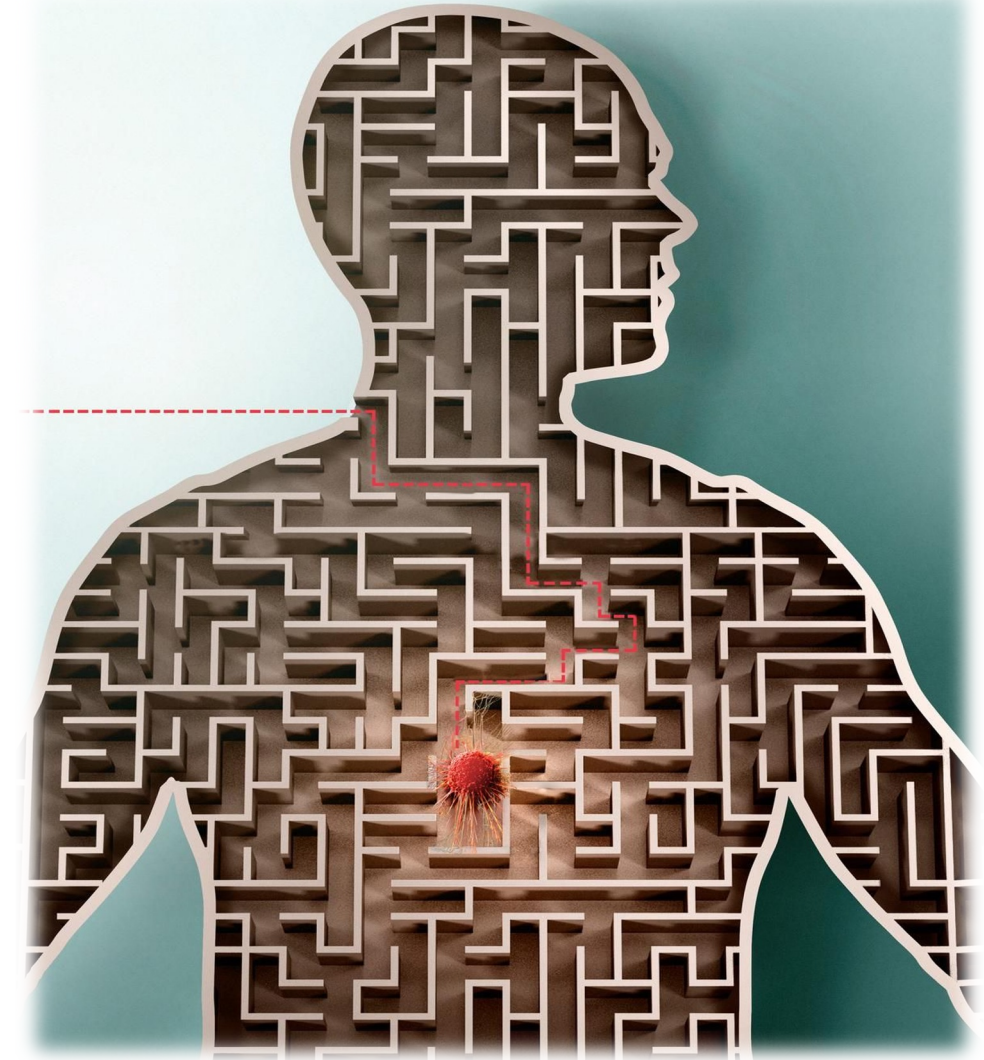


Applied Metabolic Therapy for Optimizing Cancer Treatment Outcomes



Dr. Wafaa Abdel-Hadi, MBBCH, MSc, IFMC-MD

**Chairperson & co-founder of AWARE clinic
Clinical Oncologist, Cairo University, Egypt
Functional Medicine Consultant, IFM, USA
Association for Ketogenic Metabolic Therapies**



Courtesy of Wall street Journal

Disclaimer:



- **Clinical Oncologist, Kasr Alainy Cairo University, Egypt**
- **Certified Functional Medicine Doctor, IFM, USA**
- **Chairperson & co-Founder of AWARE clinic**
- **Advisory Board & Faculty Member of the European Keto-Live Centre for Treatment & Reversing Non-Communicable Diseases.**
- **Member of The Integrative Oncology Working Group, Curriculum Committee, Texas, USA**



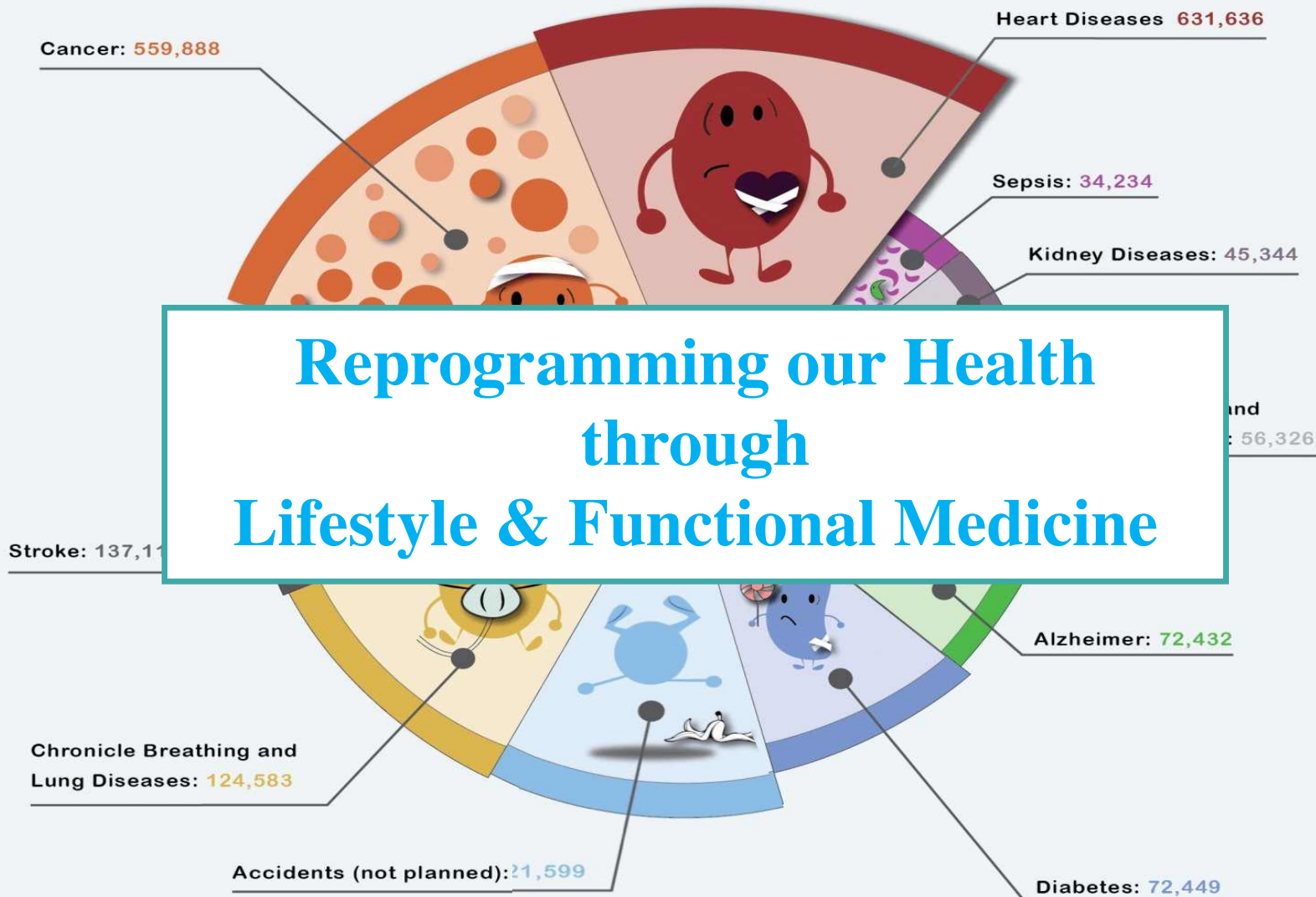


Points of Discussion:

- What did we learn so far?
- Inflammation & Cancer
- The Hallmarks of Cancer
- Tumor Microenvironment
- Which cells are we killing?
- Nature is here to help...

Top 10 Causes of Death in the USA

(according to Centers for Disease Control and Prevention)



Reprogramming our Health
through
Lifestyle & Functional Medicine

Inflammatory/Metabolic Diseases:

- Heart Diseases & Stroke
- Cancer
- Chronic Lung Diseases
- Diabetes
- Alzheimer's – NeuroDegenerative.
- Kidney Diseases
- Sepsis

Genetic Predispositions:

