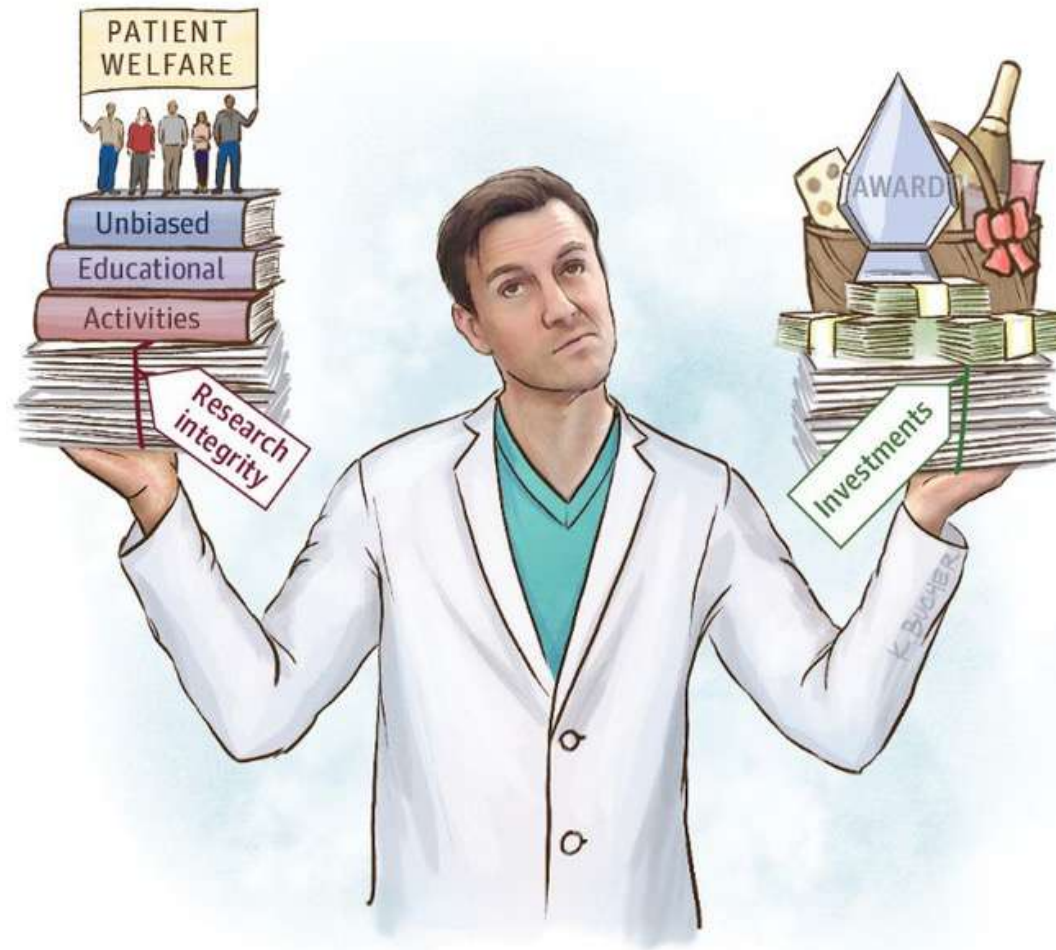


CANCER CARE

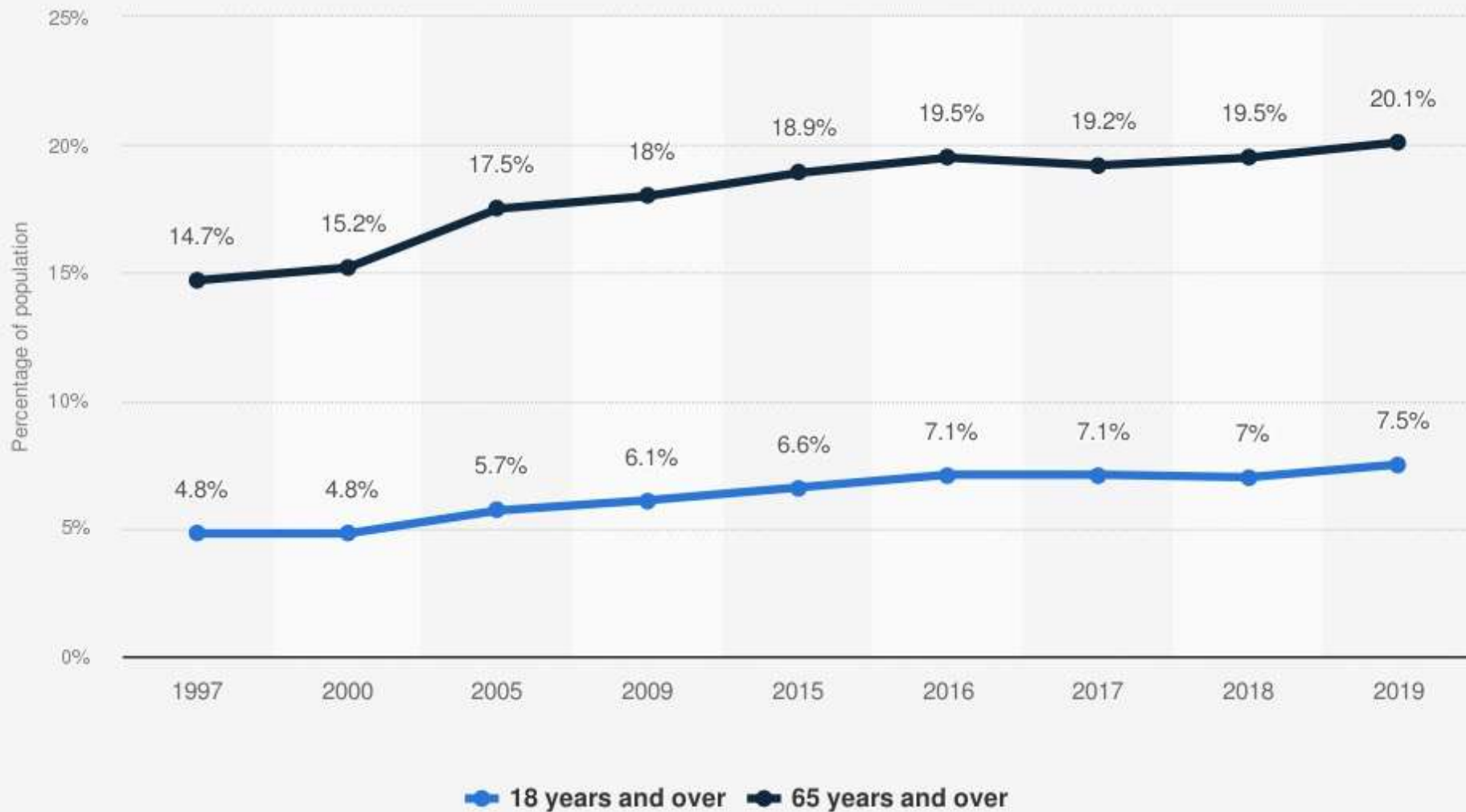
THE ROLE OF REPURPOSED DRUGS
AND METABOLIC INTERVENTIONS
IN TREATING CANCER

Paul E. Marik, MD, FCCM, FCCP

Conflicts of Interest



Percentage of U.S. population who has (or ever had) cancer between 1997 and 2019, by age



