# IVERMECTIN and CANCER, it has at least 15 anti-cancer mechanisms of action. Can Ivermectin Treat COVID-19 mRNA Vaccine Induced Turbo Cancers? - 9 Ivermectin papers reviewed

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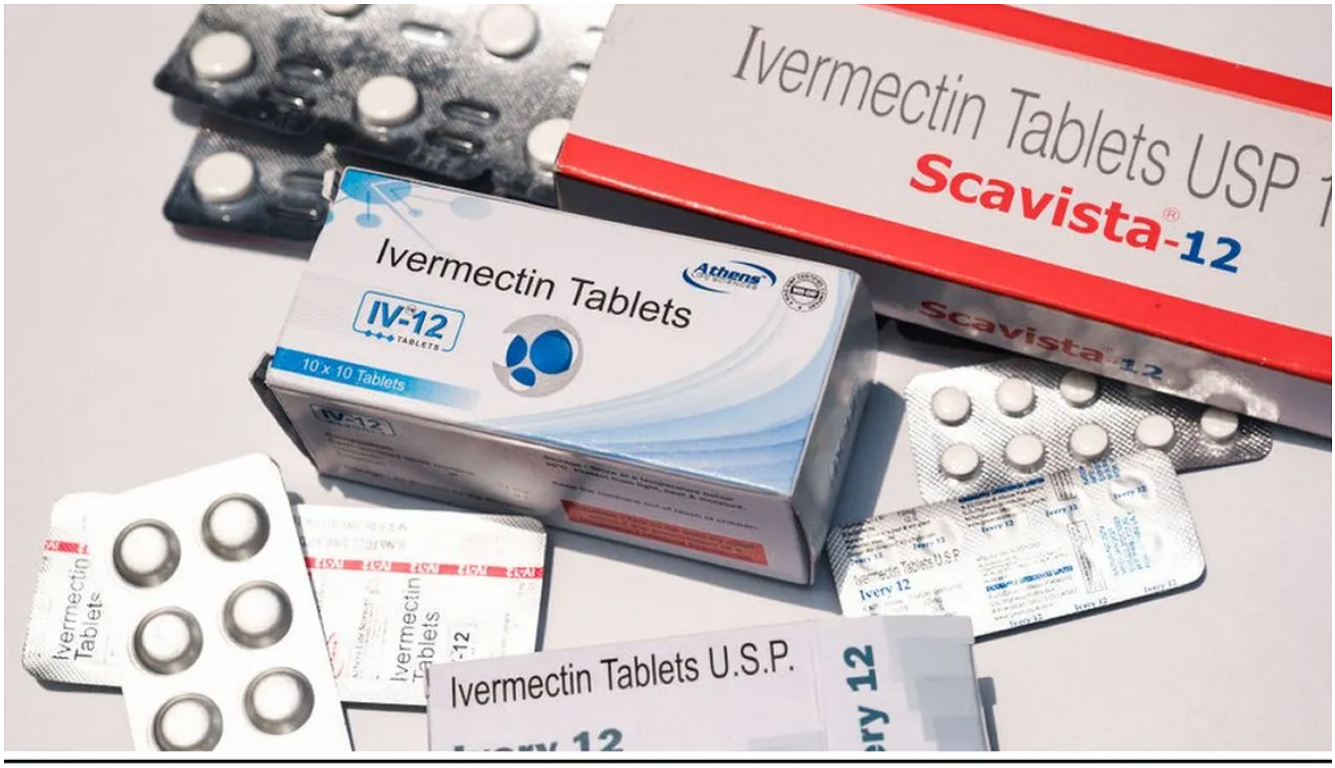


