COMBINING BIOBRAN WITH HYPERTHERMIA, CHEMOTHERAPY AND OTHER ANTICANCER TREATMENTS

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LOOKING AT CANCER FROM THREE DIFFERENT ANGLES

Dr.JOSEPH BRENNER

Medical Oncologist

• Expert in Integrative cancer therapies

• Cancer victim

Dr. JOSEPH BRENNER with Prof. Luigi DI-BELLA/Modena-Italy



Angle I: Medical Oncologist

- 1974: Fellowship in Israel as an Oncologist (Chemotherapy and RT)
- 1978-79: Felowship in RT at Rhode Island Hospital
- 1979-1982: Fellowship in Medical Oncology at Memorial Sloan Kettering Cancer Center/ New-York
- 1982-2012 Head of Oncology Wolfson Hospital/Israel

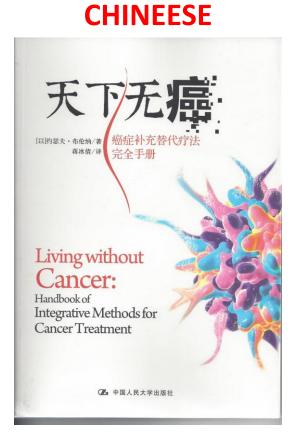
Angle II: An Expert In Cancer Integrative Medicine

- Since 1988 using integrative cancer methods for cancer patients
- 1998 the establishment of "New-Hope" clinic in Tel-Aviv for the treatment of cancer with hyperthermia, IPT, High dose Vitamin-C, Galvanotherapy, Nutrition, Supplements Mind-Body and more
- 2014 president of ICHS (International Clinical Hyperthermia Society)
- Lecturing all over the world in such subjects.

Engle III: A Cancer Victim

- 2001 Diagnosis of advanced carcinoma of prostate, PSA=20, Gleason=8
- With hyperthermia, high-dose vitamin-C infusions, supplements, nutrition and mind-body methods tumor disappeared by 95%.
- High dose-rate brachytherapy (Oakland California), hormonal therapy.
- N.E.D today, PSA=0

TEXTBOOK FOR INTEGRATIVE ONCOLOGY



HEBREW/ENGLISH/RUSSIAN



The Problem of Cancer



- Two in three born today likely to get cancer
- Half of those born since 1960 will develop cancer in their lifetime, new forecasts warn, as experts suggest it could reach two thirds among today's children
- By Laura Donnelly, Health Editor
- 6:30AM GMT 04 Feb 2015

CANCER STATISTICS

CANCER STATISICS USA-2014 (SEER):

New cases 2014: 1,669,000

- Death: 590,000=35%
- Survival 2014=65%
- Survival 2005-2012=66.5%
- One year survival: 1975=69% 2012=81% Early diagnosis, inclusion of pre-malignancies (breast and colon), improved surgical technics and care, adjuvant therapies.

Curing Cancer In the 1970th

 In the early 1970th oncologist developed treatments with RT and chemotherapy that **CUred** metastatic lethal cancers:

Metastatic testicular tumors Metastatic choriocarcinoma Early and metastatic Hodgkin's disease Some types of Non-Hodgkin's lymphomas Some types of leukemia Early and metastatic childhood osteogenic sarcomas Wilms' tumors and some other childhood cancers

Lans Armstrong: Winning Against Metastatic Testicular Tumor



In 1963 95% of patients with metastatic testicular tumors died of the disease.

In 1976 95% of patients with metastatic testicular tumors were cured.

In such case, no statistical evaluation was necessary.

Curable cancers even in metastatic stage

- Leukemia's
- Hodgkin's Lymphomas
- Some Non-Hodgkin's Lymphomas
- Childhood cancers: Wilms, Rhabdomyosarcomas, Osteogenic Sarcomas, Neuroblastomas
- Testicular Seminomas and Non-Seminomas
- Thyroid cancers
- Choriocarcinomas

23 Dec 1971: President Nixon sign on "War against Cancer"



- 40 Billion Dollars dedicated to find the cure for cancer.
- 45 years later, no cure was found even to one more cancer type.