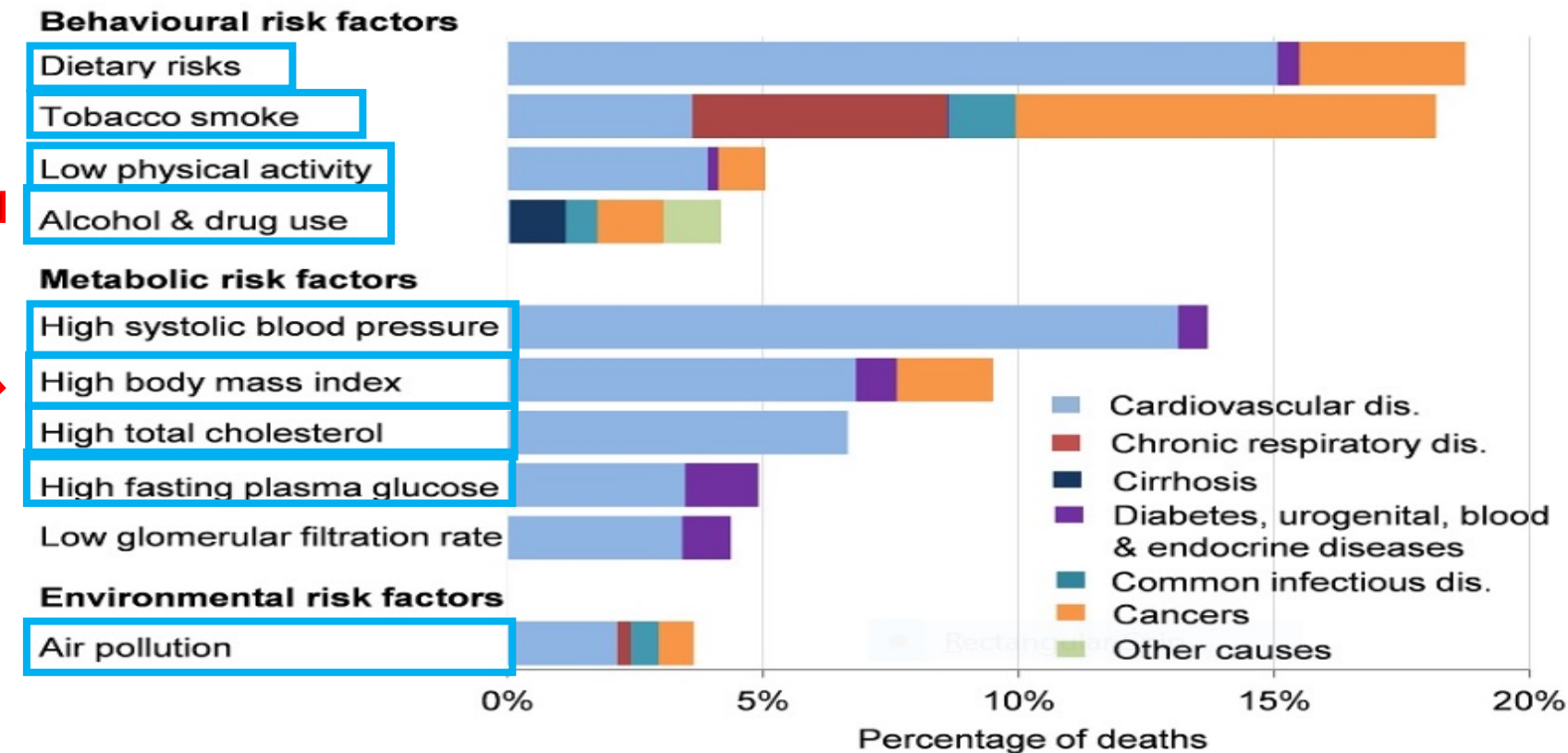
- Heart Diseases & Stroke
- Cancer
- Chronic Lung Diseases
- Diabetes
- Alzheimer's – Brain Neurodeg.
- Kidney Diseases
- Sepsis



Factors Contributing to the Global Burden of Disease:

4.1 Figure 3: attribution of deaths to risk factors and broken down by broad causes of death in England, 2013

Among those risk factors included in the GBD analysis, dietary risk factors and tobacco smoke accounted for the most deaths



Modifiable Factors!

Lifestyle & Functional Medicine

Source: GBD 2013



Consequences of Increasing GBD:

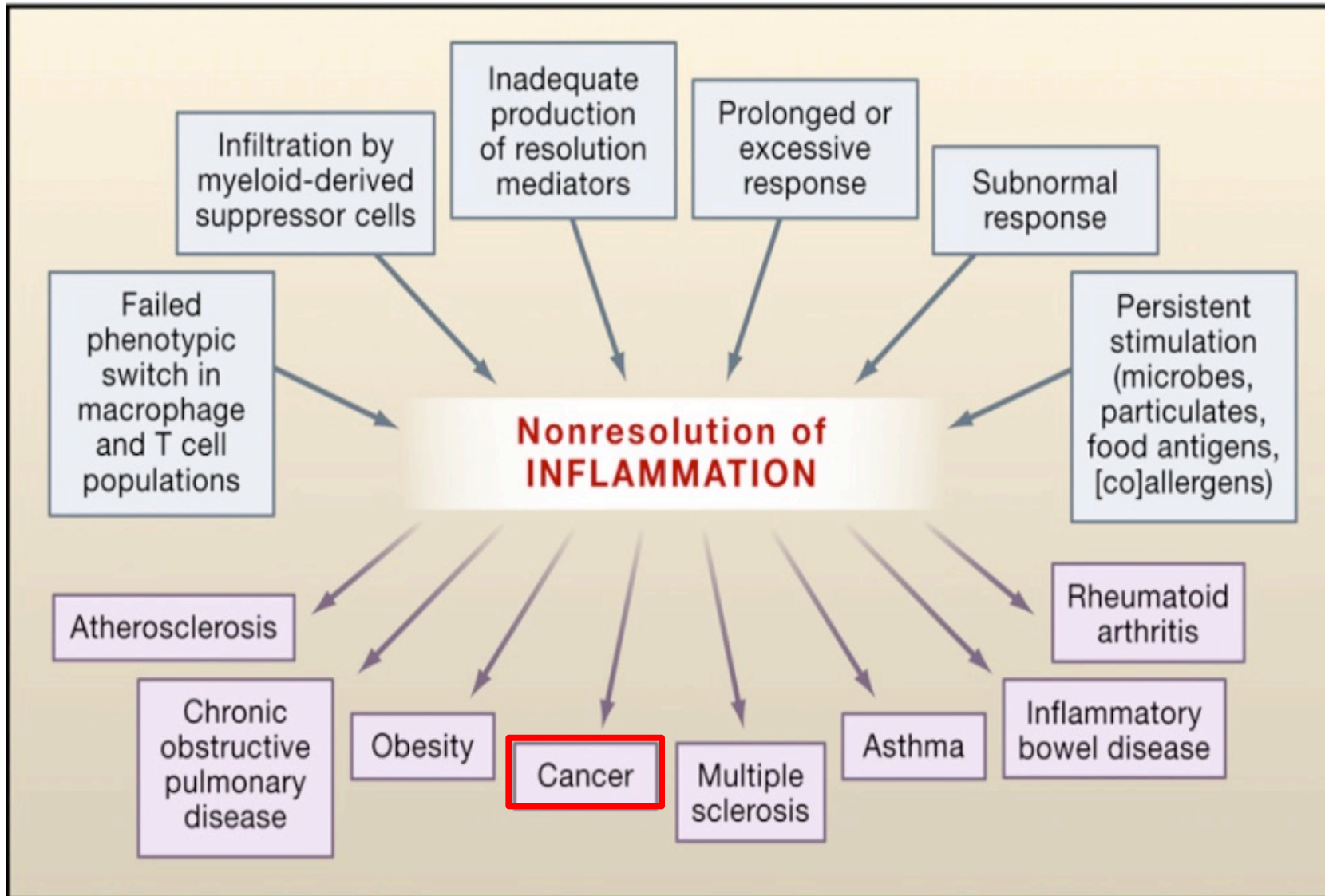
- ++ Levels of toxins in our bodies
- ++ Levels attacks of Inflammation
- **Non- Resolution of Inflammation**
- Chronic Inflammation
- Cells die and cannot regenerate
- Immune Disturbances
- Diseases start & EVOLVE!!