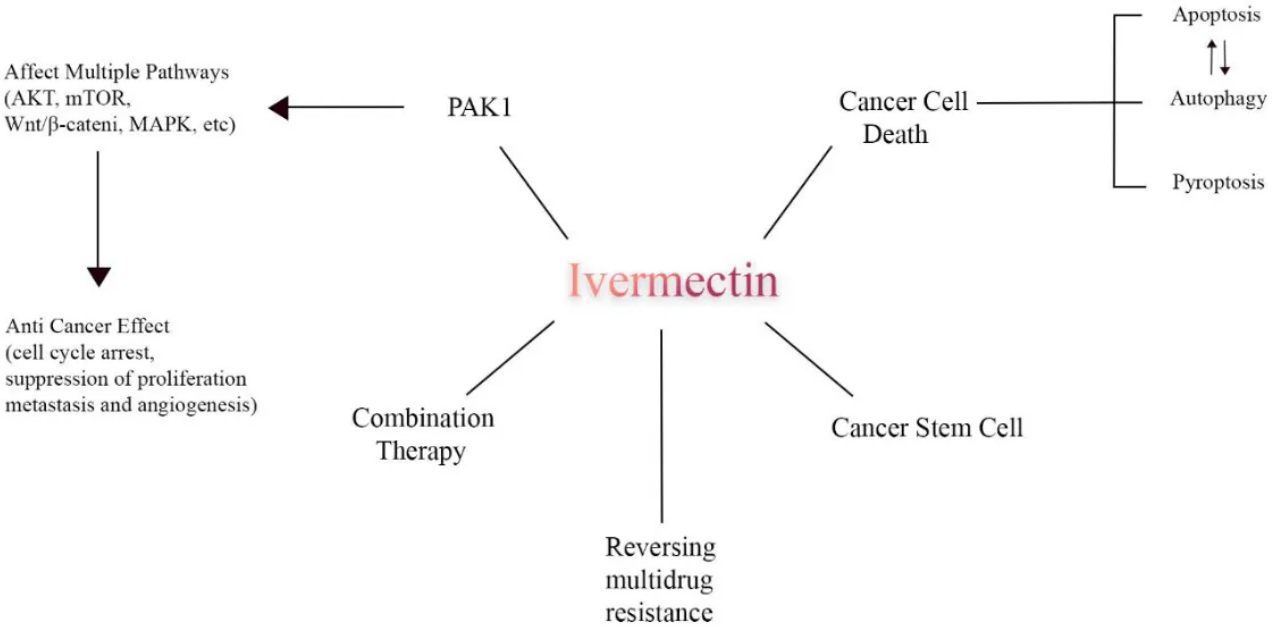




**Figure 1.** Ivermectin mechanism of action against tumors
*Lotfalizadeh N et al.*

## Papers reviewed:

- 2023 Sep.23 - Man-Yuan Li et al - Ivermectin induces nonprotective autophagy by downregulating PAK1 and apoptosis in **lung** adenocarcinoma cells

- 2023 May - Samy et al - Eprinomectin: a derivative of ivermectin suppresses growth and metastatic phenotypes of **prostate** cancer cells by targeting the β-catenin signaling pathway
- 2022 Nov - Lotfalizadeh et al - The Anticancer potential of Ivermectin: Mechanisms of action and therapeutic implications
- 2022 Oct - Jian Liu et al - Progress in Understanding the Molecular Mechanisms Underlying the Antitumour Effects of Ivermectin
- 2022 Jun - Daeun Lee et al - Ivermectin suppresses **pancreatic** cancer via mitochondria dysfunction
- 2021 Aug - Shican Zhou et al - Ivermectin has New Application in Inhibiting **Colorectal** Cancer Cell Growth
- 2021 Jan - Mingyang Tang et al - Ivermectin, a potential anticancer drug derived from an antiparasitic drug
- 2019 Sep Intuyod et al - Anti-parasitic Drug Ivermectin Exhibits Potent Anticancer Activity Against Gemcitabine-resistant **Cholangiocarcinoma** *In Vitro*
- 2018 Feb - Juarez et al - The multitargeted drug ivermectin: from an antiparasitic agent to a repositioned cancer drug

## 2018 Feb - Juarez et al - The multitargeted drug ivermectin: from an antiparasitic agent to a repositioned cancer drug

- **Satoshi Omura at the Kitasato Institute discovered Ivermectin in 1979 and was awarded a Nobel Prize in Physiology or Medicine for this discovery in 2015**
- Ivermectin was **FDA Approved for human use in 1987** to orally treat onchocerciasis, also known as river blindness, caused by the blackfly-transmitted parasite *Onchocerca volvulus*
- Ivermectin is annually taken by close to **250 million people**
- most patients treated with Ivermectin have **no side-effects** other than those caused by the immune and inflammatory responses against the parasite, such as fever, pruritus, skin rashes and malaise
- maximum concentration in plasma is reached **4-5 h after its oral administration**

- its **half-life is approximately 19 h** and is metabolized in the liver by the cytochrome CYP1A and CYP3A4 complexes, generating 10 metabolites, mostly demethylated and hydroxylated.
- Its excretion is mainly **by feces and only 1% is excreted in the urine**
- Ivermectin exerts antitumor effects in different types of cancer.

