Journal of INDEPENDENT MEDICINE

COVID-19 mRNA-Induced "Turbo Cancers"

Paul Marik[1], *Justus Hope*[2]

Abstract

The incidence of cancers has increased exponentially worldwide since the universal COVID-19 vaccination program began at the end of 2020. These cancers tend to present at an advanced stage, progress rapidly, and occur in younger patients. Additionally, some patients previously in remission have been reported to develop uncontrolled cancer relapses shortly after receiving a COVID-19 vaccination (usually a booster). The temporal association between these cancers and COVID-19 vaccination is undeniable. These observations have given rise to the term "turbo-cancers."

Although not a formally recognized oncologic classification, the term "turbo cancer" has gained traction among clinicians describing a pattern of unusually aggressive, rapidly progressing cancers—particularly among younger individuals and those previously in remission. In light of these reports, this review explores plausible biological mechanisms and available data to encourage scientific inquiry rather than premature dismissal. According to the Vaccine Event Reporting System (VAERS), the highest reported cancer risks involve the appendix, followed by breast, colorectal, laryngeal, endometrial, and hepatic cancers. A multi-hit hypothesis of oncogenesis—grounded in biological plausibility and supported by safety reports filed to VAERS—has been proposed to explain how COVID-19 vaccination may contribute to cancer development. In addition, we propose that the SARS-CoV-2 spike protein directly interferes with the fundamental pathways causing carcinogenesis, namely metabolic reprogramming, cancer stem cell propagation, apoptosis resistance, metastatic potential, and altered immune surveillance. While the prognosis of these cancers is poor, an aggressive therapeutic approach using metabolic and repurposed drugs may offer benefit.

Keywords: Turbo cancers, COVID-19 vaccines, mRNA vaccines, SARS-CoV-2 spike protein, carcinogenesis, tumor microenvironment

[1] Chief Scientific Officer, Independent Medical Alliance, Washington, DC 20036

[2] Scientific Advisor, Independent Medical Alliance, Washington, DC 20036

Corresponding author:
Paul Marik, MD
Chief Scientific Officer, Independent Medical Alliance
2001 L St NW, Suite 500, Washington, DC 20036
Email: pmarik@imahealth.org

Introduction

The observations of oncologists from around the world, as well as numerous published peer-reviewed case reports (1-12) and epidemiological data from the US, UK, and Japan, indicate that there has been an abrupt increase in the incidence of cancers beginning in 2021 and continuing into 2023, following the widespread use of the COVID-19 vaccination. (13-18) These cancers appear to be particularly aggressive, present at a late stage, and occur in younger patients. In addition, patients previously in remission have been reported to develop uncontrolled cancer relapses soon after receiving the COVID-19 vaccination (usually a booster). The

temporal association between these cancers and COVID-19 vaccination is undeniable. These observations have given rise to the term "turbo-cancers." Given its systemic impact, COVID-19 vaccination may promote malignancies in a wide range of organ systems, including those where cancer is typically rare. (16) Excess deaths from cancer have been observed in both men and women, with the greatest increase occurring among individuals aged 75 and older. (13-18) According to Craig Paardekooper of Kingston University's Department of Chemical Engineering, who analyzed the VAERS database, the risk of cancer is greatest for the appendix, followed by breast cancer, colorectal cancer, laryngeal cancer, endometrial cancer, and hepatic cancer. (16)

In the following sections, we examine how the SARS-CoV-2 spike protein may disrupt key pathways of cellular regulation and immune surveillance, contributing to oncogenesis.

Mechanistic Basis for Vaccine-Associated Carcinogenesis

COVID-19 vaccination has been demonstrated to influence cancer risk through several biological mechanisms. Angues and Bustos have proposed a multi-hit hypothesis to explain SARS-CoV-2 vaccination and oncogenesis. (19) In 2000, Hanahan and Weinberg proposed the six "hallmarks of cancer" to explain how human cells progress from normalcy to neoplastic transformation. (20) Furthermore, they proposed that genomic instability was the primary underlying mechanism driving these changes. Based on more updated data and in conjunction with the metabolic theory of cancer, (21-26) we propose a revision of the pathways leading to carcinogenesis, namely: (i) metabolic reprogramming, (ii) cancer stem cell propagation, (iii) apoptosis resistance, (iv) angiogenesis and metastatic potential, and (v) immune dysfunction with alteration of the tumor microenvironment. In this paper, we outline how the SARS-CoV-2 spike protein causes carcinogenesis via disruption of these major pathways; furthermore, we include additional mechanisms whereby spike protein may lead to carcinogenesis. This revised model, illustrated in **Figure 1**, reflects our synthesis of emerging data in conjunction with the metabolic theory of cancer.