Total Toxic Burden

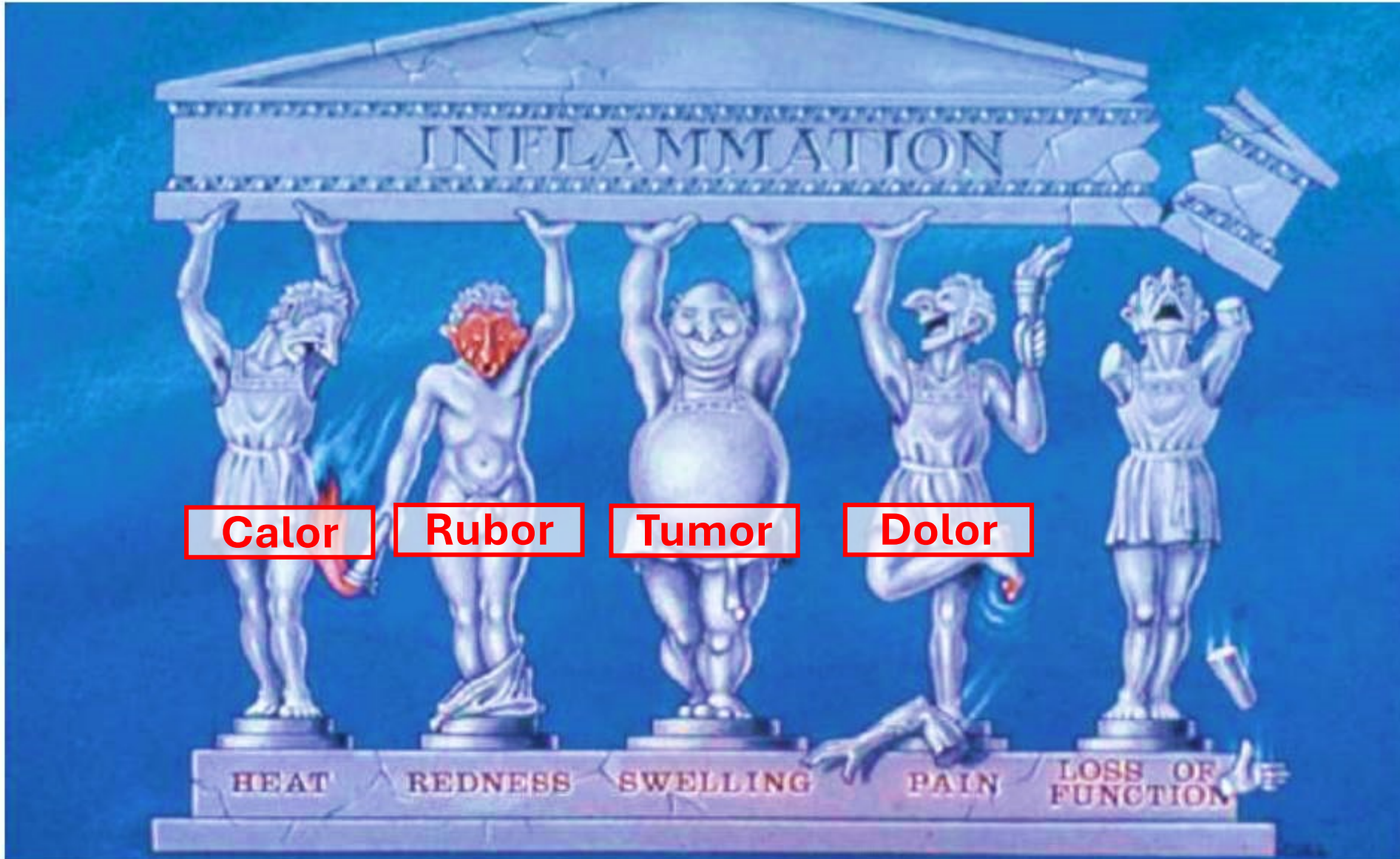




Non-Resolution of Inflammation



The five cardinal signs of **Acute Inflammation**



Tumor
Rubor
Calor
Dolor

Calor

Rubor

Tumor

Dolor

HEAT

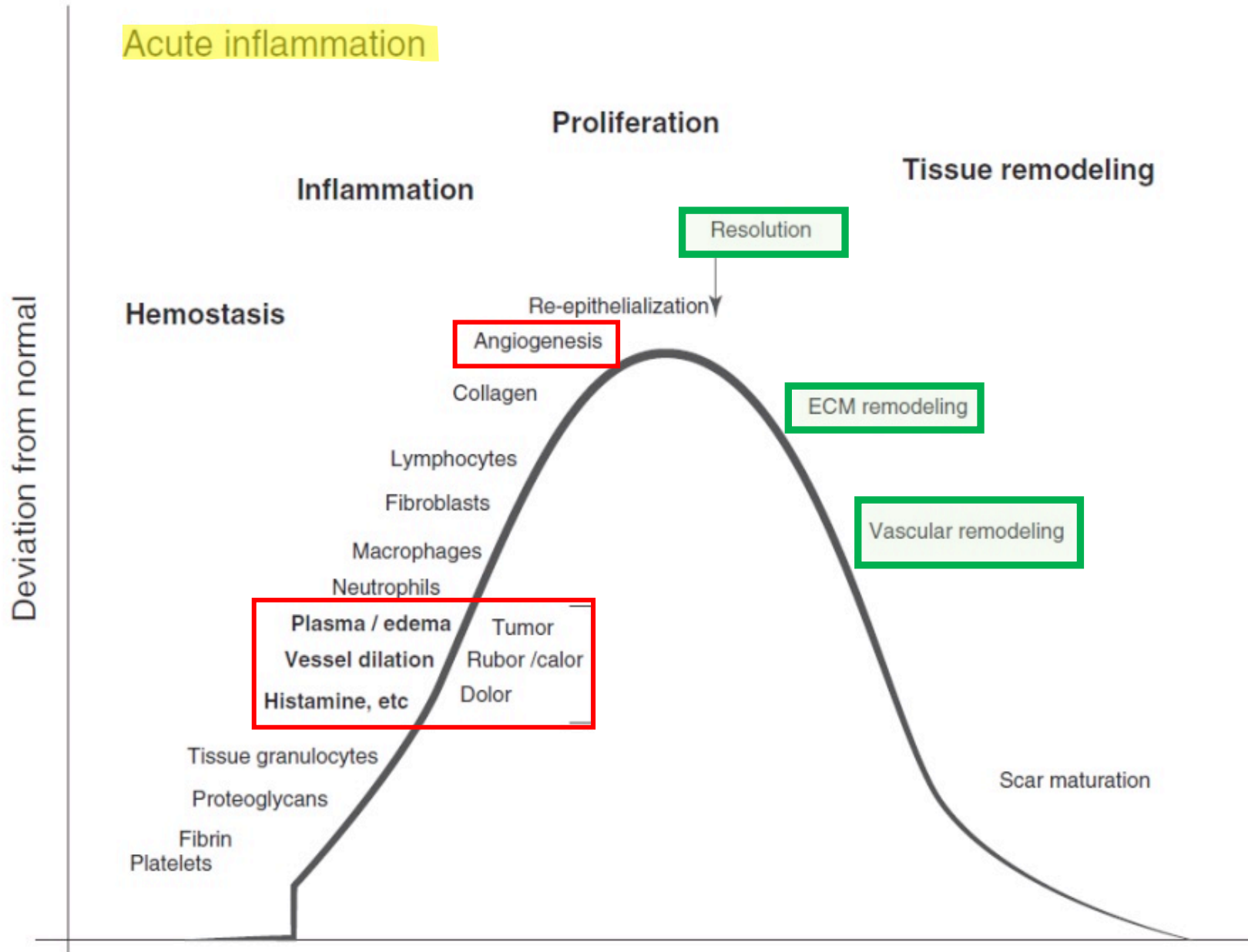
REDNESS

SWELLING

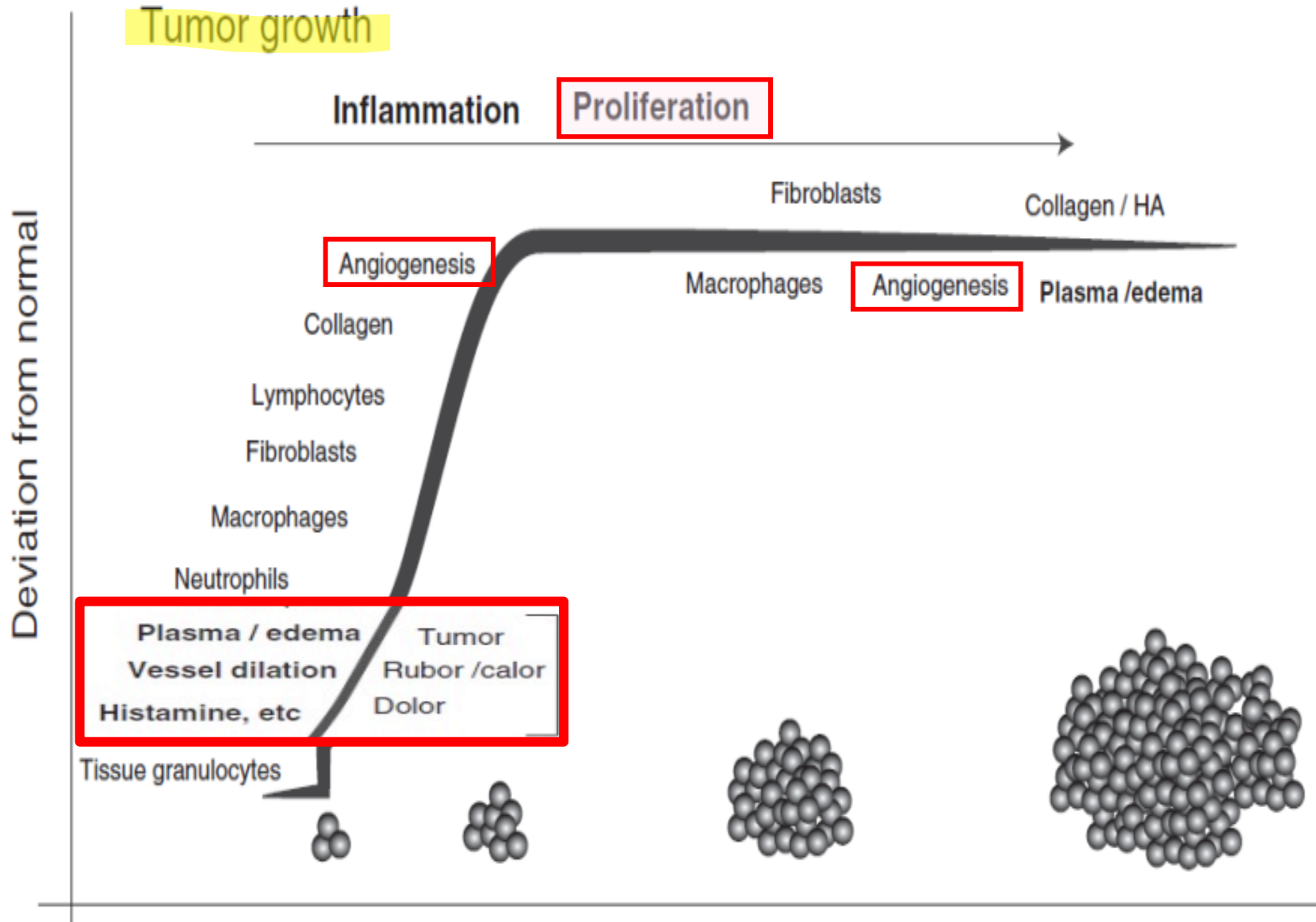
PAIN

LOSS OF
FUNCTION

Inflammation & Cancer

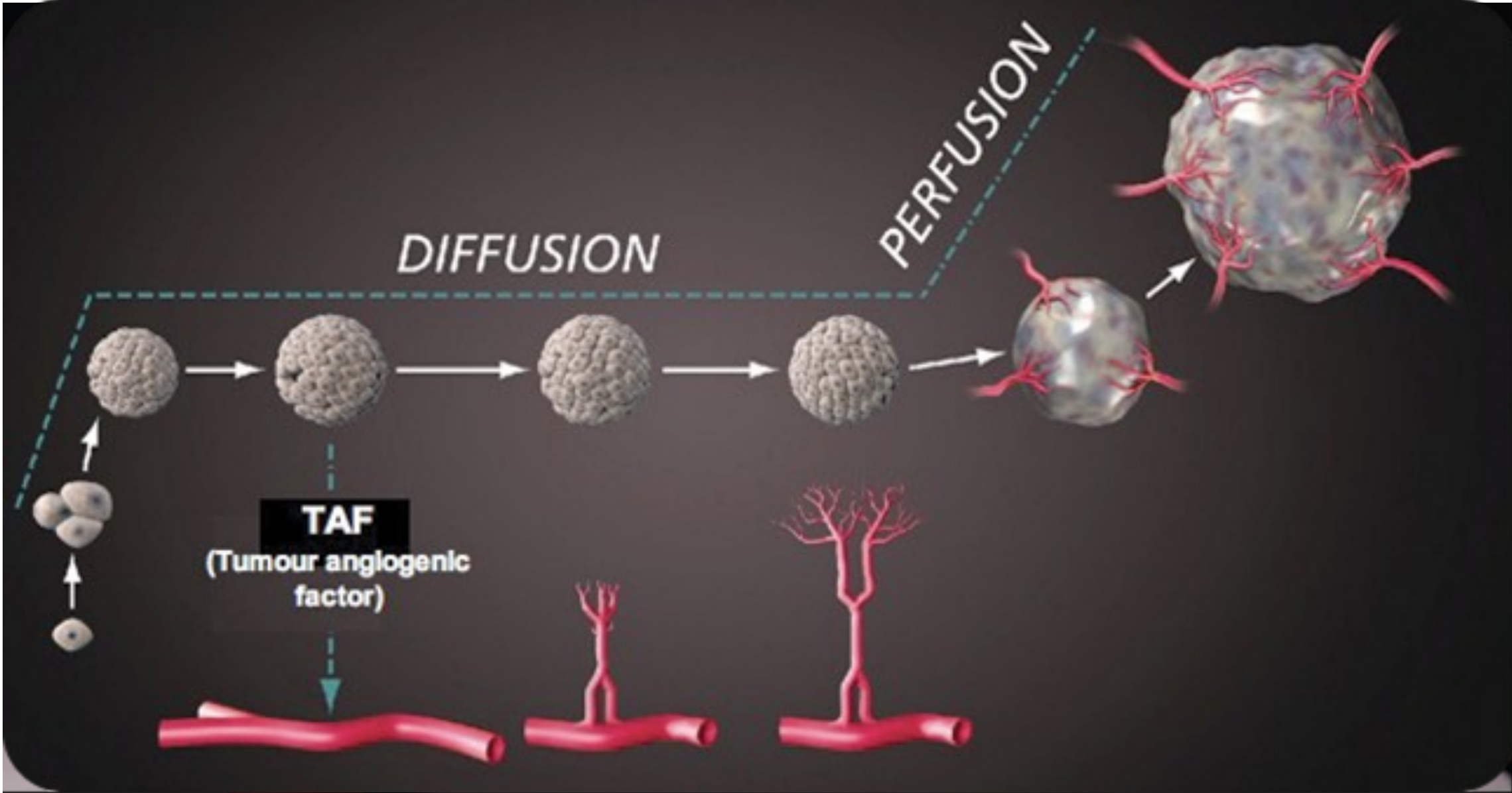


Inflammation & Cancer



