

Possible Treatment for COVID-19 mRNA Vaccine Turbo Cancer? Melatonin Regulates Oncogenic Micro RNAs or miRNA or Oncomir. Can It Counteract Pfizer's Co-miRNA-ty Vaccine?

8 papers reviewed

By <u>Dr. William Makis</u> Global Research, October 09, 2023 <u>COVID Intel</u> 8 October 2023 Theme: Science and Medicine

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Papers reviewed:

- <u>2023 Sep Putta et al</u> Melatonin: Avenues in cancer therapy and its nanotechnological advancements
- <u>2023 Jun Megerian et al</u> Melatonin and Prostate Cancer: Anti-tumor Roles and Therapeutic Application
- <u>2022 Sep Davoodvandi et al</u> Melatonin and cancer suppression: insights into its effects on DNA methylation
- 2022 Aug Florido et al Understanding the Mechanism of Action of Melatonin, Which Induces ROS Production in Cancer Cells
- <u>2022 May Monayo et al</u> The Prospective Application of Melatonin in Treating Epigenetic Dysfunctional Diseases
- <u>2022 Mar Leilei Wang et al</u> Use of Melatonin in Cancer Treatment: Where Are We?
- <u>2021 Jul Gonzalez et al</u> Melatonin as an Adjuvant to Antiangiogenic Cancer Treatments
- <u>2021 Apr Talib et al</u> Melatonin in Cancer Treatment: Current Knowledge and Future Opportunities







2023 Sep - Putta et al - Melatonin: Avenues in cancer therapy and its nanotechnological advancements

- "According to clinical investigations, melatonin has the potential to prevent and cure cancer"
- Melatonin is crucial for tumor development. Low levels of Melatonin accelerate tumor development

- At normal dose levels ranging from 10 to 50 mg/day, it can treat a variety of cancers in vivo (breast, lung, colon, liver, gastric, glioblastoma, ovarian, cervical, prostate, skin)
- There is strong proof that it reduces adverse effects while improving the therapeutic benefits of chemotherapy and radiation
- Due to its chemical characteristics, Melatonin has a restricted ability to penetrate mucosal and dermal barriers, has a shorter half-life, and is rapidly eliminated from blood circulation
- the use of Melatonin is currently limited due to its unfavourable pharmacokinetic properties.
- Nanoparticles are being developed to deliver Melatonin and potentially increase its use in cancer treatment.

2023 Jun - Megerian et al - Melatonin and Prostate Cancer: Anti-tumor Roles and Therapeutic Application

- Prostate cancer risk has been associated with exogenous factors that interfere with normal pineal secretory activity, including aging, poor sleep, and artificial light at night.
- melatonin secretion becomes circadian between the age of one to three years and gradually diminishes by 10-15% per decade
- Diminished lifetime secretion of melatonin has been suggested to be a catalyst for not only aging (dubbed "Age Clock"), but also age-related conditions like cancer
- Disruption of the circadian rhythm can increase the risk of cancer
- relationship between light exposure at night and the risk of prostate cancer
- Several reports have correlated non-standard shift work and shift work sleep disorder with poor health consequences notably on men's urologic health such as infertility, lower urinary tract symptoms, and prostate cancer
- significant increase in the risk of prostate cancer in rotating shift workers who alternate between a day and/or afternoon shift and a night shift
- Melatonin action on prostate cancer cells:
 - Melatonin prevents carcinogenesis by reducing genomic instability
 - Melatonin inhibits glucose metabolism of cancer cells
 - Melatonin inhibits DNA replication in cancer cells and cell proliferation
 - Melatonin downregulates NF-kB activities leading to promote apoptosis and inhibit cell proliferation.
 - Melatonin inhibits angiogenic processes
 - Melatonin attenuates androgen receptor activity
 - Melatonin inhibits metastasis by inhibiting enzymes that help cancer cells metastasize (Matrix metalloproteinases)
 - Melatonin inhibits initiation and progression of cancers by modulating mitochondrial activity and function (melatonin improves mitochondrial function by inhibitory effect on Akt/mTOR path)
 - melatonin has anti-inflammatory effects on inflammatory cytokines like IL-17 that promote cancer

- melatonin has anti-cancer effects by resynchronizing the circadian rhythm
- In previous clinical trials that investigated the anti-tumor effects of melatonin, the maintenance dose was mostly 20 mg per day and the duration varied from several weeks to some years (<u>Gonzalez et al</u>).
- "Considering that there were no major side effects related to melatonin except for minor psychological or neurocognitive problems (Foley et al), we recommend a higher dosage for a definite anti-tumor activity."

