Catalase

https://isom.ca/wp-content/uploads/2020/01/JOM_2001_16_3_10_The_Effect_of_Alternating_Magnetic_Field_Exposure_and-.pdf
The Effect of Alternating Magnetic Field Exposure and Vitamin C on Cancer Cells 2001
The purpose of our study was to examine the anti-tumor effect of vitamin C combined with magnetic field treatments. The inhibitory effect of vitamin C in cancer cells involves its interaction with several compounds: glutathione (GSH), hydrogen peroxide and the enzyme catalase. 17,18 In the blood, vitamin C is oxidized to dehydroascorbate (DHA). DHA is easily transported across cell membranes where it is then reduced by GSH back to vitamin C. Cancer cells have a high level of GSH compared to normal cells. The higher level of GSH for the same level of vitamin C produces more hydrogen peroxide. In normal cells, catalase inactivates hydrogen peroxide by converting it to water and oxygen. Cancer cells have a reduced (10 to 100 fold) intracellular level of catalase. This results in very high levels of hydrogen peroxide and oxidative by-products in the cancer cell. 18 Hydrogen peroxide is toxic and destroys the cancer cells.

https://pubmed.ncbi.nlm.nih.gov/25498893/
Effects of extremely low frequency electromagnetic field (ELF-EMF) on catalase, cytochrome P450 and nitric oxide synthase in erythro-leukemic cells 2015
A significant modulation of iNOS, CAT and Cyt P450 protein expression was recorded as a result of ELF-EMF exposure in both phorbol 12-myristate 13-acetate (PMA)-stimulated and non-stimulated cell lines. Modulation in kinetic parameters of CAT, CYP-450 and iNOS enzymes in response to ELF-EMF indicates an interaction between the ELF-EMF and the enzymological system.

https://www.emf-portal.org/en/article/26254
Effects of extremely low frequency electromagnetic field (ELF-EMF) on catalase, cytochrome P450 and nitric oxide synthase in erythro-leukemic cells 2015
The total enzyme activity of catalase was significantly increased in all exposed cells (groups 1-3) compared to the control group and the peak time was significantly increased in PMA-exposed cells (group 2) and PMA + magnetic field co-exposed cells (group 3) in comparison to the control group. The catalase protein expression was significantly increased in PMA + magnetic field co-exposed cells compared to PMA-exposed cells.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC11201554/
Exploring Therapeutic Potential of Catalase: Strategies in Disease Prevention and Management 2024
In cancer, disrupting the delicate balance between reactive oxygen species (ROS) generation and antioxidant defenses, including catalase, contributes to DNA damage and genomic instability. Investigations into the dual role of catalase in cancer have revealed that while its protective function in normal cells is essential, it may inadvertently support cancer cell survival.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10915913/
Therapeutic potentials of catalase: Mechanisms, applications, and future perspectives 2024
In the early stages of carcinogenesis, catalase's antioxidant properties thwart ROS-induced DNA damage and mutagenesis, thereby suppressing tumor initiation. [27,28] Conversely, in established tumors, catalase's upregulation facilitates cancer cell survival under conditions of oxidative stress, conferring a selective growth advantage and promoting tumor progression.[28] Furthermore, catalase's involvement in redox signaling pathways modulates cancer cell proliferation, angiogenesis, and metastasis, highlighting its multifaceted role in tumor biology. Harnessing catalase's dual nature as both a tumor suppressor and promoter poses intriguing therapeutic implications for cancer treatment, warranting further investigation.[1,3,27,28]

https://pubmed.ncbi.nlm.nih.gov/37424804/
Catalase as a novel drug target for metastatic castration-resistant prostate cancer 2023
Catalase is a very important enzyme in controlling OS levels. We hypothesized that catalase function is critical for the progression to mCRPC. To test this hypothesis, we used a CRISPR nickase system to create a catalase knockdown in PC3 cells, a mCRPC human-derived cell line. We obtained a $Cat^{+/-}$ knockdown cell line, which has approximately half of the transcripts for catalase, half of the protein levels, and half of catalase activity. The $Cat^{+/-}$ cells are also about twice as sensitive to H_2O_2 exposure compared to WT cells, migrate poorly, have low attachment to collagen, high attachment to Matrigel, and proliferate slowly. Using SCID mice for a xenograft model, we show that $Cat^{+/-}$ cells form smaller tumors than wild-type tumors with less collagen and no blood vessels. These results were validated via rescue experiments where functional catalase was reintroduced into the $Cat^{+/-}$ cells and the phenotypes were reversed. This study shows a novel role for catalase in deterring mCRPC development and points to a new potential drug target for mCRPC progression.