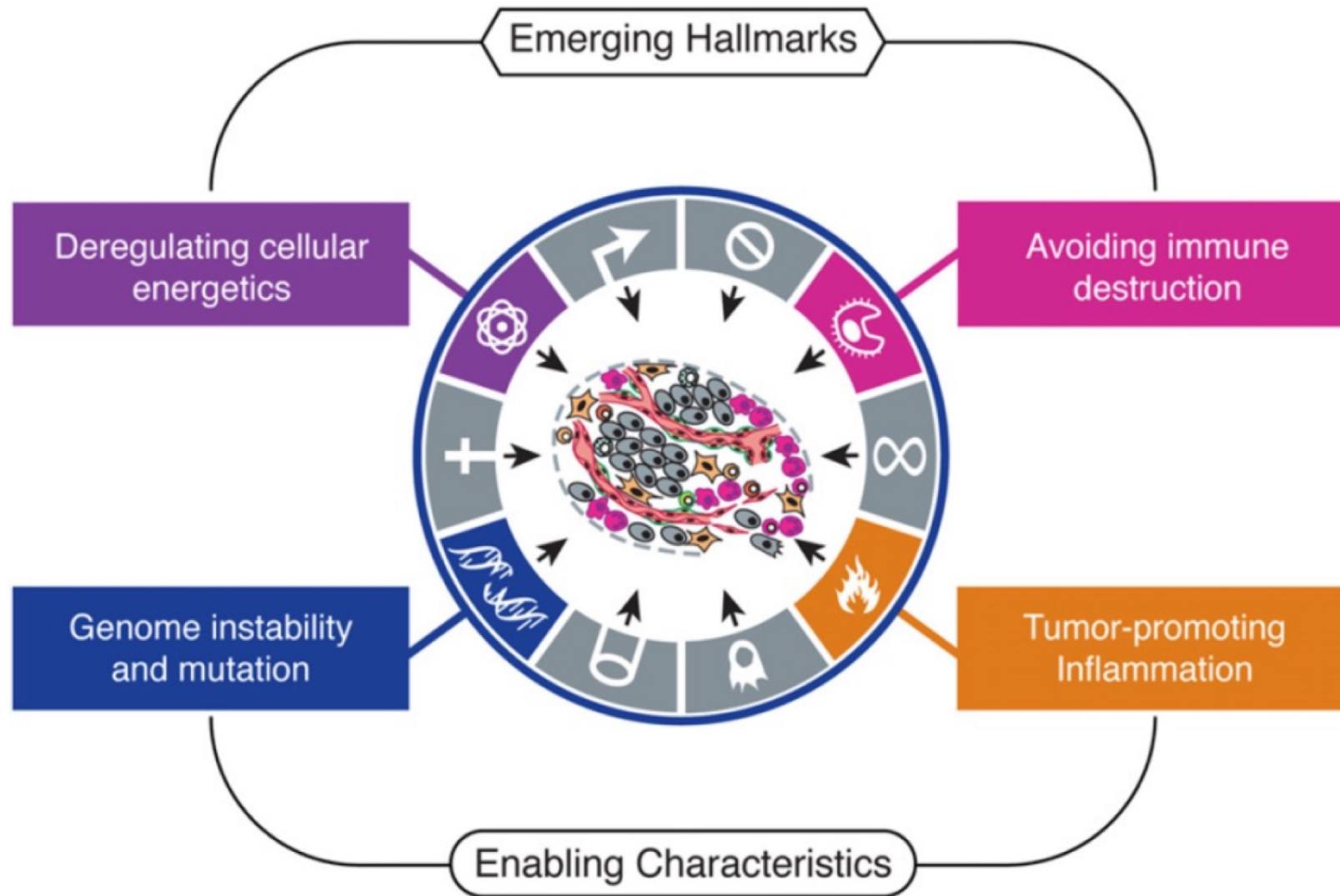
Recruitment of growth factors & starting the hallmarks of cancer

Angiogenesis

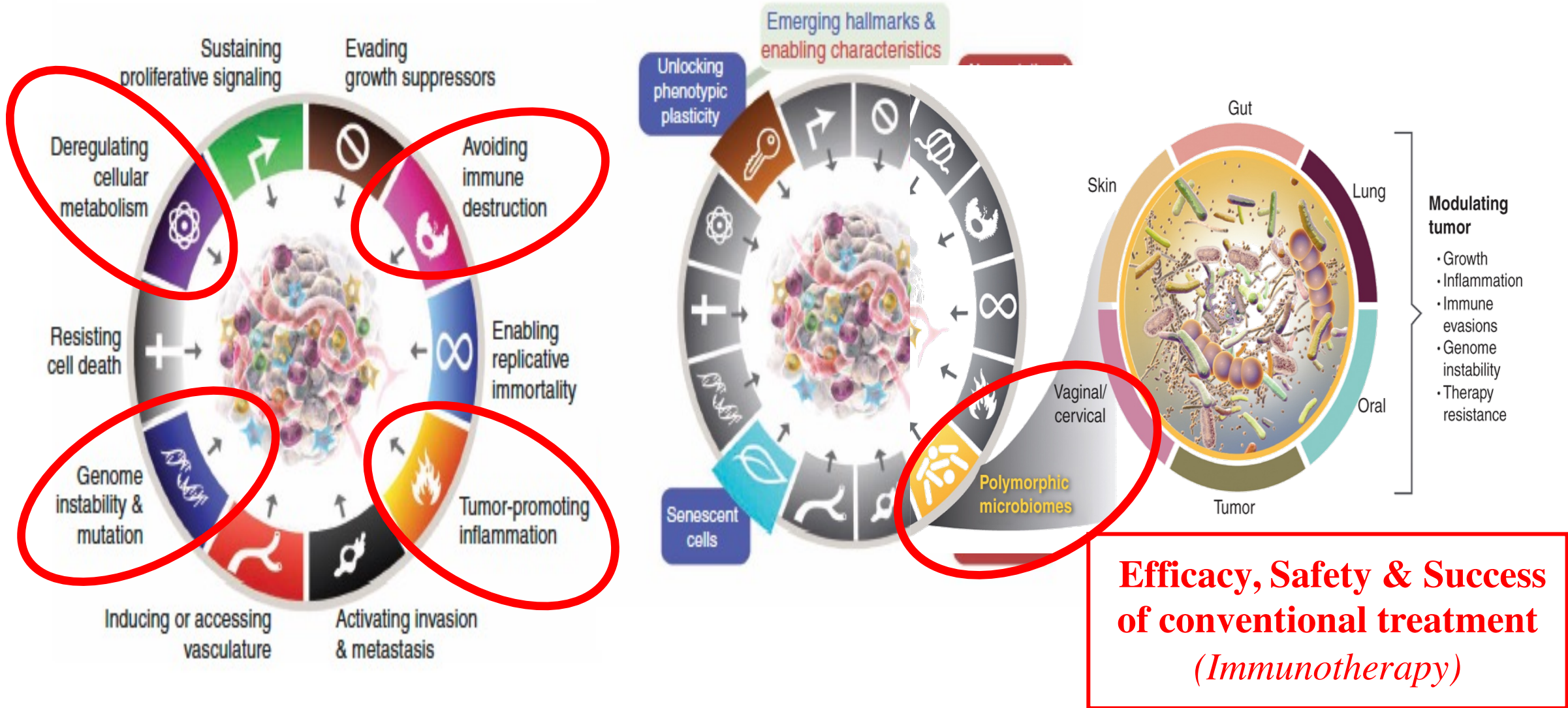




The Development of Hallmarks of Cancer



The Emerging Hallmarks of Cancer



Douglas Hanahan. *Hallmarks of Cancer: New Dimensions*. *Cancer Discov.* 2022;12(1):31-46.



Mitochondrial Dynamic Dysfunction as a Main Triggering Factor for Inflammation Associated Chronic Non-Communicable Diseases