1997: Cancer Undefeated

The New England Journal of Medicine -- May 29, 1997 -- Vol. 336, No. 22 Protection Contractor Cancer Undefeated John C. Bailar III, Heather L. Gornik

Abstract

Background. Despite decades of basic and clinical research and trials of promising new therapies, cancer remains a major cause of morbidity and mortality. We assessed overall progress against cancer in the United States from 1970 through 1994 by analyzing changes in ageadjusted mortality rates.

Methods. We obtained from the National Center for Health Statistics data on all deaths from cancer and from cancer at specific sites, as well as on deaths due to cancer according to age, race, and sex, for the years 1970 through 1994. We computed age-specific mortality rates and adjusted them to the age distribution of the U.S. population in 1990.

Results: Age-adjusted mortality due to cancer in 1994 (200.9 per 100,000 population) was 6.0 percent higher than the rate in 1970 (189.6 per 100,000). After decades of steady increases, the ageadjusted mortality due to all malignant neoplasms plateaued, then decreased by 1.0 percent from 1991 to 1994. The decline in mortality due to cancer was greatest among black males and among persons under 55 years of age. Mortality among white males 55 or older has also declined recently. These trends reflect a combination of changes in death rates from specific types of cancer, with important declines due to reduced cigarette smoking and improved screening and a mixture of increases and decreases in the incidence of types of cancer not closely related to tobacco use.

Conclusions. The war against cancer is far from over. Observed changes in mortality due to cancer primarily reflect changing incidence or early detection. The effect of new treatments for cancer or mortality has been largely disappointing. The most promising approach to the control of cancer is a national commitment to prevention, with a concomitant rebalancing of the focus and funding of research. (N Engl J Med 1997;336:1569-74.)

Source Information

From the Department of Health Studies, University of Chicago, 5841 S.Maryland Ave., MC 2007, Chicago, IL 60637-1470, where reprint requests should be addressed to Dr. Bailar. •Since the 1970th there is no cure for metastatic disease in any new cancer type. Conventional oncology is good but not good enough!

You need more then 2 hands to pull a car out of the mud

You need more than one treatment method to fight cancer



Winning the war on cancer by K.O or by points?





Integrating CAM (Complementary-Alternative Cancer Medicine) with Conventional Oncology

- Surgery
- Chemotherapy
- Radiation Therapy
- Brachytherapy
- Hormone Therapy
- Biologic Therapy
- Immuno-Therapy

Nutrition

- Habits changes
- Mind-Body therapies
- Supplements
- Anti-cancer non proved remedies.
- Detoxification
- Oxygen therapies
- IV
- IPT
- Physical anticancer methods: hyperthermia, galvano

INTEGRATIVE ONCOLOGY





Aims of Integrative Anti-Cancer Treatments

- Tumor destruction
- Improve the immune system
- Prevent side effects and organ damage of chemo and radiation
- Increase the efficiency of chemo and radiation
- Treat cancer symptoms
- Improve general condition of patients.

Combining anti-cancer treatments

- Additive effect (1+1=2)
- Synergistic effect (1+1=3)
- Reducing toxicity

TREATMENTS AT "NEW-HOPE" CLINIC

- Nutrition: General for cancer Specific for cancer type
- Detoxification
- Oral supplements

General for cancer Specific for cancer type

- I.V infusions: H.D Vit-C, Vitamins, Minerals, Homeopatic remedies, Herbs, Glutathione, ALA and more
- Hyperthermia: Superficial, Deep Local, Extensive deep local
- Galvanotherapy

Treatments by Tumor Type

Supplements for brain tumors	Food for breast cancer
Vitamin D Vitamin E Quercetine Resveretrol Selenium Bromelein Inositol Melatonin Bosevillia Green Tea Canabinoids PSK=Polysaccharide Krestin Uncaria tomentosa Berberine Noscapine Transfer Factor Viscum Album	 Fruits and vegtables Garlic, Nuts, almonds, ,Beet, Buckwheat, Whey, Rise, Salmon, Soy, Pumpkin, Olives, Cruciferous, Omega-3, Pomegranate, Celery AVOID: Avocado, Eggs (2/week), Red- Meat, Honey, Trans-Fats, Limited Milk Consumption

