WRITTEN BY
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WINNING THE CHALLENGE AGAINST BREAST CANCER STEM CELLS

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DISCLAIMER

CANCER: WHAT IF WE STARTED BY LOOKING AT THE ROOT OF THE PROBLEM?

Treating the “root of the problem” seems to be a logical approach and the only truly effective one, regardless of the issue.

Cancer is the second cause of death in the U.S. According to the latest figures (2022), 69% of survivors have lived 5+ years since their diagnosis, 47% of survivors have lived 10+ years since their diagnosis and 18% of survivors have lived 20+ years since their diagnosis in the United States.[1] Objectively not-so-glorious results, which is not surprising since the root of the problem is rarely addressed. Indeed, oncologists rarely talk about cancer stem cells. Why? Because the classic arsenal they have, namely chemotherapy and radiotherapy, is powerless to destroy them.[2] Rather than admit their inability to address the root of the problem, they prefer to pretend that the important thing is the size of the tumor. “That's very good, you are responding very well to chemotherapy: the tumor has decreased by 30% compared to the previous scan," the oncologist congratulates. The patient is delighted and full of hope.

The doctor did not tell her that the treatment only destroys the adult cancer cells, but that the youngest, most dynamic, and most aggressive are still there, ready to give birth to a new generation of cancer cells. Then a few months, or a few years later, a disaster is announced: "The cancer has returned!" Joy gives way to despair.

The truth is that the first cancer was never completely gone because not all cancer cells were properly removed. The cancer stem cells have been allowed to evolve into a new generation of cancer cells, with, of course, among them, new cancer stem cells.

So the oncologist will, for lack of anything better, offer a new series of chemotherapy, even though he knows perfectly well that the treatment remains powerless to definitively eradicate “the root of the problem”.

We cannot claim to treat cancer properly if we do not also destroy the cancer stem cells, and we should attack them from the day of diagnosis!

CANCER STEM CELLS: A NEW CHALLENGE FOR RESEARCHERS

Imagine a cell with the power to self-renew and transform into various cell types, much like a magic bean that can sprout into any plant. This is the essence of a stem cell. While healthy stem cells repair and renew our tissues, their counterparts, cancer stem cells, play a dark role in cancer.

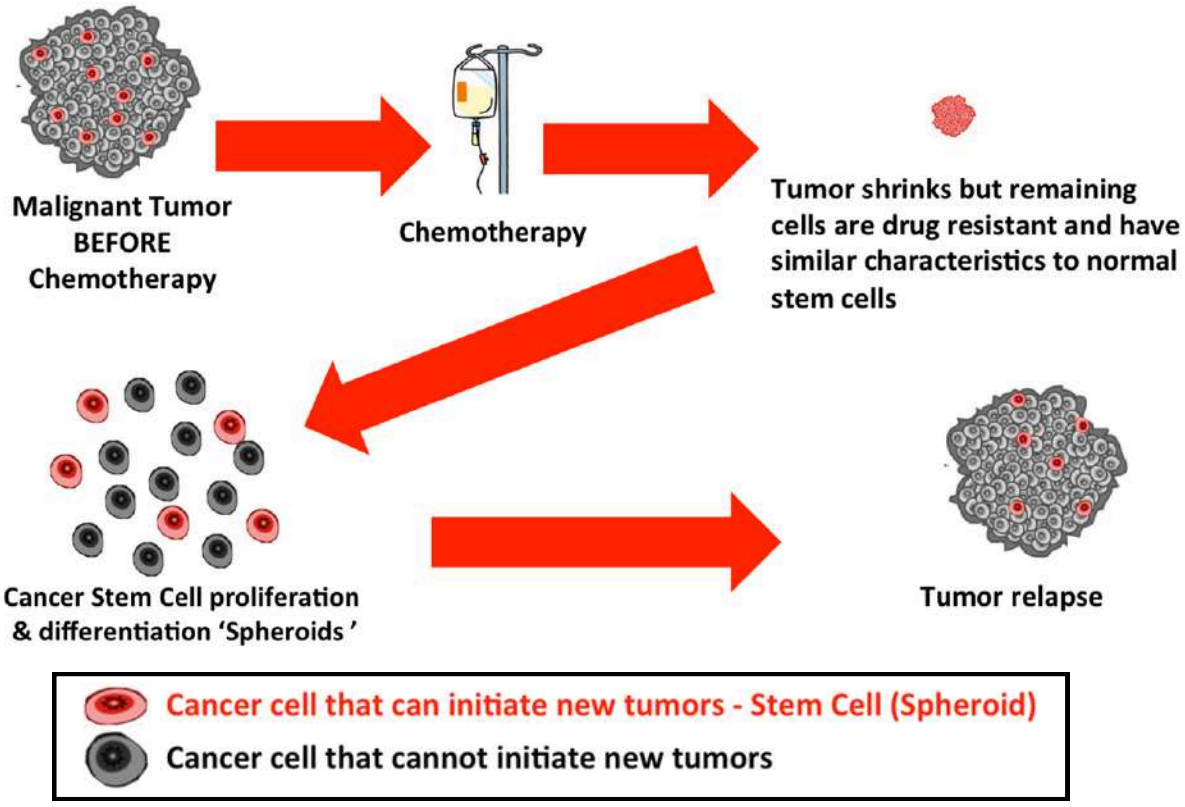
Cancer stem cells were first discovered in the late 1990s during leukemia research. This has prompted research into other cancers. Cancer stem cells are found in many cancers, including:

- Brain [3]
- Breast [4]
- Colon [5]
- Ovary [6, 7]
- Pancreas [8]
- Prostate [9, 10]
- Melanoma [11, 12, 13]
- Multiple Myeloma [14, 15]
- Non-melanoma Skin Cancer [16, 17, 18]

They're cancer cells found in all types of tumors and blood cancers that share traits with normal stem cells. This includes their ability to turn into various types of cells that make up a tumor.

Cancer stem cells have two decisive characteristics: they can self-renew indefinitely and produce new cells that fuel tumor growth.

Cancer stem cells are intrinsically more resistant to chemotherapy than adult cancer cells because they have the characteristic of dividing very little and very slowly, to the point that some scientists also call them "dormant cells". After chemotherapy, these stem cells that have resisted the treatment are able to "wake up" even after a significant latency period and acquire a rapid multiplication and evolution capacity like any classic cancer cell. They will repopulate the tumor and cause a relapse.



Some accept that the fight against cancer is not won in a single battle. Even in a patient who has been in remission for a long time, cancer can recur.

Others are actively seeking solutions: Professor Shapiro, from the departments of Biological Chemistry, Applied Mathematics, and Computer Science at the Weizmann Institute of Science (Israel), explains: "We know that in many cases, chemotherapy alone is not able to cure leukemia. Our results suggest that to completely eliminate it, we must look for a treatment that will not only eliminate the rapidly dividing cells but also target the cancer stem cells that are resistant to conventional treatment." [19]

Professor Shapiro continues to explain, "The presence of stem cells in tumors, attested by numerous studies, requires us to rethink the mechanisms of carcinogenesis. The majority of chemotherapy and radiotherapy treatments target proliferative cells by aiming precisely at the processes of their multiplication. Cancer stem cells would thus escape treatment and accumulate even more genetic alterations, develop new resistances, and transmit them to their new daughter cells, which would lead to secondary cancers more resistant to treatments than the primary tumors." [20]

According to the Ludwig Center for Cancer Stem Cell Research and Medicine, "Many new cancer treatments are evaluated based on their ability to reduce tumors, but if these treatments do not kill the cancer stem cells, the tumor is soon going to come back – often developing an unfortunate resistance to the treatment previously used. This approach could be compared to a weeding technique that would be evaluated on its ability to cut the stems as low as possible; but no matter how low the stems are cut, if the roots are not pulled out, the weeds will grow back." [21]

Although the cancer stem cell has quickly become an archetype in oncology and has imposed itself as an essential research path, there are still no therapeutic outlets with conventional products.