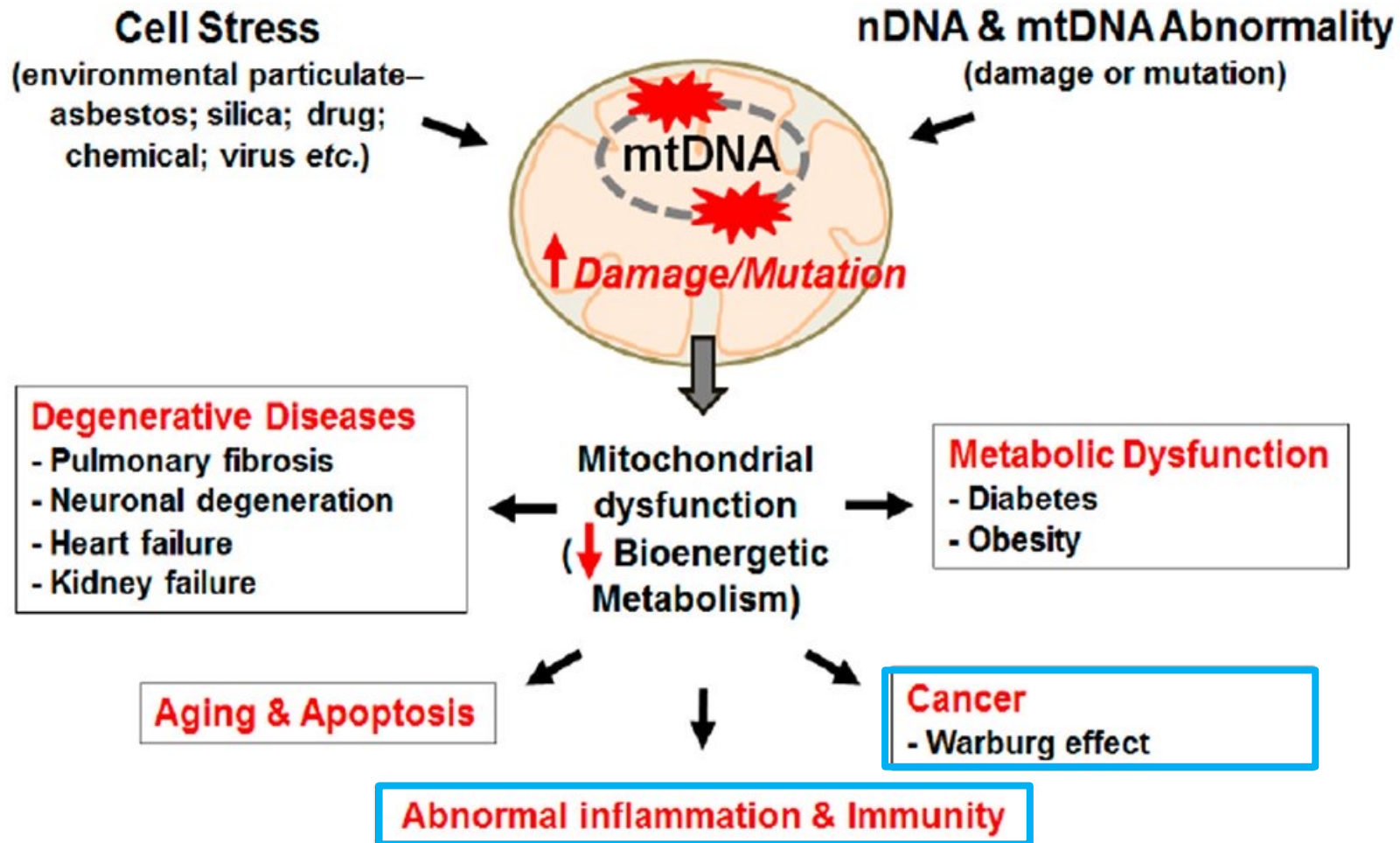
This article was published in the following Dove Press journal:
Journal of Inflammation Research

Zeleke Geto ¹
Meseret Derbew Molla²
Feyissa Challa ¹
Yohannes Belay³
Tigist Getahun ¹

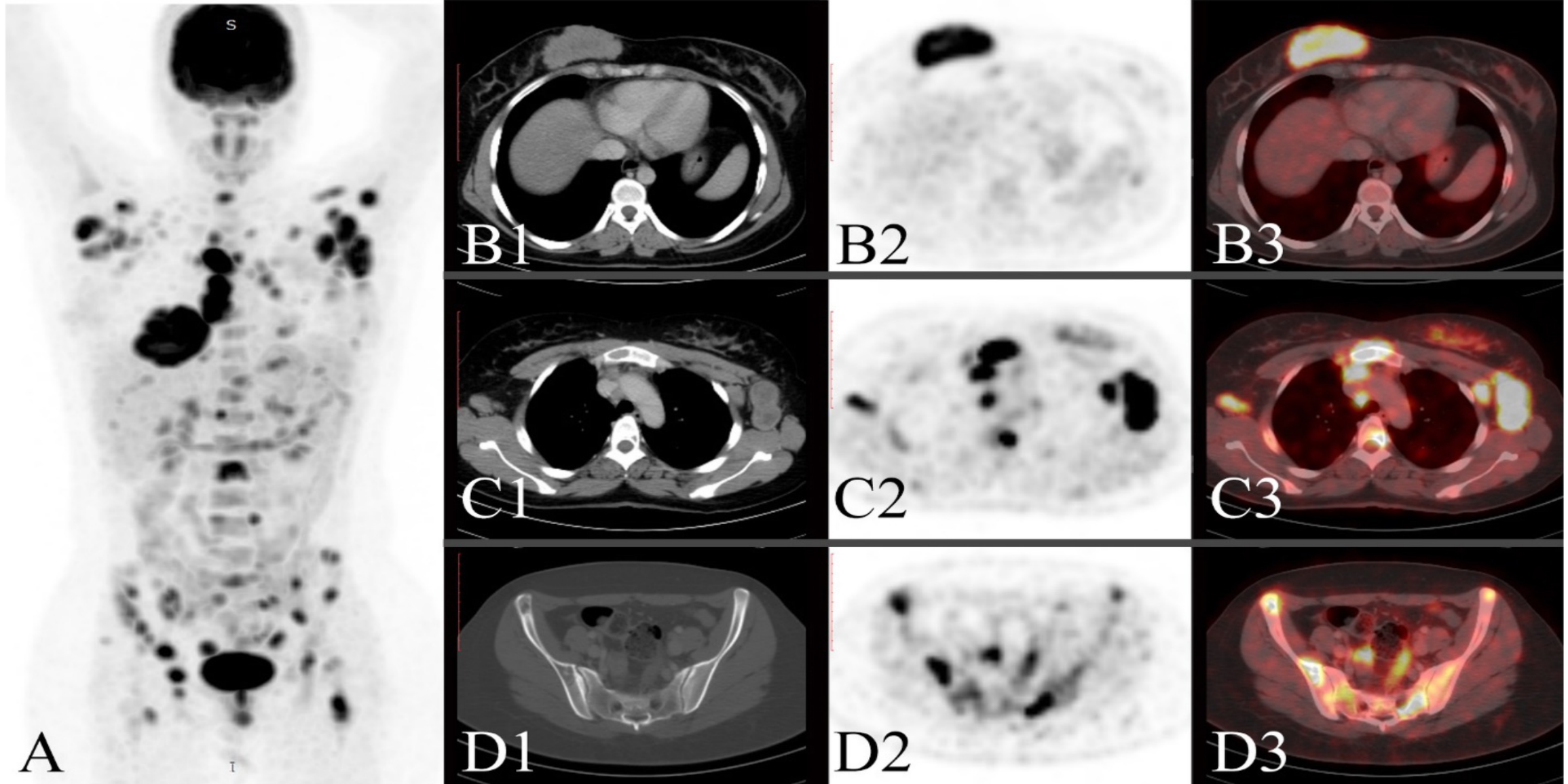
¹National Reference Laboratory for Clinical Chemistry, Ethiopian Public Health Institute, Addis Ababa, Ethiopia; ²Department of Biochemistry, School of Medicine, College of Medicine and Health Sciences, University of Gondar, Gondar, Ethiopia; ³National Reference Laboratory for Hematology and Immunology, Ethiopian Public Health Institute, Addis Ababa, Ethiopia

Abstract: Mitochondria are organelles with highly dynamic ultrastructure maintained by flexible fusion and fission rates governed by Guanosine Triphosphatases (GTPases) dependent proteins. Balanced control of mitochondrial quality control is crucial for maintaining cellular energy and metabolic homeostasis; however, dysfunction of the dynamics of fusion and fission causes loss of integrity and functions with the accumulation of damaged mitochondria and mitochondrial deoxyribose nucleic acid (mtDNA) that can halt energy production and induce oxidative stress. Mitochondrial derived reactive oxygen species (ROS) can mediate redox signaling or, in excess, causing activation of inflammatory proteins and further exacerbate mitochondrial deterioration and oxidative stress. ROS have a deleterious effect on many cellular components, including lipids, proteins, both nuclear and mtDNA and cell membrane lipids producing the net result of the accumulation of damage associated molecular pattern (DAMPs) capable of activating pathogen recognition receptors (PRRs) on the surface and in the cytoplasm of immune

Cancer, Inflammation & Cellular energetics



Cancer, Inflammation & Cellular energetics





we still
agree that

Sugar is bad!

REVIEW

Open Access

Effects of hyperglycemia on the progression of tumor diseases



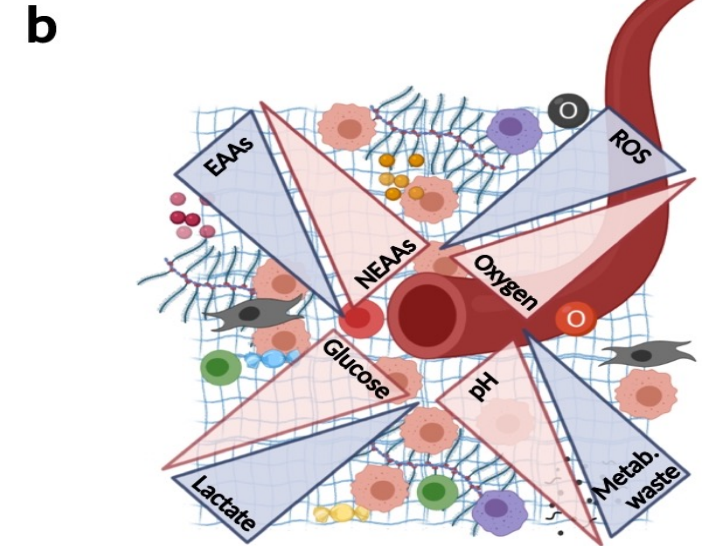
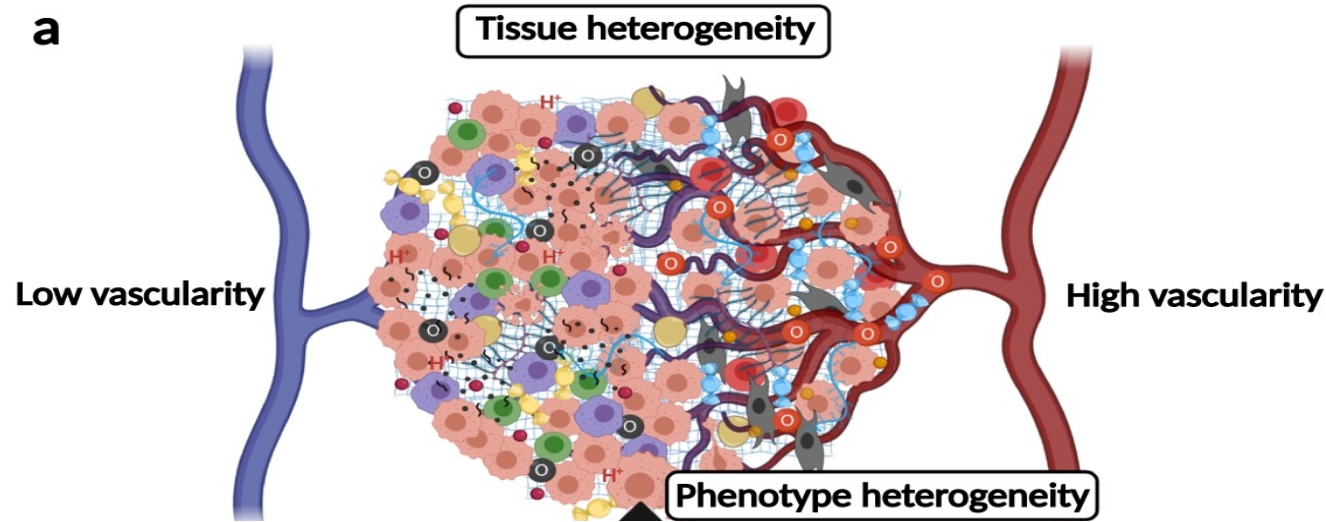
Wenjie Li^{1†}, Xuehui Zhang^{2†}, Hui Sang¹, Ying Zhou¹, Chunyu Shang¹, Yongqing Wang^{2,3*} and Hong Zhu^{1*}

Abstract

Malignant tumors are often multifactorial. Epidemiological studies have shown that hyperglycemia raises the prevalence and mortality of certain malignancies, like breast, liver, bladder, pancreatic, colorectal, endometrial cancers. Hyperglycemia can promote the proliferation, invasion and migration, induce the apoptotic resistance and enhance the chemoresistance of tumor cells. This review focuses on the new findings in the relationship between hyperglycemia and tumor development.