2022 Sep - Davoodvandi et al - Melatonin and cancer suppression: insights into its effects on DNA methylation

- Melatonin (N-acetyl-5-methoxy-tryptamine) is an endogenous hormone was discovered in bovine pineal tissue of bovine by Lerner and colleagues in 1958
- biosynthesis of melatonin also occurs in bone marrow and lymphocytes, gastrointestinal (GI) tract, and eyes, etc., and perhaps in every cell.
- Melatonin biosynthesis take places in the mitochondria of eukaryotic cells
- There is a substantial association between aberrant methylation of DNA and cancer incidence
 - epigenetic alterations over large chromatin regions in cancer diseases results in epigenetic instability, and subsequent gene expression alterations
 - disrupted epigenetic alterations such as aberrant DNA methylation in cancer cells can lead to heterogeneity of tumor cells, and subsequent poor prognosis
- Epigenetic modifications of cancers are categorized into three major processes including non-coding RNAs, histone modification, and DNA methylation.
- Results: melatonin significantly modified the status of DNA methylation, especially in breast cancer tissue.
 - Consequently, the changes in DNA methylation led to an inhibition of cancer cell proliferation, progression and metastasis
 - melatonin reversed chemo-resistance to current drug regimens

2022 Aug - Florido et al - Understanding the Mechanism of Action of Melatonin, Which Induces ROS Production in Cancer Cells

- Melatonin is synthesized by the **pineal gland** and several tissues (skin, gastrointestinal system, bone marrow, and also lymphocytes).
- Melatonin is produced by mitochondria at higher concentrations than other cellular compartments
- Melatonin is involved in multiple cellular processes, is a potent free radical scavenger and broad-spectrum antioxidant
- "Melatonin is of particular importance in the development of innovative cancer treatments due to its oncostatic impact and lack of adverse effects"
- Anti-Cancer effects:
 - Melatonin induces ROS (Reactive Oxygen Species) production in cancer cells through various pathways, which leads to apoptosis of

cancer cells.

- Melatonin stimulates antioxidant enzyme activity by regulating gene expression
- Melatonin regulates mitochondrial homeostasis
- Melatonin works in the 3 different stages of tumorigenesis: cancer initiation, progression and metastasis
 - cancer initiation Melatonin prevents DNA mutations (by free radical scavenging, inhibiting metal induced DNA damage, stimulating antioxidant enzymes, enhancing DNA repair, suppressing pro-oxidative enzymes)
 - cancer progression Melatonin impairs proliferation, impairs angiogenesis
 - metastases Melatonin impairs hypoxia-induced cancer cell migration

2022 May - Monayo et al - The Prospective Application of Melatonin in Treating Epigenetic Dysfunctional Diseases

- Due to melatonin's broad spectrum of action, epigenetic modification has been one of the fundamental tools used to unravel the possible mechanisms involved by this drug in numerous cancer types
- Melatonin decreases the activation of NF-κB by phosphorylation which decreases tumor growth and prevents metastasis

Non-coding RNA (microRNAs):

- Melatonin elevates levels of certain tumor suppressing microRNAs
 - melatonin increased levels of miR-152-3p which causes decline in cell proliferation, angiogenesis and inhibit cancer cell invasion (shown in glioblastoma cells)
 - Melatonin increased levels of miR-152-3p in breast cancer cells
 - Melatonin also increased levels of miR-16-5p which suppresses gastric cancer & breast, ovarian, cervical, hepatic, prostate, bone, lymphatic.
- Melatonin inhibits oncogenic microRNA miR-483 which is implicated in thyroid cancer, breast cancer, ovarian, colorectal, hepatocellular and pancreatic
- Melatonin inhibits oncogenic microRNA miR-155 which inhibits glioblastoma cells

Artificial Light:

- **Modern artificial lights** especially those with blue light emissions have been reported to cause a litany of health problems with cancer being among them
- environmental factors such as artificial light can cause circadian disruptions by causing desynchronization of the circadian pacemaker (SCN), resulting in decreased levels of melatonin secretions from the pineal gland
- effects of the artificial light at night associated with hormonal imbalances (decreased melatonin) and impaired circadian rhythms can cause cancer
- melatonin attenuates the effects of breast, prostate, liver, and skin cancers associated with ill-timed light exposures (early morning, late

evening, night)

melatonin resynchronizes dysregulated circadian rhythm

<u>2022 Mar - Leilei Wang et al</u> - Use of Melatonin in Cancer Treatment: Where Are We?