THE BELJANSKI® APPROACH TO WELLNESS

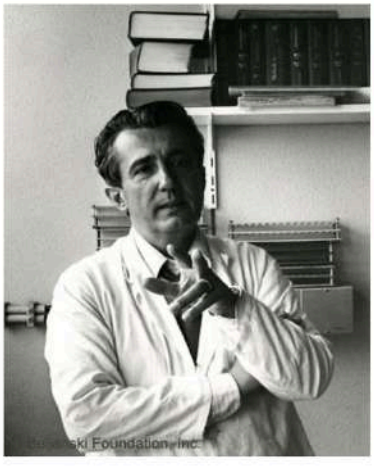
Despite the acknowledged failure of conventional therapies, such as chemotherapy and radiotherapy, we are NOT defenseless against cancer stem cells. Indeed, Nature is full of wonders that are less expensive and less toxic than conventional products. Pharmaceutical companies are not interested in them because it is almost impossible to obtain a patent for a natural molecule. And without a patent, the possibilities for return on investment are minimal.

Fortunately, a small number of researchers have delved into the wonders of nature.

Two substances with anti-cancer properties

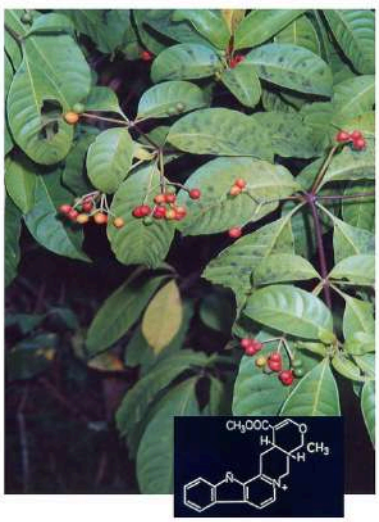
Pao Pereira

Flavopereirine



Mirko Beljanski
1923-1998

Rauwolfia Vomitoria



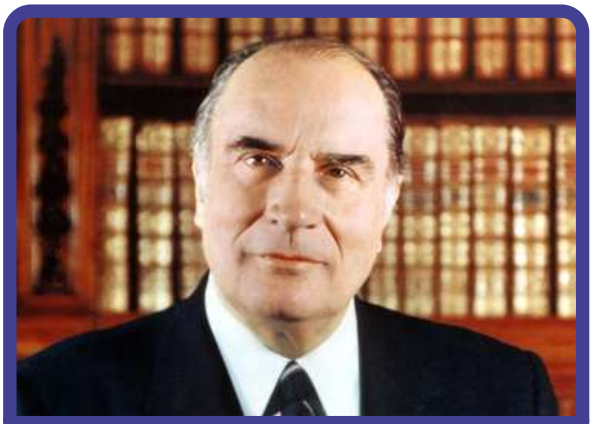
Alstonine

Dr. Mirko Beljanski, PhD. (1923-1998), a biologist working at the Pasteur Institute in France was a recognized pioneer for his research in the field of cellular biology and natural medicine. At a time when almost all of his peers were advocating a genetic solution, Dr. Mirko Beljanski was developing the concept that environmental toxins induce unregulated separation of DNA strands, a phenomenon also called "DNA destabilization."

Linking the increase of toxins in our environment to causing cancer, he focused on identifying plant compounds with anti-cancer properties, eventually leading to the development of a range of remarkable botanical extracts.

His research led him to select some plants that are particularly effective against cancer cells but without associated toxicity to the body and healthy cells: Pao Pereira (Geissospermum vellosii), Rauwolfia (after removal of reserpine), and a specific blend of green teas. These natural and non-toxic ingredients selectively block the duplication of destabilized cancerous DNA without affecting healthy DNA. They act on multiple types of cancer because they are not organ or gender specific.

When Beljanski started sharing his scientific findings and publishing his results, he faced strong opposition from traditional cancer doctors. They mocked and excluded him, despite his approach aiming to work alongside chemotherapy and radiotherapy, rather than replacing them. Even so, former French President François Mitterrand turned to Beljanski's plant extracts when diagnosed with advanced prostate cancer in 1992. It's widely recognized now that these products helped Mitterrand complete his second term. However, the pharmaceutical industry lobby didn't like this, and Beljanski suffered the consequences.



François Mitterand (1916 - 1996)

On October 9, 1996, exactly nine months after Mitterrand's death and as part of an operation named "ISA 2," a GIGN team burst into Beljanski's laboratory at 6 am with machine guns, police dogs, and a helicopter monitoring the scene. Dr. Beljanski was handcuffed roughly while all products, samples for analysis, lab notebooks, and research equipment were seized. A moving truck was brought in to take away the computers, photocopiers, and all the raw materials, without even bothering to take an inventory of what was being taken. Beljanski was ordered to remain in the laboratory while a mysterious substance was sprayed. Two months later, while all his products had been seized, Beljanski received a diagnosis of acute myeloid leukemia. The "ISA 2" operation was classified as a state secret. [22]

Beyond the tragic story of Mirko Beljanski, this attempt to destroy such a promising scientific work is a tragedy for all cancer patients who were, for a time, deprived of access to these natural therapies. Fortunately, Beljanski's devotion to understanding carcinogenesis has left a lasting legacy, inspiring a new generation of researchers and practitioners in the field of integrative medicine.

To learn more about Mirko Beljanski's fate, read "Winning the War on Cancer: The Epic Journey Towards a Natural Cure" by Sylvie Beljanski.

THE SCIENTIFIC LEGACY OF MIRKO BELJANSKI

Mirko Beljanski left a tremendous scientific legacy: beyond the innovative concepts, exposed through 133 scientific publications and two books, he developed very specific botanical extracts whose anti-cancer properties are remarkably effective. These discoveries deserved to be saved, confirmed by other scientific teams, and shared with the general public. Over the years, the Beljanski Foundation has established scientific partnerships with various university entities to fund research programs that study cancers as diverse as breast, prostate, ovarian, and pancreatic cancers.

The Beljanski Foundation is a 501 (c)(3) whose mission is to study and share knowledge of effective non-toxic natural answers that work both alone and in synergy with traditional Western medicine to cure cancer and other chronic diseases the natural way.

The foundation has collaborated with several academic institutions to further research on natural compounds and their potential anti-cancer properties. This has led to the publication of several peer-reviewed articles in scientific journals, on many cancer cell lines, including prostate, ovaries, pancreatic, and breast cancer.

The Beljanski Foundation is a non-profit organization dedicated to scientific research and education in the field of integrative oncology that combines conventional methods and natural approaches. It supports research projects aimed at exploring the properties and therapeutic applications of plant extracts discovered by Dr. Beljanski.

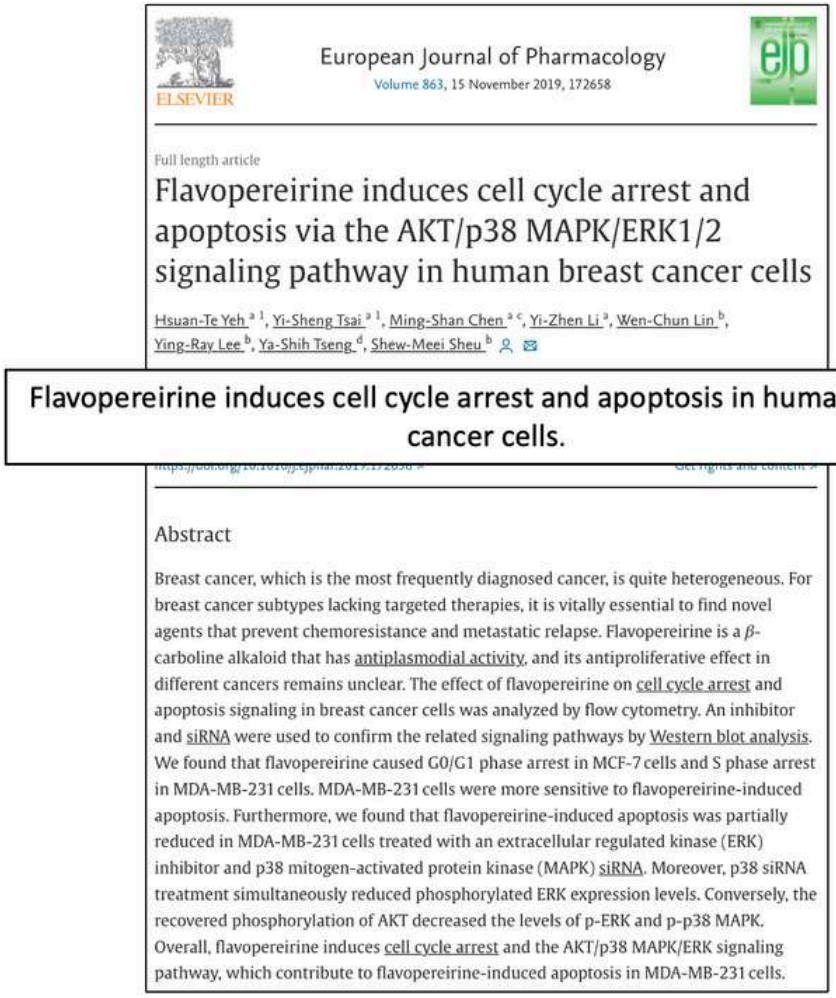
The extracts developed by Dr. Mirko Beljanski continue to be the subject of numerous scientific publications. Today, many academic institutions around the world, equipped with modern technology, have confirmed the effectiveness of the various extracts developed by Mirko Beljanski and provided a deep understanding of their multiple mechanisms of action.