https://www.degruyter.com/document/doi/10.1515/hsz-2017-0131/html#j_hsz-2017-0131_tab_002_w2aab3b7c69b1b6b1ab1b6b3Aa
Catalase, a remarkable enzyme: targeting the oldest antioxidant enzyme to find a new cancer treatment approach 2017
This locally high expression of catalase on the membrane of tumor cells is in line with the findings by Deichman's group that showed that tumor progression *in vivo* is dependent on increased resistance towards exogenous H_2O_2 (Deichman, 2000, 2002). Furthermore, localized expression of catalase on the membrane of tumor cells is not in disagreement with the finding of lower total catalase concentration in malignant cells, as the membrane comprises a minority of the total cellular material.
Furthermore, the modulation of the intracellular NO concentration has been shown to lead to the generation of cell-derived singlet oxygen that inactivates tumor cell protective catalase and reactivates intercellular ROS/RNS-mediated apoptosis-inducing signaling (Bauer, 2015; Scheit and Bauer, 2015).
Thus, as compared to normal tissues of the same origin, some authors reported an increased catalase expression in tumors (Sander et al., 2003; Hwang et al., 2007; Rainis et al., 2007), whereas other studies showed a catalase down-regulation (Marklund et al., 1982; Baker et al., 1997; Lauer et al., 1999; Chung-man et al., 2001; Cullen et al., 2003; Kwei et al., 2004), indicating that cancer cells are frequently more sensitive to an oxidative stress. For instance, we have reported an important decrease of catalase activity in different cancer cell lines, as shown in Table 2 (Verrax et al., 2009; Beck et al., 2011a; Glorieux et al., 2011).
Table 2:

Catalase enzyme activity in cells from diver origins.

Type of cells	Normal origin	Cancer origin References
Mouse hepatocytes	96.45±6.32	11.12±4.43[a,f] Verrax et al. (2009)
Human leukocytes	44.55±1.80	16.36±3.60[b,e] Beck et al. (2011a)
Human mammary epithelial cells	13.14±3.04[c]	5.44±0.88[d,e] Glorieux et al. (2016a)

https://pubmed.ncbi.nlm.nih.gov/29467594/

Catalase down-regulation in cancer cells exposed to arsenic trioxide is involved in their increased sensitivity to a pro-oxidant treatment 2018

Pro-oxidant drugs have been proposed for treating certain cancers but the resistance developed by cancer cells to oxidative stress limits its potential use in clinics. To understand the mechanisms underlying resistance to oxidative stress, we found that the chronic exposure to an H_2O_2-generating system (ascorbate/menadione, Asc/Men) or catalase overexpression (CAT3 cells) increased the resistance of cancer cells to oxidative stress, likely by increasing the antioxidant status of cancer cells.

Results: Using Resox and CAT3 cells (derived from MCF-7 breast cancer cell line) as models for cancer resistance to pro-oxidative treatment, we found that arsenic trioxide (ATO) remarkably sensitized Resox and CAT3 cells to Asc/Men treatment. Since catalase is a key antioxidant enzyme involved in detoxifying Asc/Men (as shown by siRNA-mediated catalase knockdown) that is overexpressed in resistant cells, we hypothesized that ATO might regulate the expression levels of catalase. Consistently, catalase protein level is decreased in Resox cells when incubated with ATO likely by a decreased transcriptional activity of the catalase promoter.

Conclusions: Our findings support the proposal that ATO should be administered in combination with pro-oxidant drugs to enhance cancer cell death in solid tumors.

https://pubmed.ncbi.nlm.nih.gov/29535798/

Evaluation of Potential Mechanisms Controlling the Catalase Expression in Breast Cancer Cells 2018

Development of cancer cell resistance against prooxidant drugs limits its potential clinical use. MCF-7 breast cancer cells chronically exposed to ascorbate/menadione became resistant (Resox cells) by increasing mainly catalase activity. Since catalase appears as an anticancer target, the elucidation of mechanisms regulating its expression is an important issue.