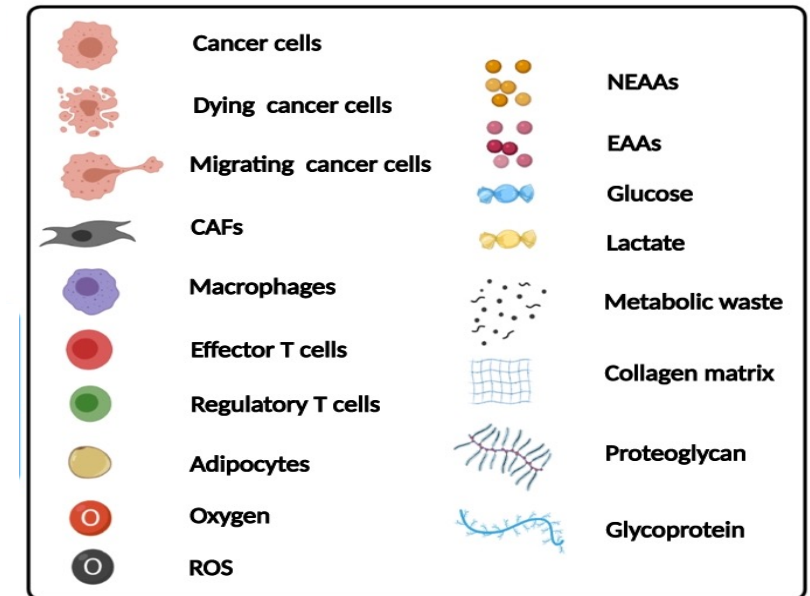
Keywords: Hyperglycemia, Tumor cells, Correlation, Mechanism, Progress

Tumor Microenvironment



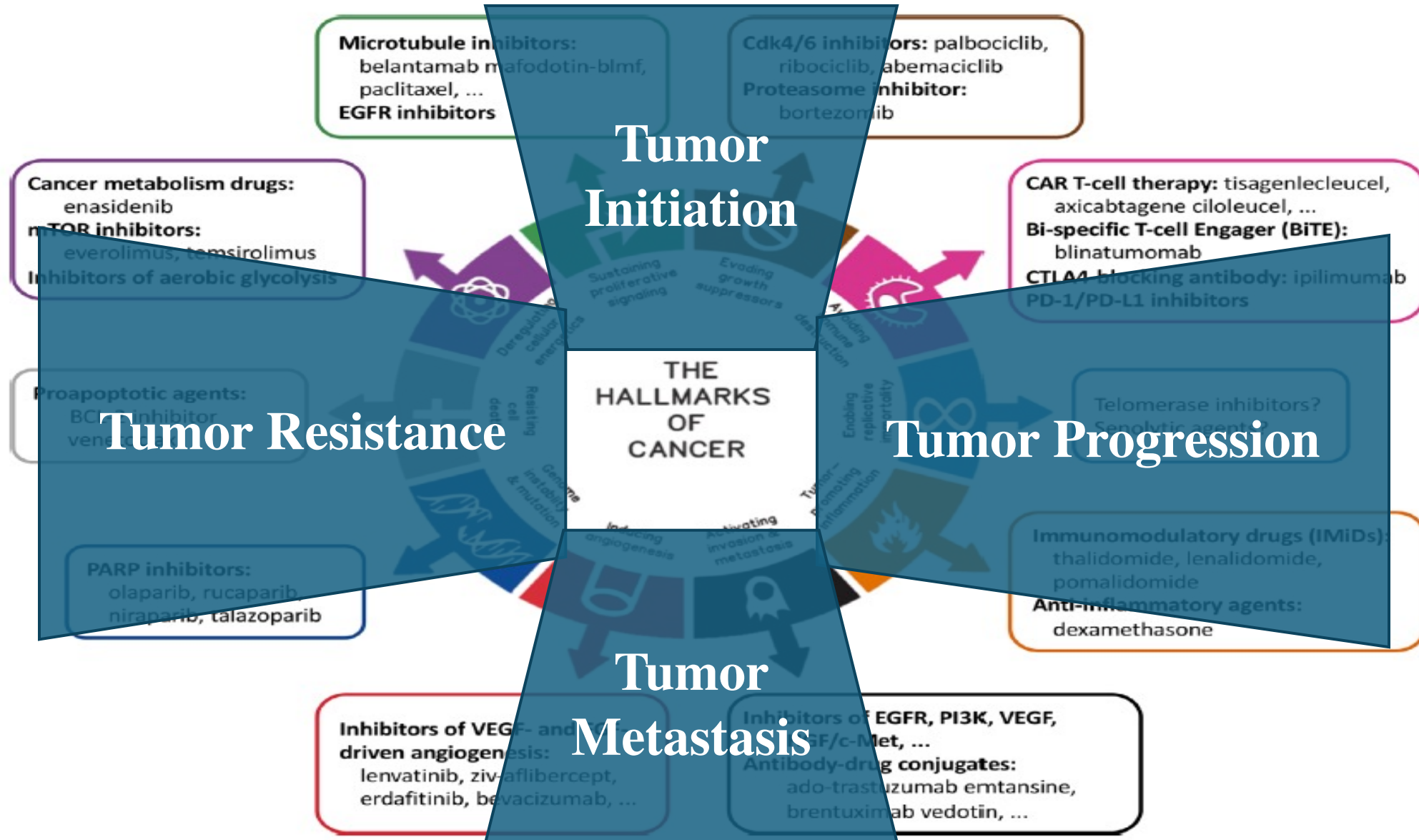
• Cancer Stem Cells Characteristics

- The ability to self-renew
- Self-sufficient
- Promote inflammation
- Resistant to chemotherapeutic drugs
- Not influenced by anti-growth signals
- Not regulated by normal cell functions including apoptosis
- Sustained by angiogenesis and flawed cellular [energy](#)



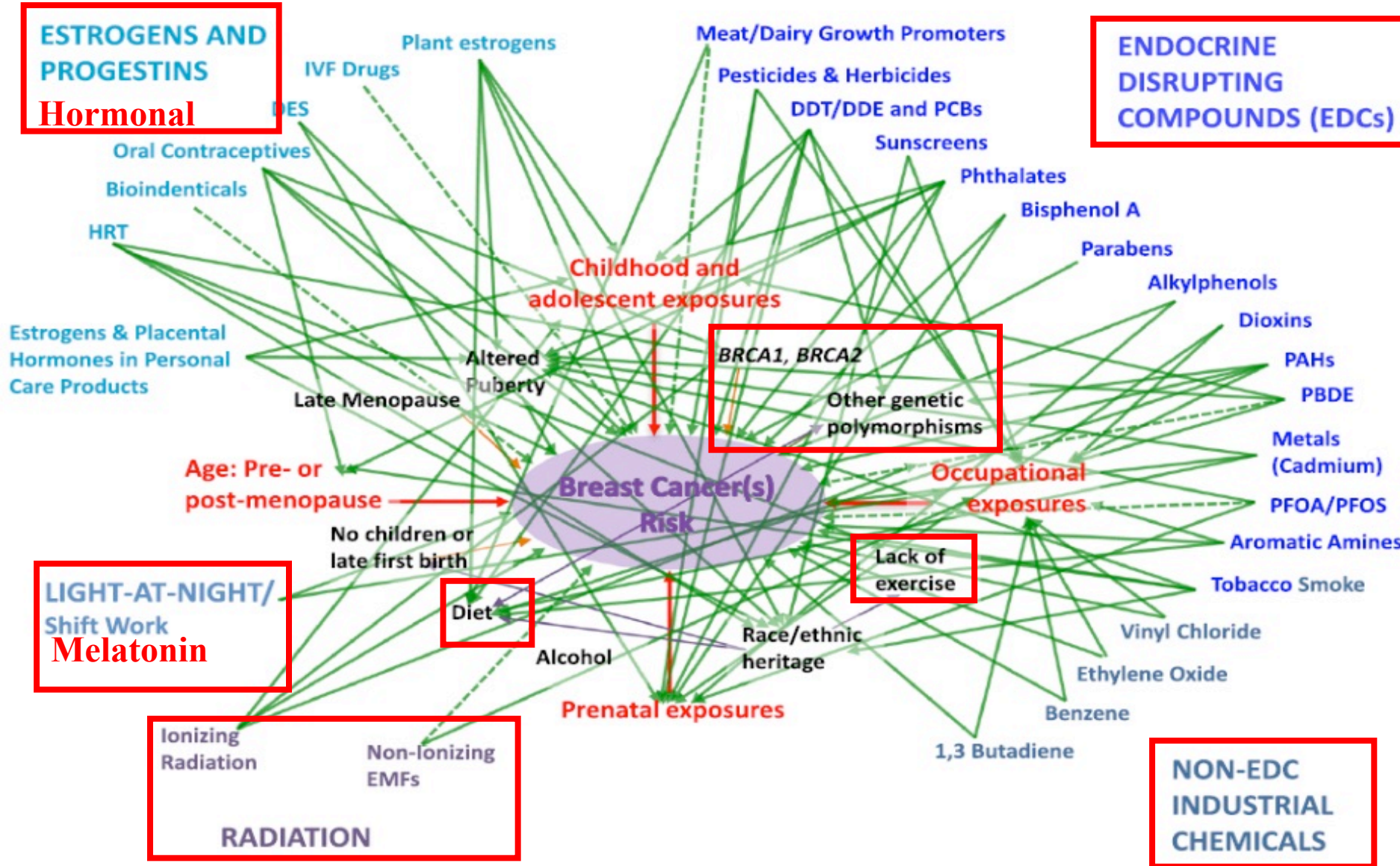


Tumor Microenvironment ... Which cells are we killing?