Metabolic Reprograming

Metabolic reprogramming is a fundamental characteristic of all cancer cells. (27) This shift occurs primarily via the Warburg effect, a metabolic phenomenon in which cancer cells preferentially use glycolysis for energy production even in oxygen-rich conditions. (28, 29) Glucose is metabolized to lactate while bypassing mitochondrial oxidative phosphorylation. Excessive lactate production from glycolysis results in metabolic acidosis in the tumor microenvironment. The Warburg effect has been reported in cancer cells associated with stereotypic chromosomal mutations, suggesting that metabolic reprogramming is a fundamental finding in all cancer cells. (30)

The spike protein induces metabolic reprogramming of cells and may thereby drive the carcinogenic process. It causes a redox shift by impairing mitochondrial function, leading to a reliance on glycolysis even in oxygen-rich conditions. (31) The main signaling pathways associated with the Warburg effect are PI3K/Akt/mTOR, in concert with the transcription factors hypoxia-inducible factor (HIF-1α), p53, and c-Myc, which modulate the activity and expression of key regulatory enzymes, including pyruvate kinase M2 (PKM2), and 3-phosphoinositide-dependent protein kinase-1 (PDK1), resulting in a metabolic profile favorable to cancer cell proliferation. (27)

Oncogenic pathways such as PI3K/Akt and HIF-1α (activated even under normoxic conditions) upregulate glycolytic enzymes (eg, hexokinase, lactate dehydrogenase A) and glucose transporters (GLUT1). MYC amplifies this effect by promoting glutaminolysis, which supplements glycolysis to support biomass synthesis. (32) Aerobic glycolysis also supports activation of pro-inflammatory cells such as neutrophils and M1 macrophages.

SARS-CoV-2 hijacks host glycolysis to fuel its replication; enhanced glucose uptake and hexokinase (HK) activity supply ribose-5-phosphate for viral RNA synthesis via the pentose phosphate pathway. (31) HIF-1α and PI3K/Akt/MAPK pathways further drive glycolytic enzymes, sustaining viral proliferation. (33-35) SARS-CoV-2 infection also upregulates HIF-1α target genes (eg, GLUT1, LDH, PDK1), promoting glycolysis. (36) This metabolic shift supports viral replication and immune cell infiltration.

Spike protein exposure increases reactive oxygen species (ROS) and monocyte chemoattractant protein 1 (MCP-1) in macrophages, amplifying endothelial damage and HIF-1α expression. (37) It also activates Toll-like receptor 4 (TLR4) signaling, which stabilizes HIF-1α in macrophages, linking innate immune activation to hypoxic responses. (35)

The S1 subunit of the spike protein represses potassium channel tetramerization domain containing 2

(KCTD2), a gene implicated in tumor suppression and cellular regulation, and may indirectly disrupt c-MYC-associated pathways. (38) The spike protein's primary role in ACE2 binding and viral entry may also indirectly influence c-MYC activity through downstream signaling or co-regulation with other viral proteins. (39)

Hexokinase (HK) initiates all major pathways of intracellular glucose utilization. Type II HK (HK2) couples glycolysis to oxidative phosphorylation via interaction with mitochondria, acting as a metabolic sensor. (40) In highly glycolytic tumors—that is, extremely aggressive ones—mitochondrial HK2 activity is increased and fosters cell growth in the hypoxic conditions of neoplastic mass accrual by enhancing glycolysis, which becomes independent of oxygen availability (the Warburg effect). (40) Spike protein exposure increases glycolysis in endothelial cells, consistent with HK2's role as a rate-limiting glycolytic enzyme. (35)

Cancer Stem Cell Propagation

Cancer stem cells (CSCs) are a subset of cancer cells that exhibit characteristics similar to those of normal stem cells, including self-renewal and the ability to differentiate into various cell types within a tumor. (41-43) These cells are believed to be responsible for tumor initiation, progression, metastasis, and recurrence due to their ability to evade conventional treatments and regenerate tumors.

SARS-CoV-2 infection may promote cancer stem cell development in multiple organs due to widespread ACE2 receptor expression and systemic inflammation. (44) One review proposed that SARS-CoV-2 infection might promote cancer stem cell development in multiple organs by altering DNA repair mechanisms and immune evasion. (44) Spike protein has been shown to promote migration, invasion, and proliferation in lung cancer cells (A549 and H1299) via TLR2-dependent pathways, increasing IL-6, IL-1β, and TNF-α production. (45) In breast cancer, spike protein binds to estrogen receptors (ER), enhancing proliferation in ER-positive cells. (46) Angiotensin II (Ang-II) may also promote cancer stem cell formation and has been linked to carcinogenesis, metastasis, and relapse. (47) This effect has been demonstrated in non-small cell lung cancer (NSCLC), where Ang-II regulates tumor aggressiveness and the number of cancer stem cells. (47)

Spike protein directly binds to Wnt3a, a key ligand in the canonical Wnt pathway. This interaction activates β-catenin signaling, facilitating viral entry into cells. (48) Similarly, spike protein interacts with Notch signaling through multiple mechanisms, exacerbating viral entry, inflammation, and tissue damage in COVID-19. The SARS-CoV-2 spike protein activates nuclear factor κB (NF-κB) signaling through multiple mechanisms, driving inflammatory responses linked to COVID-19 pathogenesis. (49) Activation of the NF-κB, Wnt, and Notch pathways are major inducers of cancer stem cell proliferation. (50)

Apoptosis Resistance and Disruption of the p53 Tumor Suppressor Pathway

Cancer cells develop resistance to apoptosis through interconnected mechanisms that disrupt both intrinsic and extrinsic cell death pathways. These adaptations allow malignant cells to evade programmed cell death, survive therapeutic interventions, and drive tumor progression. Spike protein has been implicated in p53 pathway interference and apoptosis resistance. Spike protein S2 subunit specifically interacts with proteins p53, BP1, and BRCA1. (51) The p53 BP1 is a well-established tumor suppressor; BRCA1 is frequently mutated in both breast and prostate cancer. Spike protein disrupts the binding of p53 (a tumor suppressor) to MDM2 (an E3 ligase that degrades p53), stabilizing p53 but suppressing its transcriptional activity. Singh and Singh reported that the S2 subunit of SARS-CoV-2 interacts with tumor suppressor proteins p53 and BRCA, increasing the risk of cancer. (51) Zhang and El-Deiry reported that the SARS-CoV-2 spike S2 subunit inhibits p53 activation of p21(WAF1), TRAIL death receptor DR5, and MDM2 proteins in cancer cells. (52) In lung (H460) and other cancer cells, the spike protein disrupts p53's ability to activate apoptosis-related genes like p21 and TRAIL DR5, particularly after chemotherapy exposure. (53) Altered γ-H2AX expression in spike-expressing cells suggests impaired DNA repair mechanisms. (53)