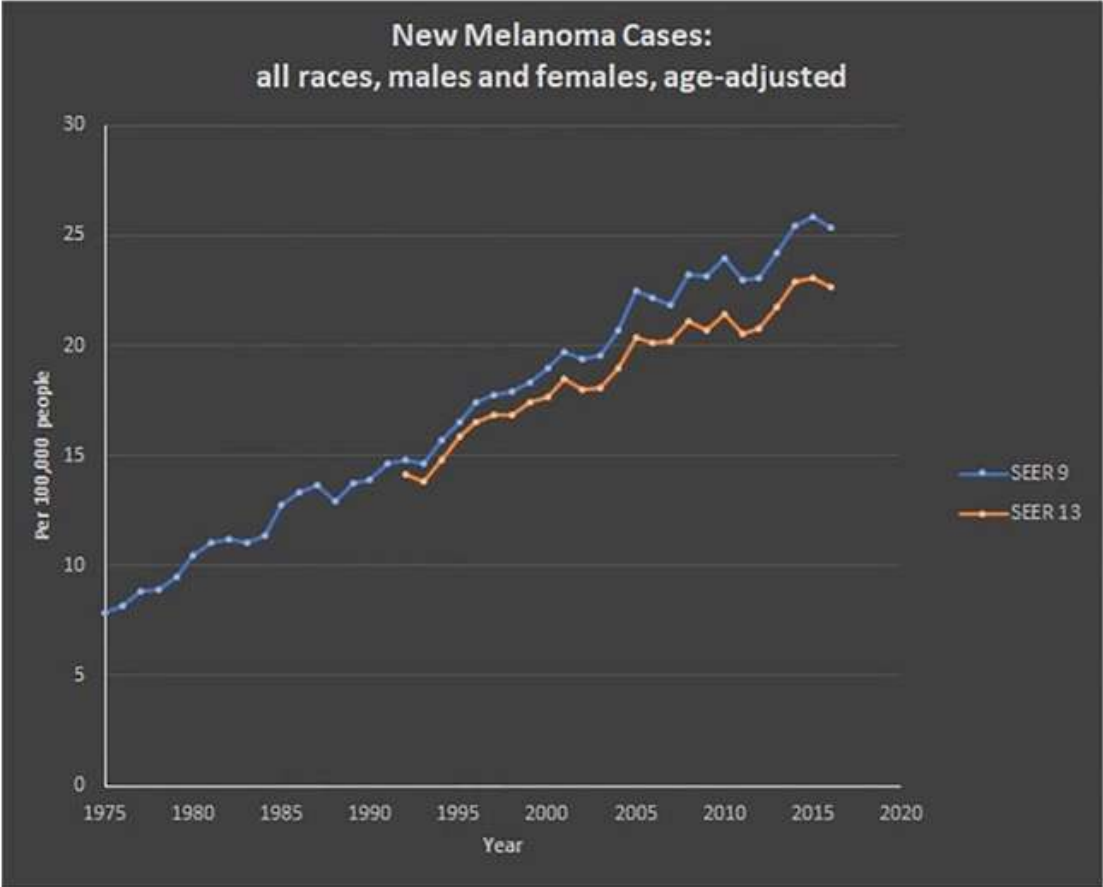
Types of Cancer (MALES)	# of cases	% of cases	Types of Cancer (FEMALES)	# of cases	% of cases
Lung & bronchus	61,170	21	Lung & bronchus	59,910	21
Prostate	34,700	11	Breast	43,170	15
Colon & rectum	28,470	9	Colon & rectum	24,080	8
Pancreas	26,620	8	Pancreas	23,930	8
Liver	19,000	6	Ovary	13,270	5
Leukemia	13,900	4	Uterus	13,030	5
ALL SITES	322,080		ALL SITES	287,740	

Table 1: Leading sites of cancer deaths - 2023 estimates (Source: American Cancer Society)

Change in Risk of Skin Cancer Over Time

Table 1
 Estimated number of new cases of nonmelanoma skin carcinoma in the United States from 1983 to 2012 (Miller and Weinstock, 1994; Rogers et al., 2010, 2015; Scotto et al., 1983).

Year	New cases of nonmelanoma skin carcinoma
1983	400,000–500,000
1992	900,000–1, 200,000
2006	3,500,000
2012	5,300,000



DISCLAIMER

- A review of the published literature.
- Options for repurposed drugs that can be used in cancer treatment.
- Not intended as a stand-alone guide to treating cancer.
- This review should not be taken as a basis to initiate treatment without guidance or avoid any treatment prescribed by your treating physician.
- The treatment interventions outlined should be used as ***adjunctive therapy*** in addition to the treatment provided by an oncologist.
- Please note that the Cancer Care review is a “living” document -- continuously updated and refined.

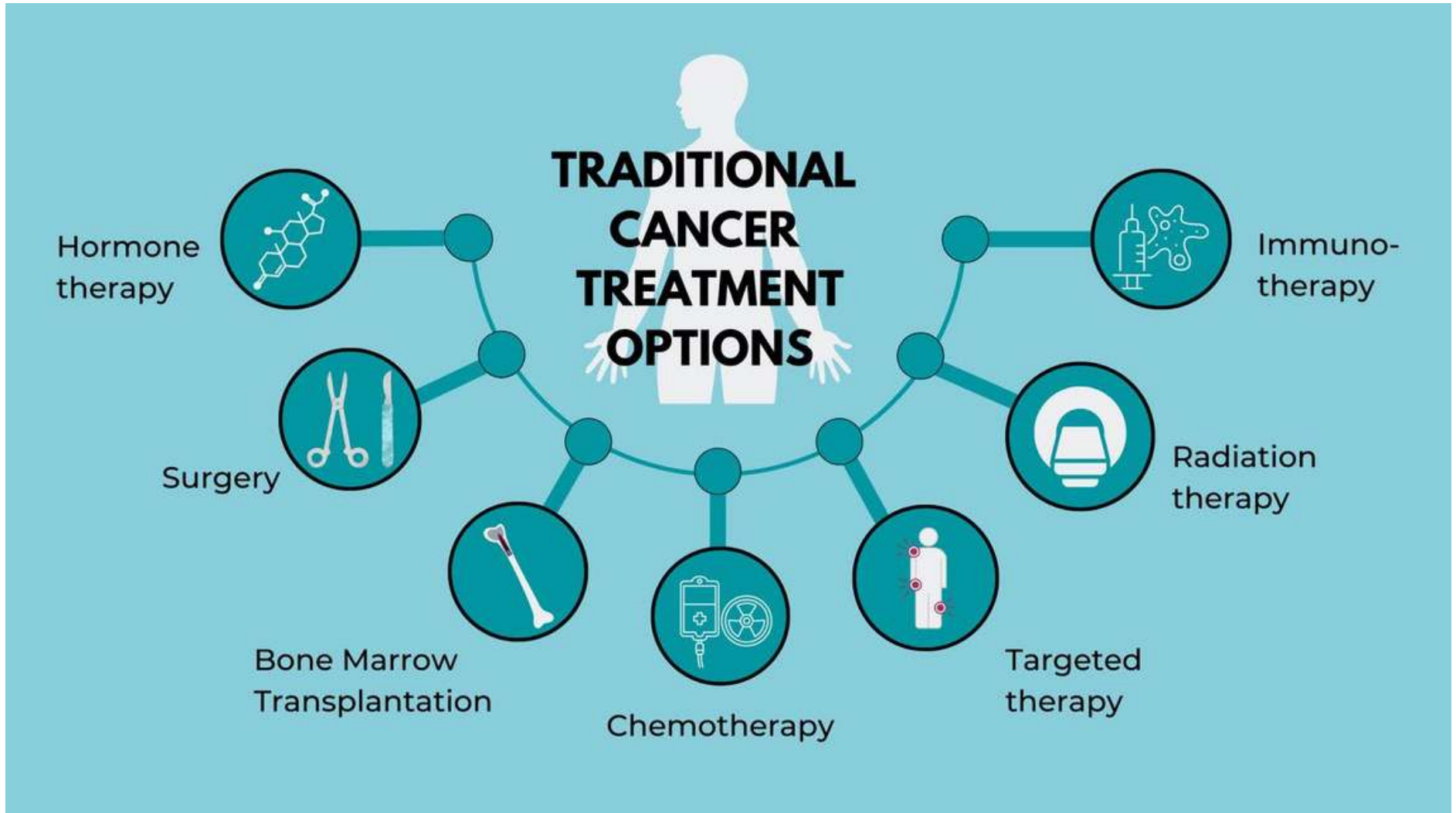


Figure 2: "Modern" cancer treatments are expensive and have limited benefit (Source: FLCCC)