- Melatonin exerts effects on tumor initiation, promotion, and progression by acting on many signaling pathways
- Melatonin inhibits oncogenic miRNAs and enhances tumor suppressor miRNAs
- Melatonin can suppress cancer stem cells that can cause relapse and metastasis
- Melatonin affects the tumor microenvironment and shifts immune system response towards the cytotoxic side by stimulating production of cytotoxic T-cells like CD8 cells or NK cells, and inhibiting T regulatory cells (Tregs) and cancer-associated fibroblasts (CAFs) that facilitate immune escape of cancer cells.
- Melatonin enhances effects of chemotherapy and reduces chemo side effects
- Melatonin sensitizes cancer cells to chemo by promoting apoptosis
- Melatonin can also enhance the effect of radiation therapy

Problems with Using Melatonin as an Anti-cancer Drug

- short half-life of 45 minutes with low oral bioavailability of 9-33%
- Melatonin is widely used clinically for the short-term management of sleep disorders, such as insomnia due to jet lag or shift work. It is typically taken orally at a dose ranging from 3 mg to 10 mg daily;
- for cancer treatment, the dosage of melatonin would be much higher
- In order to use melatonin for cancer treatment, the drug form has to be stable with a reasonable length of shelf life so as to ensure reliable drug delivery.
 However, melatonin has low water solubility and high permeability.
- Since melatonin has low water solubility and poor chemical stability in an organic solvent, novel, biocompatible vehicles need to be developed to improve the bioavailability and solubility of melatonin.
- Nanosized carriers have aroused great interest for their unique properties including increased therapeutic efficacy, reduced side effects, and improved life quality of patients.
- Nanoparticles have been used to load melatonin for cancer treatment.
- melatonin was loaded in 3D-printed magnesium-polycaprolactone to treat osteosarcoma (OS), with a high efficiency in inhibiting OS cells' proliferation, invasion, and metastasis both in vitro and in vivo (Zhang et al 2021)

Safety and Dosing

- Researchers have yet to determine the optimal dosage of melatonin for adjuvant cancer therapy or cancer prevention.
- A systematic review compared 50 studies with melatonin administration ranging from 0.3 mg-1600 mg daily for 4 weeks to 3.5 years (15 ± months, average). Twenty-six studies reported no adverse events (Foley et al 2018)
- The reported adverse events were mostly related to psychomotor and

neurocognitive dysfunctions, fatigue, and excessive sleepiness, which could be avoided by taking melatonin at night and using the proper dosage with short-term administration. (Foley et al 2018)

 However, when applied for cancer treatment, relatively high doses both in vitro (0.1–10 mM) and in vivo (5 mg-200 mg/d) and long-term duration are needed, which may cause severe side effects.

<u>2021 Jul - Gonzalez et al</u> - Melatonin as an Adjuvant to Antiangiogenic Cancer Treatments

- Melatonin shows **antiangiogenic effects** in several types of tumors.
- Combination of melatonin and chemotherapeutic agents have a synergistic effect **inhibiting angiogenesis.**
- in breast cancer, antiangiogenic action of melatonin might be explained at least in part through regulation of pro- and anti-angiogenic miRNAs
- melatonin's antiangiogenic actions also found in ovarian cancer, prostate cancer, gastric cancer, pancreatic cancer, liver cancer, colon cancer.
- melatonin exerts anti-metastatic and anti-angiogenic effects in renal carcinoma
- In vitro and in vivo results suggest that combinations of melatonin with different antitumor drugs and chemotherapeutics result in improved efficacy of treatment
- Melatonin alone has been extensively documented as an effective inhibitor of proliferation, migration, and invasion.
- Many studies have linked melatonin to inhibition of VEGF and inactivation of HIF-1α meaning that melatonin neutralizes pro-angiogenic and potentiates antiangiogenic effects induced by chemotherapeutic agents or radiation, enhancing their antitumor effectiveness.
- Conclusion: "efficacy of melatonin to sensitize cancer cells to chemotherapeutic agents or ionizing radiation makes it a molecule that can be effective as an adjuvant to these cancer treatments"

2021 Apr - Talib et al - Melatonin in Cancer Treatment: Current Knowledge and Future Opportunities

- Currently, melatonin is considered as a cell protector and not only a hormone. Studies reported essential effects of melatonin in many pathways, including oxidative stress, immune modulation, and hematopoiesis
- Suprachiasmatic nucleus (SCN) of the hypothalamus is the biological clock that regulates melatonin synthesis and secretion over 24 h.
- At night, melatonin levels increase, then start to decrease in the early morning and throughout the day.
- Elevated levels of melatonin at night stimulate target organs to enter into suitable homeostatic metabolic rhythms which help to protect the body from the development of different diseases. Therefore, exposing the body to light at night may result in disruption of melatonin production and the circadian rhythm.

