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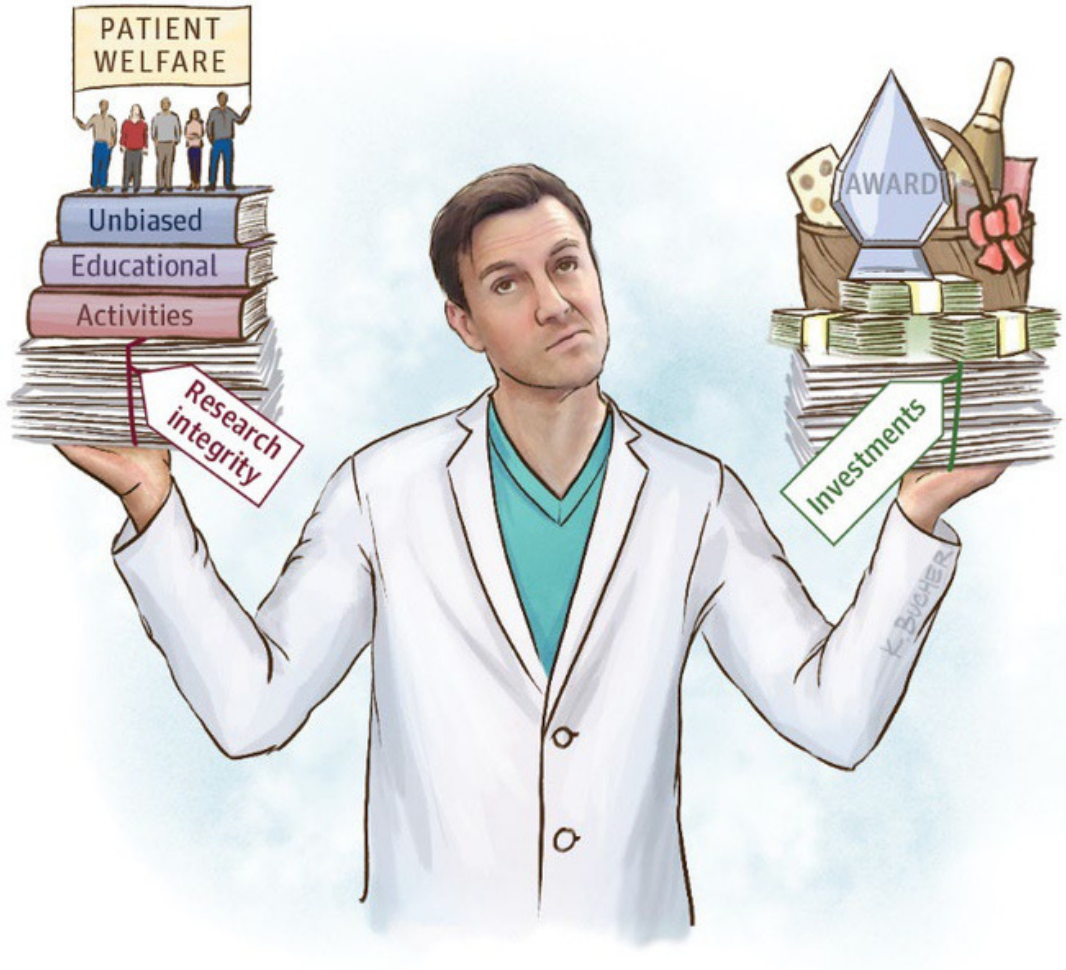
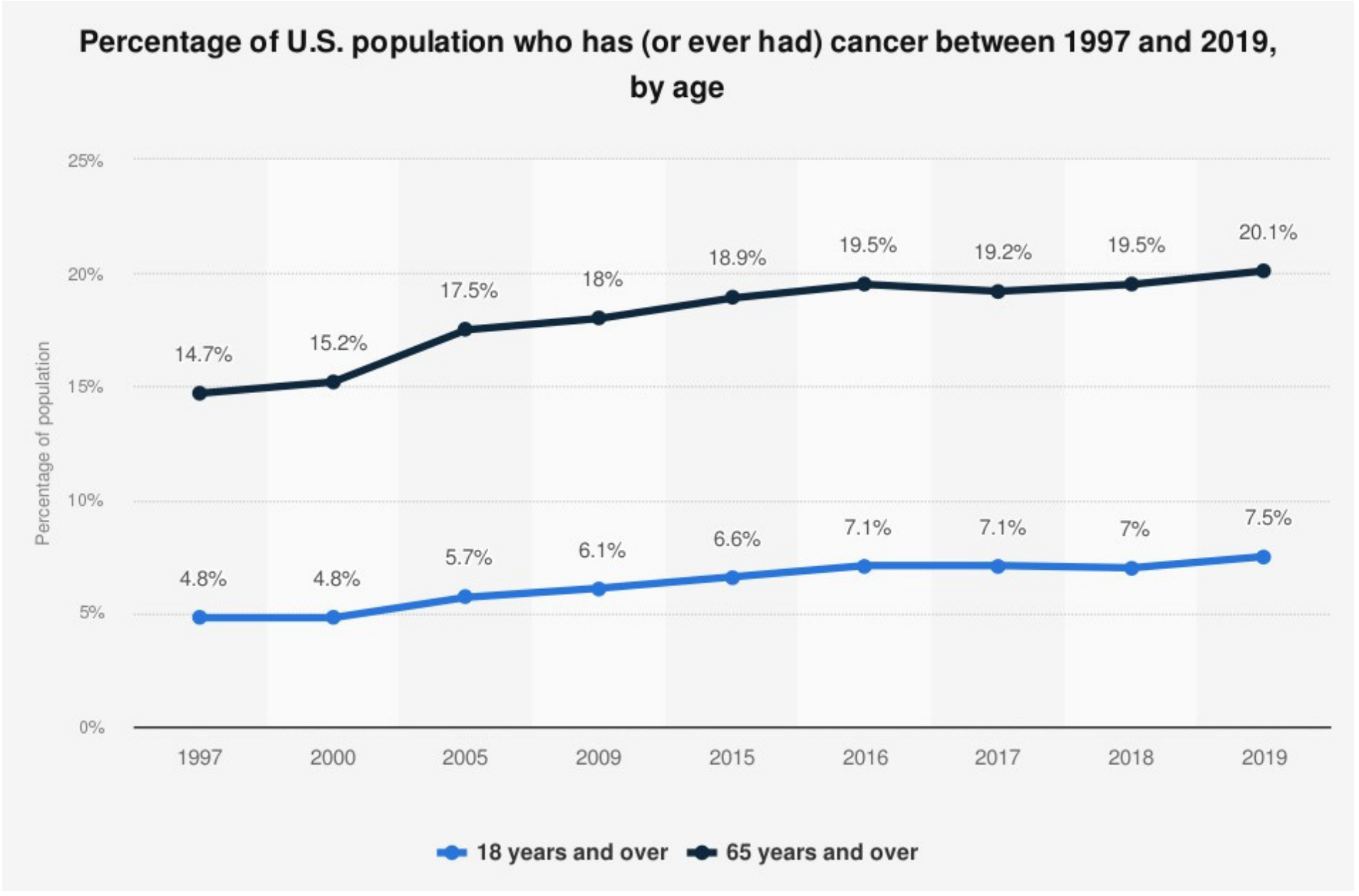
CANCER CARE

THE ROLE OF REPURPOSED DRUGS AND METABOLIC INTERVENTIONS IN TREATING CANCER

Paul E. Marik, MD, FCCM, FCCP

No Conflicts of Interest




Percentage of U.S. population who has (or ever had) cancer between 1997 and 2019, by age
Percentage of population
25%
20%
15%
10%
5%
0%
14.7%
15.2%
17.5%
18%
18.9%
19.5%
19.2%
19.5%
20.1%
4.8%
4.8%
5.7%
6.1%
6.6%
7.1%
7.1%
7%
7.5%
1997
2000
2005
2009
2015
2016
2017
2018
2019
18 years and over
65 years and over

