. https://doi.org/10.1002/9780470720493.ch2

44. Buescher, J. M., Antoniewicz, M. R., Boros, L. G., Burgess, S. C., Brunengraber, H., Clish, C. B., DeBerardinis, R. J., Feron, O., Frezza, C., Ghesquiere, B., Gottlieb, E., Hiller, K., Jones, R. G., Kamphorst, J. J., Kibbey, R. G., Kimmelman, A. C., Locasale, J. W., Lunt, S. Y., Maddocks, O. D.,

Malloy, C., … Fendt, S. M. (2015). A roadmap for interpreting (13)C metabolite labeling patterns from cells. Current opinion in biotechnology, 34, 189–201. https://doi.org/10.1016/j.copbio.2015.02.003

45. Boros, L. G., Lee, P. W., Brandes, J. L., Cascante, M., Muscarella, P., Schirmer, W. J., Melvin, W. S., & Ellison, E. C. (1998). Nonoxidative pentose phosphate pathways and their direct role in ribose synthesis in tumors: is cancer a disease of cellular glucose metabolism? Medical Hypotheses, 50(1), 55–59. https://doi.org/10.1016/s0306-9877(98)90178-5

46. Boros, Laszlo G., Lee, W.-N. P., & Cascante, M. (2002). Imatinib and chronic-phase leukemias. The New England Journal of Medicine, 347(1), 67–68. https://doi.org/10.1056/NEJM200207043470116

47. Hanahan, D., & Weinberg, R. A. (2000). The hallmarks of cancer. Cell, 100(1), 57–70. https://doi.org/10.1016/s0092-8674(00)81683-9

48. Hanahan, D., & Weinberg, R. A. (2011). Hallmarks of cancer: the next generation. Cell, 144(5), 646–674. https://doi.org/10.1016/j.cell.2011.02.013

49. Hanahan D. (2022). Hallmarks of Cancer: New Dimensions. Cancer discovery, 12(1), 31–46. https://doi.org/10.1158/2159-8290.CD-21-1059

50. Gyamfi, J., Kim, J., & Choi, J. (2022). Cancer as a Metabolic Disorder. International journal of molecular sciences, 23(3), 1155. https://doi.org/10.3390/ijms23031155

51. Tong, W. H., Sourbier, C., Kovtunovych, G., Jeong, S. Y., Vira, M., Ghosh, M., Romero, V. V., Sougrat, R., Vaulont, S., Viollet, B., Kim, Y. S., Lee, S., Trepel, J., Srinivasan, R., Bratslavsky, G., Yang, Y., Linehan, W. M., & Rouault, T. A. (2011). The glycolytic shift in fumarate-hydratase deficient kidney cancer lowers AMPK levels, increases anabolic propensities and lowers cellular iron levels. Cancer cell, 20(3), 315–327. https://doi.org/10.1016/j.ccr.2011.07.018

52. Yang, Y., Lane, A. N., Ricketts, C. J., Sourbier, C., Wei, M. H., Shuch, B., Pike, L., Wu, M., Rouault, T. A., Boros, L. G., Fan, T. W., & Linehan, W. M. (2013). Metabolic reprogramming for producing energy and reducing power in fumarate hydratase null cells from hereditary leiomyomatosis renal cell carcinoma. PloS one, 8(8), e72179. https://doi.org/10.1371/journal.pone.0072179

53. Boros, L. G., D'Agostino, D. P., Katz, H. E., Roth, J. P., Meuillet, E. J., & Somlyai, G. (2016).

Submolecular regulation of cell transformation by deuterium depleting water exchange reactions in the tricarboxylic acid substrate cycle. Medical hypotheses, 87, 69–74. https://doi.org/10.1016/j.mehy.2015.11.016

54. Olgun A. (2007). Biological effects of deuteronation: ATP synthase as an example. Theoretical biology & medical modelling, 4, 9. https://doi.org/10.1186/1742-4682-4-9

55. https://www.sciencedirect.com/topics/medicine-and-dentistry/carbohydrate-intake

56. https://www.sciencedirect.com/topics/medicine-and-dentistry/fat-intake 57. Seyfried T. N. (2012). Cancer as a metabolic disease: on the origin management and prevention of cancer. John Wiley & Sons

58. https://www.sciencedirect.com/topics/neuroscience/aconitate-hydratase

59. Lech, J. C., Dorfsman, S. I., Répás, Z., Krüger, T., Gyalai, I. M., Boros, L. G. (2021). What to feed or what not to feed-that is still the question. Metabolomics : Official journal of the Metabolomic Society, 17(12), 102. https://doi.org/10.1007/s11306-021-01855-7