Tumor Microenvironment ... Which cells are we killing?



State of the evidence 2017: an update on the connection between breast cancer and the environment. *Environ Health*. 2017 Sep 2;16(1):94.

FDA approved Treatments for Breast cancer according to Pathology & Stage



- Abraxane (Paclitaxel Albumin-stabilized Nanoparticle)
- Afinitor (Everolimus) mTOR -I
- Arimidex (Anastrozole) AI
- Aromasin (Exemestane) AI
- Cyclophosphamide CTH
- Doxorubicin Hydrochloride CTH
- Epirubicin Hydrochloride CTH
- 5-FU (Fluorouracil Injection) CTH
- Faslodex (Fulvestrant) HR
- Femara (Letrozole) AI
- Gemcitabine Hydrochloride CTH
- Herceptin (Trastuzumab) MAB
- Ibrance (Palbociclib) CDK4/6 -I
- Ixempra (Ixabepilone) CTH
- Kadcyla (Ado-Trastuzumab Emtansine) MAB + CTH
- Keytruda (Pembrolizumab) MAB
- Kisqali (Ribociclib) CDK4/6 -I
- Lapatinib Ditosylate TKI
- Lynparza (Olaparib) PARP-I (BRCA mut)
- Methotrexate Sodium CTH
- Nerlynx (Neratinib Maleate) TKI
- Perjeta (Pertuzumab) MAB
- Piqaar (Piquris) PIK3-I
- Plimparib Tosylate) PARP-I (BRCA mut)
- Provera (Megestrol Citrate) HR
- Taxotere (Docetaxel) CTH
- Tecentriq (Atezolizumab) MAB
- Tepadina (Thiotepa) CTH
- Trodelyv (Sacituzumab Govitecan-hziy) Topo2I-I
- Tucatinib TKI
- Verzenio (Abemaciclib) CDK4/6-I
- Vinblastine Sulfate CTH
- Xeloda (Capecitabine) CTH
- Zoladex (Goserelin Acetate) HR

Who takes What, Why & When?

<https://www.cancer.gov/about-cancer/treatment/drugs/breast>

Host Microenvironment ...Which cells are we reviving?



First:

- Optimize sugar levels in the body (insulin)
- Clean the body from innards: toxins, bacteria, viruses
(Immunological burden)
- Optimize spiritual beliefs and mental clarity
- Optimizing “The Recovery Fundamentals”

Then:

- Target genetic pathways → locally and systemically:
 - Nutraceuticals : oral & IV
 - HBOT, Hyperthermia, PDT, etc

Do you want to block genes and Target Pathways?

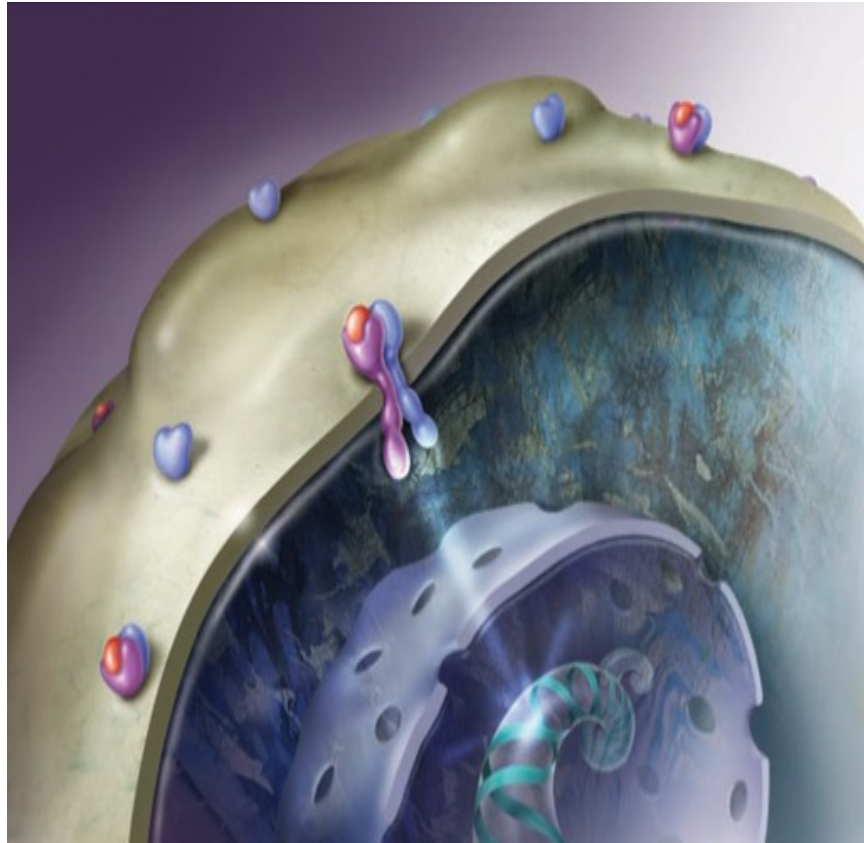


- - **Cancer Genetics:** (*analyzed in tissue biopsy*)
- *e.g BRCA, TP53, HER2, ALK, PI3K/AKT, EGFR, PD-1*

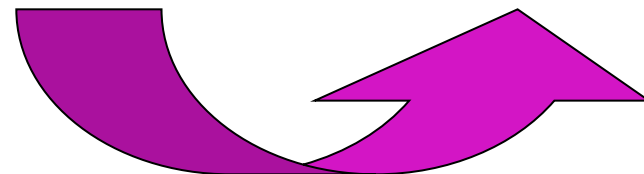
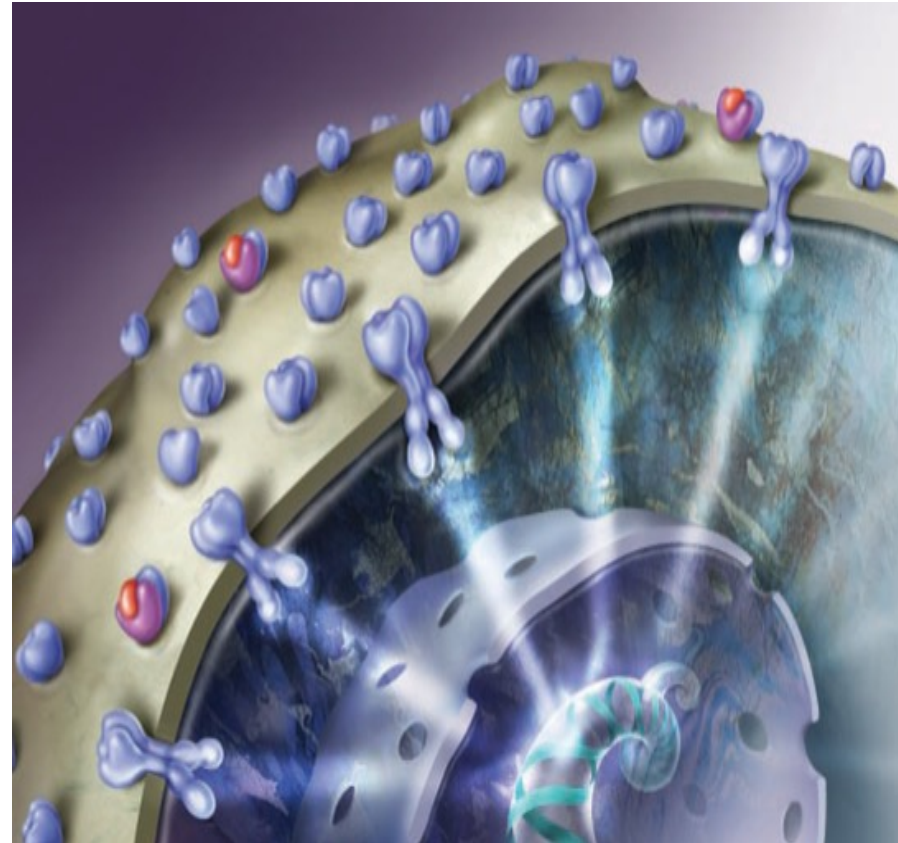
Examples of Cancer Genetics HER2-*neu* Gene (ERBB2)



Normal HER2 Expression
20 000 receptors/cell



HER2 Over Expression
2 000 000 receptors/cell



HER2 Amplification

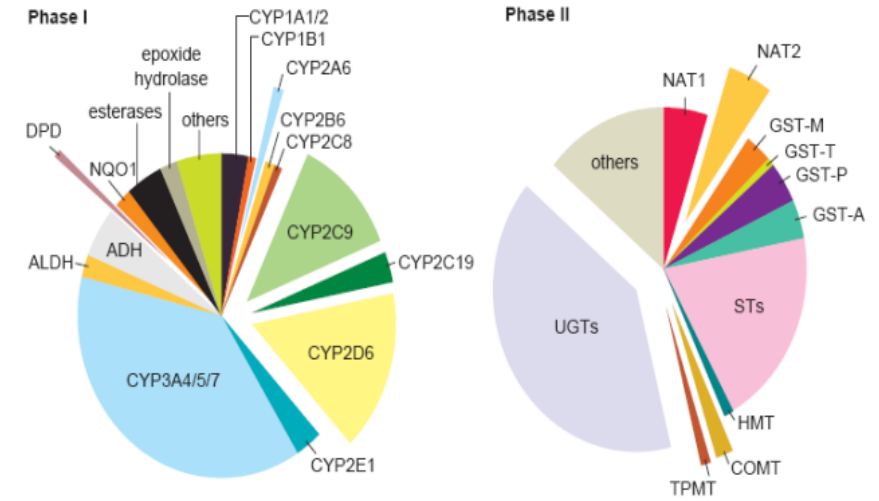


Do you want to block genes and Target Pathways?