Conventional Chemotherapy & Radiotherapy

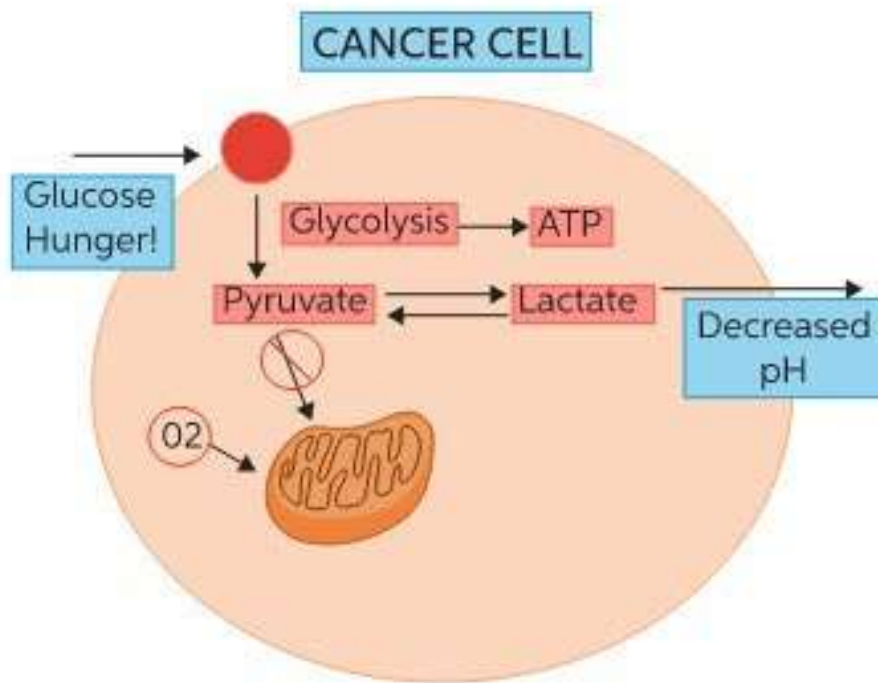
- Only target rapidly dividing cells
- Cancer Stem Cells allowed to proliferate
- Increases inflammation in TME
- Increases angiogenesis
- Increases metastatic potential
- Highly TOXIC
- Highly COSTLY

Conventional Theory of Cancer

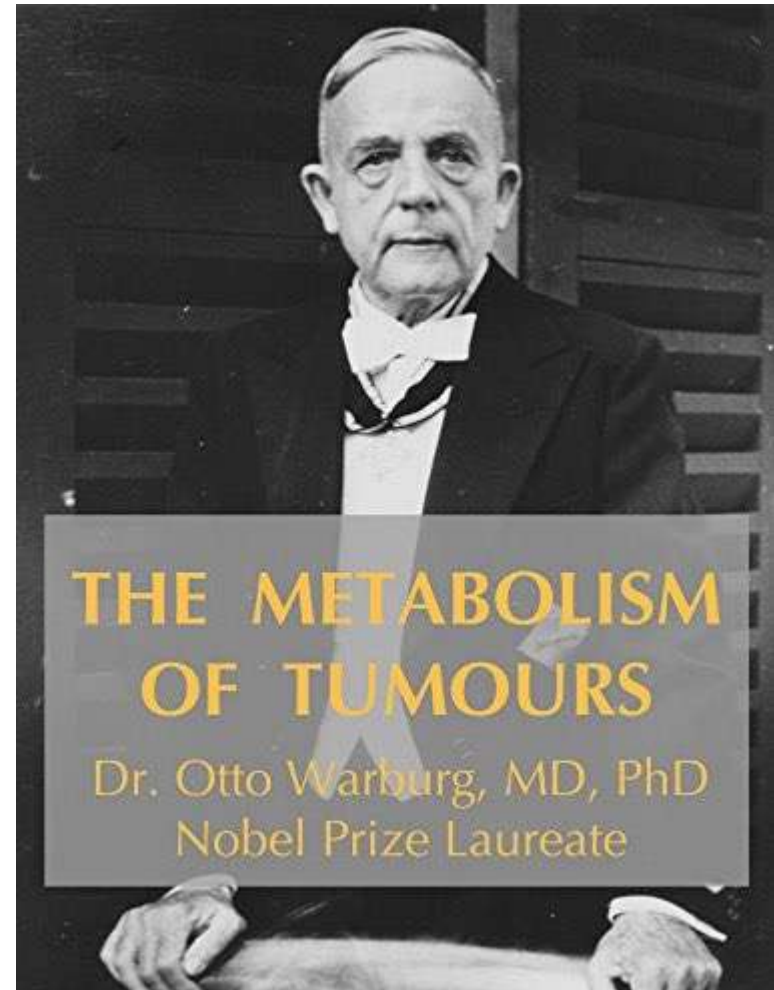
The conventional theory is that cancer is caused by genetic mutations/genomic instability, which drives a population of cells with the following six “classic” biological properties

1. Sustaining proliferative signaling
2. Evading growth suppressors
3. Resisting cell death (apoptosis)
4. Enabling replicative immortality
5. Inducing angiogenesis
6. Activating invasion and metastasis

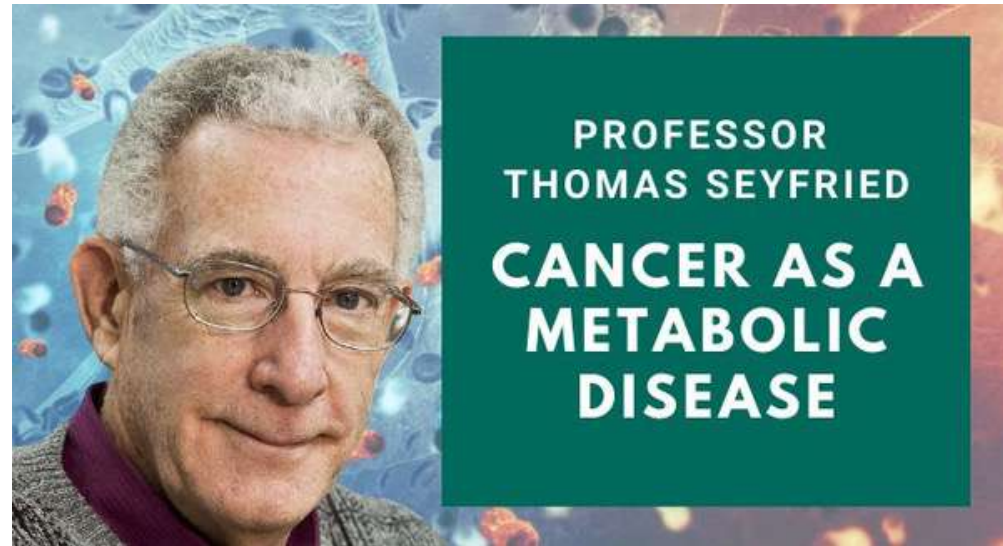
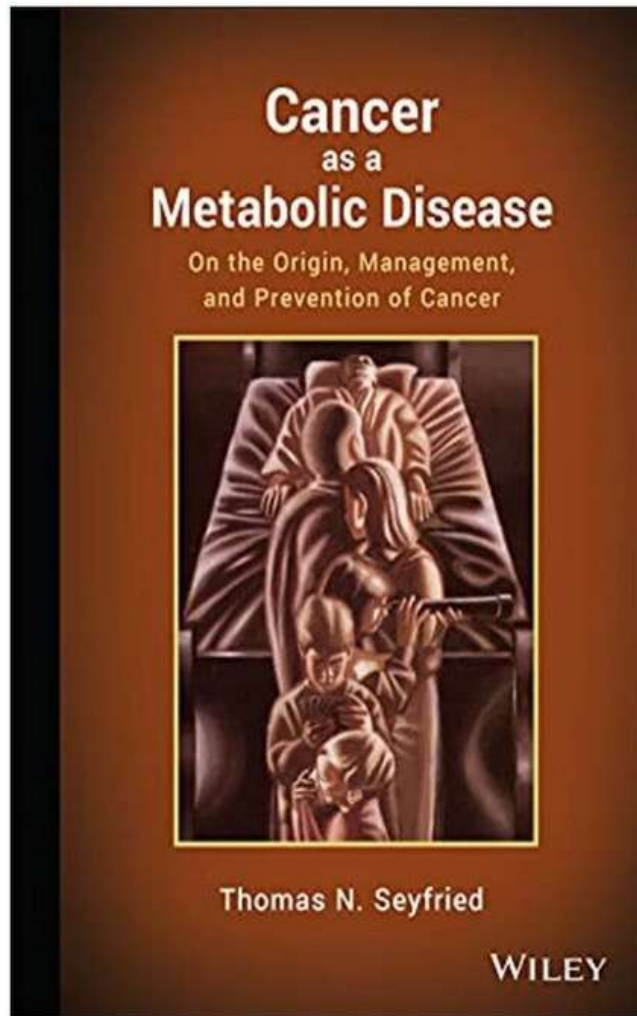
The Warburg Effect