Combining BioBran with other anti-cancer treatments

- Hyperthermia
- Chemotherapy
- Radiation Therapy
- Hormones
- Biologic Agents
- Immunotherapy
- PDT
- Supplements
- Hyperbaric Oxygen
- IVC

 BioBran is an integrated part of most treatments done at the "New-Hope" Clinic

HYPERTHERMIA

Hyperthermia

- One of the major anticancer methods.
- A selective anticancer method, causing damage to cancer cells but not to normal cells.

1997-Hyperthermia at the "New-Hope" clinic



HYPERTHERMIA

- Hyperthermia is a treatment modality using our knowledge that cancer cells are much more sensitive to heat than normal cells.
- At the heat of 41.5 centigrade and above, cancer cells die due to intracellular damaged enzymes necessary for the cell function.
- As normal cells are not affected, treatment is without any side-effects and without any damage to normal organs.

HYPERTHERMIA

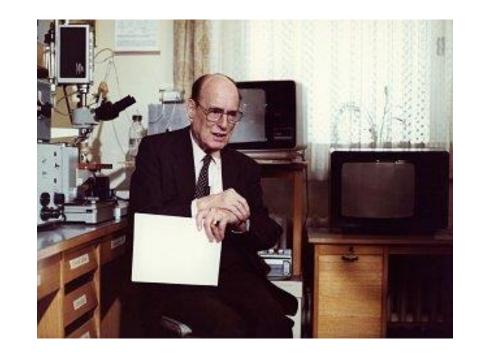
- It is used in hospitals as an invasive method: Abdominal washing with hot water in ovarian cancer surgeries, Heating the blood in limb perfusion surgeries, and more..
- 30,000 articles about hyperthermia in the literature.
- An integrated part of cancer treatments in hospitals in Germany, The-Nederland's, Italy, Japan, Korea and

Prof Von Ardenne The Founder Of Modern Hyperthermia

Dr. Alexander Von Ardenne

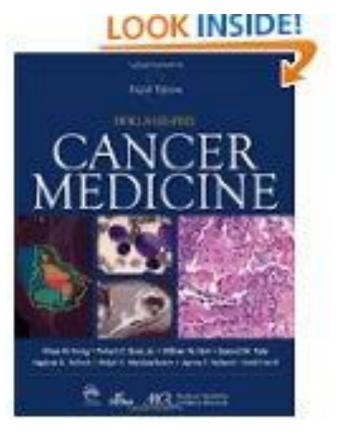


Prof Manfred Von Ardenne

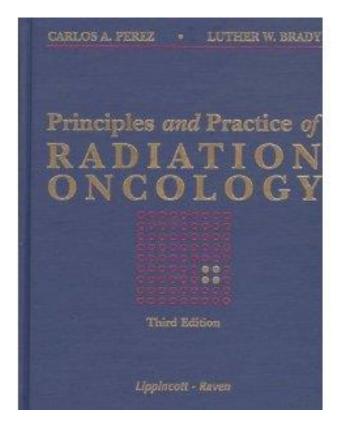


Chapters about Hyperthermia in most important Oncology Textbooks

Holland&Frei Textbook of Oncology



Prerz Textbook of Radiation Oncology



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International Journal of HYPERTHERMIA

The official journal of the

Society for Thermal Medicine

European Society for Hyperthermic Oncology

Asian Society of Hyperthermic Oncology

Special Issue: First ESHO Educational Symposium on Hyperthermia 2005



The Cochrane Report:

Concomitant hyperthermia and radiation therapy for treating locally advanced rectal cancer

- In conclusion hyperthermia seems to have an additional effect when added to radiotherapy in the treatment of advanced rectal cancer.
- After 2 years, OS was significantly better in the RHT group (HR 2.06).
- A significant higher CR rate was observed in the RHT group (RR 2.81).