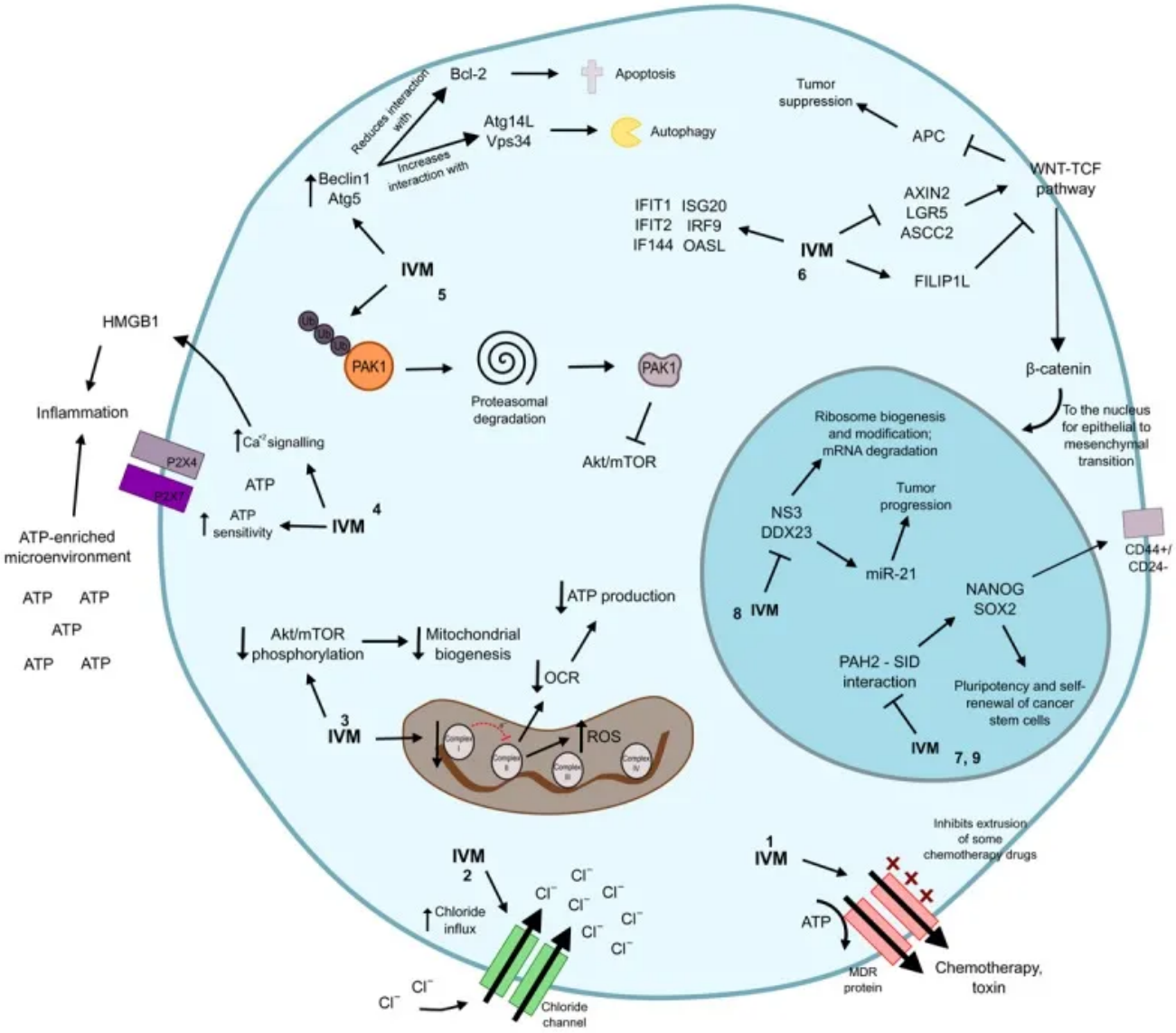


Table 2

Summary of the antitumor targets of ivermectin

| Target | Effect | References |
|---|---|---|
| MDR protein | Inhibition | [39] |
| Chloride channel | Increase of activity | [44] |
| Akt/mTOR pathway | Inhibition | [47] |
| P2X7/P2X7 receptors | Activation | [50,51] |
| PAK1 protein | Inhibition | [9,54] |
| WNT-TCF pathway | Inhibition | [57,58] |
| SIN3 domain | Inhibition | [59] |
| NS3 DDX23 helicase | Inhibition | [64] |
| *Nanog/Sox2/Oct4* genes | Downregulation | [67] |

## What this means Clinically:

- Chloride channel - **Acute myeloid leukemia** - induced cell death
- Akt/mTOR path - **glioblastoma, renal cancer cell lines** - inhibition of mitochondrial biogenesis or function, oxidative stress, DNA damage
- P2X7 (ICD) overexpression promotes tumor growth and metastases - ivermectin potentiates immunogenic cell death (ICD) in **triple negative breast cancer** cells
- PAK1 (Autophagy) - **glioblastoma and ovarian cance**r cell lines - Ivermectin promotes autophagy through this pathway
- WNT-TCF pathway - **glioblastoma, colon cancer, melanoma** - Ivermectin exerts anti-proliferative function through this pathway (possibilities to use Ivermectin to

block WNT-TCF dependent cancers like **breast, skin, lung**)

- SIN3 Domain - **breast cancer** (Ivermectin acts as epigenetic modulator to alter gene expression and decrease tumor growth)
- NS3 helicase - **glioma cells** - Ivermectin had anti-tumor effects by acting as helicase inhibitor

### In Vitro Studies:

- **breast cancer, ovarian, prostate, colon, pancreas, head and neck, melanoma** - inhibits cell proliferation, induction of apoptosis, autophagy, reversion of tamoxifen resistance, inhibits metastases