Melatonin Effects on Cancer Cells

• Melatonin preserves genomic stability – scavenges free radicals, inhibits

metal induced DNA damage, stimulates antioxidant enzymes, enhances DNA repair, inhibits pro-oxidative enzymes

- Melatonin inhibits cancer cell proliferation (most critical and controlling pathways are hypoxia-inducible factor-1 (HIF-1), NF-κB s, PI3K/Akt, insulin-like growth factor receptor (IGF-1R), cyclin-dependent kinases (CDK), and estrogen receptor signaling)
- Melatonin promotes apoptosis of cancer cells (melatonin increases expression of pro-apoptotic mediators such as BAX/BAK, Apaf-1, caspases, and p53, p38, p-JNK)
- Melatonin inhibits angiogenesis
- Melatonin counteracts cancer cell immune evasion melatonin can increase production of T-cells and NK cells, modulate the immune system
- Melatonin decreases pro-tumor inflammation
- Melatonin inhibits glucose metabolism of cancer cells
- Melatonin inhibits cancer cell metastasis by several mechanisms

Melatonin Can Treat These Cancers:

- gastric cancer numerous pathways
- glioblastoma Melatonin showed an anticancer effect against glioblastoma, and it was also reported to overcome the multi-drug resistance in glioblastoma
- prostate cancer melatonin suppressed growth and metastasis
- lung cancer (NSCLC) Melatonin administration remarkably enhanced apoptosis, in addition to inhibition of proliferation, invasion, and metastasis
- ovarian cancer (TLR-4 signaling pathway involved)
- colorectal cancer inhibited proliferation and promoted apoptosis
- liver cancer melatonin promoted autophagy and apoptosis
- renal cell cancer melatonin promoted apoptosis and inhibited metastasis
- oral cancer

Melatonin as Adjuvant Treatment to Chemo and Radiation

- melatonin used alongside radiotherapy is able to augment the impact of ionizing radiation on tumors and can also prevent radiation's toxic effects on normal cells
- efficiency of chemotherapy can be enhanced by the concomitant prescription of melatonin; side effects of the former are also ameliorated.
- Data also indicate that melatonin increases survival and improves quality of life
- It is thought that the capacity of melatonin to scavenge free radicals together with its antioxidant characteristics, are responsible for the improved outcomes

Melatonin Safety Profile and Dosing

- Based on human trials and reported use, melatonin seems to have a high safety profile especially when used in appropriate doses and short term.
- Although the doses used in the published studies are 10-50 mg/day higher than those used for other indications (0.5-5.0 mg/d), none of the studies found any severe adverse effects linked to melatonin;

- The most common side effects are excess sedation and somnolence.
- half-life time of oral melatonin was approximately 45 min (28-126 min)
- melatonin appears safe, since no side effects have been reported, even with doses up to 100 mg/kg administered in 72 h (<u>Gitto et al</u>), or when a dose of 10 mg/kg was administered once daily for 5 days (<u>Aly et al</u>)
- Melatonin has short plasma half-life, variable oral absorption, and low variable bioavailability in addition to its poor solubility and stability.
- Therefore, conventional oral dosage forms (immediate release) are unsuitable candidates for melatonin delivery.
- To overcome these limitations, many pharmaceutical formulations have been developed using different approaches



Source: 2017 - Ya Li et al - Melatonin for the prevention and treatment of Cancer)

My Take...

I have recently covered high dose Ivermectin and Fenbendazole for the possible treatment of very aggressive COVID-19 mRNA Vaccine Turbo Cancers, as these patients are not being given any options by their Oncologists and Turbo Cancers are resistant to conventional chemo and radiation.

Melatonin has extensive anti-cancer properties.

Where I find Melatonin particularly incredible, is its ability to regulate numerous cancer related micro RNAs, specifically by enhancing tumor suppressor miRNAs and inhibiting

oncogenic miRNAs.