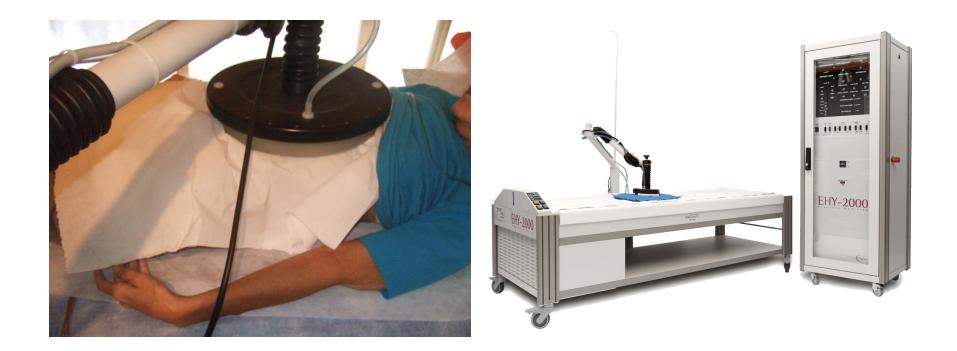
The Cochrane Report:

Combined use of hyperthermia and radiation therapy for treating locally advanced cervix carcinoma

- . The results do suggest a better outcome for patients treated with the combination of radiotherapy with hyperthermia.
- Thus following treatment a complete disappearance of the tumor was observed more regularly, regrowth of the tumor at the site of origin during follow up was observed less frequently and more patients were still alive at last follow-up.

 Treatment related side effects were not increased by the addition of hyperthermia to standard radiotherapy.

Limited Field Deep Local-Regional Hyperthermia



Wide-Field Deep Local-Regional Hyperthermia



Bilateral lungs hyperthermia

Allow us to treat bilateral lungs disease, pleural effusions, lymphatic spread of breast cancer



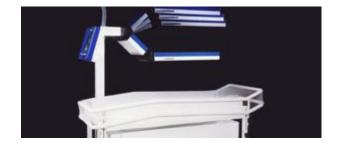
Whole abdomen hyperthermia

Allow us to treat diffused abdominal and pelvic carcinomatosis such as in ovarian and colonic cancer, ascites, bi-lobar liver metastasis



Von Ardenne Whole Body Hyperthermia





Heckel Whole-Body Hyperthermia





Superficial Hyperthermia



 Treatment of skin tumors or skin metastasis of deep seated tumors

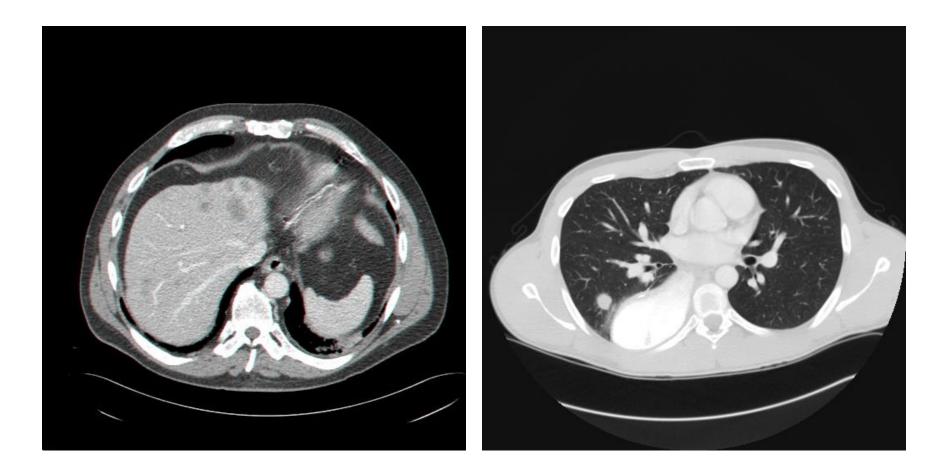
Intra-prostatic hyperthermia





- January 2010: 62 Y.O with adenocarcinoma of pancreas, liver and lung metastasis. No surgery.
- Chemotherapy FOLFIRI+ Hyperthermia to abdomen and lungs, HDVC and supplements including Biobran.
- August 2012: no metastasis in the liver and lungs. Operated to remove the pancreatic tumor: no tumor cells found.
- **2013**: died of multiple bone metastasis.