Angiogenesis and Metastasis

Emerging research suggests that the SARS-CoV-2 spike protein may influence cancer progression by promoting angiogenesis and metastasis. Spike protein may promote angiogenesis by upregulating vascular endothelial growth factor (VEGF). (19, 44) This is linked to dysregulation of the renin-angiotensin-aldosterone system (RAAS) via ACE2 downregulation, which normally suppresses VEGF. Spike protein activates NF-κB, a transcription factor that enhances pro-survival pathways and angiogenesis in breast cancer cells. (54) This interaction with the renin-angiotensin system induces pro-inflam-

matory cytokines (IL-6, TNF-α) linked to metastasis.

The N-terminal domain (NTD) of the spike protein's S1 subunit contains a galectin-fold with structural homology to human galectin-3 (Gal-3). (55) This domain enables the spike protein to mimic Gal-3's sugar-binding properties. The spike protein's structural homology with human Gal-3 is linked to cancer aggressiveness and metastasis. Gal-3 itself drives NF-κB-mediated inflammation, amplifying IL-6 and TNF-α production. (44) The SARS-CoV-2 spike protein induces lung cancer migration and invasion in a TLR2-dependent manner. (45) In vitro studies demonstrate that spike protein increases MMP9 (matrix metalloproteinase) expression in colorectal cancer cells, facilitating tissue invasion. (45)

Immune Disruption and the Tumor Microenvironment

The tumor microenvironment (TME) is a dynamic ecosystem that surrounds a tumor and is composed of cancer cells, nonmalignant host cells, signaling molecules, blood vessels, and extracellular components. It plays a critical role in tumor progression, metastasis, and therapy resistance by fostering reciprocal interactions between cancer cells and their surroundings. (56-60)

Spike protein exposure may induce non-specific IgG4 antibodies, which activate inhibitory FcγRIIB receptors on macrophages and natural killer (NK) cells. (61) This interaction suppresses phagocytosis of tumor cells and promotes an immunosuppressive TME. Elevated IgG4 correlates with aggressive cancers and poor prognosis in preclinical models. (61) Jordakieva et al demonstrated that IgG4 in colorectal cancer synergizes with macrophages in shaping an immunosuppressive microenvironment that impairs anticancer effector cell functions. (62) Abue et al reported that repeated COVID-19 booster vaccinations are associated with poorer overall survival in patients with pancreatic cancer. (63) In their analysis, high levels of IgG4 induced by vaccination, correlated with a detrimental prognosis in these patients.

Lymphopenia with low CD4+ cells, low CD8+ cells, and low natural killer cells is exceedingly common after the COVID-19 vaccines. (64-67) SARS-CoV-2 spike proteins may bind to lymphocytes via ACE2-independent pathways, potentially triggering apoptosis. (68, 69) Repeated antigen exposure from vaccine boosters may lead to upregulated PD-1 expression on T cells, particularly in those with preexisting lymphopenia. (67) Lymphopenia is closely linked to impaired immune surveillance. Lymphocyte depletion undermines the body's ability to detect and eliminate malignant cancer cells, increasing susceptibility to cancer progression and mortality.

The SARS-CoV-2 spike protein may exacerbate myeloid-derived suppressor cell (MDSC)-mediated immunosuppression in the TME by inhibition of the p53 pathway. (53) Spike protein may enhance MDSC immunosuppression indirectly by promoting pro-inflammatory cytokines (eg, IL-6, IL-1β), which drive MDSC expansion and activation. (70) The SARS-CoV-2 spike protein also influences macrophage behavior, which may extrapolate to tumor-associated macrophages (TAMs) in the TME. Spike protein downregulates type I interferons (IFNAs) and protocadherins within 5 hours of exposure. (71) This early suppression of interferon signaling could impair antitumor immunity, as IFNAs are vital for activating immune cells against tumors.

Additional Proposed Mechanisms of Carcinogenesis

As previously proposed by Angues and Bustos, (19) several additional mechanisms may contribute to vaccine-related carcinogenesis, including:

- **EBV (Epstein-Barr virus).** Chronic EBV viral infection (and other herpes viruses) may be reactivated following the mRNA vaccination. (72, 73) EBV is an oncogenic virus that can convert normal cells into cancer cells by modulating the central metabolic pathways or hampering genomic integrity mechanisms, consequently inhibiting the apoptotic machinery and/or enhancing cell proliferation. (74)
- **SV40 DNA sequences.** SV40 (a known oncogenic virus) has been historically linked to polio vaccines. The detection of SV40 sequences in the COVID-19 vaccine vials raises the possibility of oncogenic potential. (75-78)
- **N1-methyl-pseudouridine.** Evidence from melanoma models suggests that the inclusion of N1-methyl-pseudouridine (m1Ψ) in mRNA vaccines may promote cancer growth and metastasis, whereas non-modified mRNA vaccines induce opposite effects, suggesting that COVID-19 mRNA vaccines could aid cancer development. (79)
- **Lipid nanoparticles (LNPs).** LNPs used in mRNA vaccines can accumulate in tumors via the enhanced permeability and retention (EPR)

effect.