60. Zhang, X., Gaetani, M., Chernobrovkin, A., Zubarev, R. A. (2019). Anticancer Effect of Deuterium Depleted Water - Redox Disbalance Leads to Oxidative Stress. Molecular cellular proteomics : MCP, 18(12), 2373–2387. https://doi.org/10.1074/mcp.RA119.001455

61. Kovács, B. Z., Puskás, L. G., Nagy, L. I., Papp, A., Gyöngyi, Z., Fórizs, I., Czuppon, G., Somlyai, I., Somlyai, G. (2022). Blocking the Increase of Intracellular Deuterium Concentration Prevents the Expression of Cancer-Related Genes, Tumor Development, and Tumor Recurrence in Cancer Patients. Cancer control : journal of the Moffitt Cancer Center, 29, 10732748211068963. https://doi.org/10.1177/10732748211068963

62. Yavari, K., Kooshesh, L. (2019). Deuterium Depleted Water Inhibits the Proliferation of Human MCF7 Breast Cancer Cell Lines by Inducing Cell Cycle Arrest. Nutrition and cancer, 71(6), 1019–1029. https://doi.org/10.1080/01635581.2019.1595048

63. Somlyai, G, Laskay, G, Berkényi, T, et al. The biological effects of deuterium-depleted water, a possible new tool in cancer therapy. Zeitschrift für Onkologie (ger) Journal of Oncology. 1998;30:91–94.

64. Somlyai, G, Laskay, G, Berkényi, T, Jákli, GY, Jancsó, G. Naturally occurring deuterium may have a central role in cell signalling. In: Heys, JR, Melillo, DG, eds. Synthesis and Applications of Isotopically Labelled Compounds. John Wiley and Sons; 1998: 137–141.

65. Somlyai, G., Molnár, M., Laskay, G., Szabó, M., Berkényi, T., Guller, I., Kovács, A. (2010). A természetben megtalálható deutérium biológiai jelentosége: a deutériumdepletio daganatellenes hatása [Biological significance of naturally occurring deuterium: the antitumor effect of deuterium depletion]. Orvosi hetilap, 151(36), 1455–1460. https://doi.org/10.1556/OH.2010.28865

66. Basov, A., Fedulova, L., Baryshev, M., Dzhimak, S. (2019). Deuterium-Depleted Water Influence on the Isotope 2H/1H Regulation in Body and Individual Adaptation. Nutrients, 11(8), 1903. https://doi.org/10.3390/nu11081903

67. Wang, H.; Zhu, B.; Liu, C.; Fang, W.; Yang, H. [Deuterium-depleted water selectively inhibits nasopharyngeal carcinoma cell proliferation in vitro]. Nan fang yi ke da xue xue bao = J. South. Med. Univ. 2012, 32, 1394–1399. PMID: 23076171.

68. Gyöngyi, Z, Somlyai, G. Deuterium depletion can decrease the expression of c-myc, Ha-ras and p53 gene in carcinogen-treated mice. In Vivo. 2000;14:437–439. PMID: 10904878.

69. Bild, W., Stefanescu, I., Haulica, I., Lupuşoru, C., Titescu, G., Iliescu, R., Nastasa, V. (1999). Research concerning the radioprotective and immunostimulating effects of deuterium-depleted water. Romanian journal of physiology : physiological sciences, 36(3-4), 205–218.

70. Yaglova, N. V., Obernikhin, S. S., Timokhina, E. P., Diatropova, M. A., Diatropov, M. E., Yaglov, V. V. (2021). Impact of Reduced Deuterium Intake on Thermoregulation. Bulletin of experimental biology and medicine, 171(5), 572–575. https://doi.org/10.1007/s10517-021-05271-8

71. Rasooli, A., Fatemi, F., Hajihosseini, R., Vaziri, A., Akbarzadeh, K., Mohammadi Malayeri, M. R., Dini, S., Foroutanrad, M. (2019). Synergistic effects of deuterium depleted water and Mentha longifolia L. essential oils on sepsis-induced liver injuries through regulation of cyclooxygenase-2. Pharmaceutical biology, 57(1), 125–132. https://doi.org/10.1080/13880209.2018.1563622

72. Fatemi, F., Golbodagh, A., Hojihosseini, R., Dadkhah, A., Akbarzadeh, K., Dini, S., Malayeri, M. (2020). Anti-inflammatory Effects of Deuterium-Depleted Water Plus Rosa Damascena Mill. Essential Oil Via Cyclooxygenase-2 Pathway in Rats. Turkish journal of pharmaceutical sciences, 17(1), 99–107. https://doi.org/10.4274/tjps.galenos.2018.24381

73. Krempels, K., Somlyai, I, Somlyai, G. A retrospective evaluation of the effects of deuterium depleted water consumption on four patients with brain metastases from lung cancer. IntegrCancer Ther. 2008;7(3):172–181. doi:10.1177/1534735408322851