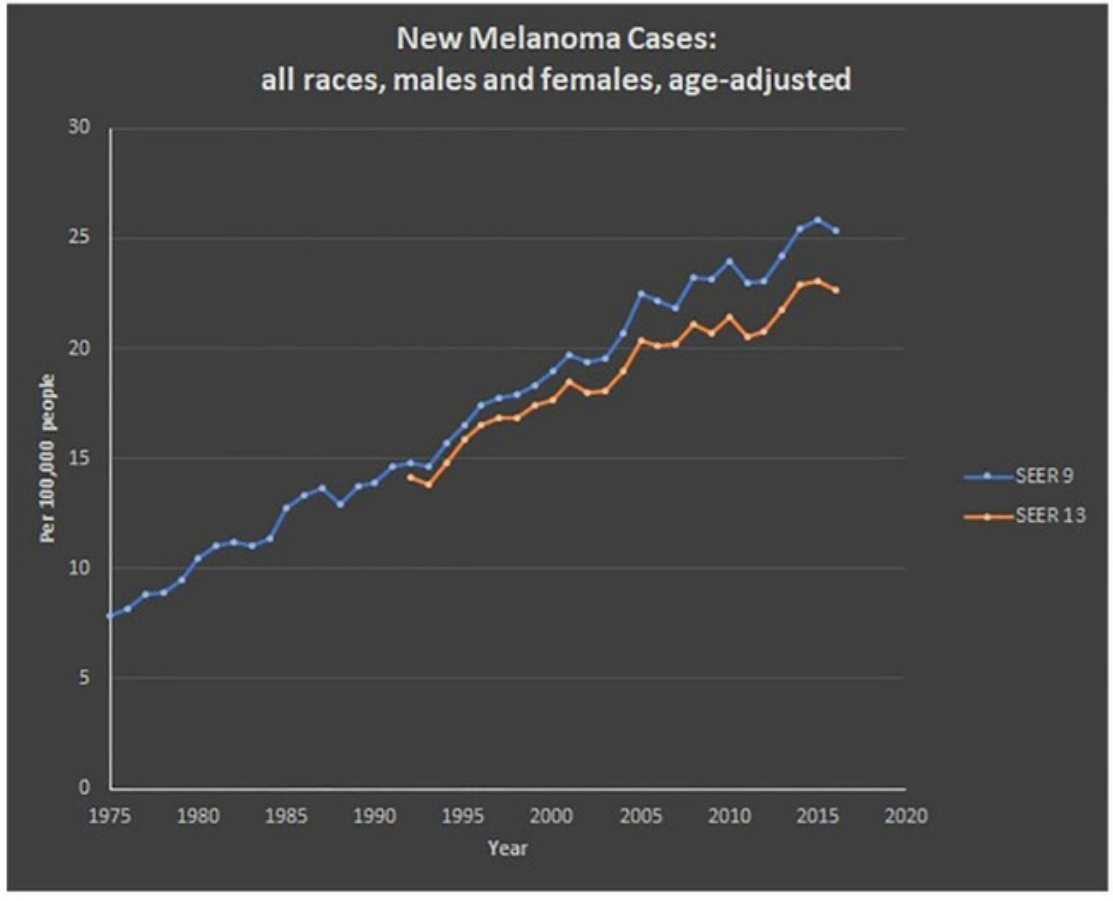
Types of Cancer (MALES)	# of cases	% of cases	Types of Cancer (FEMALES)	# of cases	% of cases
Lung & bronchus	61,170	21	Lung & bronchus	59,910	21
Prostate	34,700	11	Breast	43,170	15
Colon & rectum	28,470	9	Colon & rectum	24,080	8
Pancreas	26,620	8	Pancreas	23,930	8
Liver	19,000	6	Ovary	13,270	5
Leukemia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

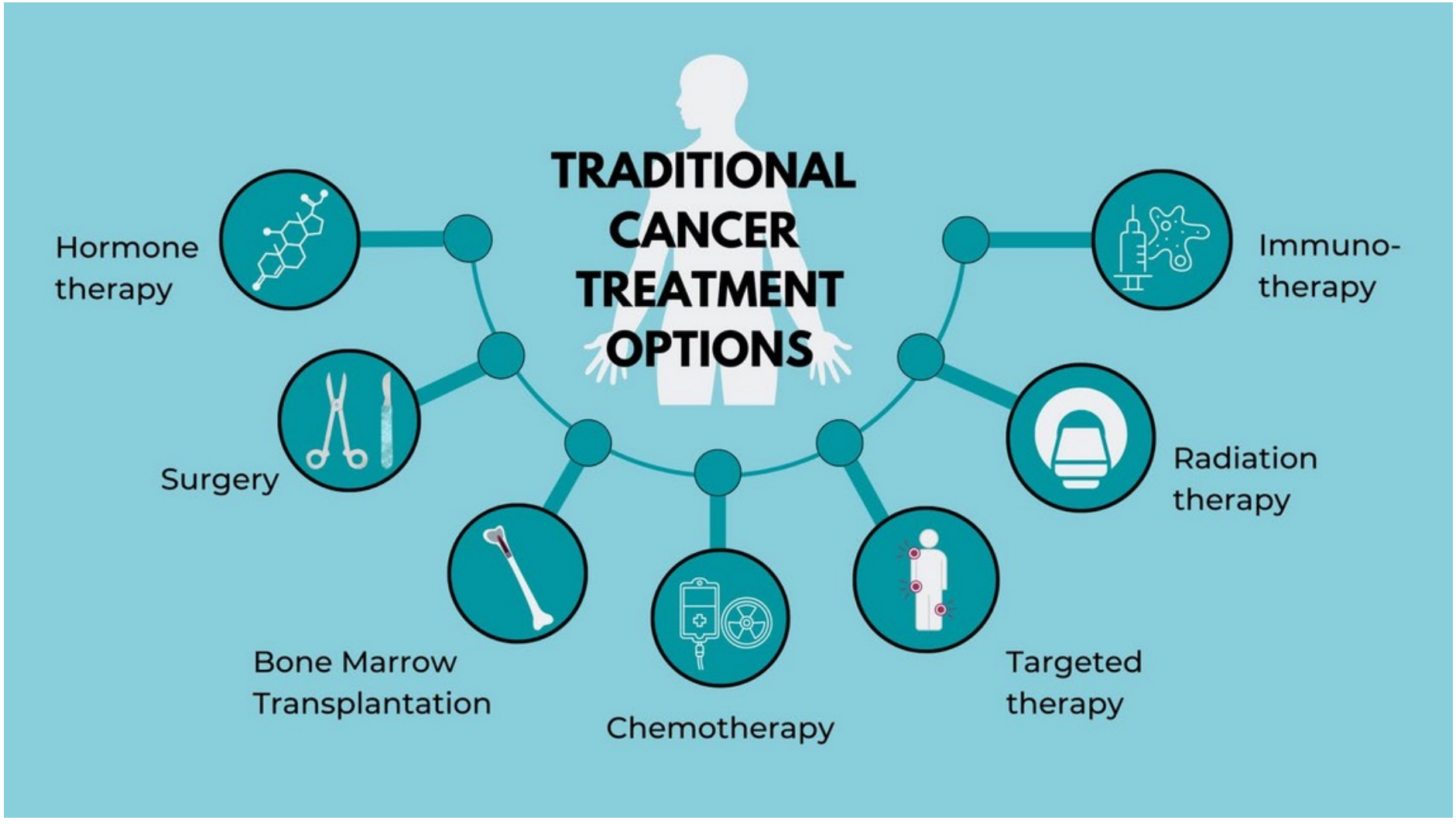


Figure 2: "Modern" cancer treatments are expensive and have limited benefit (Source: FLCCC)