- **glioblastoma** - growth inhibition, apoptosis, and anti-angiogenesis

### In Vivo Studies (done on immune deficient mice):

- **acute myeloblastic leukemia** - reduce tumor volume up to 70%
- **glioblastoma** - reduce tumor volume up to 50%
- **breast cancer** - reduce tumor volume up to 60%
- **glioma** - reduce tumor volume up to 50% (at 0.24mg/kg), however at human dose equivalent to **0.8mg/kg** tumors were **not detectable!**
- **colon cancer** - reduce tumor volume up to 85%
- median dose employed was equivalent to **0.4 mg/kg in humans** from 10 to 42 days (oral, intraperitoneal or intra-tumoral)
- the *in vitro* and *in vivo* antitumor activities of Ivermectin are achieved at **concentrations that can be clinically reachable** based on the human pharmacokinetic studies done in healthy and parasited patients

## 2019 Sep Intuyod et al - Anti-parasitic Drug Ivermectin Exhibits Potent Anticancer Activity Against Gemcitabine-resistant Cholangiocarcinoma *In Vitro*

- Ivermectin studied on cholangiocarcinoma cells that were chemo resistant (gemcitabine)

- Ivermectin inhibited cancer cell proliferation and colony formation in a **dose and time dependent manner**(!)
- Ivermectin caused **S-phase cell cycle arrest and cell death**
- Conclusion: "**Ivermectin might be useful as an alternative treatment for cholangiocarcinoma, especially in patients who do not respond to chemo.**"

## 2021 Jan - Mingyang Tang et al - Ivermectin, a potential anticancer drug derived from an antiparasitic drug

- specific mechanism of **IVM-mediated cytotoxicity in tumor cells is unclear**; it may be related to the effect of IVM on various signaling pathways
- IVM seems to induce **mixed cell death in tumor cells**