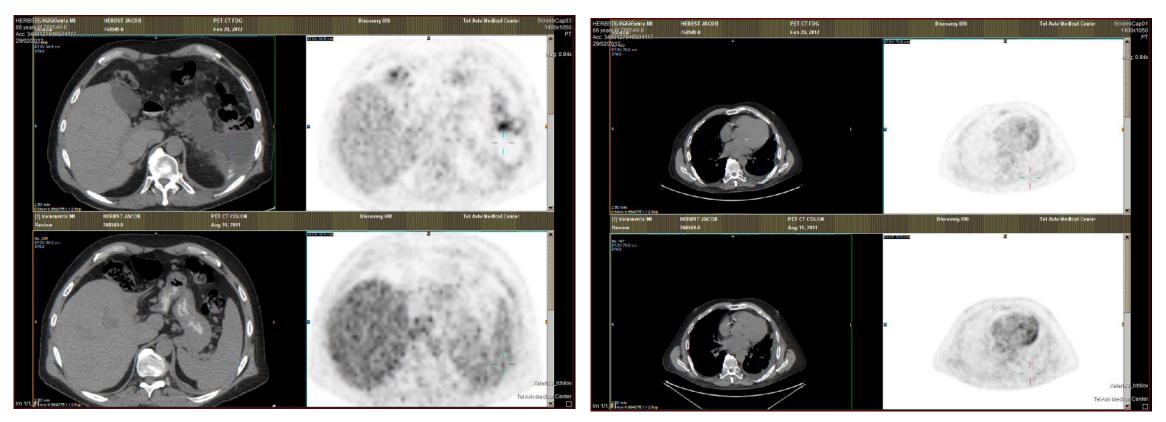
January 2010



August 2012

ABDOMEN

LUNGS





Ca Rectum with hugh recurrent pelvic mass

Tumor response to hyperthermia alone

3 Dec 2008

23 June 2009



Locally advanced breast cancer (refused surgery) treated with EHY-3000 to the whole chest and superficial hyperthermia

Before treatments



After treatments



RT+Hyperthermia



K.L

- 44 Y.O born in Russia, american citizen, living in Singapore.
- 2010 Ca Rt. Breast, S/P mastectomy + ALND.
- 14 June 2013 presented in my clinic with stage IV recurrent metastatic breast cancer.
- PET 3.6.13: Metastasis to the chest wall as well to internal mammary, supra and infra-clavicular and sub-capsular lymph nodes.
- She was treated for 3 months with hormonal therapy (Tamoxifen) combined with Hyperthermia (superficial and deep), Galvanotherapy, IV vitamins infusions and oral supplements.
- With the above treatments a complete remission was achieved detected by complete disappearance of the skin metastasis, return of tumor markers to the normal range and a complete normal PET-CT.

• Currently N.E.D

Sylvia-miracle response of terminal rectal cancer

- Rectal cancer, recurrent huge pelvic mass
- Failed chemotherapy
- Terminal state
- Hyperthermia only
- 75% reduction of pelvic mass
- Walking, eating, weight gain
- Died due to radiation therapy treatment



Ca Rectum with hugh recurrent pelvic mass

Tumor response to hyperthermia alone

3 Dec 2008

23 June 2009



COMBIENED EFFECT OF BIOBRAN AND HYPERTHERMIA

- Membrane-bound Hsp70 provides a tumor-specific target structure for lytic natural killer (NK) cells of the innate immune system.
- BioBran increase NK cells cytotoxicity.
- Cancer cells develop HSP after the hyperthermia treatment to protect themselves from another heat shock.
- The HSP appears on the cancer cell membrane for a period of 48 hours.
- During this period, NK cells activated by BioBran are able to destroy these cancer cells.