All these studies confirm the activity of the extracts on a very large number of cancer lines, regardless of the sex of the patient, the organ affected, and the advancement of the disease.

All those studies can be directly downloaded from the website of The Beljanski Foundation.

French traditional media persisted in presenting Dr. Mirko Beljanski as a quack whose theories never materialized! Nevertheless, several teams of scientists from all over the world have now taken an interest in the benefits of flavopereirine, the active molecule of Pao Pereira, and have published their results in internationally renowned journals. Thus, twenty-three years after the destruction of Mirko Beljanski's laboratory, the European Journal of Pharmacology published that flavopereirine (the active molecule of the Pao Pereira extract) induces cell cycle arrest and apoptosis in human breast cancer cells. [23]

Pao Pereira: mechanism of action



European Journal of Pharmacology
Volume 863, 15 November 2019, 172658

Full length article

Flavopereirine induces cell cycle arrest and apoptosis via the AKT/p38 MAPK/ERK1/2 signaling pathway in human breast cancer cells

Hsuan-Te Yeh [a 1], Yi-Sheng Tsai [a 1], Ming-Shan Chen [a c], Yi-Zhen Li [a], Wen-Chun Lin [b], Ying-Ray Lee [b], Ya-Shih Tseng [d], Shew-Meei Sheu [b]

Flavopereirine induces cell cycle arrest and apoptosis in human breast cancer cells.

Abstract

Breast cancer, which is the most frequently diagnosed cancer, is quite heterogeneous. For breast cancer subtypes lacking targeted therapies, it is vitally essential to find novel agents that prevent chemoresistance and metastatic relapse. Flavopereirine is a β-carboline alkaloid that has antiplasmodial activity, and its antiproliferative effect in different cancers remains unclear. The effect of flavopereirine on cell cycle arrest and apoptosis signaling in breast cancer cells was analyzed by flow cytometry. An inhibitor and siRNA were used to confirm the related signaling pathways by Western blot analysis. We found that flavopereirine caused G0/G1 phase arrest in MCF-7 cells and S phase arrest in MDA-MB-231 cells. MDA-MB-231 cells were more sensitive to flavopereirine-induced apoptosis. Furthermore, we found that flavopereirine-induced apoptosis was partially reduced in MDA-MB-231 cells treated with an extracellular regulated kinase (ERK) inhibitor and p38 mitogen-activated protein kinase (MAPK) siRNA. Moreover, p38 siRNA treatment simultaneously reduced phosphorylated ERK expression levels. Conversely, the recovered phosphorylation of AKT decreased the levels of p-ERK and p-p38 MAPK. Overall, flavopereirine induces cell cycle arrest and the AKT/p38 MAPK/ERK signaling pathway, which contribute to flavopereirine-induced apoptosis in MDA-MB-231 cells.

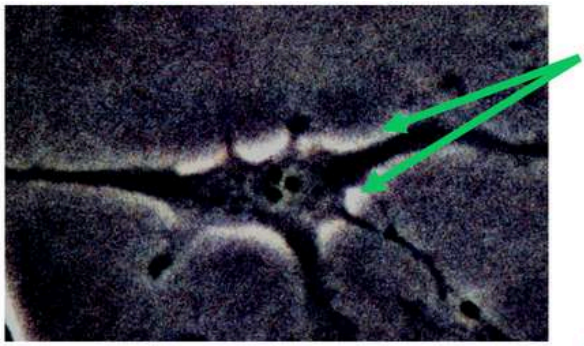
The following year, the International Journal of Molecular Sciences published the benefit of flavopereirine for triple-negative breast cancers. [24]

What is more, is that those two extracts are selective. Scientists have recognized that the electrical polarity of cancerous cells is opposite that of normal cells. It is known that healthy cells, have a membrane that is essentially positively charged (+) and impenetrable to many substances. On the contrary, cancer cells have a negatively charged (-) membrane, which is porous. Mirko Beljanski was thus able to observe that the fluorescent Pao Pereira and Rauwolfia Vomitoria extracts remained outside healthy cells but entered cancerous ones.

Both extracts target destabilized DNA, which is characteristic of all cancer cells of all types. By binding specifically to the damaged DNA structure in cancer cells, the extracts leave the normal process of DNA replication and cell division in healthy cells unaffected, demonstrating the non-toxicity of the extracts.

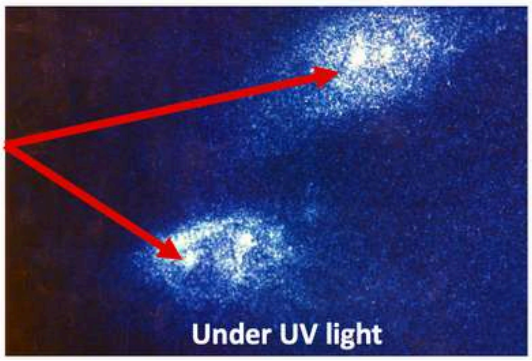
Working selectively at the level of the DNA, the Beljanski extracts are therefore not organ or gender specific.

Selectivity of Action of Pao Pereira



Naturally fluorescent, *Pao pereira* can be seen outside a **healthy cell** (astrocyte), unable to penetrate its non-porous membrane

The *Pao pereira* extract can be seen penetrating the **cancerous cell** (glioblastoma)