Table 2. Summary of the anticancer mechanism of IVM

| Mechanism | Cancer type | References |
|---|---|---|
| **Inhibit Wnt pathway** | Breast cancer, Colorectal cancer | [33,41] |
| **Inhibit Akt/mTOR pathway** | Breast cancer, Ovarian cancer, Glioma | [32,60,64] |
| **Inhibit MAPK pathway** | NasopharyngealcarcinomaMelanoma | [69,73] |
| **Inhibit YAP1 protein** | Gastric cancer, liver cancer | [39,43] |
| **Inhibit PAK1 protein** | Breast cancer, Ovarian cancer, Nasopharyngeal carcinoma, Melanoma | [32,58,69,73,96] |
| **Inhibit HSP27** | Prostate cancer, Lung cancer Colorectal cancer | [50] |
| **Induce mitochondrial dysfunction** | Renal cell carcinoma, GliomaLeukemia | [48,53,63] |
| **Inhibit cancer stem cells** | Breast cancer | [95,96] |
| **Inhibit p-glycoproteinand MDR protein** | Colorectal cancer, Breast cancerLeukemia | [22,104] |
| **Activate P2 × 7 receptor** | Breast cancer | [37] |
| **Inhibit SIN3 domain** | Breast cancer | [36] |
| **Inhibit DDX23 helicase** | Glioma | [66] |
| **Activate chloride channels** | Leukemia | [51] |
| **Increase TFE3 Activity** | Melanoma | [74] |
| **Inhibit KPNB1 protein** | Ovarian cancer | [59] |

- **CONCLUSIONS**: Ivermectin selectively inhibits the proliferation of tumors at a dose that is not toxic to normal cells and can reverse the MDR (multi-drug resistance) of tumors.
- In healthy volunteers, the **dose was increased to 2 mg/kg**, and **no serious adverse reactions were found**

- Unfortunately, there have been **no reports of clinical trials of IVM as an anticancer drug**
- large number of research results indicate that IVM affects multiple signaling pathways in tumor cells and inhibits proliferation, IVM may cause antitumor activity in tumor cells through specific targets
- **Ivermectin regulates the tumor microenvironment, inhibits the activity of tumor stem cells and reduces tumor angiogenesis and tumor metastasis.**
- It has become increasingly clear that **Ivermectin can induce a mixed cell death mode involving apoptosis, autophagy and pyroptosis** depending on the cell conditions and cancer type.
- **Ivermectin can enhance the sensitivity of chemotherapeutic drugs and reduce the production of resistance**. Therefore, IVM should be used in combination with other drugs to achieve the best effect

## 2022 Jun - Daeun Lee et al - Ivermectin suppresses pancreatic cancer via mitochondria dysfunction

- Poster presentation from South Korea
- Ivermectin was combined with gemcitabine in pancreatic cancer
- Ivermectin-gemcitabine combination inhibited pancreatic cancer cell proliferation via **G1 arrest of cell cycle**
- in vivo experiments showed ivermectin-gemcitabine significantly suppressed **tumor growth of pancreatic cancer** compared with gemcitabine alone
- Conclusion: "**Ivermectin could be a potential antitumor drug for the treatment of pancreatic cancer**"