In line with our previous report, chromatin remodeling appears as the main regulator of catalase expression in breast cancer after chronic exposure to an oxidative stress

https://pubmed.ncbi.nlm.nih.gov/27591797/

Chromatin remodeling regulates catalase expression during cancer cells adaptation to chronic oxidative stress 2016

Regulation of ROS metabolism plays a major role in cellular adaptation to oxidative stress in cancer cells, but the molecular mechanism that regulates catalase, a key antioxidant enzyme responsible for conversion of hydrogen peroxide to water and oxygen, remains to be elucidated.

This regulatory mechanism plays an important role in redox adaptation to chronic exposure to H_2O_2 in breast cancer cells. Our study suggests that cancer adaptation to oxidative stress may be regulated by transcriptional factors through chromatin remodeling, and reveals a potential new mechanism to target cancer cells.

https://pubmed.ncbi.nlm.nih.gov/26117330/

Regulation of catalase expression in healthy and cancerous cells 2015

Deciphering the molecular mechanisms that regulate catalase expression could, therefore, be of crucial importance for the future development of pro-oxidant cancer chemotherapy.

https://pubmed.ncbi.nlm.nih.gov/35763649/

Effects of ERCC5 rs751402 Polymorphism on Oxidative Stress and the Impact of Curcumin on Catalase Activity in Breast Carcinogenesis 2022

Results: It showed that this polymorphism involved in oxidative stress ($p < 0.05$) and curcumin caused the antiproliferative effect by the catalase activity increase ($p < 0.05$).

Conclusion: Our study indicated that ERCC5 rs751402 polymorphism may contribute to the etiology of breast carcinogenesis about the failure of oxidative stress protection and lead to breast carcinogenesis. The antiproliferative effect of curcumin may be associated with catalase activity and protect breast carcinogenesis.

https://www.sciencedirect.com/science/article/abs/pii/S0891584921003750

Browsing the oldest antioxidant enzyme: catalase and its multiple regulation in cancer 2021

Catalase, as well as other antioxidant enzymes, plays an important dichotomous role in cancer. Therefore, therapies aimed at either reverting the increased or further escalating catalase levels could be effective, depending on the metabolic landscape and on the redox status of cancer cells.

Reflecting this role of ROS, catalase plays a dichotomous role in cancer as both a tumor suppressor and a prosurvival protein during tumor progression.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5106370/

Tumor cells have decreased ability to metabolize H2O2: Implications for pharmacological ascorbate in cancer therapy 2016

Ascorbate (AscH−) functions as a versatile reducing agent. At pharmacological doses (P-AscH−; [plasma AscH−] ≥≈20 mM), achievable through intravenous delivery, oxidation of P-AscH− can produce a high flux of H2O2 in tumors. Catalase is the major enzyme for detoxifying high concentrations of H2O2. We hypothesize that sensitivity of tumor cells to P-AscH− compared to normal cells is due to their lower capacity to metabolize H2O2. Rate constants for removal of H2O2 (kcell) and catalase activities were determined for 15 tumor and 10 normal cell lines of various tissue types. A differential in the capacity of cells to remove H2O2 was revealed, with the average kcell for normal cells being twice that of tumor cells. The ED50 (50% clonogenic survival) of P-AscH− correlated directly with kcell and catalase activity. Catalase activity could present a promising indicator of which tumors may respond to P-AscH−.

Studies have shown that all but one human cancer cell type, a human renal adenocarcinoma, have low levels of both catalase and GPx [29]. This suggests that the vast majority of cancer cells may lack the biochemical machinery needed to detoxify higher fluxes of H_2O_2 efficiently. While in general, the levels of catalase are low in cancer cells, catalase activity appears to vary greatly across different cancer cell lines [28]. This may correspond to a differential capacity to remove H_2O_2 and differential sensitivity to H_2O_2 -producing agents (*i.e.* P-AscH$^-$). We hypothesize that the sensitivity of tumor cells to P-AscH$^-$ compared to normal cells is due to their lower capacity to remove extracellular H_2O_2; across different tumor cell types there will also be a differential sensitivity to P-AscH$^-$ that is correlated with their individual capacities to remove extracellular H_2O_2, as reflected by k_{cell} of H_2O_2 removal and catalase activity.