COVID-19 mRNA Vaccines may be generating oncogenic miRNAs that are causing Turbo Cancers (!

After all, it's in the name of Pfizer's COVID-19 mRNA Vaccine:



It's posts like this that keep me up at night:



Well I guess Pfizer knew that modifying RNA with pseudouridine would produce pseudouridylated micro-RNA and we would all live happily ever after.

So they called it co-mirna-ty. Yay.

@NarfGb @Fynnderella1 @DoorlessCarp @Kevin_McKernan @NestCommander



At least these are more fun:



Oncogenic miRNAs (ONCOMIR)

Oncogenic <u>miRNAs</u> or **ONCOMIRS** are overexpressed in a variety of cancer types and act through a variety of downstream targets. Multiple oncomirs are consistently overexpressed in a variety of cancer types such as miR-21, miR-31, miR-135, miR-155, and miR-17-92 family of oncomirs.

These act in a variety of manners to downregulate <u>tumor suppressor</u> pathways, upregulate oncogenic pathways, and even alter <u>epigenetic</u> machinery.

In other words: THEY PROMOTE CANCER.

What to do with Melatonin?

So Melatonin has been proven to regulate oncogenic miRNAs in a number of cancers, but can it regulate Pfizer's or Co-miRNA-ty's oncogenic miRNAs?

MAYBE. No one has asked. Well, I'm asking but I don't know the answer.

Melatonin has been shown to treat **breast**, **colon**, **lung**, **hepatobiliary**, **ovarian and prostate cancers** – which just happen to also be the same cancers that show up after Pfizer or Moderna COVID-19 mRNA Vaccination but in **Stage 4 Turbo Variety!**

For Cancer treatment the dosing starts at a minimum of 20mg / day but all the studies admit that the dose must be much higher. But how high?

Some people are taking 60mg to 720mg per day, presumably safely:

- see article by <u>William Faloon A Case for Higher Dose Melatonin</u>
- Integrative Medicine Center of Western Colorado uses 180mg to 720mg per day

Melatonin can improve the immune system, it can prevent cancer and it can treat cancer. Perhaps it can treat mRNA Vaccine Turbo Cancer also.

But what are the optimal doses for each of these indications?

I honestly don't know.

*

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The Worldwide Corona Crisis, Global Coup d'Etat

Against Humanity

by Michel Chossudovsky

Michel Chossudovsky reviews in detail how this insidious project "destroys people's lives". He provides a comprehensive analysis of everything you need to know about the "pandemic" — from the medical dimensions to the economic and social repercussions, political underpinnings, and mental and psychological impacts.

"My objective as an author is to inform people worldwide and refute the official narrative which has been used as a justification to destabilize the economic and social fabric of entire countries, followed by the imposition of the "deadly" COVID-19 "vaccine". This crisis affects humanity in its entirety: almost 8 billion people. We stand in solidarity with our fellow human beings and our children worldwide. Truth is a powerful instrument."

Reviews

This is an in-depth resource of great interest if it is the wider perspective you are motivated to understand a little better, the author is very knowledgeable about geopolitics and this comes out in the way Covid is contextualized. —**Dr. Mike Yeadon**

In this war against humanity in which we find ourselves, in this singular, irregular and massive assault against liberty and the goodness of people, Chossudovsky's book is a rock upon which to sustain our fight. –**Dr. Emanuel Garcia**

In fifteen concise science-based chapters, Michel traces the false covid pandemic, explaining how a PCR test, producing up to 97% proven false positives, combined with a relentless 24/7 fear campaign, was able to create a worldwide panic-laden "plandemic"; that this plandemic would never have been possible without the infamous DNA-modifying Polymerase Chain Reaction test – which to this day is being pushed on a majority of innocent people who have no clue. His conclusions are evidenced by renown scientists. —**Peter Koenig**

Professor Chossudovsky exposes the truth that "there is no causal relationship between the virus and economic variables." In other words, it was not COVID-19 but, rather, the deliberate implementation of the illogical, scientifically baseless lockdowns that caused the shutdown of the global economy. -**David Skripac**

A reading of Chossudovsky's book provides a comprehensive lesson in how there is a global coup d'état under way called "The Great Reset" that if not resisted and defeated by freedom loving people everywhere will result in a dystopian future not yet imagined. Pass on this free gift from Professor Chossudovsky before it's too late. You will not find so much valuable information and analysis in one place. –**Edward Curtin**

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