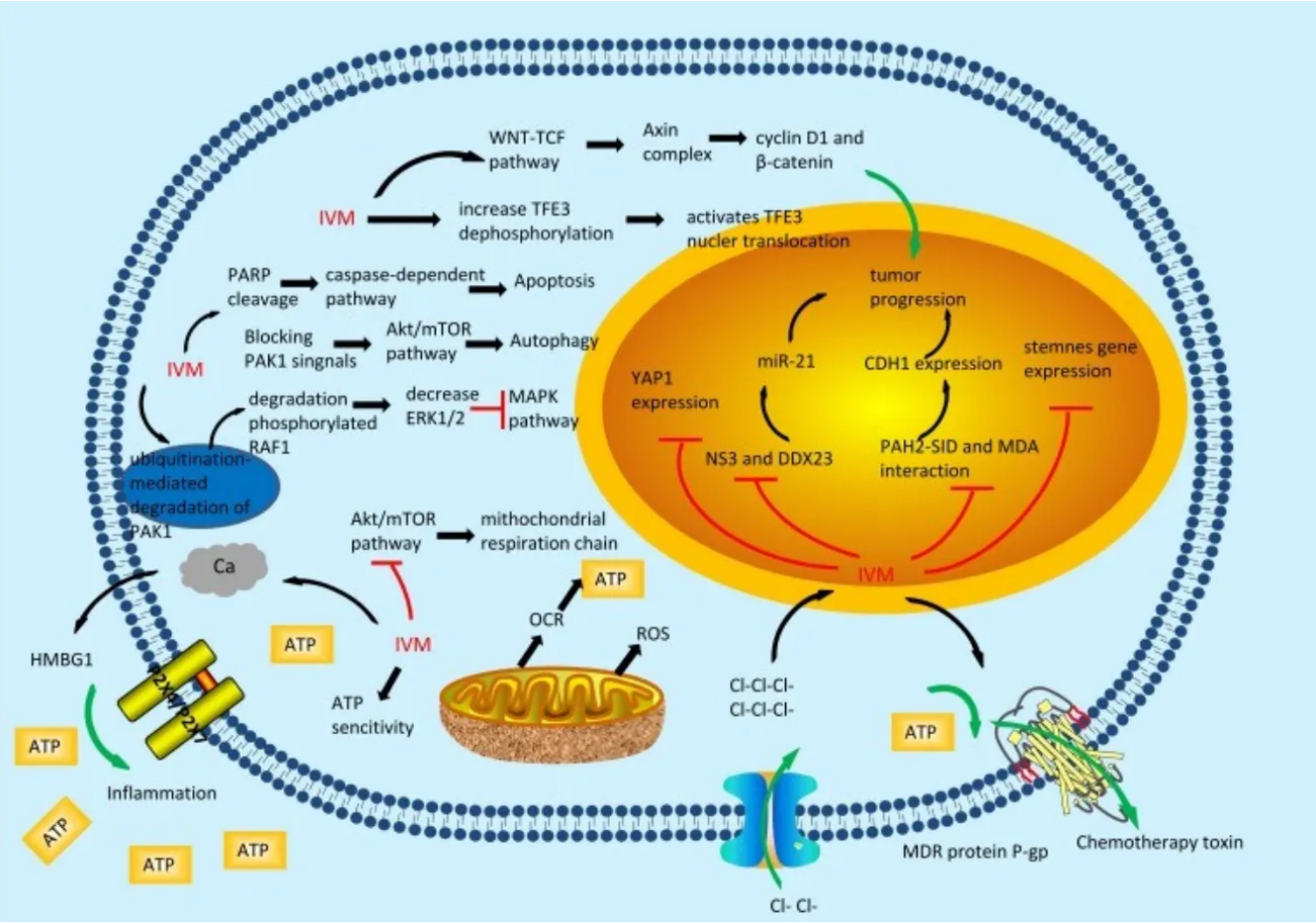
## 2021 Aug - Shican Zhou et al - Ivermectin has New Application in Inhibiting Colorectal Cancer Cell Growth

- Colorectal cancer is 3rd most common cancer worldwide, lacks effective therapy
- Ivermectin tested on colorectal cancer cell lines
- **Ivermectin dose-dependently inhibited colorectal cancer growth**

- promoted cell apoptosis
- promoted total and mitochondrial ROS production (reactive oxygen species)
- induced colorectal cancer cell **S-phase arrest**

- Conclusion: **Ivermectin might be a new potential anticancer drug therapy for human colorectal cancer**

## 2022 Oct - Jian Liu et al - Progress in Understanding the Molecular Mechanisms Underlying the Antitumor Effects of Ivermectin




- PAK1 (**Autophagy**) - Ivermectin, acts as PAK1 inhibitor and inhibits growth of **breast cancer, ovarian cancer, glioblastoma and NF2** tumors and involved in cell death in **Nasopharyngeal carcinoma and melanoma.**

