Free Radicals and Antioxidants., 2026; 16(1):7-8.
https://www.antiox.org

Commentary

The Antioxidant Paradox in Cancer: When Neutralizing Free Radicals Protects the Tumor

Mueen Ahmed KK*

Manuscript Technomedia LLP, No. 22 (New No. 40), 3rd Cross, Vivekananda Nagar, Bengaluru, Karnataka, INDIA.

For half a century, the public has absorbed a simple message: free radicals damage DNA, DNA damage causes cancer, and antioxidants mop up free radicals-therefore antioxidants should prevent cancer. The logic is so intuitive that antioxidant supplements remain a multibillion-dollar industry marketed substantially on cancer-prevention claims. Yet a striking body of experimental and clinical evidence has converged on an uncomfortable conclusion: once a malignancy has begun, supplemental antioxidants may do the opposite of what is intended, helping cancer cells survive and spread. This is the antioxidant paradox, and it deserves far wider appreciation than it currently receives.

The conceptual key is that oxidative stress is not uniformly bad for the organism, nor uniformly bad for the tumor. According to PubMed, Reactive Oxygen Species (ROS) operate on a gradient: at low levels they activate signaling pathways that promote proliferation and survival, while at higher levels they damage or kill cells by oxidizing proteins, lipids, and nucleic acids. The original rationale for antioxidant chemoprevention was that reducing ROS would lower the mutation rate and delay cancer initiation. But the same review notes that dietary supplementation with antioxidants has generally proven ineffective or detrimental in clinical trials, and crucially, that high ROS levels limit cancer cell survival during certain windows of cancer initiation and progression-so supplementation during those windows may instead promote cancer cell survival and progression.

The most provocative experimental support comes from animal models of metastasis. According to PubMed, administration of the antioxidant N-acetylcysteine increased lymph node metastases in an endogenous mouse model of malignant melanoma while having no effect on the size or number of primary tumors. The same study found that both N-acetylcysteine and a soluble vitamin E analog markedly increased the migration and invasive properties of human melanoma cells, that this effect depended on new glutathione synthesis, and that it operated through activation of the small GTPase RHOA-demonstrating a previously unappreciated role for antioxidants and the glutathione system in melanoma progression. This is a mechanistic finding, not a statistical fluke: the antioxidants did not merely correlate with worse outcomes; they actively drove the invasive phenotype.

Lung cancer tells a parallel story with an additional molecular twist. According to PubMed, long-term supplementation with N-acetylcysteine and vitamin E promoted KRAS-driven lung cancer metastasis in mice by reducing free heme levels and stabilizing the transcription factor BACH1, which in turn activated glycolytic genes, increased glucose uptake and lactate secretion, and stimulated glycolysis-dependent metastasis of both mouse and human lung cancer cells. Strikingly, the researchers found that targeting BACH1 normalized glycolysis and prevented antioxidant-induced metastasis, confirming that the antioxidants were acting through a specific, identifiable signaling axis rather than some vague systemic effect. The tumor, in effect, exploits the reduced oxidative environment that supplementation provides.

These findings dovetail with what is known about the Keap1-Nrf2 pathway, the cell's master regulator of endogenous antioxidant defense. According to PubMed, this system functions as a double-edged sword: Nrf2 activity protects normal cells and makes them resistant to oxidative and electrophilic stress, but elevated Nrf2 activity also helps cancer cells survive and proliferate. Tumors frequently hijack this very pathway to build resistance against the oxidative stress that would otherwise destroy them as they detach, circulate, and colonize distant sites. Flooding such a system with exogenous antioxidants is, from the tumor's perspective, an unearned gift.

None of this means that every antioxidant is dangerous in every cancer context, and the literature retains genuine nuance. According to PubMed, selenium and certain selenoproteins present a more complicated picture, with various studies suggesting that selenium compounds can negatively affect cancer progression and that *in vitro* and animal work has linked selenium supplementation to reduced cell migration, invasion, angiogenic factors, microvessel density, and metastasis in several cancer types-leading some to propose selenium as a potential anti-metastatic as well as preventive agent. The contrast underscores that "antioxidant" is not a single pharmacological category; mechanism, dose, chemical form, and cancer type all matter, and the epidemiological data even for selenium remain described as somewhat controversial.

OPEN ACCESS

Manuscript TECHNOMEDIA

DOI: 10.5530/fra.20260004

Copyright Information :
Copyright Author (s) 2026 Distributed under Creative Commons CC-BY 4.0

Publishing Partner : Manuscript Technomedia. [www.mstechnomedia.com]

The practical message is one of caution rather than blanket prohibition. The intuitive prevention narrative-free radicals are bad, antioxidants are good-collapses under scrutiny once a tumor exists, because the very oxidative stress that supplements suppress is also a barrier the cancer must overcome to progress and metastasize. For oncology, this has inverted some thinking entirely, with researchers now exploring pro-oxidant strategies that exacerbate oxidative stress or block the metabolic adaptations that confer oxidative-stress resistance. For the general public and for patients in particular, the prudent course is to obtain antioxidants from whole foods rather than high-dose supplements, and for anyone with a cancer diagnosis to treat self-prescribed antioxidant megadosing not as harmless insurance but as a genuinely open question with real potential for harm.

REFERENCES

Chen, Y.-C., Prabhu, K. S., & Mastro, A. M. (2013). Is selenium a potential treatment for cancer metastasis? Nutrients, 5(4), 1149-1168. https://doi.org/10.3390/nu5041149

Deshmukh, P., Unni, S., Krishnappa, G., & Padmanabhan, B. (2016). The Keap1-Nrf2 pathway: Promising therapeutic target to counteract ROS-mediated damage in cancers and neurodegenerative diseases. Biophysical Reviews, 9(1), 41-56. https://doi.org/10.1007/s12551-016-0244-4

Gill, J. G., Piskounova, E., & Morrison, S. J. (2017). Cancer, oxidative stress, and metastasis. Cold Spring Harbor Symposia on Quantitative Biology, 81, 163-175. https://doi.org/10.1101/sqb.2016.81.030791

Le Gal, K., Ibrahim, M. X., Wiel, C., Sayin, V. I., Akula, M. K., Karlsson, C., Dalin, M. G., Akyürek, L. M., Lindahl, P., Nilsson, J., & Bergo, M. O. (2015). Antioxidants can increase melanoma metastasis in mice. Science Translational Medicine, 7(308), 308re8. https://doi.org/10.1126/scitranslmed.aad3740

Wiel, C., Le Gal, K., Ibrahim, M. X., Jahangir, C. A., Kashif, M., Yao, H., Ziegler, D. V., Xu, X., Ghosh, T., Mondal, T., Kanduri, C., Lindahl, P., Sayin, V. I., & Bergo, M. O. (2019). BACH1 stabilization by antioxidants stimulates lung cancer metastasis. Cell, 178(2), 330-345. e22. https://doi.org/10.1016/j.cell.2019.06.005

Correspondence:
Dr. Mueen Ahmed KK
Manuscript Technomedia LLP, No. 22 (New No. 40), 3rd Cross, Vivekananda Nagar, Bengaluru, Karnataka, INDIA.
Email: mueen.ahmed@gmail.com

Cite this article: Ahmed KKM. The Antioxidant Paradox in Cancer: When Neutralizing Free Radicals Protects the Tumor. Free Radicals and Antioxidants. 2026;16(1):7-8.