Conventional Chemotherapy & Radiotherapy

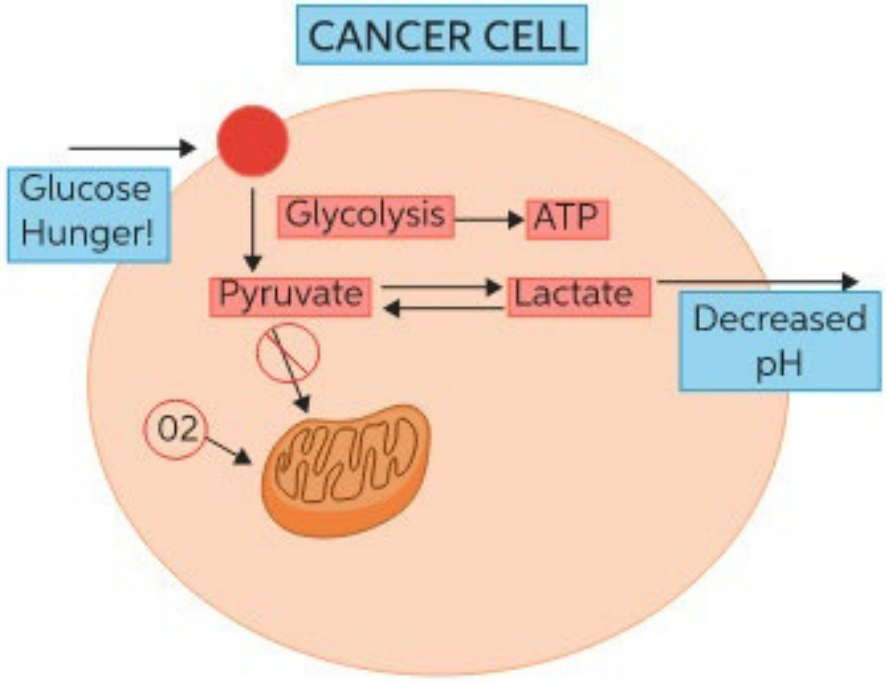
- Only target rapidly dividing cells
- Cancer Stem Cells allowed to proliferate
- Increases inflammation in TME
- Increases angiogenesis
- Increases metastatic potential
- Highly TOXIC
- Highly COSTLY