- Apoptosis (Caspase Dependent) - Ivermectin induces apoptosis in **glioblastoma, chronic myeloid leukemia cells, also breast cancer, ovarian cancer.**
- Immunogenic Cell Death (ICD - P2X7 signaling) - ivermectin induces cell death in **triple negative breast cancer.**
- YAP1 Inhibition - **hepatocellular and cholangiocarcinoma, colorectal cancer, ovarian cancer, gastric cancer** - ivermectin exerts anti-tumor effects
- WNT Path (cancer progression - differentiation, metastasis, cell senescence, tumor initiation, tumor growth) - Ivermectin inhibits this path - **inhibits colon cancer and lung cancer**, ivermectin also limits formation of cancer stem cells.
- TF3 Path - ivermectin stimulates **apoptosis of melanoma** cells.
- RNA Helicase Inhibition - ivermectin inhibits cell invasion and proliferation of **glioma** cells
- SID Peptide (SIN3A/B) - Ivermectin inhibits breast cancer progression, also restores tamoxifen sensitivity
- Akt/mTOR inhibition - Ivermectin inhibits mitochondrial respiration - glioblastoma, CML leukemia (**some cancers like breast, leukemia and lymphoma are more metabolically active and depended on mitochondria - more responsive to ivermectin inhibition**)
- ivermectin is an **angiogenesis inhibitor**
- ivermectin has **anti-mitotic activity**

In humans, toxicity of ivermectin is very low, no serious adverse reactions have been found in healthy volunteers at dose up to **120 mg** (**~2 mg/kg**) (Reference: GuzzoCA, FurtekCI, PorrasAG, et al. Safety, tolerability, and pharmacokinetics of escalating high doses of ivermectin in healthy adult subjects. *J Clin Pharmacol*. 2002;42(10):1122–1133.)

## 2023 May - Samy et al - Eprinomectin: a derivative of ivermectin suppresses growth and metastatic phenotypes of prostate cancer cells by targeting the β-catenin signaling pathway

- Ivermectin (derivative) inhibits prostate cancer cell viability, migration capacities

- Ivermectin induces **apoptosis, autophagy** (via ROS)
- Ivermectin downregulates expression of **cancer stem cell markers**
- Conclusion: Ivermectin has tremendous potential to target metastatic prostate cancer cells and provides new avenues for therapeutic approaches to advanced prostate cancer

## 2023 Sep.23 - Man-Yuan Li et al - Ivermectin induces nonprotective autophagy by downregulating PAK1 and apoptosis in lung adenocarcinoma cells

- Ivermectin was studied on lung adenocarcinoma cells
- Ivermectin strikingly impeded colony formation and viability of cancer cells, along with **cell proliferation, caused apoptosis and enhanced autophagy**
- Ivermectin efficiently **suppressed cellular growth of lung adenocarcinoma** cells in vivo among nude mice

## My Take...

**Ivermectin exerts anti-cancer effects through at least 15 different pathways proven in the medical literature, both in vitro and in vivo!**

**(You get a nice summary of these 15 pathways from the 2021 paper by Mingyang Tang et al.)**

### First, let's quickly summarize the anti-cancer mechanisms (a quick summary can be found in 2022 paper by Loftalizadeh et al):

- **Ivermectin induces tumor cell death**: apoptosis, autophagy, pyroptosis
- **Ivermectin inhibits tumor initiation and tumor progression** (via WNT inhibition, YAP1 inhibition)
- **Ivermectin inhibits tumor growth and proliferation** (via Akt/mTOR inhibition, MAPK inhibition)
- **Ivermectin stops cancer cell migration, invasion and metastasis** (via PAK1 inhibition - seen in 70% of all cancers, EMT inhibition, RNA Helicase inhibition)

- **Ivermectin causes cancer cell mitochondrial dysfunction** (inhibits mitochondrial biogenesis, increases reactive oxygen species selectively only in cancer cells)
- **Ivermectin regulates tumor microenvironment** (to inhibit tumor growth and progression, via P2X7 path, ICD - mediates immunogenic cell death)
- **Ivermectin inhibits cancer stem cells** (**which are responsible for tumor initiation, progression and recurrence**)
- **Ivermectin inhibits tumor angiogenesis** (tumor blood vessel creation)
- **Ivermectin has anti-mitotic activity** (interacts with mammalian tubulin)
- **Ivermectin is an epigenetic regulator of cancer to inhibit cancer progression** (alters gene expression to inhibit cancer progression, SIN3A, EMT)
- **Ivermectin can overcome tumor multidrug resistance**