Common effects of hyperthermia and BioBran

- BioBran appears to stimulate the production of inflammatory cytokines IFN-gamma, TNF-alpha² and IL-6.
 Hyperthermia increases the production of TNF-alpha and IL-6.
- Biobran has antioxidant properties. Hyperthermia enhances antioxidants activity.
- Both Hyperthermia and BioBran increase the production of apoptosis of cancer cells.

BIOBRAN AND CURCUMIN

- Synergistic apoptotic effect of arabinoxylan rice bran (MGN-3/Biobran) and curcumin (turmeric) on human multiple myeloma cell line U266 in vitro.
 Department of Otalaryngology, Charles Drew University of Medicine and Science, Los Angeles, CA 90059, USA Neoplasma. 2011;58(2):118-23
- MGN-3 and curcumin synergize in the induction of U266 cell apoptosis

BIOBRAN AND TAXOL

- Modified arabinoxylan from rice bran, MGN-3/biobran, sensitizes metastatic breast cancer cells to paclitaxel in vitro.
- <u>Ghoneum M¹</u>, <u>Badr El-Din NK</u>, <u>Ali DA</u>, <u>El-Dein MA</u>.
- Anticancer Res. 2014 Jan;34(1):81-7.
- MGN-3 increased the susceptibility of both types of cancer cells to paclitaxel by over 100-fold.
- Mechanistically, MGN-3 works synergistically with paclitaxel by causing DNA damage, enhancing apoptosis, and inhibiting cell proliferation in 4T1 cells.

BIOBRAN AND DOUNORUBICIN

- MGN-3/Biobran, modified arabinoxylan from rice bran, sensitizes human breast cancer cells to chemotherapeutic agent, daunorubicin.
- <u>Gollapudi S¹</u>, <u>Ghoneum M</u>.
- <u>Cancer Detect Prev.</u> 2008;32(1):1-6
- Treatment with MGN-3 increased susceptibility of BCCs to DNR (5.5fold for MCF-7 and 2.5-fold for HCC70 cells) as compared to BCCs treated with DNR alone. The sensitizing effect of MGN-3 was associated with increased accumulation of DNR in cancer cells.

Reducing side effects of chemotherapy in breast cancer patients

- The Profesional Medical Journal Jan-Feb 2013;20(1): 013-016. Department, Nishtar Hospital Multan.
- Group A: Chemo+BioBran Group B: Chemo alone
- There was a significant reduction in: Tiredness Anorexia Hair loss Nausea and vomiting
- Weigh loss
- **Conclusions:** The study showed that, by helping to optimize the immune system, Biobran MGN-3 can not only help maximize treatment success, but also minimize treatment side effects and improve quality of life during treatment and in recovery.

Combining BioBran with chemotherapy reduce side effects and increase survival

- Bran Arabinoxylan Derivative (MGN-3, BioBran) for Progressive Cancer" Clinical Pharmacology and Therapy, 2004
- Randomized study comparing chemotherapy without BioBran to chemotherapy combined with bioBran.
- At the end of the study there was a 50% higher survival rate of the BioBran group compare to chemo alone group and better QOL mainly by improving appetite.

BIOBRAN AND RT

- Lab tests suggest that BioBran MGN-3 arabinoxylan complex could help to protect against some of the side-effects of radiotherapy.
- Mice given MGN-3 prior to radiotherapy were protected from damage to their blood cell counts and did not suffer from a reduction in cells in their bone marrow.
- MGN-3 was also associated with protection against weight loss and fatigue.

Arabinoxylan rice bran (MGN-3) enhances the effects of interventional therapies for the treatment of hepatocellular carcinoma: a three-year randomized clinical trial.