Selectivity of Action of Rauwolfia vomitoria

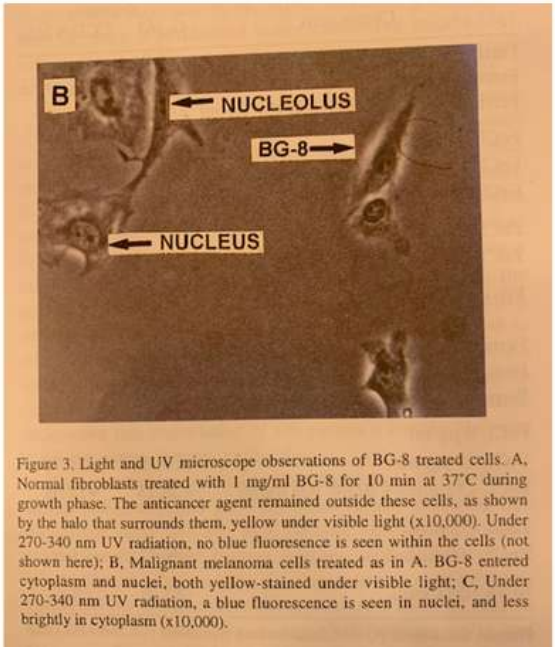


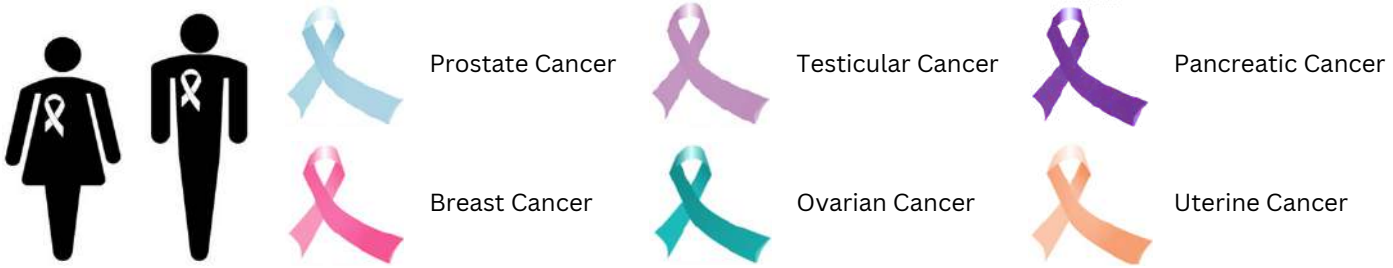
Figure 3. Light and UV microscope observations of BG-8 treated cells. A, Normal fibroblasts treated with 1 mg/ml BG-8 for 10 min at 37°C during growth phase. The anticancer agent remained outside these cells, as shown by the halo that surrounds them, yellow under visible light (x10,000). Under 270-340 nm UV radiation, no blue fluoresence is seen within the cells (not shown here); B, Malignant melanoma cells treated as in A. BG-8 entered cytoplasm and nuclei, both yellow-stained under visible light; C, Under 270-340 nm UV radiation, a blue fluorescence is seen in nuclei, and less brightly in cytoplasm (x10,000).

BELJANSKI, S. CROCHET, "The selective anticancer agents PB-100 and BG-8 are active against human melanoma cells, but do not affect **non malignant** fibroblasts".
International Journal of Oncology 8:1143-1148,1996.

PB-100 : Pao Pereira
BG-8 : Rauwolfia vomitoria

The beauty of this selectivity of action is that Women's and Men's cancers can now be addressed with the same natural approach that has already given hope to so many.

Women's and Men's Cancers: Same Approach



PAO PEREIRA AND RAUWOLFIA VOMITORIA: TWO OF NATURE'S WONDERS

Anticancer Activity, Alone, and in Synergy With Chemotherapy

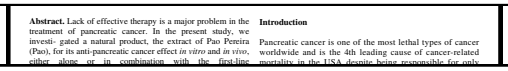
Several studies conducted at Kansas University Medical Center and at Columbia University have confirmed that extracts from Pao Pereira and Rauwolfia Vomitoria are active against a broad spectrum of cancers, including the ovarian and pancreatic cancers, as well as very advanced prostate cancers.

The synergistic action of Pao Pereira and Rauwolfia Vomitoria extracts with various chemotherapies, such as Carboplatin (commonly recommended for ovarian cancer), or Gemcitabine (recommended for pancreatic cancer), has also been confirmed.

For example, mice with pancreatic tumors were treated with Pao extract and Gemcitabine, either alone or in combination. While Gemcitabine alone did not provide significant inhibition, treatment with Pao alone suppressed tumor growth by 70 to 72% and by 78% when combined with Gemcitabine. [25]


ONCOLOGY REPORTS 30: 149-156, 2013

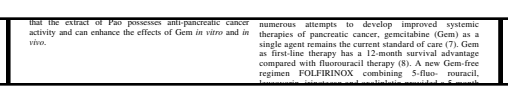
Pao treatment possessed low toxicity as no toxic effect was observed associated with the treatments. At the end of the experiments, major organs (kidney, liver and spleen) were subjected to haematoxylin and eosin (H&E) staining and histological analysis. No tissue damage was detected in any of the groups.


Abstract. Lack of effective therapy is a major problem in the treatment of pancreatic cancer. In the present study, we investi- gated a natural product, the extract of Pao Pereira (Pao), for its anti-pancreatic cancer effect *in vitro* and *in vivo*, either alone or in combination with the first-line

Introduction

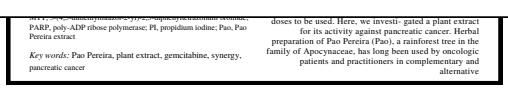
Pancreatic cancer is one of the most lethal types of cancer worldwide and is the 4th leading cause of cancer-related mortality in the USA despite being responsible for only

The extract of Pao Pereira (Pao) exhibited strong inhibition in PANC - 1 tumors throughout the course of the experiment, reaching >70% inhibition even when tumors did not respond to Gem anymore.
Consistent with the in vitro dose the reduction effect for Gem, the combination of Pao and Gem had a better effect than Gem in vivo.


that the extract of Pao possesses anti-pancreatic cancer activity and can enhance the effects of Gem *in vitro* and *in vivo*.

numerous attempts to develop improved systemic therapies of pancreatic cancer, gemcitabine (Gem) as a single agent remains the current standard of care (7). Gem as first-line therapy has a 12-month survival advantage compared with fluorouracil therapy (8). A new Gem-free regimen FOLFIRINOX combining 5-fluo- rouracil,

In addition, by the dose-reduction effect, Pao allowed for lower concentrations of Gem while achieving an equivalent cytotoxicity in cancer cells with higher Gem concentrations alone. This may P decrease the toxicity associated with chemotherapy.


PARP, poly-ADP ribose polymerase; PI, propidium iodine; Pao, Pao Pereira extract

Key words: Pao Pereira, plant extract, gemcitabine, synergy, pancreatic cancer

doses to be used. Here, we investi- gated a plant extract for its activity against pancreatic cancer. Herbal preparation of Pao Pereira (Pao), a rainforest tree in the family of Apocynaceae, has long been used by oncologic patients and practitioners in complementary and alternative

Similarly, extracts of Pao Pereira or Rauwolfia Vomitoria combined with Carboplatin worked particularly well, even against chemotherapy-resistant ovarian cancer cells. [26]

Furthermore, studies conducted at Columbia University and Nanjing University on prostate cancer have demonstrated that due to multiple mechanisms of action, Pao Pereira had a beneficial effect at all stages of the disease, from benign prostate hyperplasia [27] (i.e, a prostate swollen by inflammation, but without developed cancer - a very common condition in men over fifty years old is often associated with an increased urge to urinate), to declared prostate cancer, [28] and even very advanced prostate cancer no longer responding to hormonal treatments. [29]

Comparable results have also been obtained with Rauwolfia Vomitoria. [30, 31]

Those publications can be directly downloaded from the website of The Beljanski Foundation.

Multiple Chemotherapy Drugs ...

- Lomustine is an alkylating agent, one of a family of chemotherapy drugs that attaches alkyl groups to DNA thus preventing DNA replication and cell division.
- Docetaxel is an anti-mitotic agent, one of a family of chemotherapy drugs that prevents cells from dividing by disrupting microtuble function.
- Carboplatin is one of the platinum-based drugs that bind to DNA and interfere with DNA repair.
- Gemcitabine is a nucleoside analog resembling cytidine that is incorporated into DNA and that blocks further DNA synthesis.
- When applied together to lung cancer cell lines, gemcitabine and docetaxel were antagonistic with one another and thus cannot be taken together.

Source: Theodossiou C, Cook JA, Fisher J, et al. Interaction of gemcitabine with pacitaxel and cisplatin in human tumor cell lines. International Journal of Oncology, 1998, 12, pp. 825-32.

... and still, we have synergy !

Experiments conducted by Dr. Beljanski's group in Paris, by Dr. Katz's group in New York, and by Dr. Drisko's group at Kansas, show that the Pao and/or Rauwolfia extracts forms highly effective combinations with four different chemotherapeutic drugs with four different mechanisms of action.

This suggests that the extracts will work together with a broad spectrum of anti-tumor drugs.

Anti-inflammatory Benefits

The anti-inflammatory activity observed with Pao Pereira extract, as well as that of Rauwolfia Vomitoria, is a new application of great importance. Indeed, the link between inflammation and aging is a very active research topic in the field of the biology of aging: As individuals age, their immune system can become more reactive, which can lead to chronic inflammation, often called "inflammaging". This low-grade, persistent inflammation is associated with many age-related diseases, such as cardiovascular diseases, type 2 diabetes, neurodegenerative diseases, and even some types of cancer. In Alzheimer's disease, markers of inflammation are observed in the brains of patients.