- **Retrotransposon activation.** Spike protein may unsilence retrotransposable elements, contributing to genomic instability.
- **Reverse transcription.** Potential reverse-transcription and genomic integration of foreign RNA are sources of genomic instability. A study by Acevedo-Whitehouse and Bruno discusses the possibility that parts of the SARS-CoV-2 genome might undergo reverse transcription and genomic integration within infected cells, leading to persistent transcription of the integrated sequences. (80)
- **Codon optimization of mRNA.** Codon optimization of COVID-19 vaccines may lead to dysregulation of the RNA G-quadruplex (G4)-protein binding system, altering the translational regulation of cellular microRNAs. (19)

Despite this overwhelming body of evidence, mainstream medicine continues to perpetuate the false narrative that turbo cancers are "biologically implausible and there is no preclinical, nor clinical, evidence to support it." (81)

Risk Stratification and Preventive Measures

The concept of COVID-19 vaccine-induced turbo cancer is considered an anti-vaccination conspiracy theory by mainstream medicine; however, the overwhelming body of published evidence cited here suggests otherwise. As a result, risk factors for developing turbo cancers have not been well studied. However, patients with a strong family history of cancer, those in remission from prior malignancies, individuals over the age of 75 years, and patients who have received at least one booster dose appear to be at increased risk. Based on the use of the following nutraceuticals, we have developed the ROOT4 protocol for cancer prophylaxis—a preventive strategy comprising EGCG (green tea extract), curcumin, vitamin D, and omega-3 fatty acids (manuscript in press). This protocol should be considered for patients identified as high-risk.

Conclusion

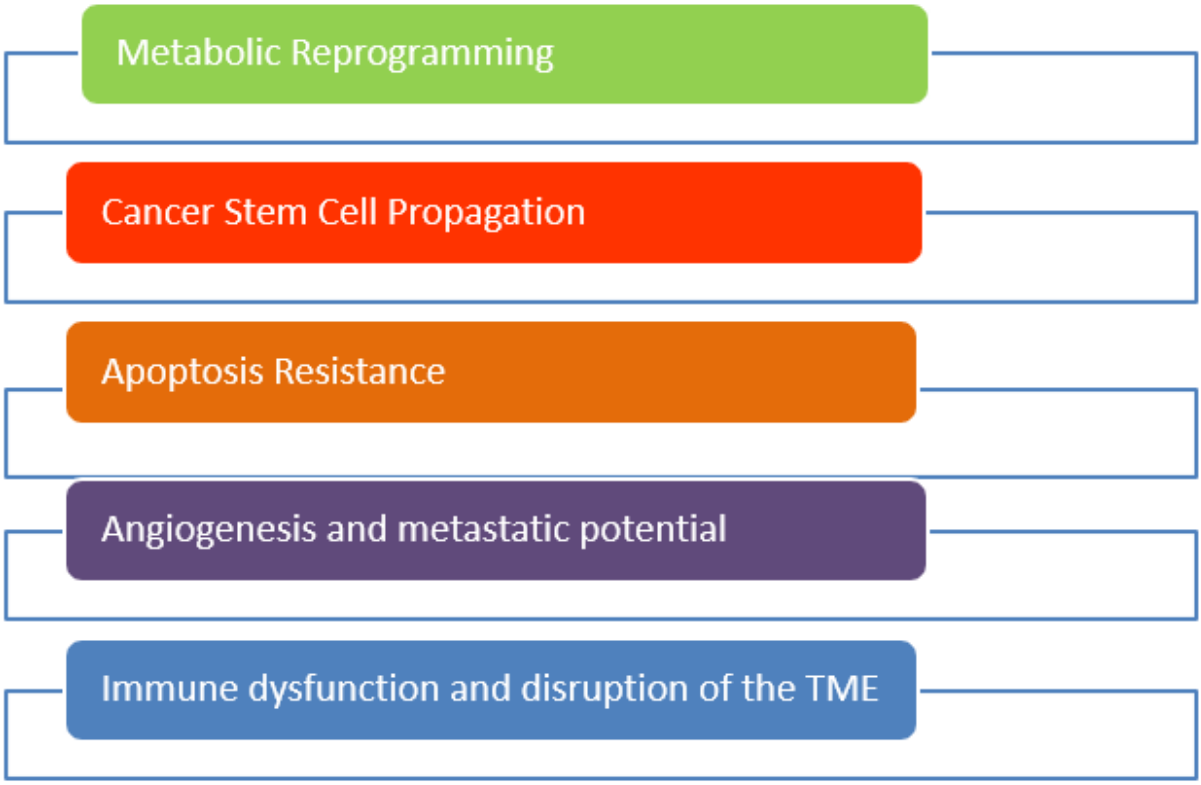
The emergence of turbo cancers following COVID-19 vaccination—marked by unusually aggressive behavior, relapse in remission cases, and occurrence in younger individuals—represents a concerning clinical pattern that warrants urgent scientific scrutiny. While mainstream discourse has largely dismissed these cancers as coincidental or biologically implausible, the mechanistic data presented in this review suggest otherwise. The SARS-CoV-2 spike protein may interfere with core regulatory pathways of carcinogenesis, including metabolic reprogramming, immune surveillance, apoptosis resistance, and stem cell proliferation.