When catalase was inhibited using 3-amino-1,2,4-triazole (3-AT) in HepG2 cells, which have a high basal level of catalase activity, there was a 4.6-fold decrease in the rate constant at which these cells remove extracellular H_2O_2 (Fig. 3A). These results both suggest and support the important role of catalase in the removal of high concentrations of extracellular H_2O_2.

We observed that both increasing and decreasing the catalase activity had a significant effect on the rate constant of H2O2 removal and further investigated whether similar manipulation of basal catalase activity would affect the cells' sensitivity to P-AscH−.

Increasing the catalase activity within the same cell line (MIA PaCa-2) increased resistance to P-AscH− (Fig. 5B).

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8073689/

Catalase Modulates the Radio-Sensitization of Pancreatic Cancer Cells by Pharmacological Ascorbate 2021

Pancreatic cancer cells (PDACs) are more susceptible to an oxidative insult than normal cells, resulting in greater cytotoxicity upon exposure to agents that increase pro-oxidant levels. Pharmacological ascorbate (P-AscH$^-$), i.e., large amounts given intravenously (IV), generates significant fluxes of hydrogen peroxide (H_2O_2), resulting in the killing of PDACs but not normal cells. Recent studies have demonstrated that P-AscH$^-$ radio-sensitizes PDAC but is a radioprotector to normal cells and tissues. Several mechanisms have been hypothesized to explain the dual roles of P-AscH− in radiation-induced toxicity including the activation of nuclear factor-erythroid 2-related factor 2 (Nrf2), RelB, as well as changes in bioenergetic profiles. We have found that P-AscH− in conjunction with radiation increases Nrf2 in both cancer cells and normal cells. Although P-AscH− with radiation decreases RelB in cancer cells vs. normal cells, the knockout of RelB does not radio-sensitize PDACs. Cellular bioenergetic profiles demonstrate that P-AscH− with radiation increases the ATP demand/production rate (glycolytic and oxidative phosphorylation) in both PDACs and normal cells. Knocking out catalase results in P-AscH− radio-sensitization in PDACs. In a phase I trial where P-AscH− was included as an adjuvant to the standard of care, short-term survivors had higher catalase levels in tumor tissue, compared to long-term survivors. These data suggest that P-AscH− radio-sensitizes PDACs through increased peroxide flux. Catalase levels could be a possible indicator for how tumors will respond to P-AscH−.

https://medicine.uiowa.edu/content/why-high-dose-vitamin-c-kills-cancer-cells

Why high-dose vitamin C kills cancer cells 2017

"Our results suggest that cancers with low levels of catalase are likely to be the most responsive to high-dose vitamin C therapy, whereas cancers with relatively high levels of catalase may be the least responsive," he explains.

A future goal of the research is to develop methods to measure catalase levels in tumors.

https://pubmed.ncbi.nlm.nih.gov/25458956/

Significance of blood serum catalase activity and malondialdehyde level for survival prognosis of ovarian cancer patients 2014

Significantly lower CAT (28.2±15.5 vs. 36.1±14.6nmol/L/min, P=0.019) activity and higher MDA levels (8.7±3.0 vs. 6.7±2.7nmol/L, P=0.002) were observed in cancer patients compared with healthy volunteers.

https://www.nature.com/articles/cdd2012102

The critical role of catalase in prooxidant and antioxidant function of p53 2012

The tumor suppressor p53 is an important regulator of intracellular reactive oxygen species (ROS) levels, although downstream mediators of p53 remain to be elucidated.