Anaerobic Glycolysis
Defective Mitochondria



Origins of Cancer



Cancer is a METABOLIC Disease not a Genetic Disease

“No researcher can point to any single mutation or combination of mutations and say with confidence that it is alone the cause of cancer. Nor can researchers point to a series of cellular systems rendered dysfunctional by mutations and make the same claims with confidence.”

- Travis Christofferson (Tripping Over The Truth)

“We may have to turn our main research focus away from decoding the genetic instructions behind cancer and toward understanding the metabolism within cancer cells.”

- James Watson, Father of DNA

The Tumor Microenvironment

- Myeloid derived stem cells (MDSC)
- T-regulatory cells (Tregs)
- Tumor associated macrophages
- Platelets
- Natural Killer Cells (NK cells)
- Cytotoxic T cells

The Tumor Microenvironment

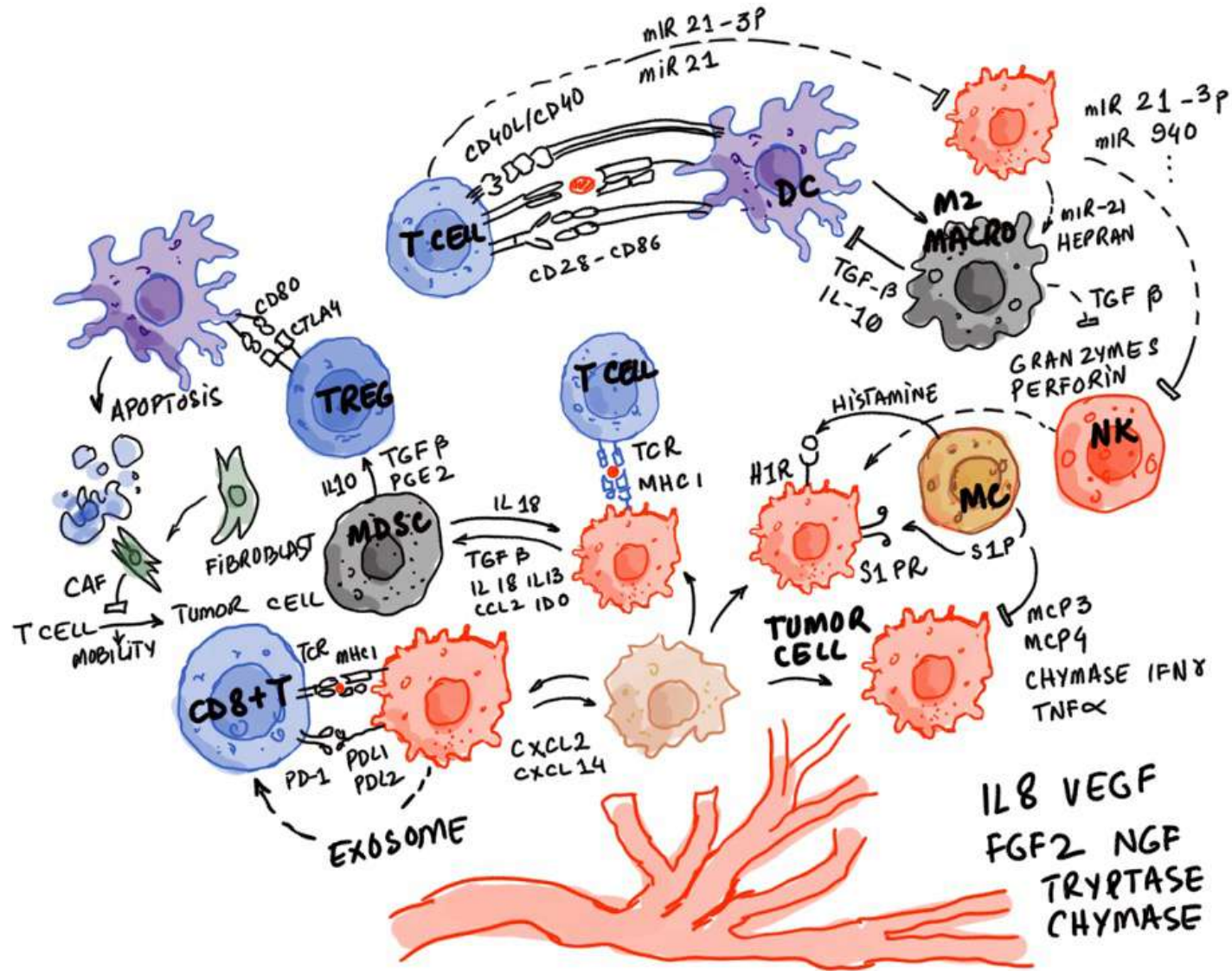


Illustration courtesy of Dr. Mobeen Syed

Cancer Stem Cells

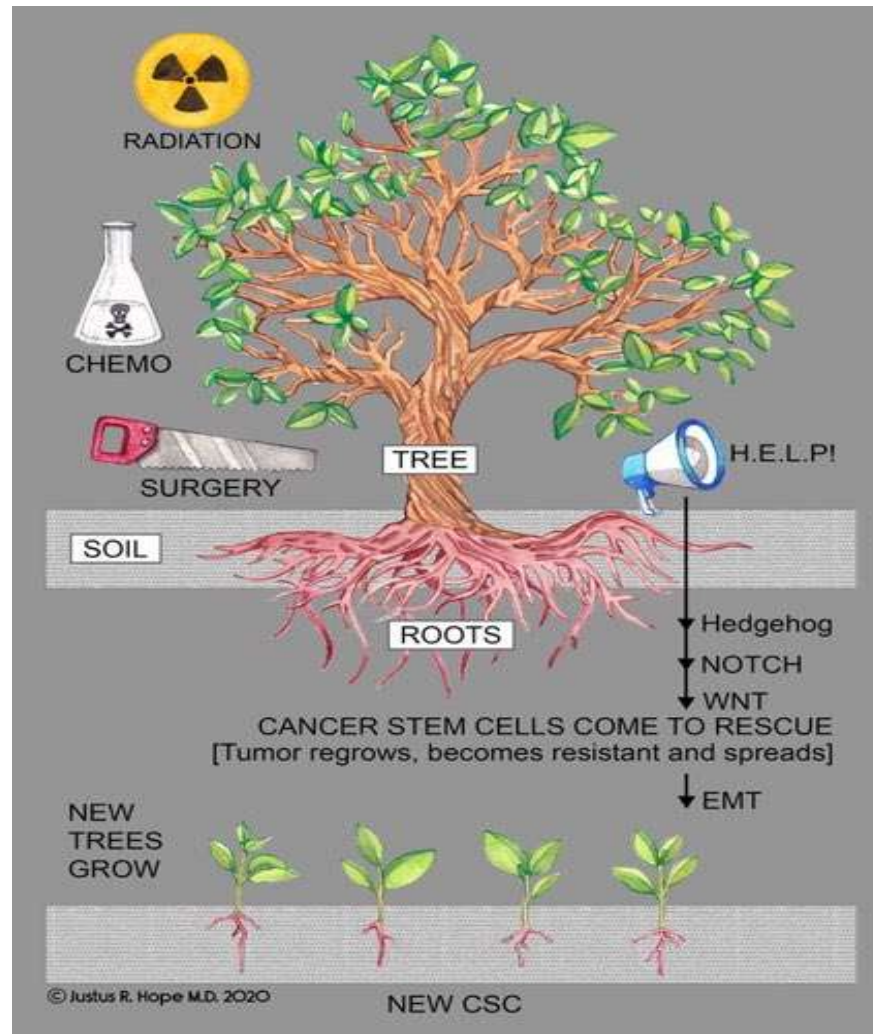
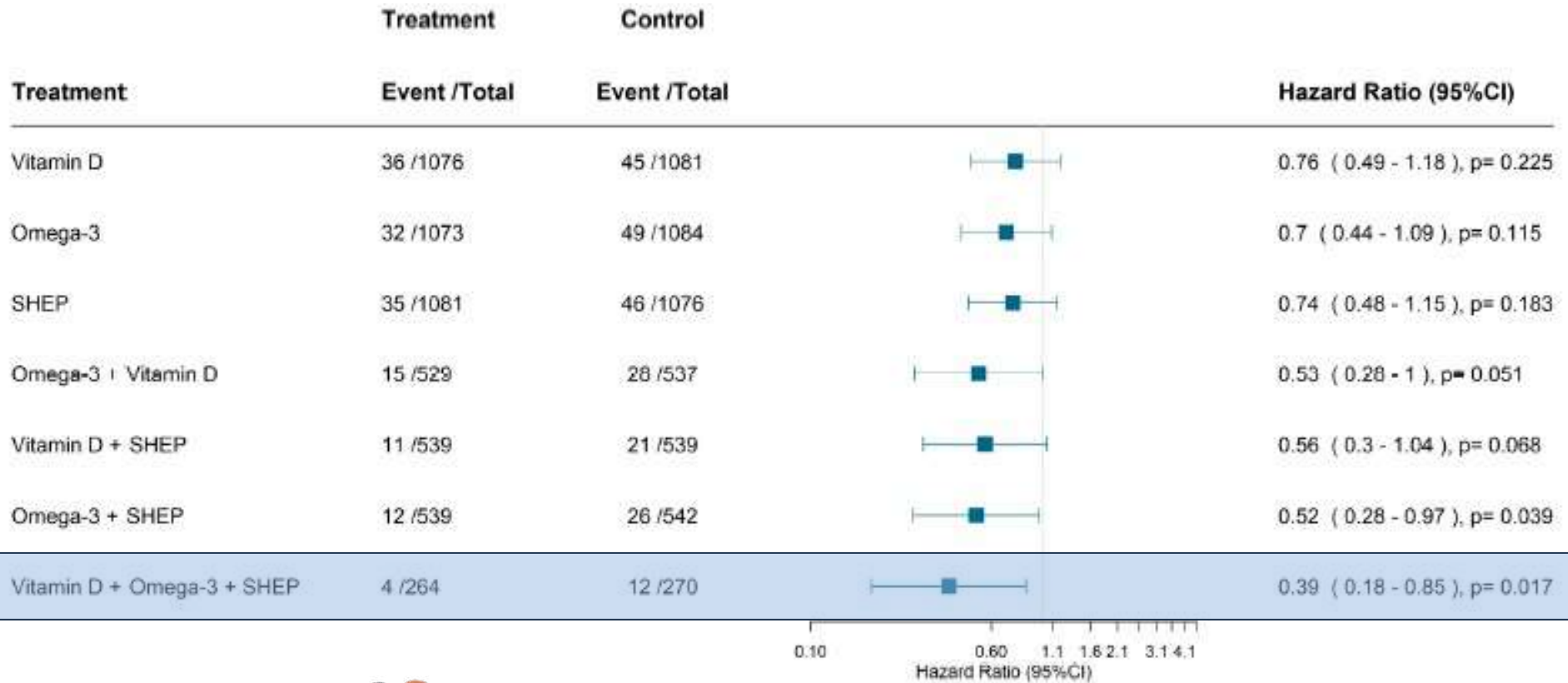


Figure: Cancer stem cells are the root of cancer (Source: Dr. Justus Hope)

60-80% of Cancers are Preventable

- Tackle insulin resistance (40% of all cancers)
- Quit smoking
- Limit alcohol
- Get enough Vitamin D
- Avoid processed foods
- Avoid sugary drinks and pure fruit juice
- Get enough exercise (aerobic and resistance training)
- Stress reduction
- 8 hours quality sleep

Vitamin D, Omega-3 FA and Home Exercise to Prevent Cancer: An RCT



Bischoff-Ferrari et al. *Front Aging* 2022;3:852643



Vitamins and Nutrients

- Vitamin D3:
 - 5000 u/day and adjusted according to Vitamin D3 (25OH D3 > 60 mg/dl ~ 100mg/dl)
- Omega 3 fatty acids:
 - 2-4 g/day
- Green tea catechins:
 - 500-1000 mg/day
- Melatonin:
 - 0.75 – 5 mg (extended/slow release) at night
- Metformin:
 - 250 mg - 2000 mg daily

Hierarchy of evidence for the stratification of repurposed drugs/nutraceuticals

(reviewed > 1,200 peer reviewed papers)

- Meta analysis of observational and/or randomized controlled trials.
- RCTs and/or prospective observational studies.
- Epidemiological studies
- Case reports and case series
- *In Vivo/in Vitro* models
 - Killing cancer cells
 - Killing stem cells
 - Synergy with chemotherapeutic drugs
 - Improvement in tumor microenvironment

If the only tool you have is a hammer the world looks like a nail!



Metabolic Interventions to Control Cancer: TOP 10

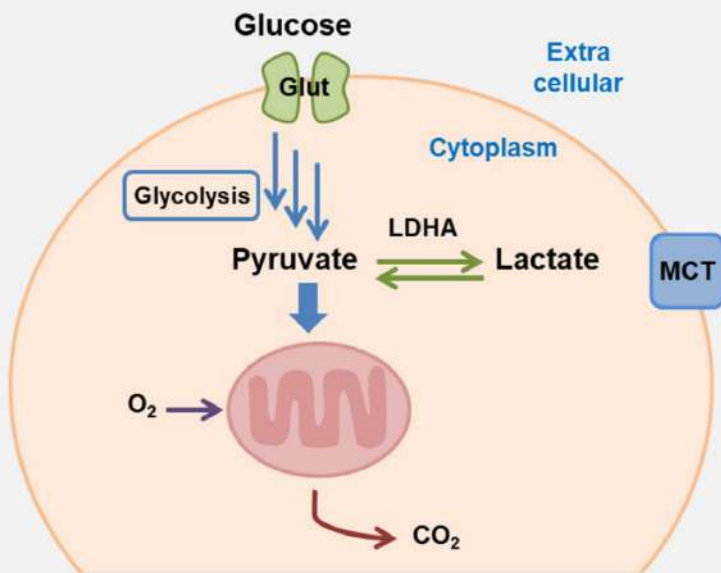
1. A low carbohydrate, high-fat diet, ketogenic diet + Time Restricted eating
2. Green tea catechins: 500-100 mg daily
3. Melatonin: start 1 mg and increase to 20-30 mg at night
 - (extended/low release)
4. Vitamin D3: 20 000 to 50 000 IU/day.
 - Dosage should be adjusted by blood vitamin D levels aiming for a 25-OH vitamin D level of ~ 100 ng/dl.
5. **Metformin: 1000 mg BID**
6. Curcumin: (nanocurcumin) 600 mg twice daily
7. **Mebendazole: 100 – 200 mg/day**
8. Omega- 3 FATTY ACIDS 4g/day
9. Berberine: 500 – 600 mg BID.
 - Metformin and berberine can be used together or alternating (for one month then switching) depending on the blood glucose levels.
10. Exercise; walking, high-intensity interval training, cycling etc.
 - Stress reduction