Additional mechanisms such as EBV reactivation, SV40 DNA sequences, reverse transcription, and codon optimization may further contribute to genomic instability and oncogenic transformation. Given the consistent temporal association and biological plausibility, it is imperative to investigate these phenomena with objectivity and scientific rigor. Proactive risk stratification, enhanced postvaccination surveillance, and early, targeted prophylactic strategies, such as the ROOT4 protocol, may help mitigate the potential impact of these malignancies.

Acknowledgment

The authors have no conflicts of interest to declare.

Figure 1. Proposed mechanisms by which the SARS-CoV-2 spike protein may promote carcinogenesis



Legend: These include metabolic reprogramming, cancer stem cell propagation, apoptosis resistance, angiogenesis and metastatic potential, and immune dysfunction resulting in disruption of the tumor microenvironment (TME).

References

1. Panou E, Nikolaou V, Marinos L, et al. Recurrence of cutaneous T-cell lymphoma post viral vector COVID-19 vaccination. *J Eur Acad Dermatol Venereol*. 2022;36(2):e91-e3. doi.org/10.1111/jdv.17736
2. Cavanna L, Grassi SO, Ruffini L, et al. Non-Hodgkin lymphoma developed shortly after mRNA COVID-19 vaccination: report of a case and review of the literature. *Medicina (Kaunas)*. 2023;59(1):157. doi.org/10.3390/medicina59010157
3. Sekizawa A, Hashimoto K, Kobayashi S, et al. Rapid progression of marginal zone B-cell lymphoma after COVID-19 vaccination (BNT162b2): a case report. *Front Med (Lausanne)*. 2022;9:963393. doi.org/10.3389/fmed.2022.963393
4. Bae E, Bae S, Vaysblat M, Abdelwahed M, Sarkar K, Bae S. Development of high-grade sarcoma after second dose of Moderna vaccine. *Cureus.* 2023;15(4):e37612. doi.org/10.7759/cureus.37612
5. Goldman S, Bron D, Tousseyn T, et al. Rapid progression of angioimmunoblastic T cell lymphoma following BNT162b2 mRNA vaccine booster shot: a case report. *Front Med (Lausanne)*. 2021;8:798095. doi.org/10.3389/fmed.2021.798095
6. Barnett C, Mehta N, Towne WS, Babagbemi K, Sales RM. Metastatic melanoma in the breast and axilla: a case report. *Clin Imaging*. 2022; 85:78-82. doi.org/10.1016/j.clinimag.2022.02.014
7. Bharathidasan K, Tran V, Ghafouri SR, Rehman S, Brandi L. Metastatic prostatic adenocarcinoma presenting as generalized lymphadenopathy unmasked by a COVID booster vaccine. *Clin Case Rep*. 2023;11(12):e8278. doi.org/10.1002/ccr3.8278
8. Gentilini P, Lindsay JC, Konishi N, Fukushima M, Polykretis P. A case report of acute lymphoblastic leukaemia (ALL)/lymphoblastic lymphoma (LBL) following the second dose of Comirnaty®: An Analysis of the Potential Pathogenic Mechanism Based on of the Existing Literature. *Preprints*. 2024. doi.org/10.20944/preprints202403.1661.v2
9. Mizutani M, Mitsui H, Amano T, et al. Two cases of axillary lymphadenopathy diagnosed as diffuse large B-cell lymphoma developed shortly after BNT162b2 COVID-19 vaccination. *J Eur Acad Dermatol Venereol*. 2022;36 (8):e613-e615. doi.org/10.1111/jdv.18136
10. Tachita T, Takahata T, Yamashita S, et al. Newly diagnosed extranodal NK/T-cell lymphoma, nasal type, at the injected left arm after BNT162b2 mRNA COVID-19 vaccination. *Int J Hematol*. 2023;118(4):503-507. doi.org/10.1007/s12185-023-03607-w
11. White E, Fazio N, Tourmouzis K, et al. Unilateral conjunctival classic Kaposi sarcoma following a COVID 19 booster. *Am J Ophthalmol Case Rep.* 2024;34:101986. doi.org/10.1016/j.ajoc.2023.101986
12. Zamfir MA, Moraru L, et al. Hematologic malignancies diagnosed in the context of the mRNA COVID-19 vaccination campaign: a report of two cases. *Medicina (Kaunas)*. 2022;58(7):874. doi.org/10.3390/medicina58070874
13. Alegria C, Nunes Y. Trends in death rates from neoplasms in the US for all ages and detailed analysis for 75–84. *ResearchGate*. 2024. doi.org/10.13140/RG.2.2.16221.01760
14. Alegria C, Wiseman DM, Nunes Y. US - death trends for neoplasms ICD codes: C00–D48, ages 15-44. *Research Gate*. 2024. doi.org/10.13140/RG.2.2.16068.64645
15. Alegria C, Nunes Y. UK - death and disability trends for malignant neoplasms, ages 15-44. *Research Gate*. 2024. doi.org/10.13140/RG.2.2.34374.45123
16. Paardekooper C. Cancer and COVID vaccines. *medRxiv*. Preprint posted online 2023. doi.org/10.1101/2023.03.15.23287234
17. Akkus E, Karaoglan B, Akyol C, et al. Types and rates of COVID-19 vaccination in patients with newly diagnosed microsatellite stable and instable non-metastatic colon cancer. *Cureus*. 2024;16(6):e61780. doi.org/10.7759/cureus.61780
18. Gibo M, Kojima S, Fujisawa A, Kikuchi T, Fukushima M. Increased age-adjusted cancer mortality after the third mRNA-lipid nanoparticle vaccine dose during the COVID-19 pandemic in Japan. *Cureus*. 2024;16:e57860. doi.org/10.7759/cureus.57860
19. Valdes Angues R, Perea Bustos Y. SARS-CoV-2 vaccination and the multi-hit hypothesis of oncogenesis. *Cureus*. 2023;15(12):e50703. doi.org/10.7759/cureus.50703
20. Hanahan D, Weinberg RA. The hallmarks of cancer. *Cell*. 2000;100(1):57–70. doi.org/10.1016/S0092-8674(00)81683-9
21. Seyfried TN, Chinopoulos C. Can the mitochondrial metabolic theory explain better the