There is also some concern regarding the long-term use of certain medications such as non-steroidal anti-inflammatory drugs (such as ibuprofen or naproxen) often used to alleviate pain and reduce inflammation in various conditions, and their possible link to cancer. Research suggests that high doses and prolonged use of non-steroidal anti-inflammatory drugs may increase the risk of certain types of cancer, particularly gastrointestinal cancers (like stomach and colon cancer).

The benefit of anti-inflammatory activity, associated with anti-cancer activity, makes this combination a win/win approach for the patient.

Different Stages of Cancer Progression
The Prostate Example

Precancerous | **Cancerous** | **Advanced Cancer**

The team at The Beljanski Foundation shares all these results with you on the website www.beljanski.org so that you can make informed decisions to help restore and maintain optimal health.

Beljanski®
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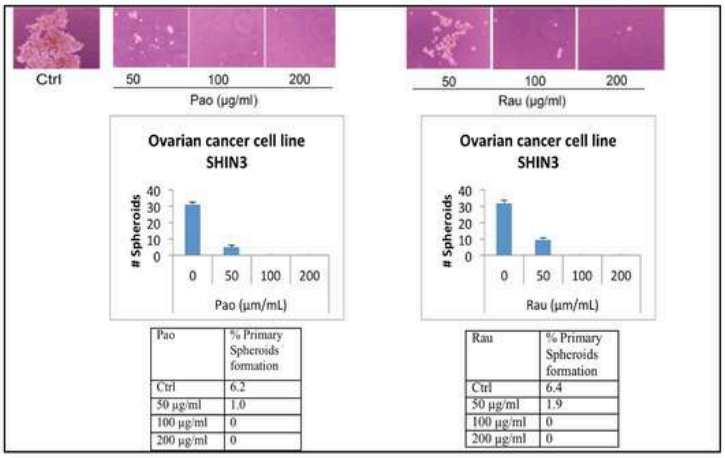
Anti-inflammatory activity, anti-cancer activity, synergy with chemotherapies... what if these little wonders could do even more?

BELJANSKI EXTRACTS AND CANCER STEM CELLS

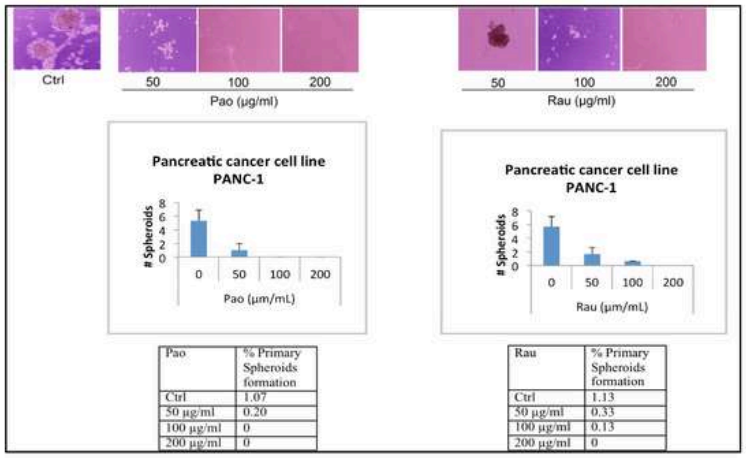
It must be remembered that Mirko Beljanski passed away in 1998, and at that time, cancer stem cells were not yet a topic of discussion. But beyond the confirmation of the activity of the extracts on numerous cancers (Mirko Beljanski had already published on this subject), new studies have shed light on their multiple mechanisms of action for identifying and destroying cells with altered DNA, at different stages of the disease. Therefore, it seemed legitimate to question their activity against cancer stem cells.

In vitro studies of the activity of *Pao pereira* and *Rauwolfia vomitoria* on Ovarian Cancer stem cells SHIN3 at doses $ 200 µg/ml and on Pancreatic Cancer Stem Cells PANC-1 at Doses ≤ 200 µg/ml



Pao	% Primary Spheroids formation
Ctrl	6.2
50 µg/ml	1.0
100 µg/ml	0
200 µg/ml	0

Rau	% Primary Spheroids formation
Ctrl	6.4
50 µg/ml	1.9
100 µg/ml	0
200 µg/ml	0

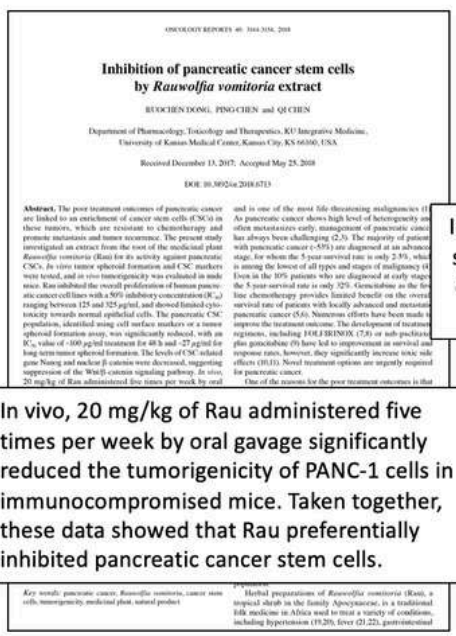


Pao	% Primary Spheroids formation
Ctrl	1.07
50 µg/ml	0.20
100 µg/ml	0
200 µg/ml	0

Rau	% Primary Spheroids formation
Ctrl	1.13
50 µg/ml	0.33
100 µg/ml	0.13
200 µg/ml	0

Given the crucial importance of cancer stem cells in the progression of cancer, the Beljanski Foundation asked Dr. Chen at Kansas University Medical Center to test the activity of the extracts on pancreatic cancer and ovarian cancer stem cells. Pancreatic and ovarian cancers were chosen for this experiment because they are generally very difficult to cure. They are usually detected very late, and often, the tumor cells become resistant to the drugs chosen for treatment. However, the in vitro study revealed that all cancer stem cells had been completely eradicated by the natural extracts within hours, and this was archived without any harm to healthy cells! An in vivo study (on mice) thus complemented the initial results. The research team at Kansas University Medical Center concluded that in mice that had developed pancreatic or ovarian cancers, the extracts destroyed both primary cancer cells and cancer stem cells, due to different mechanisms of action depending on the type of cells. The absence of toxicity to healthy cells and the very good tolerance of the extracts taken orally (gavage) throughout the duration of the study was also confirmed. [32, 33, 34]

Cancer Stem Cells / Pao pereira and Rauwolfia vomitoria



Inhibition of pancreatic cancer stem cells by *Rauwolfia vomitoria* extract

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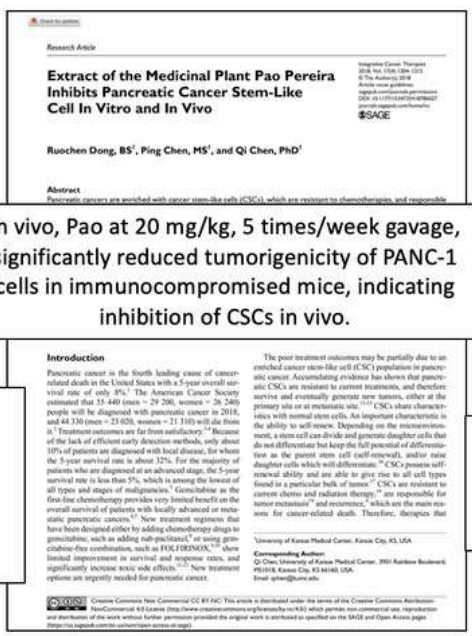
Abstract. The poor treatment outcomes of pancreatic cancer are linked to an enrichment of cancer stem cells (CSCs) in these tumors, which are resistant to chemotherapy and promote metastasis and tumor recurrence. The present study investigated an extract from the root of the medicinal plant *Rauwolfia vomitoria* (Rau) for its activity against pancreatic CSCs. *In vitro* tumor spheroid formation and CSC markers were tested, and *in vivo* tumorigenicity was evaluated in nude mice. Rau inhibited the overall proliferation of human pancreatic cancer cell lines with a 50% inhibitory concentration (IC_{50}) ranging between 125 and 325 µg/ml, and showed limited cytotoxicity towards normal epithelial cells. The pancreatic CSC population, identified using cell surface markers or a tumor spheroid formation assay, was significantly reduced, with an IC_{50} value of ~100 µg/ml treatment for 48 h and ~27 µg/ml for long-term tumor spheroid formation. The levels of CSC related gene Nanog and nuclear β-catenin were decreased, suggesting suppression of the Wnt/β-catenin signaling pathway. *In vivo*, 20 mg/kg of Rau administered five times per week by oral gavage significantly reduced the tumorigenicity of PANC-1 cells in immunocompromised mice. Taken together, these data showed that Rau preferentially inhibited pancreatic cancer stem cells.