 *Over the Counter*

 *Requires a prescription*

Warburg Phenomenon

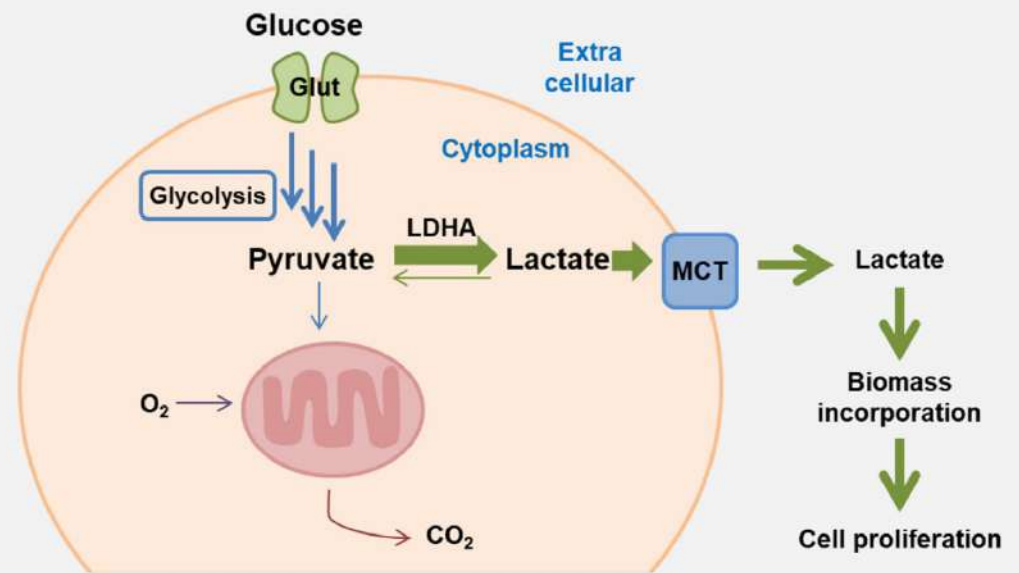
(A) Normal cell



Oxidative Phosphorylation
~38 mol ATPs/
mol glucose

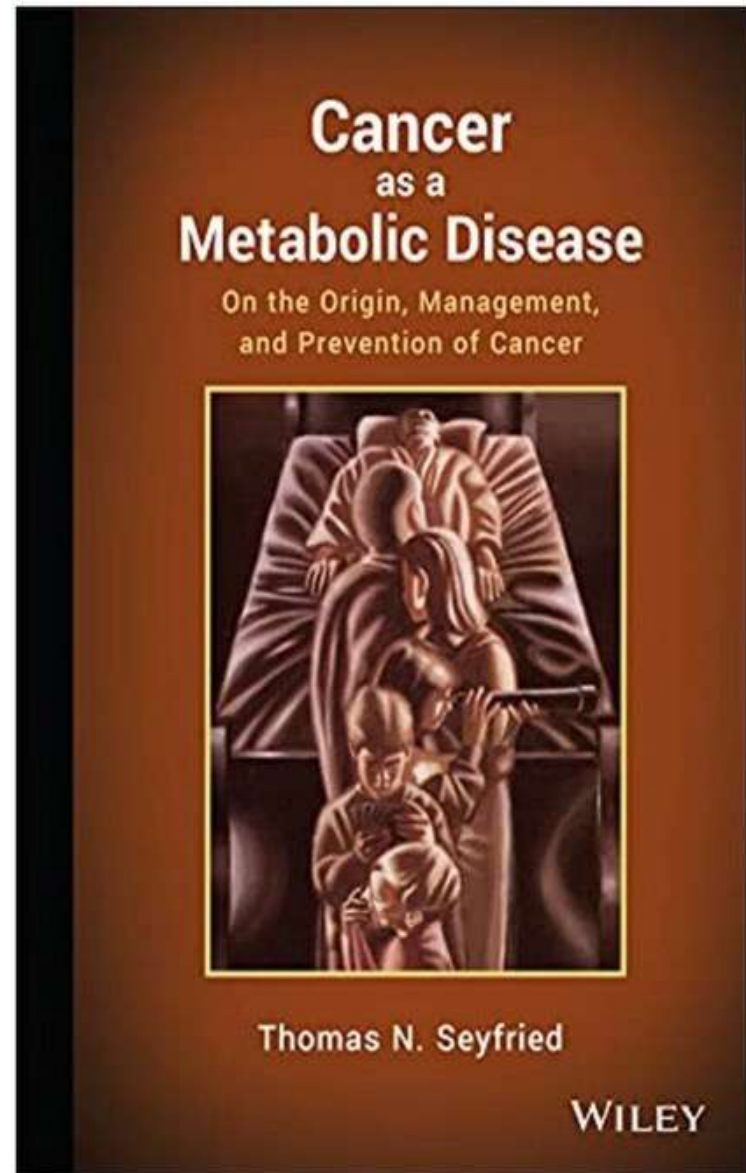
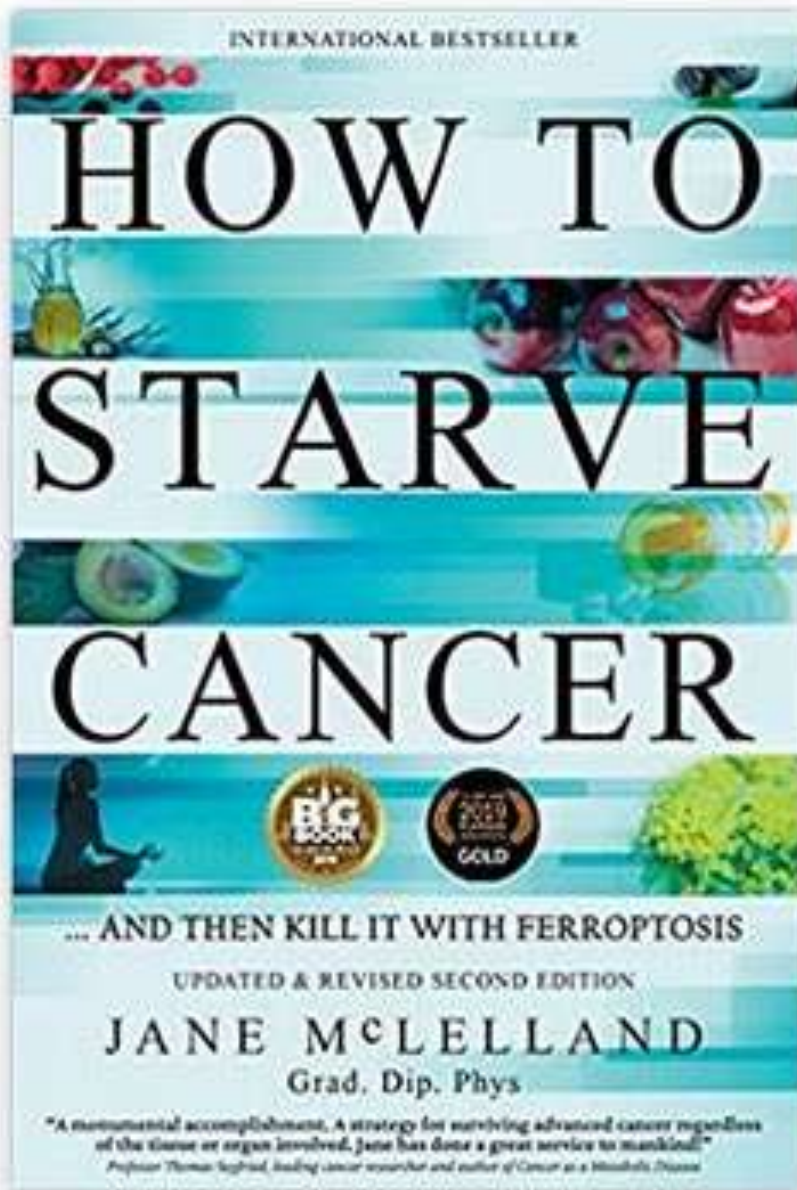
Anaerobic glycolysis
2 mol ATPs/
mol glucose