origin and management of cancer than can the somatic mutation theory? *Metabolites*. 2021;11 (9):572. doi.org/10.3390/metabo11090572
22. Seyfried TN. *Cancer as a Metabolic Disease. On the Origin, Management, and Prevention of Cancer*. Hoboken, NJ: Wiley; 2012.
23. Seyfried TN, Flores RE, Poff AM, D'Agostino DP. Cancer as a metabolic disease: implications for novel therapeutics. *Carcinogenesis*. 2014; 35(3):515–27. doi.org/10.1093/carcin/bgt480
24. Seyfried TN, Huysentruyt LC. On the origin of cancer metastasis. *Crit. Rev. Oncog*. 2013;18: 43–73. doi.org/10.1615/CritRevOncog.v18.i1-2.40
25. Seyfried TN, Shelton LM. Cancer as a metabolic disease. *Nutrition Metab (Lond)*. 2010;7: 7. doi.org/10.1186/1743-7075-7-7
26. Christofferson T. *Tripping Over the Truth: The Metabolic Theory of Cancer.* Charleston, SC: CreateSpace; 2014.
27. Jaworska M, Szczudło J, Pietrzyk A, et al. The Warburg effect: a score for many instruments in the concert of cancer and cancer niche cells. *Pharmacol Rep*. 2023;75(4):876–890. doi.org/10.1007/s43440-023-00504-1
28. Warburg O. On the origin of cancer cells. *Science*. 1956;123(3191):309–14. doi.org/10.1126/science.123.3191.309
29. Warburg O, Wind F, Negelein E. The metabolism of tumors in the body. *J. Gen. Physiol*. 1927;6:519–30. doi.org/10.1085/jgp.8.6.519
30. Patel H, Paracha A, Singhal A, Wang K, Gostanian N. Clinical Warburg effect in a patient with mantle cell lymphoma: a case report. *Cureus*. 2024;16(4):e58768. doi.org/10.7759/cureus.58768
31. Schwartz L, Aparicio-Alonso M, Henry M, Radman M, Attal R, Bakkar A. Toxicity of the spike protein of COVID-19 is a redox shift phenomenon: a novel therapeutic approach. *Free Radic Biol Med*. 2023;206:106-110. doi.org/10.1016/j.freeradbiomed.2023.05.034
32. Liu C, Jin Y, Fan Z. The mechanism of Warburg effect-induced chemoresistance in cancer. *Front Oncol*. 2021;11:698023. doi.org/10.3389/fonc.2021.698023
33. Icard P, Lincet H, Wu Z, et al. The key role of Warburg effect in SARS-CoV-2 replication and associated inflammatory response. *Biochimie*. 2021;180:169-177. doi.org/10.1016/j.biochi.2020.11.010
34. Campos MF, Constant LE, Teixeira DE, et al. SARS-CoV-2 spike protein increases angiotensin converting enzyme-2 expression and promotes an increase in glucose uptake in endothelial cells. *Acta Virol*. 2024;68:12136. doi.org/10.3389/av.2024.12136
35. Appelberg S, Gupta S, Svensson Akusjärvi S, et al. Dysregulation in Akt/mTOR/HIF-1 signaling identified by proteo-transcriptomics of SARS-CoV-2 infected cells. *Emerg Microbes Infect*. 2020;9(1):1748-1760. doi.org/10.1080/22221751.2020.1799723
36. Jana S, Heaven MR, Stauft CB, et al. HIF-1α-dependent metabolic reprogramming, oxidative stress, and bioenergetic dysfunction in SARS-CoV-2-infected hamsters. *Int J Mol Sci*. 2022;24(1):1–20. doi.org/10.3390/ijms24010001
37. Barhoumi T, Alghanem B, Shaibah H, et al. SARS-CoV-2 coronavirus spike protein-induced apoptosis, inflammatory, and oxidative stress responses in THP-1-like-macrophages: potential role of angiotensin-converting enzyme inhibitor (perindopril). *Front Immunol.* 2021; 12:728896. doi.org/10.3389/fimmu.2021.728896
38. Nahalka J. 1-L transcription of SARS-CoV-2 spike protein S1 subunit. *Int J Mol Sci*. 2024;25(8):1–10. doi.org/10.3390/ijms25081999
39. Zhang L, Jackson CB, Mou H, et al. SARS-CoV-2 spike-protein D614G mutation increases virion spike density and infectivity. *Nat Commun.* 2020;11(1):6013. doi.org/10.1038/s41467-020-19808-4
40. Chiara F, Castellaro D, Marin O, et al. Hexokinase II detachment from mitochondria triggers apoptosis through the permeability transition pore independent of voltage-dependent anion channels. *PLoS One*. 2008;3(3):e1852. doi.org/10.1371/journal.pone.0001852
41. Capp JP. Cancer stem cells: from historical roots to a new perspective. *J Oncol*. 2019;2019: 5189232. doi.org/10.1155/2019/5189232
42. Telang N. Stem cell models for cancer therapy. *Int J Mol Sci.* 2022;23(13):7055. doi.org/10.3390/ijms23137055
43. Walcher L, Kistenmacher AK, Suo H, et al. Cancer stem cells-origins and biomarkers: perspectives for targeted personalized therapies. *Front Immunol.* 2020;11:1280. doi.org/10.3389/fimmu.2020.01280
44. Jahankhani K, Ahangari F, Adcock IM, Mortaz E. Possible cancer-causing capacity of COVID-19: is SARS-CoV-2 an oncogenic agent? Biochimie. 2023;213:130-138. doi.org/10.1016/j.biochi.2023.05.014
45. Kim MJ, Kim JY, Shin JH, et al. The SARS-CoV-2 spike protein induces lung cancer migra-