Key words: pancreatic cancer, *Rauwolfia vomitoria*, cancer stem cells, tumorigenicity, medicinal plant, natural product

Herbal preparations of *Rauwolfia vomitoria* (Rau), a tropical shrub in the family Apocynaceae, in a traditional folk medicine in Africa used to treat a variety of conditions, including hypertension (19,20), fever (21,22), gastrointestinal



Research Article

Extract of the Medicinal Plant Pao Pereira Inhibits Pancreatic Cancer Stem-Like Cell In Vitro and In Vivo

Ruochen Dong, BS[1], Ping Chen, MS[1], and Qi Chen, PhD[1]

Abstract

Pancreatic cancers are enriched with cancer stem-like cells (CSCs), which are resistant to chemotherapies, and responsible

Introduction

Pancreatic cancer is the fourth leading cause of cancer-related death in the United States with a 5-year overall survival rate of only 8%.[1] The American Cancer Society estimated that 55 440 (men = 29 200, women = 26 240) people will be diagnosed with pancreatic cancer in 2018, and 44 330 (men = 23 020, women = 21 310) will die from it.[1] Treatment outcomes are far from satisfactory.[2-4] Because of the lack of efficient early detection methods, only about 10% of patients are diagnosed with local disease, for whom the 5-year survival rate is about 32%. For the majority of patients who are diagnosed at an advanced stage, the 5-year survival rate is less than 5%, which is among the lowest of all types and stages of malignancies.[1] Gemcitabine as the first-line chemotherapy provides very limited benefit on the overall survival of patients with locally advanced or metastatic pancreatic cancers.[5,6] New treatment regimens that have been designed either by adding chemotherapy drugs to gemcitabine, such as adding nab-paclitaxel,[7] or using gemcitabine-free combinations, such as FOLFIRINOX,[8,9] show limited improvement in survival and response rates, and significantly increase toxic side effects.[10,11] New treatment options are urgently needed for pancreatic cancer.

The poor treatment outcomes may be partially due to an enriched cancer stem-like cell (CSC) population in pancreatic cancer. Accumulating evidence has shown that pancreatic CSCs are resistant to current treatments, and therefore survive and eventually generate new tumors, either at the primary site or at metastatic site.[12,13] CSCs share characteristics with normal stem cells. An important characteristic is the ability to self-renew. Depending on the microenvironment, a stem cell can divide and generate daughter cells that do not differentiate but keep the full potential of differentiation as the parent stem cell (self-renewal), and/or raise daughter cells which will differentiate.[14] CSCs possess self-renewal ability and are able to give rise to all cell types found in a particular bulk of tumor.[15] CSCs are resistant to current chemo and radiation therapy,[16] are responsible for tumor metastasis[17] and recurrence,[18] which are the main reasons for cancer-related death. Therefore, therapies that

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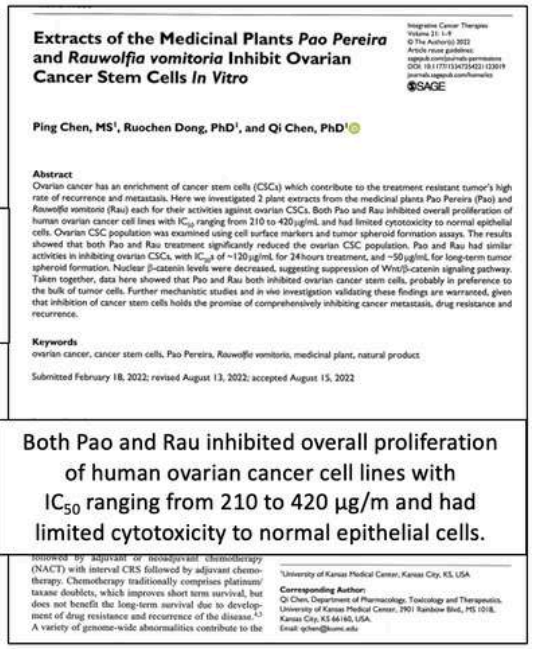

Extracts of the Medicinal Plants *Pao Pereira* and *Rauwolfia vomitoria* Inhibit Ovarian Cancer Stem Cells *In Vitro*

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Abstract

Ovarian cancer has an enrichment of cancer stem cells (CSCs) which contribute to the treatment resistant tumor's high rate of recurrence and metastasis. Here we investigated 2 plant extracts from the medicinal plants Pao Pereira (Pao) and *Rauwolfia vomitoria* (Rau) each for their activities against ovarian CSCs. Both Pao and Rau inhibited overall proliferation of human ovarian cancer cell lines with IC_{50} ranging from 210 to 420 µg/mL and had limited cytotoxicity to normal epithelial cells. Ovarian CSC population was examined using cell surface markers and tumor spheroid formation assays. The results showed that both Pao and Rau treatment significantly reduced the ovarian CSC population. Pao and Rau had similar activities in inhibiting ovarian CSCs, with IC_{50}s of ~120 µg/mL for 24 hours treatment, and ~50 µg/mL for long-term tumor spheroid formation. Nuclear β-catenin levels were decreased, suggesting suppression of Wnt/β-catenin signaling pathway. Taken together, data here showed that Pao and Rau both inhibited ovarian cancer stem cells, probably in preference to the bulk of tumor cells. Further mechanistic studies and *in vivo* investigation validating these findings are warranted, given that inhibition of cancer stem cells holds the promise of comprehensively inhibiting cancer metastasis, drug resistance and recurrence.

Keywords

ovarian cancer, cancer stem cells, Pao Pereira, *Rauwolfia vomitoria*, medicinal plant, natural product

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followed by adjuvant or neoadjuvant chemotherapy (NACT) with interval CRS followed by adjuvant chemotherapy. Chemotherapy traditionally comprises platinum/taxane doublets, which improves short term survival, but does not benefit the long-term survival due to development of drug resistance and recurrence of the disease.[4,5] A variety of genome-wide abnormalities contribute to the

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In vivo, Pao at 20 mg/kg, 5 times/week gavage, significantly reduced tumorigenicity of PANC-1 cells in immunocompromised mice, indicating inhibition of CSCs in vivo.

In vivo, 20 mg/kg of Rau administered five times per week by oral gavage significantly reduced the tumorigenicity of PANC-1 cells in immunocompromised mice. Taken together, these data showed that Rau preferentially inhibited pancreatic cancer stem cells.

Both Pao and Rau inhibited overall proliferation of human ovarian cancer cell lines with IC_{50} ranging from 210 to 420 µg/m and had limited cytotoxicity to normal epithelial cells.