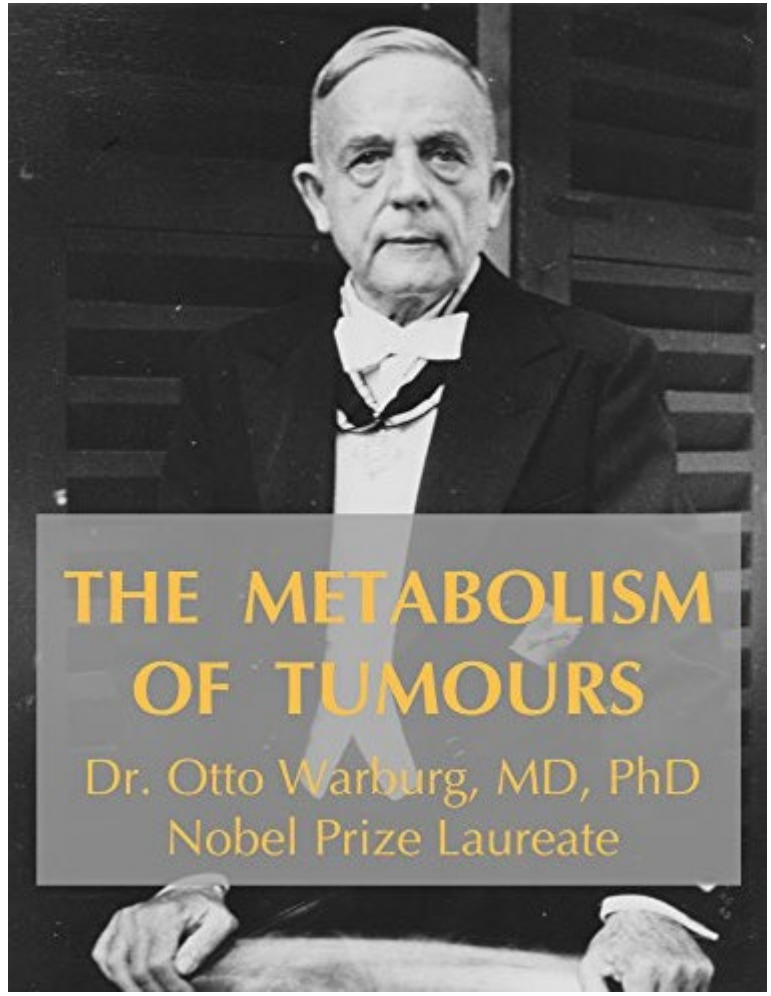
Conventional Theory of Cancer

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

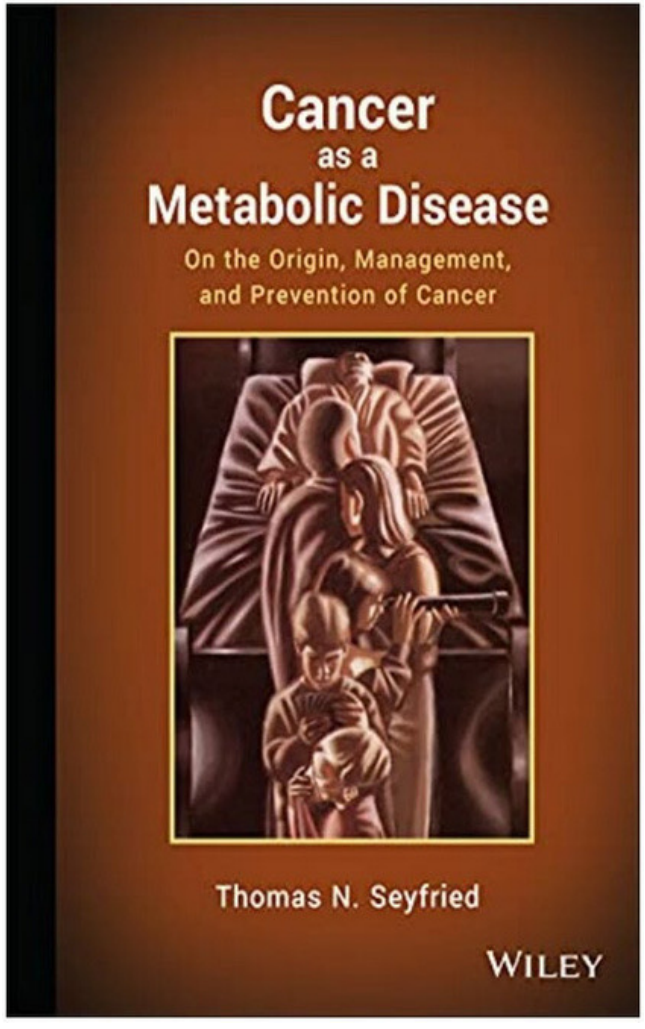


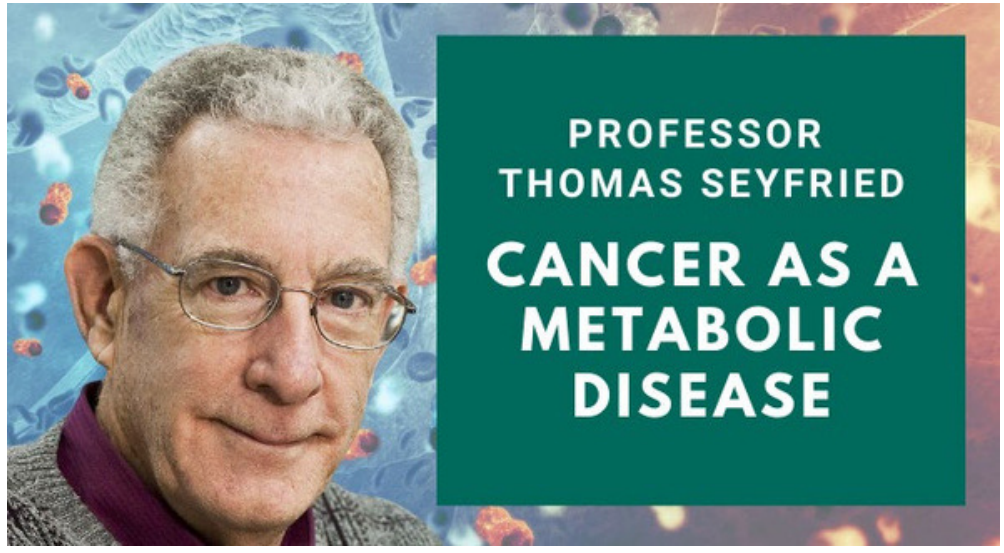


Anaerobic Glycolysis

Defective Mitochondria

Origins of Cancer





metabolites

MDPI

Concept Paper

Can the Mitochondrial Metabolic Theory Explain Better the Origin and Management of Cancer than Can the Somatic Mutation Theory?

Thomas N. Seyfried [1,*] and Christos Chinopoulos [2]

Concept Paper

Can the Mitochondrial Metabolic Theory Explain Better the Origin and Management of Cancer than Can the Somatic Mutation Theory?

- The absence of gene mutations and chromosomal abnormalities in some cancers
- The identification of numerous driver gene mutations in normal human tissue
- The general absence of cancers in chimpanzees despite having about 98% gene and protein sequence identity with humans even at the BRCA1 locus
- Theodor Boveri, the person most recognized as the originator of the SMT never directly studied cancer and was highly apologetic for his general lack of knowledge about the disease
- Normal mitochondria can down-regulate multiple oncogenic pathways and abnormal growth in tumor cells