- Department of Hepatogastroenterology, The 108 Military Central Hospital, Hanoi, Vietnam. <u>Anticancer Res.</u> 2010 Dec; 30(12):5145-51.
- Patients in the IT (Interventional Therapy=transarterial oily chemoembolization (TOCE) or a combination of TOCE and percutaneous ethanol injection treatment (PEIT). IT +MGN-3 group showed:

Lower recurrence of the disease, 31.6% (12/38), as compared to 46.7% (14/30) for the control;

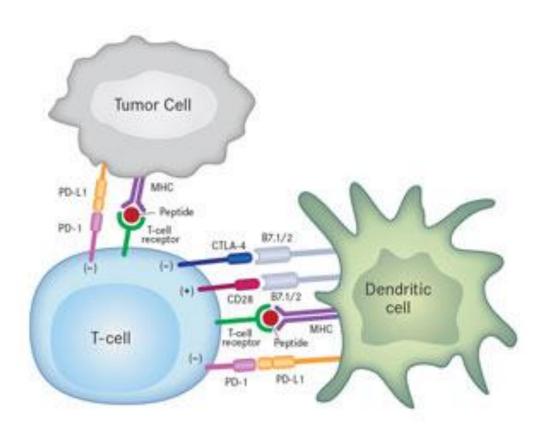
Higher survival after the second year, 35%, as compared to 6.7% for the control;

Significantly lower alpha-fetoprotein level, a 38% decrease (p = 0.0001), as compared to baseline value, while the control showed no significant change;

A significant decrease in tumor volume, in contrast to the control, which showed no significant change

BioBran and Checkpoints Inhibitors

- Checkpoints inhibitors are the most exciting new drugs in the field of cancer.
- After 50 years of standstill, there are new drugs that produce impressive tumor regressions that last sometimes long periods.
- Now oncologists admit that treatment progress until now was limited if any.
- Pembrolisumab (Kytroda) and Nivolumab (Optivo) are the major new drugs available in the market.
- Impressive effects were demonstrated in Melanoma, Lung Cancer, Bladder Cancer, Renal Carcinoma, Hodgkin's Lymphoma.



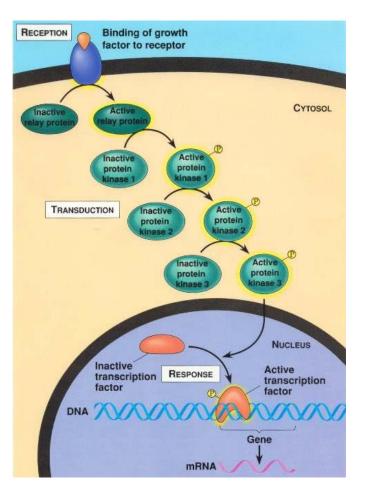
Checkpoints blockade

- Cancer cells present on cell surface antigens (MHC) that when legate to T-cell receptors are recognized as foreign antigens and provoke the immune system to react and destroy these cells.
- Many tumor cells contains on their cell membrane protein named PD-L1 which combine with a PD-1 receptor on the Tcell. This will downregulate the activated T-cells against foreign tumor cells.
- The inhibition of the PD-L1 ligation to the PD-1 receptors will discover the tumor cell as a foreign cell and activate the T-cells against it.

BioBran and checkpoins inhibitors

- As the treatments of cancers with checkpoints inhibitors is available only in the last few years, no studies of BioBran with the conjunction with these drugs are available.
- But, as the checkpoints inhibitors expose the cancer cell to the immune system, the ability of the immune cells to confront the tumor cells is very important.
- BioBran has the ability to improve the function of the immune system cells therefor using checkpoints inhibitors together with BioBran has the potential to be a very effective combination against cancer.

BioBran and Biologic Drugs



 Signal transduction is the way by which growth factors from outside to the cells legate to special receptors on the cell surface and by this, they create a signal that it is transferred through the cytoplasm by several molecule reaching finally the cell nucleus to influence the DNA to uncontrolled replication creating by this a tumor cell.

BioBran and biologic drugs

- Some of these drugs are apoptosis inducers, therefor are synergistic with BioBran.
- In other drugs BioBran may help reducing side effects and toxicity



- Glivec
- Afinitor

In conclusion

- BioBran has its own activity against cancer.
- Combining BioBran with other anticancer methos: Increased activity Reduced Toxicity