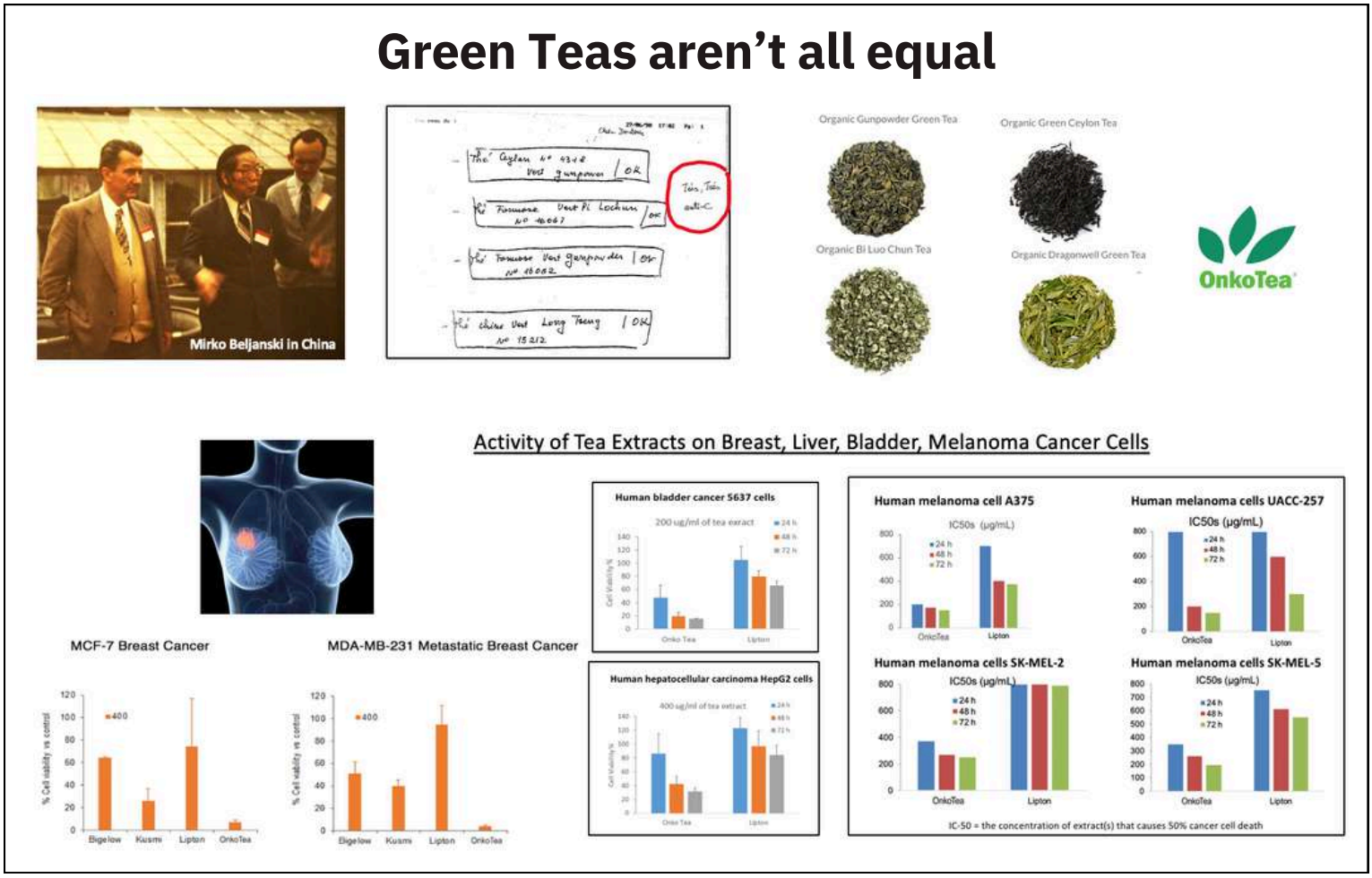
The data showing how extracts of Pao Pereira and Rauwolfia Vomitoria treat ovarian and pancreatic cancer stem cells is excellent news for patients suffering from these cancers. This breakthrough, highlighting the effect of the two extracts on cancer stem cells changes the game not only for patients but also for the oncologists who care for these patients.

Given their broad-spectrum anti-cancer activity – already solidly documented – and the absence of toxicity of these extracts, Pao Pereira and Rauwolfia Vomitoria deserve to be studied more thoroughly against stem cells of many types of cancer in both men and women.

AND GREEN TEA?

The origin of green tea dates back over 5,000 years in China. For a long time, green tea was very expensive and only accessible to wealthy Chinese society. It was not until the 14th century that green tea became accessible to the general public. Nowadays, green tea is widely appreciated for its taste and health benefits.

During a study trip to China, Dr. Mirko Beljanski received a large box of samples filled with several teas known for their interesting health properties. Back at the Pasteur Institute, Dr. Beljanski tested each one and noted the positive results on a sheet of paper. Unfortunately, this list was lost and only found twenty years later. Four names of green teas had the handwritten note "very very anti-C."



A blend of these four green teas (OnkoTea®) was created without delay, and sent to Kansas University Medical Center, to evaluate its activity on cancer cells. For good measure and for comparison purpose, several other teas were also evaluated, namely Bigelow® mint green tea, Kusmi® Chinese green tea, and Lipton® black tea.

The activity of all these teas on breast cancer cells, melanoma, liver, and bladder was tested. The results showed that the effects of each of these teas on cell proliferation depended on their concentration. At a high concentration, all teas inhibited cells from various cancer lines, but the specific combination of green teas (OnkoTea®) identified by Dr. Mirko Beljanski showed the best inhibitory effect. Most specifically, this new blend of green teas was far superior to the others in inhibiting the growth of two breast cancer cell lines, including one highly metastatic cell line. [35]

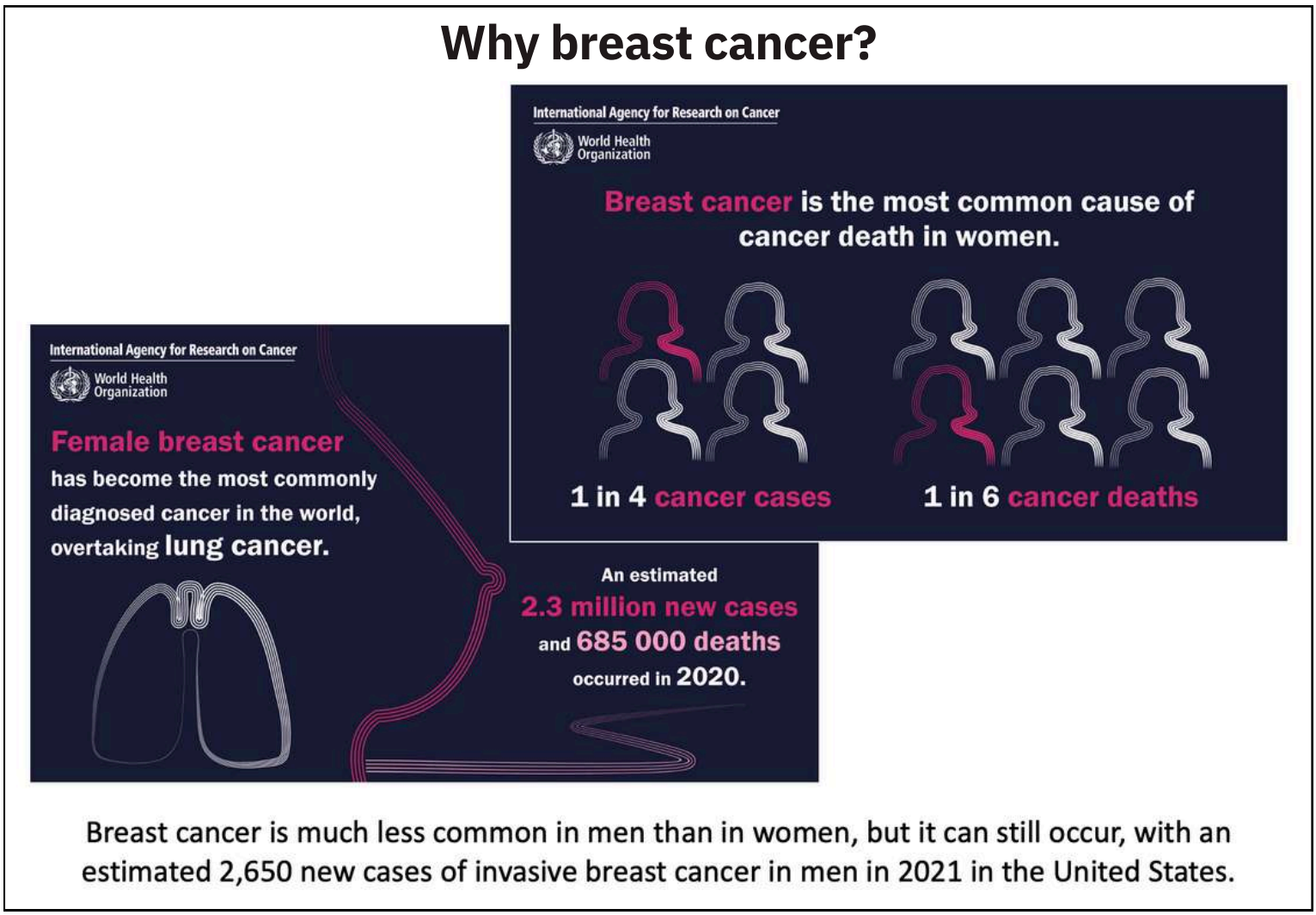
Green teas have long been associated with antioxidant benefits, but new research conducted by Kansas University Medical Center and the Beljanski Foundation shows that OnkoTea®, like the extracts of Pao Pereira and Rauwolfia Vomitoria, is active against a broad spectrum of cell lines with a destabilized DNA structure.