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

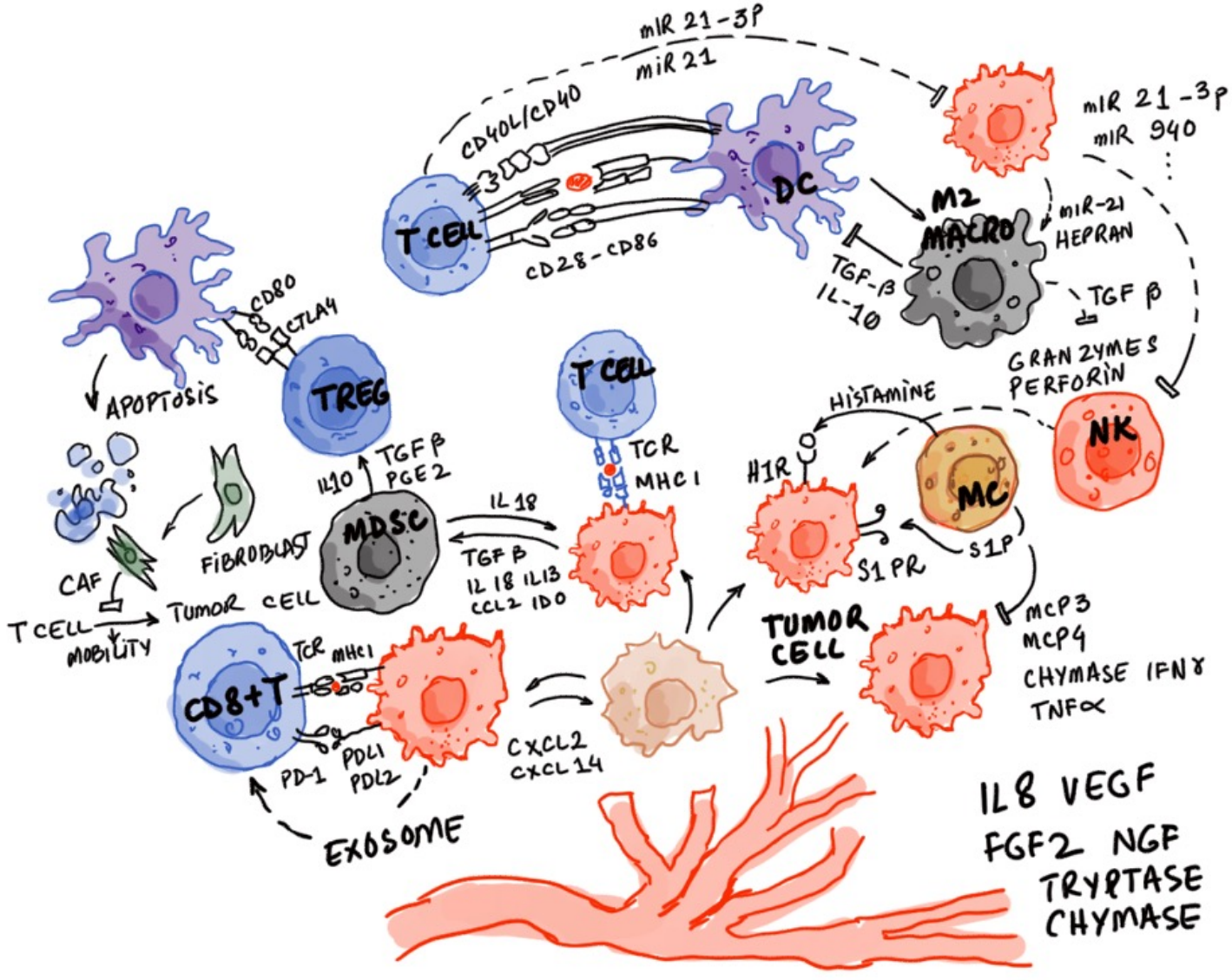


Illustration courtesy of Dr. Mobeen Syed

Cancer Stem Cells

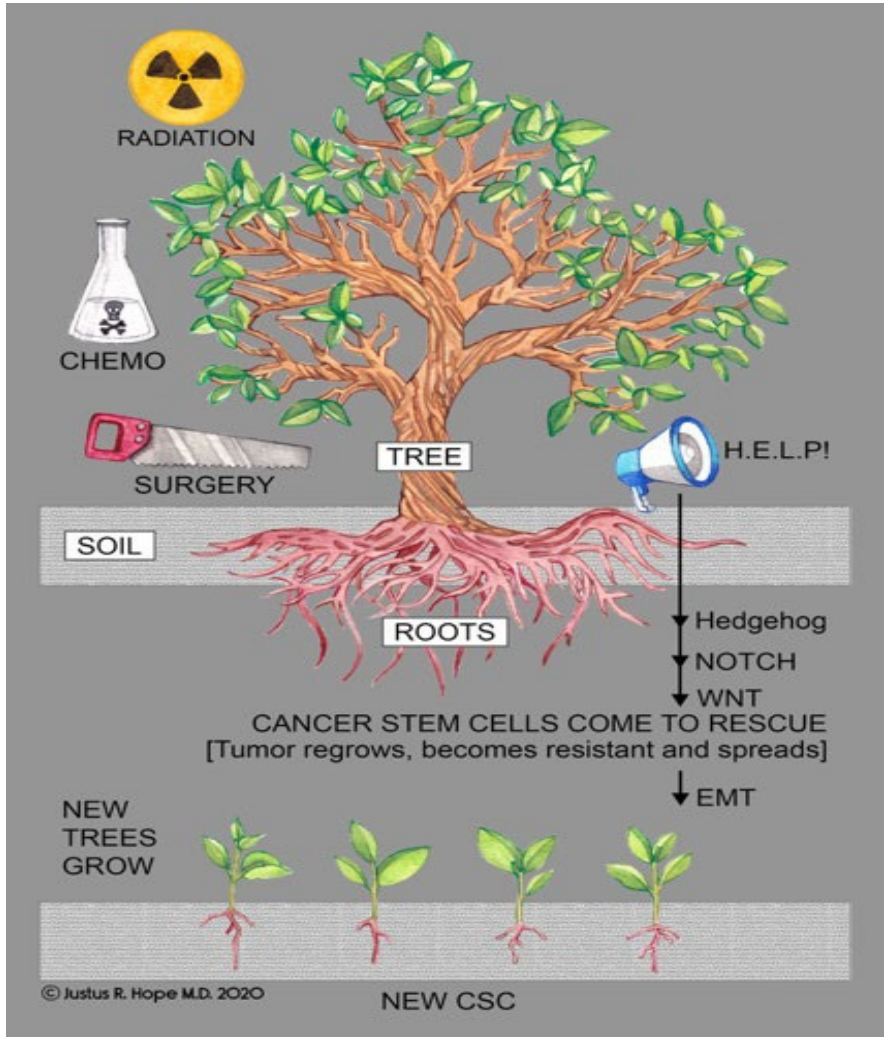


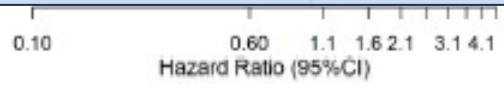
Figure: Cancer stem cells are the root of cancer (Source: Dr. Justus Hope)

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
- Limit exposure to carcinogens

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

Treatment	Treatment Event /Total	Control Event /Total	Hazard Ratio (95%CI)
Vitamin D	36 /1076	45 /1081	0.76 (0.49 - 1.18), p= 0.225
Omega-3	32 /1073	49 /1084	0.7 (0.44 - 1.09), p= 0.115
SHEP	35 /1081	46 /1076	0.74 (0.48 - 1.15), p= 0.183
Omega-3 + Vitamin D	15 /529	28 /537	0.53 (0.28 - 1), p= 0.051
Vitamin D + SHEP	11 /539	21 /539	0.56 (0.3 - 1.04), p= 0.068
Omega-3 + SHEP	12 /539	26 /542	0.52 (0.28 - 0.97), p= 0.039
Vitamin D + Omega-3 + SHEP	4 /264	12 /270	0.39 (0.18 - 0.85), p= 0.017



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!

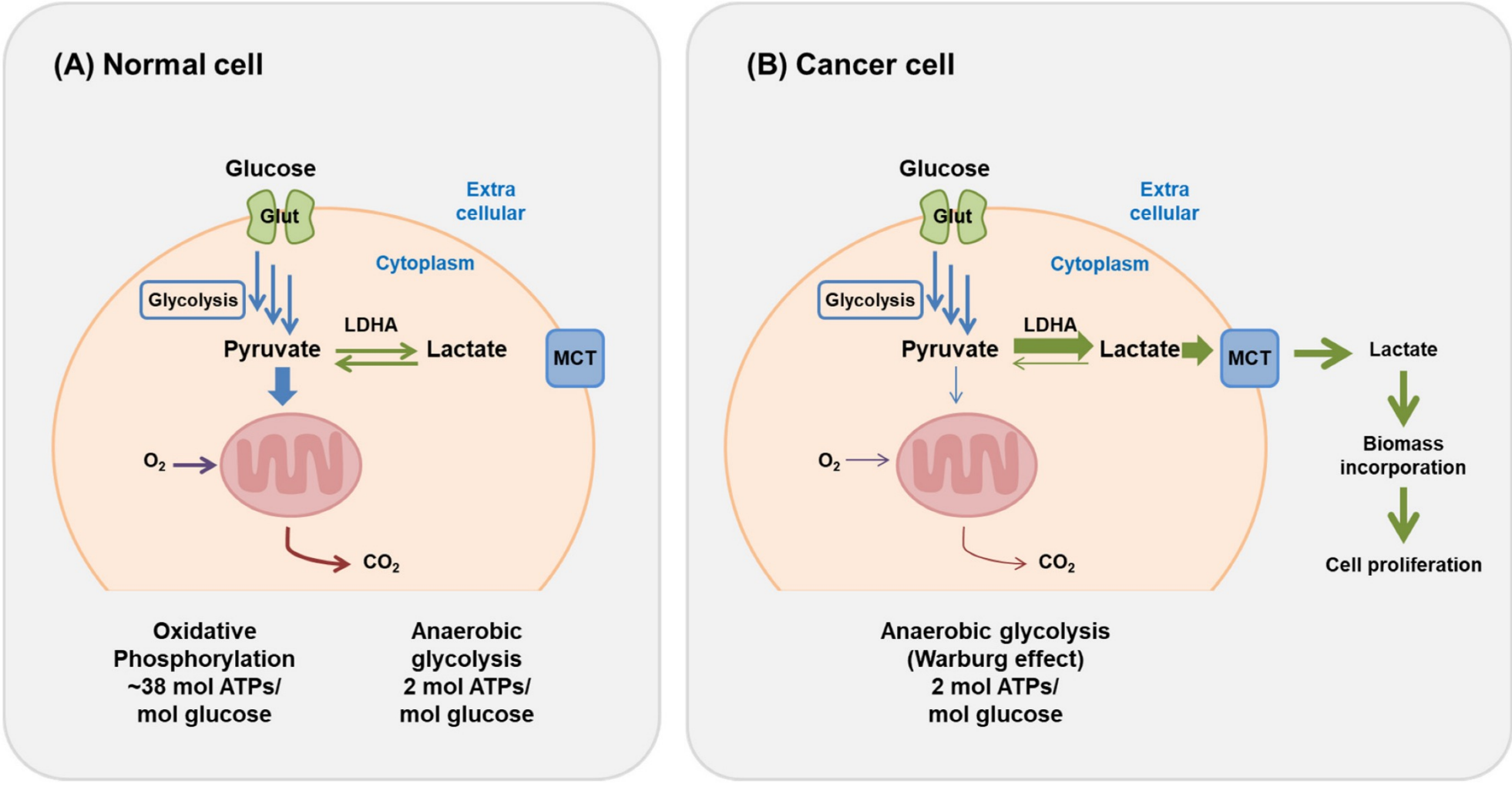
Metabolic Interventions to Control Cancer: TOP 12

1. A low-carbohydrate, high-fat, ketogenic diet + time-restricted eating
2. Exercise, stress reduction, and quality sleep
3. Vitamin D3: 20,000 to 50,000 IU daily
   - Dosage should be adjusted by blood vitamin D levels aiming for a 25-OH vitamin D level of ~ 100 ng/ml.
4. Melatonin: start 1 mg and increase to 20-30 mg nightly (extended/slow release)
5. Green tea catechins: 500-1,000 mg daily
6. Metformin: 1,000 mg twice daily
7. Curcumin: (nanocurcumin) 600 mg twice daily
8. Mebendazole: 100-200 mg daily
9. Omega-3 fatty acids: 4 g daily
10. Berberine: 500-600 mg twice daily
    - Metformin and berberine can be used together or alternating (for one month then switching) depending on blood glucose levels.
11. Atorvastatin: 40 mg twice daily or Simvastatin 20 mg twice daily
12. Disulfiram: 80 mg three times daily or 500 mg once daily

