Oxygen and Cancer

https://www.nature.com/articles/nrc2540
The impact of O2 availability on human cancer 2008
During the past century it has been established that regions within solid tumours experience mild to severe O_2 deprivation owing to aberrant vascular function. These hypoxic regions are associated with altered cellular metabolism, as well as increased resistance to radiation and chemotherapy.

https://blog.dana-farber.org/insight/2019/11/cancer-and-oxygen-whats-the-connection/
Cancer and Oxygen: What's the Connection?
The difference in oxygen levels between cancer cells and normal cells continues to inspire research.
Normal human cells need just the right amount of oxygen — not too much nor too little — to survive and stay healthy. This critical balance is regulated by an intricate oxygen-sensing process in the body, the discovery of which earned the 2019 Nobel Prize in Medicine shared by Dana-Farber scientist **William G. Kaelin, Jr., MD**, and two other researchers. This mechanism enables people to adapt to living at high altitudes and bring more oxygen to cells during exercise — but it can also be hijacked by cancer cells for their own survival.
Cancer cells often are starved of oxygen — a condition called hypoxia. One instance where this might occur is when enlarging tumors outgrow the network of blood vessels that supplies tumor cells with oxygen.
Hypoxia in tumors is also a major factor in their resistance to immunotherapy agents.
Another unproven idea about oxygen and cancer is that, since many tumors thrive in oxygen-deprived (hypoxic) conditions, giving cancer cells extra oxygen might shut them down or even kill them. That's the notion behind hyperbaric oxygen therapy

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3510426/
Hyperbaric oxygen therapy and cancer—a review
Hypoxia is a critical hallmark of solid tumors and involves enhanced cell survival, angiogenesis, glycolytic metabolism, and metastasis.
Based on the present as well as previous reviews, there is no evidence indicating that HBO neither acts as a stimulator of tumor growth nor as an enhancer of recurrence. On the other hand, there is evidence that implies that HBO might have tumor-inhibitory effects in certain cancer subtypes, and we thus strongly believe that we need to expand our knowledge on the effect and the mechanisms behind tumor oxygenation.

https://www.jbc.org/article/S0021-9258(20)33918-1/fulltext
Oxygen availability and metabolic reprogramming in cancer 2017
Because O_2 serves as an electron acceptor in oxidative phosphorylation, a central adaptation to hypoxia is a shift toward non-oxidative forms of carbon metabolism and ATP production, such as anaerobic glycolysis (Fig. 1*A*).

https://pubmed.ncbi.nlm.nih.gov/30739528/
Hyperbaric oxygen rescues lung cancer cells from chemical hypoxia-induced low differentiation and apoptosis resistance 2018
Hypoxia induces vigorous growth and a higher malignant phenotype in solid tumors. Hyperoxic treatment using hyperbaric oxygen (HBO) has previously been shown as a highly effective method to attenuate hypoxia. We aimed to investigate the effect of HBO on hypoxia-induced malignancy of lung cancer cells.
HBO could serve as a reliable adjuvant treatment targeting the hypoxia microenvironment in solid tumors.

https://pubmed.ncbi.nlm.nih.gov/34367973/
Hyperbaric Oxygen Therapy Represses the Warburg Effect and Epithelial-Mesenchymal Transition in Hypoxic NSCLC Cells via the HIF-1α/PFKP Axis 2021
Background: Tumor cells initiate hypoxia-induced mechanisms to fuel cell proliferation, invasion, and metastasis, largely mediated by low O_2-responsive Hypoxia-Inducible Factor 1 Alpha (HIF-1α). Therefore, hyperbaric oxygen therapy (HBO) is now being studied in cancer patients, but its impact upon non-small-cell lung cancer (NSCLC) cell metabolism remains uncharacterized.
Conclusions: HBO's repression of the Warburg effect, repression of hyperproliferation, and repression of EMT in hypoxic NSCLC cells is dependent upon HIF-1α downregulation. HIF-1α's target gene PFKP functions as a central mediator of HBO's effects in hypoxic NSCLC cells and may represent a metabolic vulnerability in NSCLC tumors.

https://pubmed.ncbi.nlm.nih.gov/38226837/
Hypoxia promotes non-small cell lung cancer cell stemness, migration, and invasion via promoting glycolysis by lactylation of SOX9 2024
Lung cancer is the deadliest form of malignancy and the most common subtype is non-small cell lung cancer (NSCLC). Hypoxia is a typical feature of solid tumor microenvironment. In the current study, we clarified the effects of hypoxia on stemness and metastasis and the molecular mechanism.
Conclusion: Hypoxia induced the lactylation of SOX9 to promote stemness, migration, and invasion via promoting glycolysis. The findings suggested that targeting hypoxia may be an effective way for NSCLC treatment and reveal a new mechanism of hypoxia in NSCLC.

https://pubmed.ncbi.nlm.nih.gov/38279461/
Evaluation of use of hyperbaric oxygen in suppression of hyper-proliferation in hypoxic NSCLC cells 2023
Hyperbaric oxygen therapy (HBO) is being researched as a potential adjuvant treatment for solid malignancies, such as NSCLC. It can reduce tumour hypoxia and has been found to slow tumour growth, stop dedifferentiation, and reduce apoptosis resistance in hypoxic NSCLC cells. Though HBO has shown promise in treating various cancers, more study is required to determine its precise mechanism of action in NSCLC.
After HBO treatment, glucose absorption was reduced while intracellular ATP levels were maintained. Overexpression of HIF-1a was able to counteract the effect of HBO on glycolytic gene expression. PFKP is a possible therapeutic target because HBO reduces the Warburg effect in NSCLC cells by downregulating HIF-1.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3140692/
The impact of O2 availability on human cancer 2008
During the last century, it has been established that regions within solid tumors experience mild to severe oxygen deprivation, due to aberrant vascular function. These hypoxic regions are associated with altered cellular metabolism, as well as increased resistance to radiation and chemotherapy.
Ambient air is 21% O_2 (150 mm Hg); however, most mammalian tissues exist at 2%-9% O_2 (on average 40 mm Hg). "Hypoxia" is usually defined as ≤ 2% O_2, while severe hypoxia or "anoxia" is defined as ≤ 0.02% O_2.
As described by Otto Warburg in the 1920s, rapidly dividing tumor cells display increased glycolysis, even in the presence of oxygen. As a consequence, lactic

acid concentrations are elevated, acidifying the environment.

Gray used Ehrlich mouse ascites tumor cells irradiated in vitro and in mice under various O_2 conditions. Similar to what had been shown in plants and insect tissues, Gray found that the ascites tumor cells showed a dependence of radiation sensitivity on O_2 tension both *in vitro* and *in vivo*. Sensitivity was about three times greater under well-oxygenated conditions as compared to anoxic conditions [19,20]. Subsequently, Churchill-Davidson published a cytological evaluation of damage in patient tumors after radiation. One half of the tumor was irradiated while patients breathed pure O_2 at three atmospheres pressure, the other half while patients were breathing room air. Significantly more damage was observed in the half irradiated under high O_2 conditions [21].

Similarly, hypoxic cells were later found to be more resistant to many commonly used chemotherapeutic agents [25,26]