NEW PROJECT: BREAST CANCER STEM CELLS

In light of all these results, the Beljanski Foundation has chosen to collaborate once again with Kansas University Medical Center, this time to study the activity of a specific blend of Pao Pereira, Rauwolfia Vomitoria, and OnkoTea® green tea on breast cancer stem cells.

Why breast cancer?

Because breast cancer is one of the most common cancers globally.



According to the Global Cancer Observatory Report, "Breast cancer is the most commonly occurring cancer in women and one of the most common cancers overall. There were more than 2.3 million new cases of breast cancer in women in 2020. It is also the most common cause of death in women (Breast cancer is much less common in men than in women but is often of poor prognosis)." [36]

Good news!
We have a lot of breast cancer survivors

There are more than **4 million breast cancer survivors** in the United States, including women still being treated and those who have completed treatment.

Bad news!

Up to **30% of people** who have been treated for breast cancer may experience a **recurrence**

The good news is that there are many "survivors" of breast cancer. The survival rate is the percentage of people in a group with the same disease who survive, and who do not die from it. In medicine, the survival rate is generally limited to the 5-year survival rate, which is the percentage of people who are still alive five years after being diagnosed with the disease. Of course, it varies depending on many factors, including the stage of cancer at diagnosis, the individual characteristics of the patient, and the quality of medical care received. But generally speaking, saying that a person has survived five years after the initial diagnosis does not mean that their treatment is over, or that the person has been able to return to their "previous life." Cancer survivors often face many adverse psychological and physical events as a result of cancer and conventional treatments. They also often suffer from a worse quality of life than people without cancer. And there is always the fear of recurrence, because, as previously seen, conventional cancer treatment does not address the problem of cancer stem cells. According to the website of the Marie Curie Institute, "Cancer can recur at the level of the breast itself (local recurrence) or at a distance, in other organs or tissues, which are metastases. The risk of recurrence and the severity of it depends on the size of the initial tumor, the involvement of the lymph nodes, treatments... For all types of cancer combined, there is a peak of local recurrence or the appearance of metastases two years after treatment." [37]

Why choose a mix of Pao Pereira, Rauwolfia Vomitoria, and OnkoTea® green tea? Because previous studies have confirmed significant activity of each of these ingredients on breast cancer cells, and because Pao Pereira and Rauwolfia Vomitoria have already demonstrated their ability to inhibit the development of ovarian and pancreatic cancer stem cells.

The Kansas University Medical Center is advancing a research program on breast cancer stem cells, supported by funds raised at the Beljanski Integrative Cancer Conference held in Jacksonville, Florida, in October 2023. The necessary extracts for the study were supplied by Maison Beljanski who launched *Womabel*®* for that purpose.

NEW!

Womabel®*

Pao pereira
Rauwolfia vomitoria
& Green tea extracts

The Beljanski Foundation anticipates sharing the findings of this research at their forthcoming conference, scheduled to take place in Austin, Texas, from April 25-27, 2025.

The results are likely to lead to a new publication which will be featured on The Beljanski Foundation website. The hope is to improve the odds of all the many women who are breast cancer survivors and live with the anxiety that their cancer will come back.

Let's put an end to the breast cancer epidemic!

Unless we tackle cancer stem cells, we will never see the end of breast cancer epidemic

What we need is a treatment that addresses ALL cancer cells!

But there is more! Since Pao pereira and Rauwolfia vomitoria selectively target cancerous cells wherever they are located... the Beljanski Foundation is already contemplating its next project: Prostate cancer stem cells!

The Beljanski Foundation relies on grants and donations from people like you. Our work is made possible by the generous donations of individuals who believe in our mission and share our commitment to making the discoveries of Dr. Mirko Beljanski available to as many people as possible.

Support The Beljanski Foundation by donating today!

*Source: https://www.maisonbeljanski.com/

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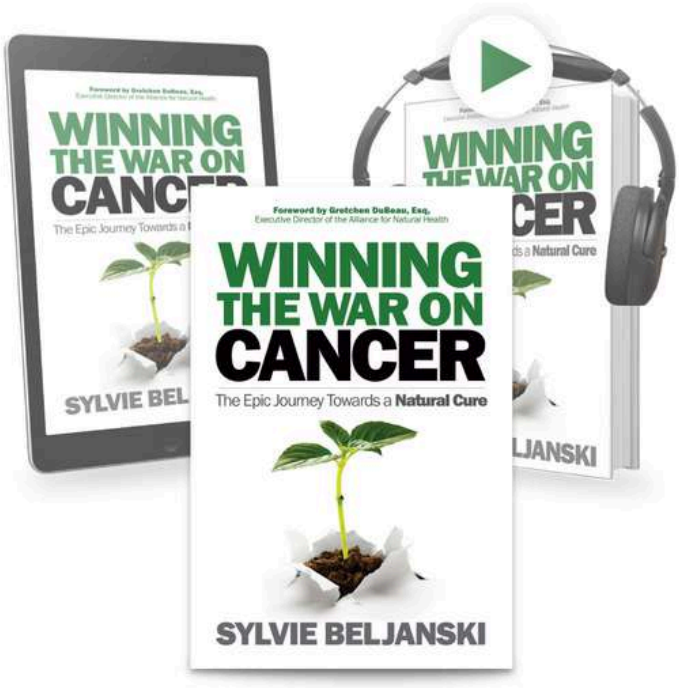

WINNING THE WAR ON CANCER

Click here to get a FREE chapter

100% of the author's proceeds from "Winning The War On Cancer" will be donated to The Beljanski Foundation, Inc. a 501(c)(3) non-profit organization, to help fund anticancer research to cure cancer the natural way.

HERE IS WHAT PEOPLE ARE SAYING ABOUT "WINNING THE WAR ON CANCER: THE EPIC JOURNEY TOWARDS A NATURAL CURE"

Zack H. on OnlineBookClub.org ★★★★★

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Vivienne Nat ★★★★★

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Marika P. on OnlineBookClub.org ★★★★★

"As people who are on the receiving end of medical treatments, we are unaware of the struggles that scientists face in the pharmaceutical industry. Dr. Mirko Beljanski was a victim of an unfair government that aimed at destroying any evidence of the scientist's research, together with the promising results he had obtained in treating different types of cancer. It was then his daughter who salvaged what little was left and gave the newfound treatment back to the whole medical community."

Florence Nalianya ★★★★★

"Story of hope and determination that could lead us to a cancer-free world. I loved reading this book so much. It's a book of hope for everybody as far as health is concerned ."

Anna S. on OnlineBookClub.org ★★★★★

"This has been a smooth read for me, and I so much appreciate how well-written and well-researched this book is. I must say that what I like in this book, which I so much appreciate and also find to be one of its greatest strengths, is its thorough grounding in scientific research, with numerous published articles and treatment protocols cited throughout."

THE BELJANSKI INTEGRATIVE CANCER CONFERENCE 2025

THE BELJANSKI CANCER TALK SHOW

LET'S TALK ABOUT CANCER

Welcome to "The Beljanski Cancer Talk Show", a podcast series dedicated to exploring comprehensive and integrative approaches to cancer treatment and chronic diseases.

Our journey delves into the world of holistic health, examining how it complements traditional medicine in the fight against cancer.

In each episode, we'll be discussing various aspects of holistic care, including nutrition, mental health, alternative therapies, and lifestyle changes, with a focus on how these elements collectively support the body, mind, and spirit during cancer treatment and beyond.

We will feature expert guests - oncologists, naturopaths, nutritionists, psychologists, and survivors, all sharing their insights and experiences.

Whether you're a patient, a caregiver, or someone interested in holistic health, this series offers valuable perspectives and practical advice to empower and inspire you on your journey.

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