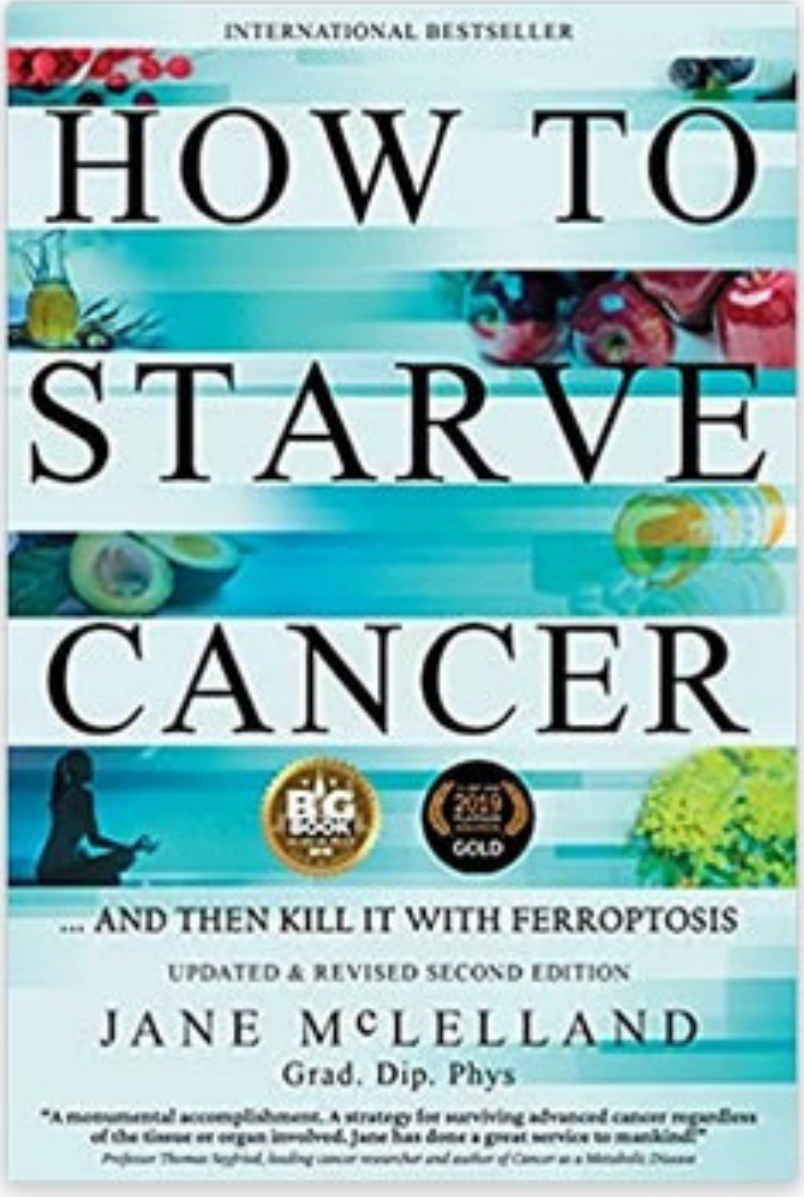
Over the Counter

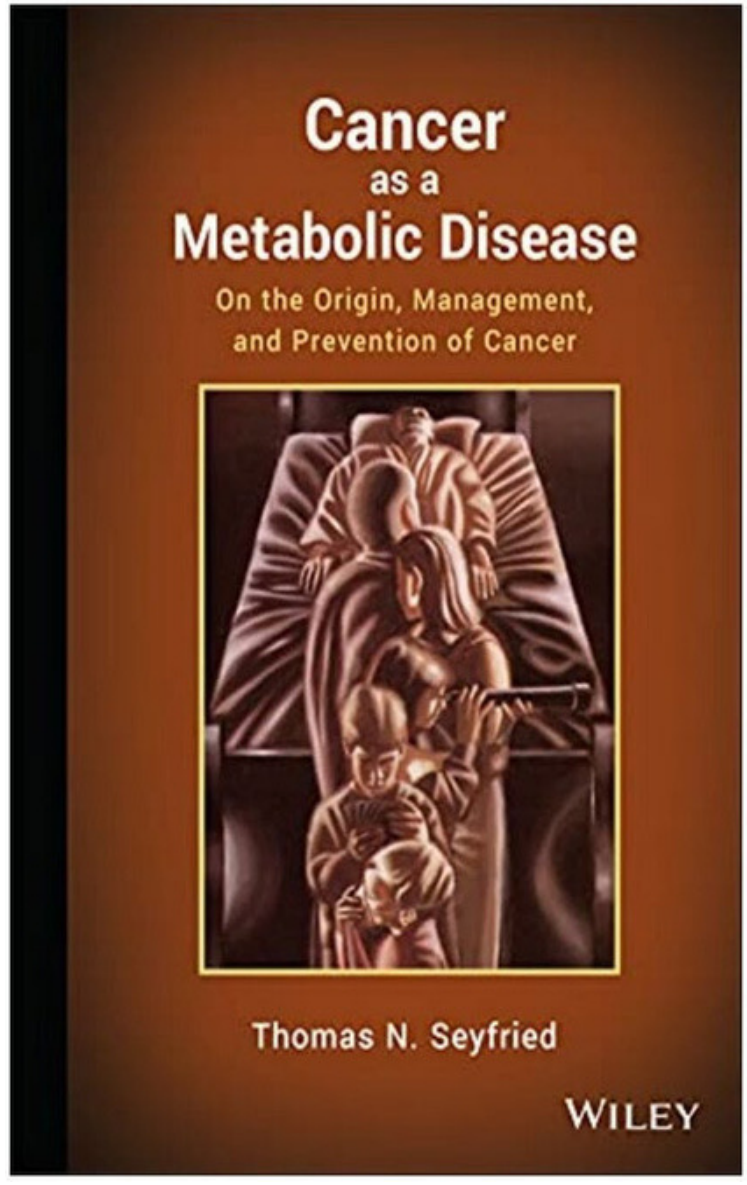
Requires a prescription

Warburg Phenomenon

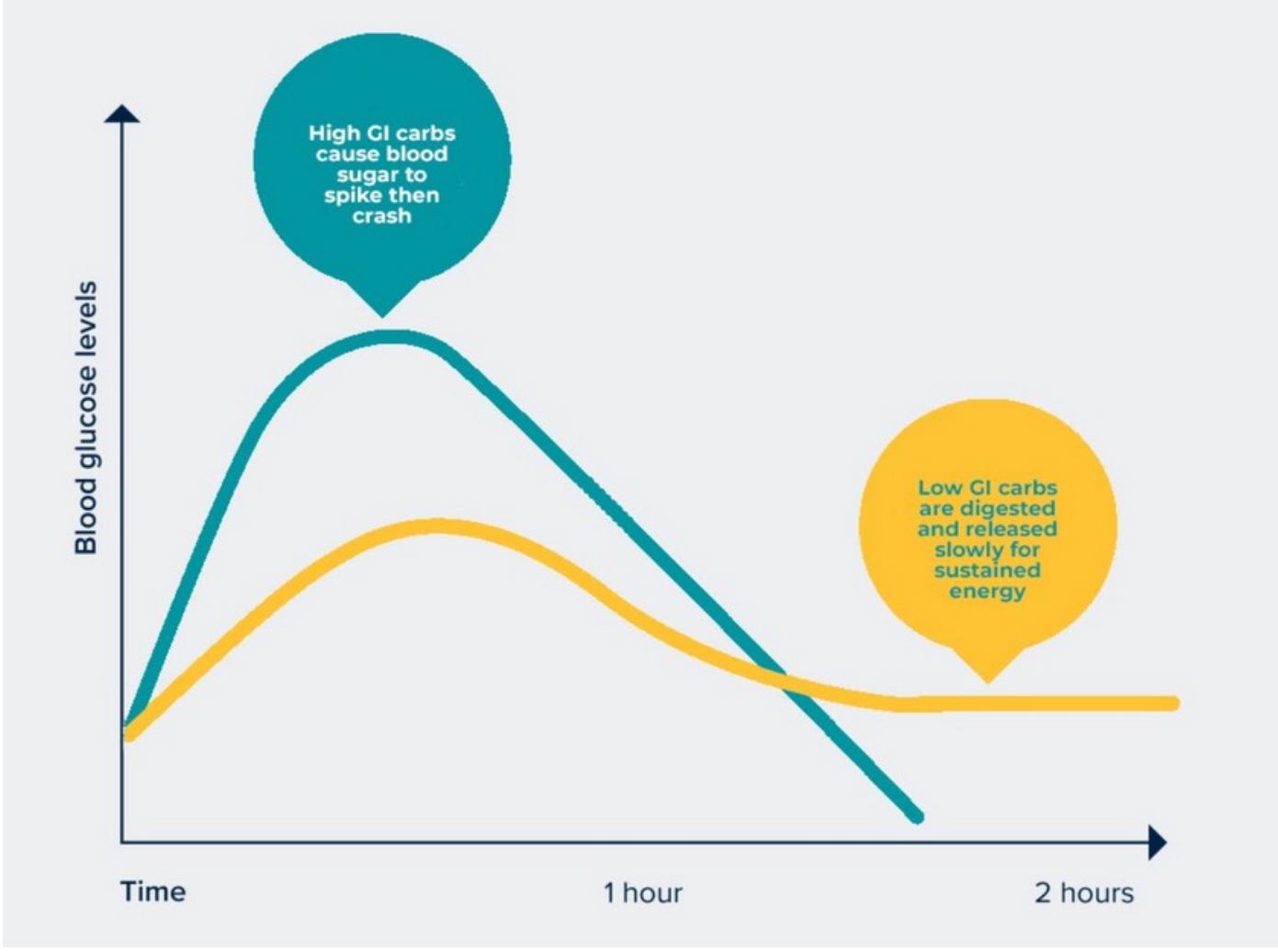


Wikimedia license: https://commons.wikimedia.org/wiki/File:Differences_in_glycolysis_pathways_between_normal_cells_and_cancer_cells.webp


INTERNATIONAL BESTSELLER
HOW TO
STARVE
CANCER
... AND THEN KILL IT WITH FERROPTOSIS
UPDATED & REVISED SECOND EDITION
JANE McLELLAND
Grad. Dip. Phys
"A monumental accomplishment. A strategy for surviving advanced cancer regardless of the tissue or organ involved. Jane has done a great service to mankind."