(B) Cancer cell

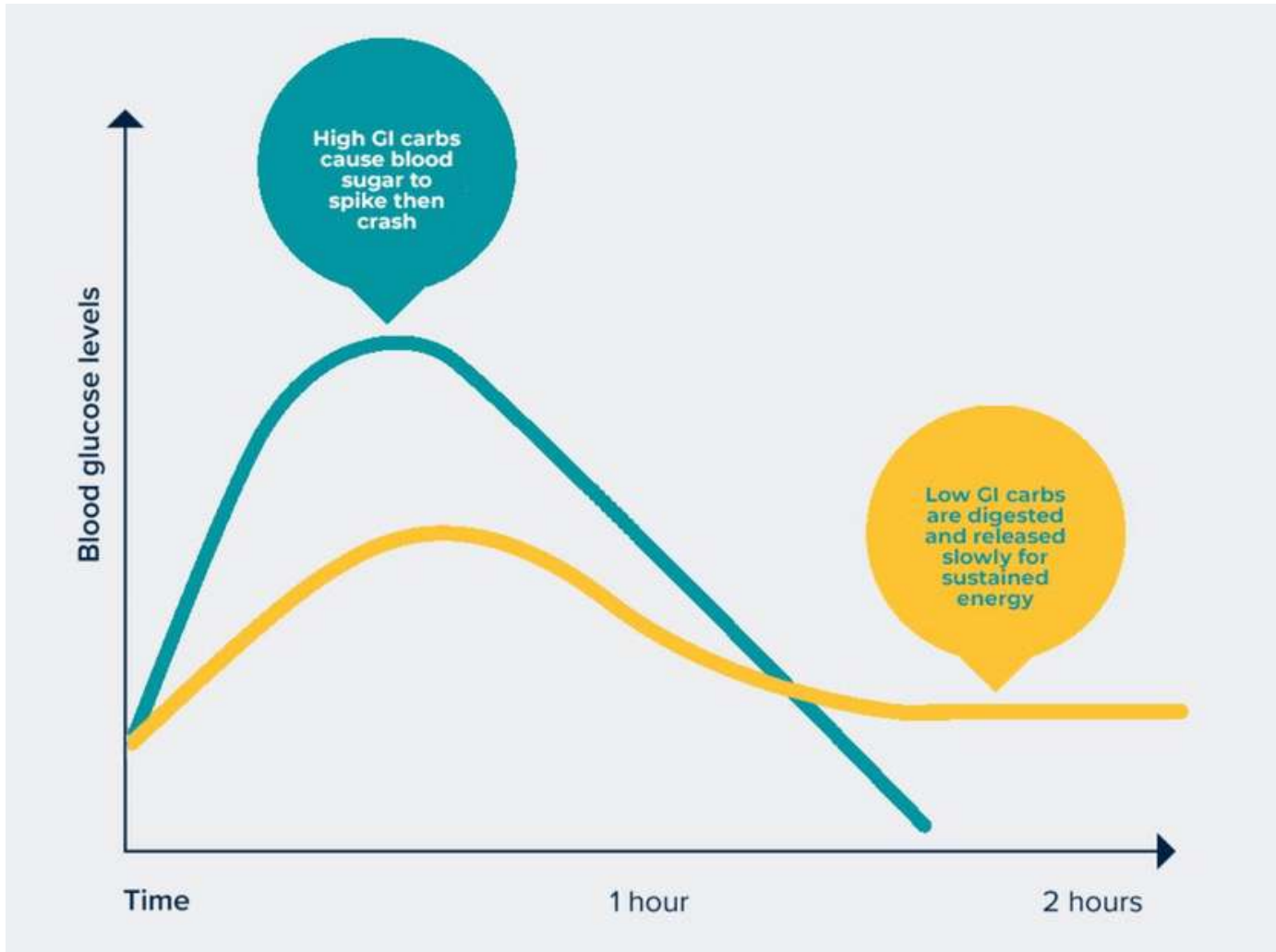


Anaerobic glycolysis
(Warburg effect)
2 mol ATPs/
mol glucose

Wikimedia license: https://commons.wikimedia.org/wiki/File:Differences_in_glycolysis_pathways_between_normal_cells_and_cancer_cells.webp



Glucose Management



The blood glucose profile of high and low glycemic index foods (Source: adapted from Glycemic Index Foundation)

Glucose Management

ARTICLE

Dietary Insulin Load and Cancer Recurrence and Survival in Patients With Stage III Colon Cancer: Findings From CALGB 89803 (Alliance)

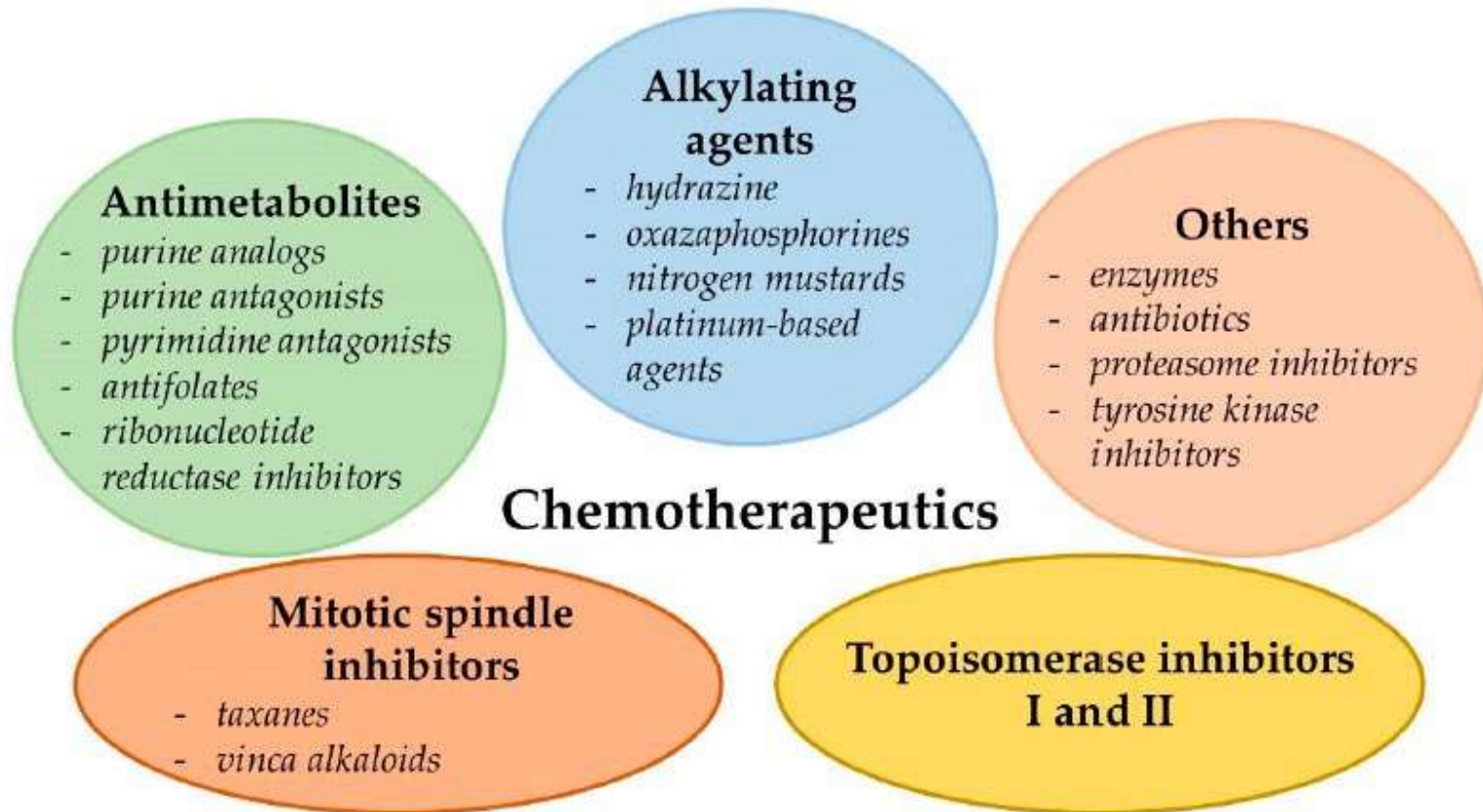
Conclusion:

Patients with resected stage III colon cancer who consumed a high-insulinogenic diet were at increased risk of recurrence and mortality



JNCI J Natl Cancer Inst (2019) 111(2): djy098

Chemotherapy



**Over 50 chemotherapeutic drugs
All target actively dividing cell**

Traditional “chemo” fails for solid tumors because:

- Solid tumors are composed of heterogeneous population of cells many of which are slowly growing.
- Most of the tumor cells are in the rest phase of the cell cycle.
- Chemotherapy does not improve the cancer microenvironment (which promotes cancer cell proliferation) and likely makes it worse.
- Chemotherapy enhances rather than kills cancer stem cells.
- Cancer cells become resistant to the chemotherapeutic agent.

Chemotherapy vs Repurposed Drugs

	Chemotherapy	Repurposed Drugs
Tumor Cell population	Actively dividing cells only (~ 10% of cells)	All malignant cells
Tumor selectivity	++	+++
Tumor Stem Cells	Enhances	Suppresses/kills
Effect on adaptive immunity	Suppressive	Enhances
Effect on Tumor Microenvironment	Negative effect	Improves/enhances
Myelotoxic	Yes	No
Severe systemic side effects	Yes	No
Tumor cell resistance develops	Yes	No
Cost	+++++	+

Chemotherapy “Curable” Cancer

Cancer Curable	Improves Survival	Palliation Only (metastatic)
Choriocarcinoma	Breast cancer	Colorectal, gallbladder
Acute lymphatic leukemia	Ovarian Cancer	Pancreatic, stomach
Chronic lymphatic leukemia	ALL in adults	Esophageal, liver
Acute promyelocytic leukemia	AML	Prostate, bladder, kidney
Testicular cancer	Thyroid Cancer	Endometrial and cervical
Ovarian germ cell tumor	Small cell lung cancer	NSCLC (lung cancer)
Hodgkin's lymphoma	Multiple myeloma	Brain, adrenal, melanoma
High Grade non-Hodgkin's lymphoma	Osteosarcoma	Adenocarcinoma primary unknown
Rare childhood malignancies	Wilms tumor	H&N cancer

Role of Chemotherapy and Repurposed Drugs

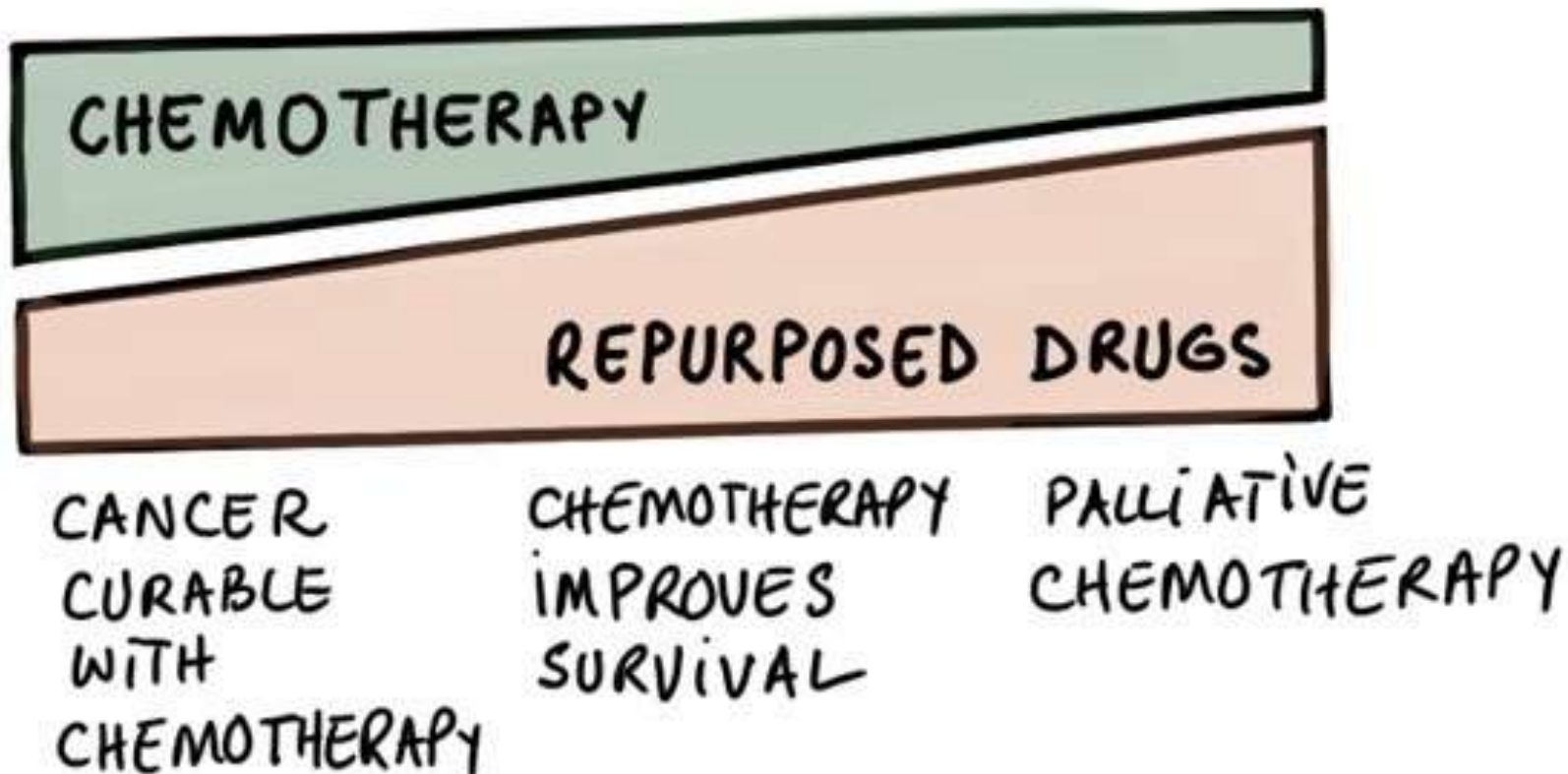


Illustration courtesy of Dr. Mobeen Syed

Surgically “Curable” Disease. Five-year survival for local disease* with surgical removal

Cancer	5-year Survival (%)
Breast	99
Prostate	99
Thyroid	99
Melanoma of skin	99
Endometrial cancer	95
Kidney cancer	93
Ovarian cancer	92
Uterine Cervix	93
Colorectal	91

* Local disease; An invasive malignant cancer confined entirely to the organ of origin

Personalized Management of Cancer

Repurposed Drugs & Metabolic Rx

Chemotherapy

Surgery

Stress Management & sleep

Review the **CANCER CARE** monograph

- Go to FLCCC.net
- Select “Medical Evidence” on main menu
- Under “Reviews & Monographs”

flccc.net/cancer-care

Thank you