tion and invasion in a TLR2-dependent manner. *Cancer Commun (Lond)*. 2024;44(2):273–277. doi.org/10.1002/cac2.12485
46. Sommariva M, Dolci M, Triulzi T, et al. Impact of in vitro SARS-CoV-2 infection on breast cancer cells. *Sci Rep*. 2024;14(1):13134. doi.org/10.1038/s41598-024-63804-3
47. Deshayes F, Nahmias C. Angiotensin receptors: a new role in cancer? *Trends Endocrinol Metab*. 2005;16(7):293-299. doi.org/10.1016/j.tem.2005.07.009
48. Melano I, Chen HJ, Ngwira L, et al. Wnt3a facilitates SARS-CoV-2 pseudovirus entry into cells. *Int J Mol Sci*. 2023;25(1):217. doi.org/10.3390/ijms25010217
49. Khan S, Shafiei MS, Longoria C, et al. SARS-CoV-2 spike protein induces inflammation via TLR2-dependent activation of the NF-KB pathway. *bioRxiv*. Preprint posted online March 16, 2021. doi.org/10.1101/2021.03.16.435700
50. Borlongan MC, Wang H. Profiling and targeting cancer stem cell signaling pathways for cancer therapeutics. *Front Cell Dev Biol*. 2023;11: 1125174. doi.org/10.3389/fcell.2023.1125174
51. Singh N, Bharara Singh A. S2 subunit of SARS-nCoV-2 interacts with tumor suppressor protein p53 and BRCA: an in silico study. *Transl Oncol*. 2020;13(10):100814. doi.org/10.1016/j.tranon.2020.100814
52. Zhang S, El-Deiry WS. SARS-CoV-2 spike S2 subunit inhibits p53 activation of p21(WAF1), TRAIL death receptor DR5 and MDM2 proteins in cancer cells. *bioRxiv*. Preprint posted online March 1, 2024. doi.org/10.1101/2024.03.01.123456
53. Zhang S, El-Deiry WS. Transfected SARS-CoV-2 spike DNA for mammalian cell expression inhibits p53 activation of p21(WAF1), TRAIL death receptor DR5 and MDM2 proteins in cancer cells and increases cancer cell viability after chemotherapy exposure. *Oncotarget*. 2024;15:275–284. doi.org/10.18632/oncotarget.123456
54. Huang HC, Liao CC, Wang SH, et al. Hyperglycosylated spike of SARS-CoV-2 gamma variant induces breast cancer metastasis. *Am J Cancer Res*. 2021;11(10):4994-5005.
55. Schroeder JT, Bieneman AP. The S1 subunit of the SARS-CoV-2 spike protein activates human monocytes to produce cytokines linked to COVID-19: relevance to Galectin-3. *Front Immunol*. 2022;13:831763. doi.org/10.3389/fimmu.2022.831763
56. Kumar V, Patel S, Tcyganov E, Gabrilovich DI. The nature of myeloid-derived suppressor cells in the tumor microenvironment. *Trends Immunol.* 2016;37(3):208–220. doi.org/10.1016/j.it.2016.01.004
57. Kumari N, Choi SH. Tumor-associated macrophages in cancer: recent advancements in cancer nanoimmunotherapies. *J Exp Clin. Cancer Res*. 2022;41(1):68.
58. Li C, Jiang P, Wei S, Xu X, Wang J. Regulatory T cells in tumor microenvironment: new mechanisms, potential therapeutic strategies and future prospects. *Mol. Cancer*. 2020;19(1):116. doi.org/10.1186/s12943-020-01234-1
59. Pan Y, Yu Y, Wang X, Zhang T. Tumor-associated macrophages in tumor immunity. *Front Immunol.* 2020;11:583084. doi.org/10.3389/fimmu.2020.583084
60. Zhang Y, Zhai Z, Duan J, et al. Lactate: the mediator of metabolism and immunosuppression. *Front Endocrinol (Lausanne)*. 2022;13: 901495. doi.org/10.3389/fendo.2022.901495
61. Uversky VN, Redwan EM, Makis W, Rubio-Casillas A. IgG4 antibodies induced by repeated vaccination may generate immune tolerance to the SARS-CoV-2 spike protein. *Vaccines (Basel)*. 2023;11(5):991. doi.org/10.3390/vaccines11050991
62. Jordakieva G, Bianchini R, Reichhold D, et al. IgG4 induces tolerogenic M2-like macrophages and correlates with disease progression in colon cancer. *Oncoimmunology*. 2021;10(1): 1880687. doi.org/ 10.1080/2162402X.2021.1880687
63. Abue M, Mochizuki M, Shibuya-Takashi R, et al. Repeated COVID-19 vaccination as a poor prognostic factor in pancreatic cancer: a retrospective, single-center cohort study. *Preprints*. Published online April 2025. doi.org/10.20944/preprints202504.1167.v1
64. Mulligan MJ, Lyke KE, Kitchin N, et al. Phase I/II study of COVID-19 RNA vaccine BNT162b1 in adults. *Nature*. 2020;586(7830): 589–593. doi.org/10.1038/s41586-020-2639-4
65. Gerlach J, Baig AM. Effects of COVID-19 and vaccination on the human immune system: cases of lymphopenia and autoimmunity. *Future Virol*. 2023;18:339–341. doi.org/10.2217/fvl-2022-0282
66. Seban RD, Richard C, Nascimento-Leite C, et al. Absolute lymphocyte count after COVID-19 vaccination is associated with vaccine-induced hypermetabolic lymph nodes on ^{18}F-FDG PET/CT: a focus in breast cancer care. *J Nucl Med*. 2022;63(8):1231-1238. doi.org/10.2967/jnumed.121.263119