Professor Thomas Seyfried, leading cancer researcher and author of Cancer as a Metabolic Disease


Cancer
as a
Metabolic Disease
On the Origin, Management,
and Prevention of Cancer
Thomas N. Seyfried
WILEY

Glucose Management



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

Glucose Management

ARTICLE

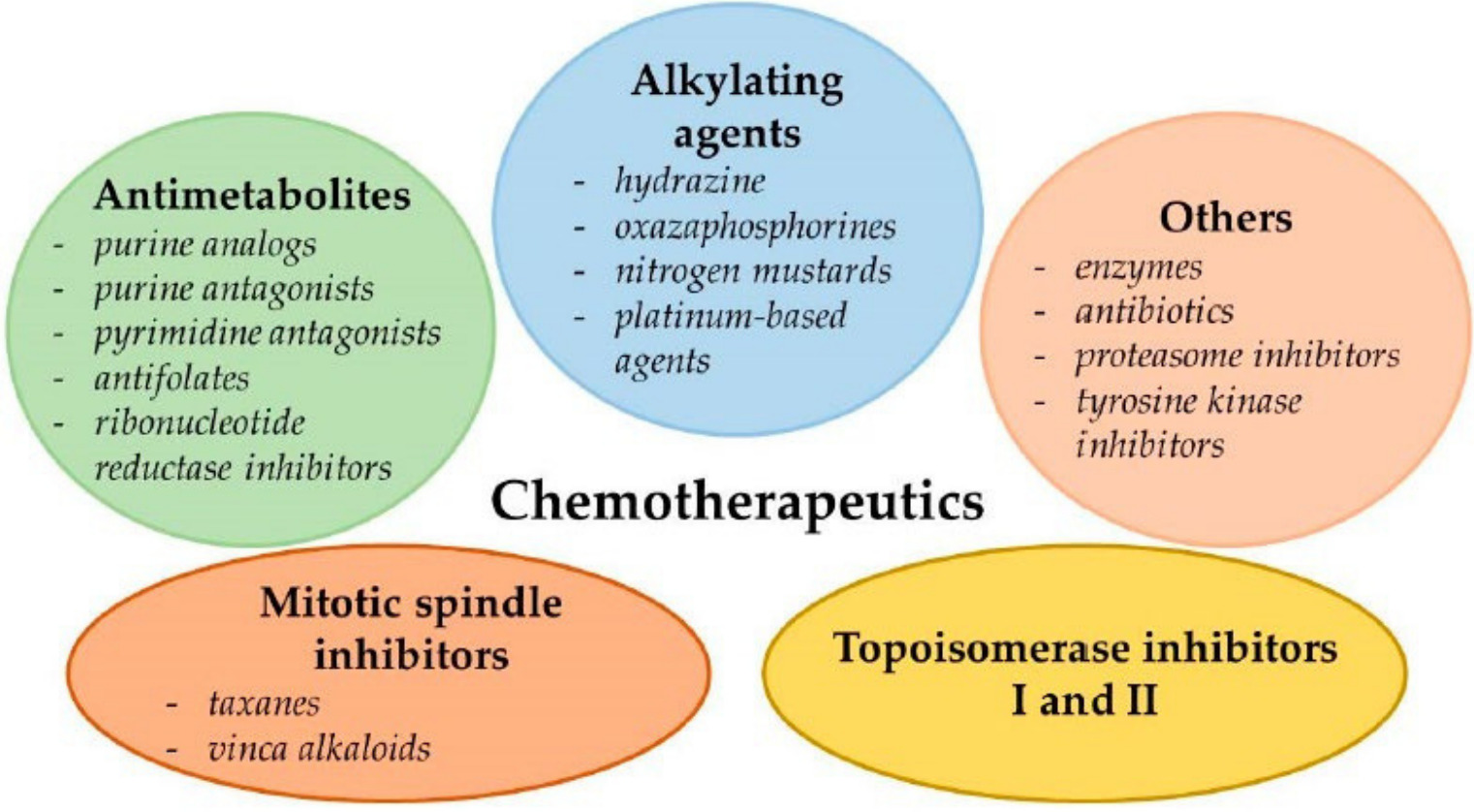
Dietary Insulin Load and Cancer Recurrence and Survival in Patients With Stage III Colon Cancer: Findings From CALGB 89803 (Alliance)