## What cancers can Ivermectin treat?

- The top 5 COVID-19 mRNA Vaccine Induced Turbo Cancers are: **lymphomas, brain cancers, breast cancers, colon cancers and lung cancers** (signals also seen in leukemias, hepatobiliary cancers, testicular cancers, sarcomas and melanomas)
- Ivermectin has been shown to kill these cancer cells (in vitro or in vivo):
- **breast cancer, especially triple negative breast cancer** which is often seen in COVID-19 mRNA Vaccinated women and has the worst prognosis.
- **glioblastoma** and gliomas (glioblastomas are often seen in COVID-19 mRNA Vaccinated individuals)
- **leukemias, both AML and CML** (these are the most aggressive and quickly lethal mRNA Turbo Cancers)
- **colorectal cancer** (Stage 4 Colon cancers common in COVID-19 mRNA vaccinated)
- **hepatobiliary cancers**: hepatocecullar carcinoma, cholangiocarcinoma, pancreatic cancer (major signal with COVID-19 mRNA Vaccines)
- **lung cancer** (Stage 4 lung cancers in COVID-19 mRNA Vaccinated)
- **melanoma** (definite signal in COVID-19 mRNA vaccinated)
- **renal cell cancer** (possible signal with mRNA Turbo Cancers) **and** **urothelial carcinoma**

- **ovarian cancer** (possible signal with mRNA Turbo Cancers)
- **gastric cancer**
- **prostate cancer** (possible signal with mRNA Turbo Cancers)
- **Nasopharyngeal cancer**

**There is almost no literature on Ivermectin and lymphomas which are probably the most common COVID-19 mRNA vaccine turbo cancers - this must be investigated.**

## What dose of Ivermectin to treat COVID-19 mRNA Vaccine Turbo Cancer?

- Guzzo et al published a paper in 2022 on the "**Safety, tolerability, and pharmacokinetics of escalating high doses of Ivermectin in healthy adult subjects**"
- The highest dose tested to be safe with no side effects, was **2 mg/kg**.
- Max concentration in plasma is **4 hours** after oral intake
- **Half life is 18 hours**
- **Dr.David E. Scheim PhD, Blacksburg VA also wrote an interesting article on Ivermectin Safety in Sep.7, 2021 (Source)**
- Several studies have shown that Ivermectin's **anti-cancer effects are DOSE-DEPENDENT (higher dose = better response)**

## Warning: not to be taken as medical advice - hypothetical situation: if I was faced with a COVID-19 Vaccine Induced Turbo Cancer or an advanced stage cancer, I would be looking at an Ivermectin dose of 2mg/kg orally, daily or every two days.

### Dr. Justus Hope MD published an article on Aug.29, 2023 that discusses anecdotal cases of Stage 4 Colon cancer, Stage 4 Ovarian Cancer responding to Ivermectin with dramatic drop in Tumor markers.

Also mentioned is a "**High Dose Ivermectin" regimen of 2mg/kg per day** for a doctor with Stage 4 Gallbladder cancer, taken for over a year, **with visual side effects for a few**

**days initially which resolved.**

Also described is a case of enlarged Prostate suspicious for cancer, and a 5 week **Ivermectin 45mg/day regimen** that dropped PSA from 89.1 to 10.9 with resolution of nocturnal urinary frequency. **For a 100kg man, that is a dose of 0.45mg/kg,** significantly lower than the **2 mg/kg** safe dose published by Guzzo et al.

The article describes a cancer patient with a neck tumor and lung metastases on a **High Dose Ivermectin** regimen of **2.45mg/kg daily.**

## I believe that it is a reasonable hypothesis that COVID-19 mRNA Vaccine Turbo Cancer patients could benefit from High Dose Ivermectin regimens, such as 2mg/kg and we urgently need more research to be done in this area.

## (mRNA Vaccine Induced Turbo Cancers such as leukemias, glioblastomas, breast cancers (including triple negative), colon cancers, hepatobiliary cancers, lung cancers, melanomas, renal cell cancers, ovarian cancers, prostate cancers - as there is already evidence in the literature)

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