Here, we demonstrate that p53 upregulates intracellular ROS levels through suppression of catalase activity: first, p53 and catalase can form a stable complex both *in vitro* and *in vivo*. Second, p53 protein is able to inhibit catalase activity *in vitro*.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8730328/

Tumor Suppressor p53: Biology, Signaling Pathways, and Therapeutic Targeting 2021

TP53 is the most commonly mutated gene in human cancer with over 100,000 literature citations in PubMed. This is a heavily studied pathway in cancer biology and oncology with a history that dates back to 1979 when p53 was discovered. The p53 pathway is a complex cellular stress response network with multiple diverse inputs and downstream outputs relevant to its role as a tumor suppressor pathway.

https://bmccomplementmedtherapies.biomedcentral.com/articles/10.1186/1472-6882-12-61

Natural resistance to ascorbic acid induced oxidative stress is mainly mediated by catalase activity in human cancer cells and catalase-silencing sensitizes to oxidative stress 2012

Ascorbic acid demonstrates a cytotoxic effect by generating hydrogen peroxide, a reactive oxygen species (ROS) involved in oxidative cell stress. A panel of eleven human cancer cell lines, glioblastoma and carcinoma, were exposed to serial dilutions of ascorbic acid (5-100 mmol/L). The purpose of this study was to analyse the impact of catalase, an important hydrogen peroxide-detoxifying enzyme, on the resistance of cancer cells to ascorbic acid mediated oxidative stress.

Results

The tested human cancer cell lines demonstrated obvious differences in their resistance to ascorbic acid mediated oxidative cell stress. Forty-five percent of the cell lines had an EC50 > 20 mmol/L and fifty-five percent had an EC50 < 20 mmol/L. With an EC50 of 2.6–5.5 mmol/L, glioblastoma cells were the most susceptible cancer cell lines analysed in this study. A correlation between catalase activity and the susceptibility to ascorbic acid was observed. To study the possible protective role of catalase on the resistance of cancer cells to oxidative cell stress, the expression of catalase in the breast carcinoma cell line BT-20, which cells were highly resistant to the exposure to ascorbic acid (EC50: 94,9 mmol/L), was silenced with specific sh-RNA. The effect was that catalase-silenced BT-20 cells (BT-20 KD-CAT) became more susceptible to high concentrations of ascorbic acid (50 and 100 mmol/L).

Conclusions

Fifty-five percent of the human cancer cell lines tested were unable to protect themselves against oxidative stress mediated by ascorbic acid induced hydrogen peroxide production. The antioxidative enzyme catalase is important to protect cancer cells against cytotoxic hydrogen peroxide. Silenced catalase expression increased the susceptibility of the formerly resistant cancer cell line BT-20 to oxidative stress.

https://www.sciencedirect.com/science/article/abs/pii/S0891584912003656

Maintenance of higher H2O2 levels, and its mechanism of action to induce growth in breast cancer cells: Important roles of bioactive catalase and PP2A 2012

We conclude that inhibition of catalase bioactivity by O2- leads to an increase in steady-state levels of H2O2 in HBC cells, which in turn inhibits PP2A activity, leading to phosphorylation of ERK 1/2 and Akt and resulting in HBC (human breast cancer) cell proliferation.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6527626/

Intracellular catalase activity instead of glutathione level dominates the resistance of cells to reactive oxygen species 2019

Collectively, catalase activity instead of glutathione level dominates the resistance of cells to ROS.

Catalase, a scavenger of H_2O_2, efficiently decomposes H_2O_2 to water and dioxygen to protect cells against H_2O_2 stress (Martins and English 2014). It was reported that H_2O_2-resistant cells exhibited high catalase activity

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7731207/

Use of H2O2 to Cause Oxidative Stress, the Catalase Issue 2020

Addition of hydrogen peroxide (H_2O_2) is a method commonly used to trigger cellular oxidative stress. However, the doses used (often hundreds of micromolar) are

disproportionally high with regard to physiological oxygen concentration (low micromolar). In this study using polarographic measurement of oxygen concentration in cellular suspensions we show that H_2O_2 addition results in O_2 release as expected from catalase reaction. This reaction is fast enough to, within seconds, decrease drastically H_2O_2 concentration and to annihilate it within a few minutes. Firstly, this is likely to explain why recording of oxidative damage requires the high concentrations found in the literature. Secondly, it illustrates the potency of intracellular antioxidant (H_2O_2) defense. Thirdly, it complicates the interpretation of experiments as subsequent observations might result from high/transient H_2O_2 exposure and/or from the diverse possible consequences of the O_2 release.