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

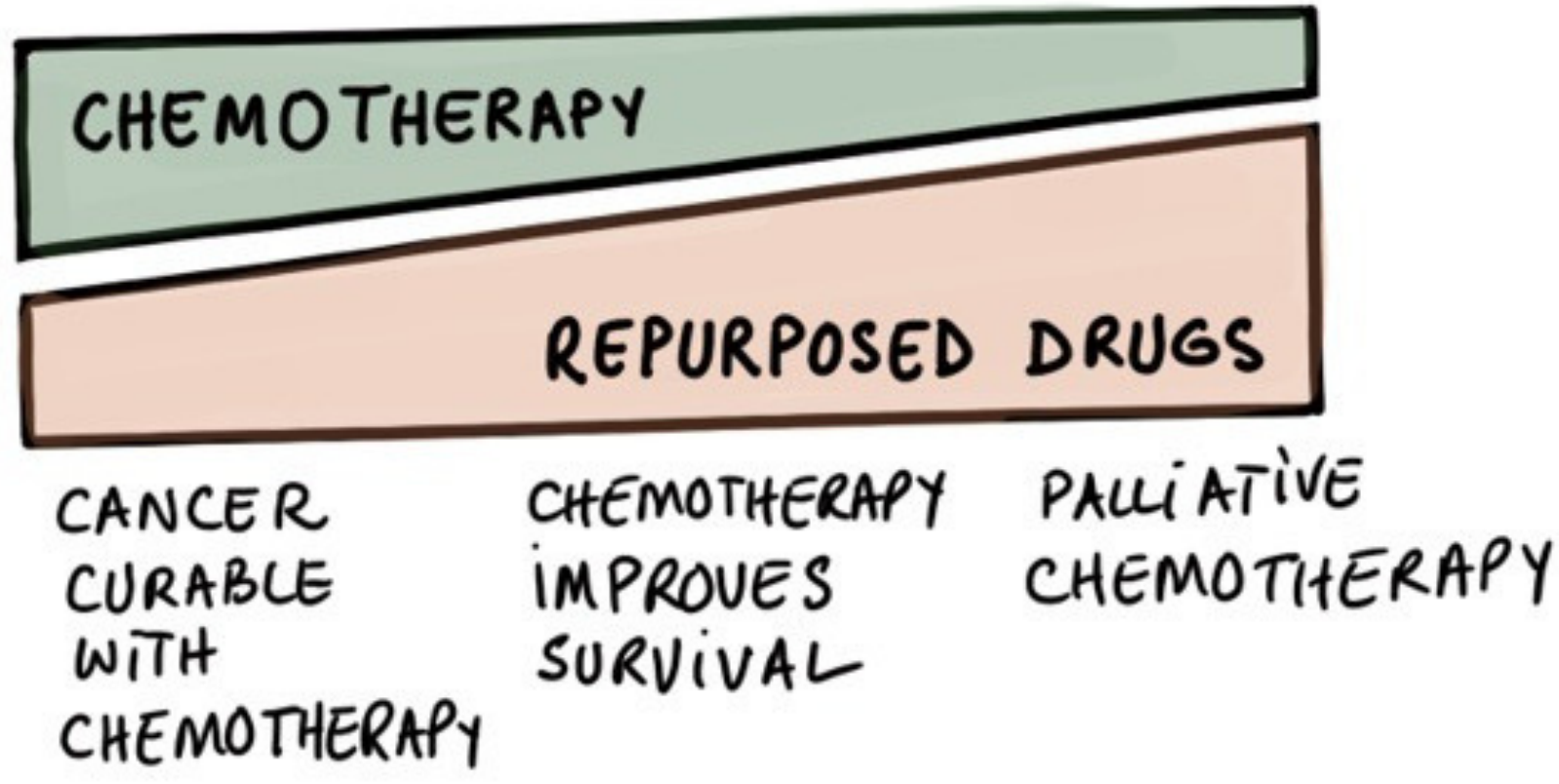


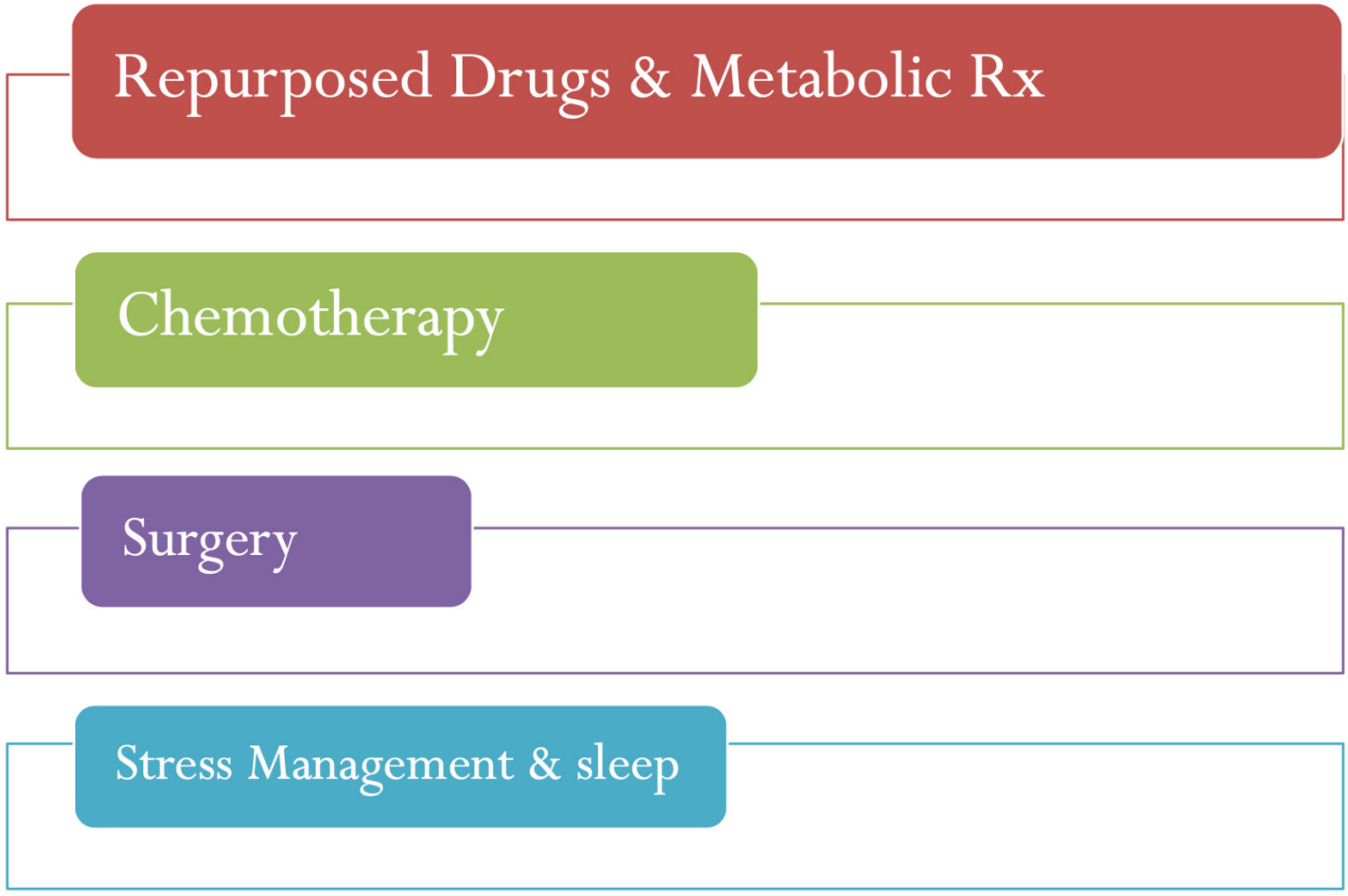
Illustration courtesy of Dr. Mobeen Syed

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



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- Under “Reviews & Monographs”

flccc.net/cancer-care

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