67. Benitez Fuentes JD, Mohamed Mohamed K, de Luna Aguilar A, et al. Evidence of exhausted lymphocytes after the third anti-SARS-CoV-2 vaccine dose in cancer patients. *Front Oncol.* 2022;12:975980. doi.org/10.3389/fonc.2022.975980
68. Kuklina EM. T lymphocytes as targets for SARS-CoV-2. *Biochemistry (Mosc).* 2022;87 (6):566-576. doi.org/10.1134/S0006297922060046
69. Okada K, Tagami T, Otaguro T, et al. Early lymphopenia as a predictor of COVID-19 outcomes: a multicenter cohort study. *Acute Med Surg.* 2025;12(1):e70044. doi.org/10.1002/ams2.70044
70. Grassi G, Notari S, Gili S, et al. Myeloid-derived suppressor cells in COVID-19: the paradox of good. *Front Immunol*. 2022;13:842949. doi.org/10.3389/fimmu.2022.842949
71. Miltner N, Linkner TR, Ambrus V, et al. Early suppression of antiviral host response and protocadherins by SARS-CoV-2 spike protein in THP-1-derived macrophage-like cells. *Front Immunol*. 2022;13:999233. doi.org/10.3389/fimmu.2022.999233
72. Nakamura H, Nagasawa Y, Kobayashi H, et al. Successful treatment of SARS-CoV-2 vaccination-related activation of rheumatoid arthritis with positive findings for Epstein-Barr virus. *Intern Med.* 2022;61(13):2073-2076. doi.org/10.2169/internalmedicine.0614-21
73. Shafiee A, Amini MJ, Arabzadeh Bahri R, et al. Herpesviruses reactivation following COVID-19 vaccination: a systematic review and meta-analysis. *Eur J Med Res.* 2023;28(1):278. doi.org/10.1186/s40001-023-01238-9
74. Costanzo M, De Giglio MAR, Roviello GN. Deciphering the relationship between SARS-CoV-2 and cancer. *Int. J Mol. Sci.* 2023;24(9): 7803. doi.org/10.3390/ijms24097803
75. Chakraborty S. The bloodstream of mRNA vaccinated individuals (both Pfizer and Moderna) shows DNA expression vector contamination, including SV40 and kanamycin-resistant gene sequences. *OSF Preprints.* Published April 12, 2024. Accessed May 18, 2025. https://osf.io/hzyn3
76. Kammerer U, Schulz V, Steger K. BioNTech RNA-Based COVID-19 injections contain large amounts of residual DNA including an SV40 promoter/enhancer sequence. *Sci Public Health Policy Law*. 2024;5:2019-2024.
77. Šenigl F, Soikkeli A, Prost S, et al. The SV40 virus enhancer functions as a somatic hypermutation-targeting element with potential oncogenic activity. *bioRxiv*. Preprint posted online April 2024. doi.org/10.1101/2024.04.10.123456
78. Speicher DJ, Rose J, Gutschi LM, Wiseman D, McKernan K. DNA fragments detected in monovalent and bivalent Pfizer/BioNTech and Moderna modRNA COVID-19 vaccines from Ontario, Canada: exploratory dose response relationship with serious adverse events. *medRxiv*. Preprint posted online October 20, 2023. doi.org/10.31219/osf.io/mjc97
79. Rubio-Casillas A, Cowley D, Raszek M, Uversky VN, Redwan EM. Review: N1-methyl-pseudouridine (m1Ψ): friend or foe of cancer? *Int J Biol Macromol*. 2024;267(Pt 1): 131427. doi.org/10.1016/j.ijbiomac.2024.131427
80. Okoro EO, Ikoba NA, Okoro BE, Akpila AS, Salihu MO. Paradoxical increase in global COVID-19 deaths with vaccination coverage: World Health Organization estimates (2020-2023). *Int J Risk Saf Med.* Published online April 23, 2025. doi.org/10.1177/09246479251336610
81. Furlow B. Cancer misinformation puts patients in harm's way. *Lancet Oncol*. 2024;25(2):165-166. doi.org/10.1016/S1470-2045(24)00034-9