- **Cancer – Genetic mutations:** (analyzed in tissue biopsy)
- e.g BRCA, TP53, HER2, ALK, PI3K/AKT, EGFR, PD-1

- **Host- Blueprint/Software Genetics:**

- ***DNA Protection, Damage & Repair.*** (Vulnerability)
- ***Inflammation & Anti-oxidant protection*** (FIRE)
- ***Methylation & Detoxification genes*** (Toxic Burden & Drug metabolism)
- ***Hormone Support & Neurotransmitters*** (Messengers)
- ***Macronutrient Metabolism*** (The Right Diet)
- ***Cardiovascular Health, Blood health*** (Blood Viscosity,Oxygen,Stamina)





Combined effect of *CYP1B1*, *COMT*, *GSTP1*, and *MnSOD* genotypes and risk of postmenopausal breast cancer

Conclusion: Individual susceptibility to breast cancer incidence may be increased by combined effects of the high-risk genotypes in *CYP1B1*, *COMT*, and *MnSOD* estrogen metabolic genes.

Significant associations were observed among women with two high-risk genotypes in ***CYP1B1* and *COMT*** (OR, 2.0; 95% CI, 1.1 to 3.5) and two high-risk genotypes in ***COMT* and *MnSOD*** (OR, 2.0; 95% CI, 1.0 to 3.8), compared to those with low-risk genotypes.

Blueprint/software genetics for **Optimizing Treatments**

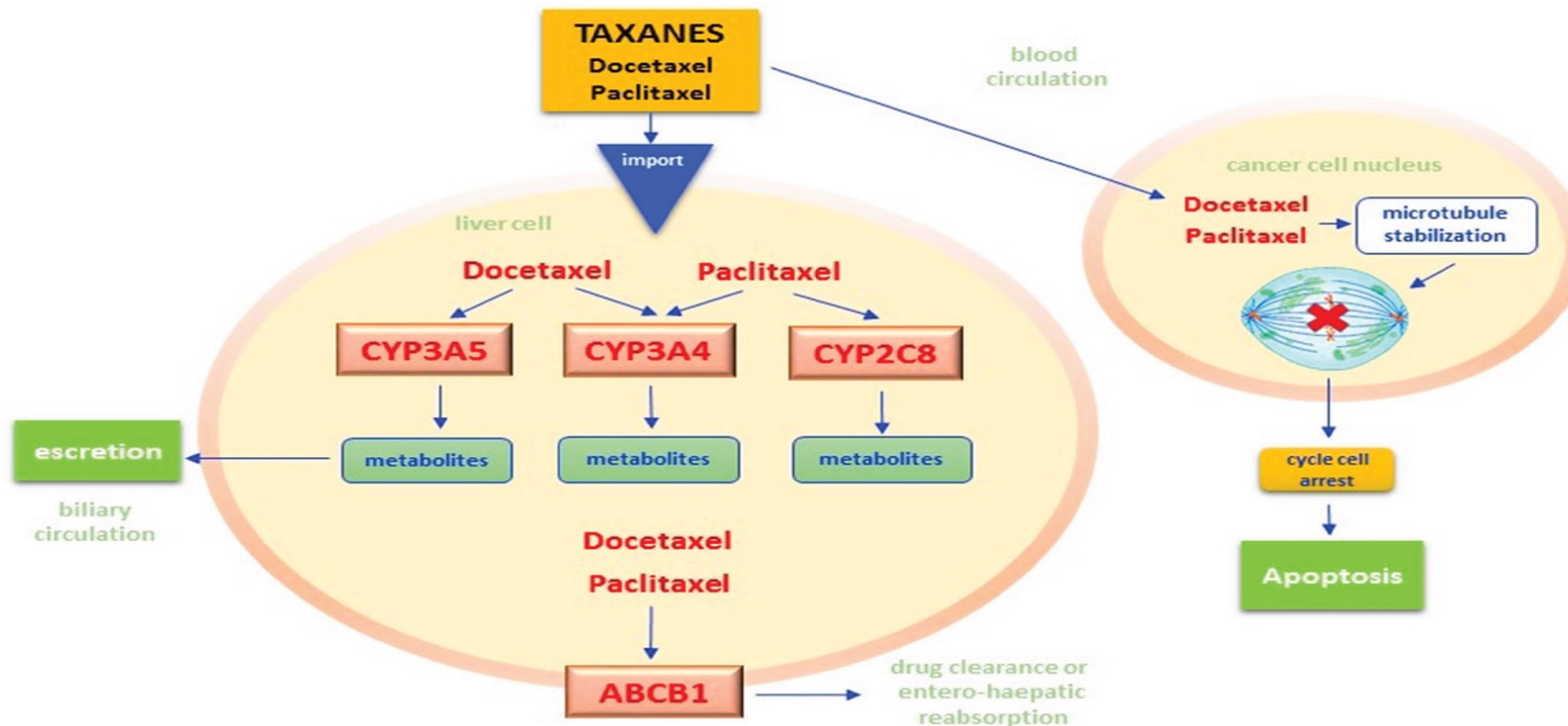


www.oncotarget.com

Oncotarget, 2018, Vol. 9, (No. 38), pp: 25355-25382

Review

SNPs in predicting clinical efficacy and toxicity of chemotherapy: walking through the quicksand



*Metabolized
&
Eliminated
Properly?*

Role of Nutraceuticals / Supplements?



YOU cannot supplement yourself out of a bad diet!



Need a quick good start







Nature is here to Help...



Hindawi
BioMed Research International
Volume 2022, Article ID 5425485, 18 pages
<https://doi.org/10.1155/2022/5425485>

Review Article

Plants in Anticancer Drug Discovery Mechanism to Chemoprevention

Arif Jamal Siddiqui ¹, Sadaf Jahan ², Ritu Sir
Syed Amir Ashraf ⁶, Andleeb Khan ⁷, Ranjay
Santharaj Balakrishnan ^{8,9}, Riadh Badraoui 

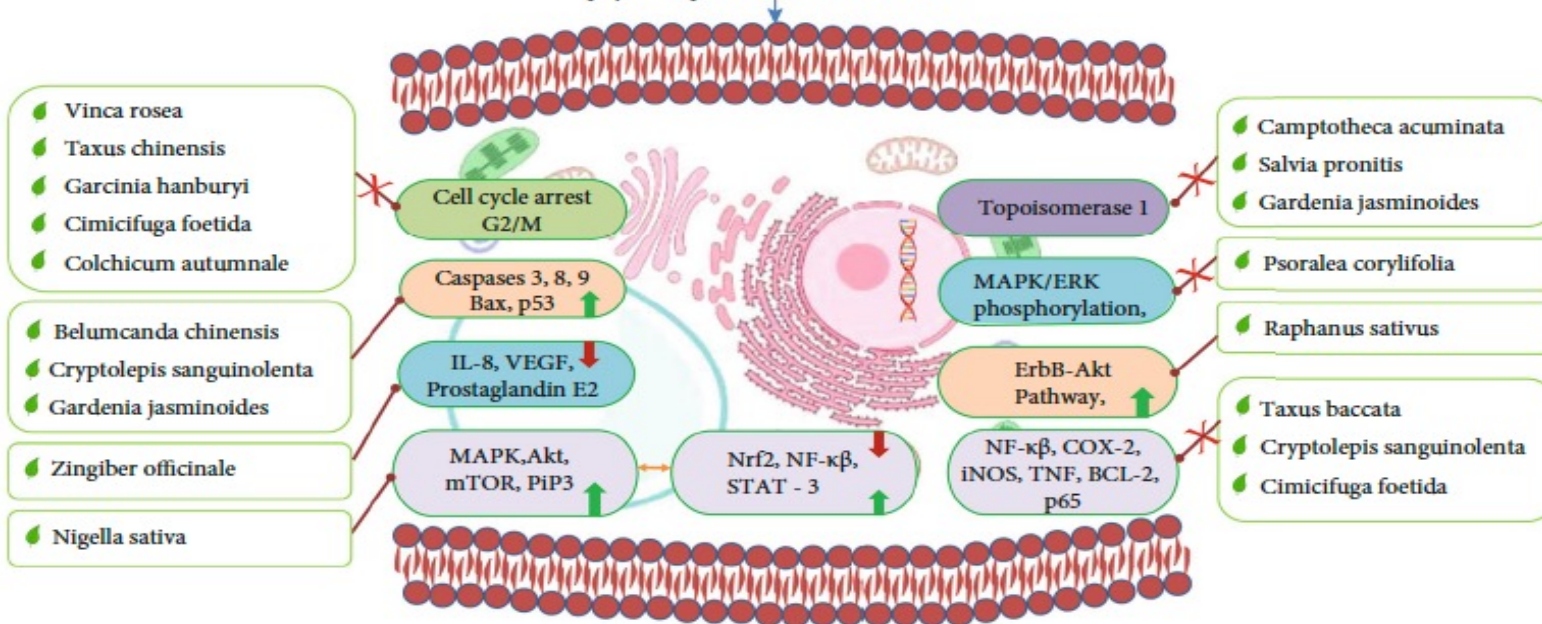
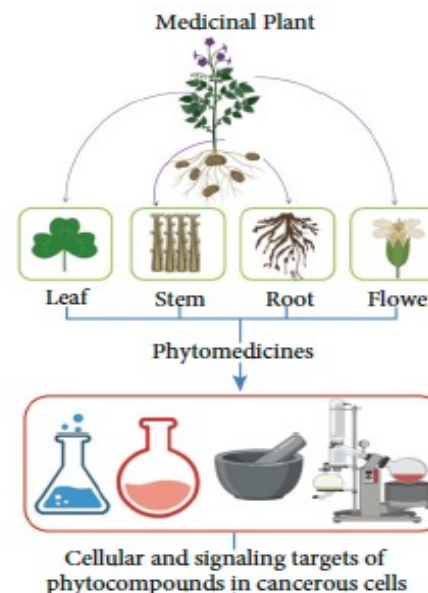
¹Department of Biology, College of Science, University of Hail, Hail, Saudi Arabia

²Department of Medical Laboratory Sciences, College of Applied Medical Sciences, Al-Majmaah 11952, Saudi Arabia

³Department of Environmental Sciences, School of Earth Sciences, Central Board of Secondary Education, New Delhi, India

⁴Faculty of Applied Sciences and Biotechnology, Shoolini University of Technology and Management, Himachal Pradesh, India

⁵Department of Biotechnology, University Institute of Biotechnology, Chandigarh State Hwy, Punjab, India





Contents lists available at [ScienceDirect](https://www.sciencedirect.com)

Biomedicine & Pharmacotherapy

journal homepage: www.elsevier.com/locate/bioph

Review

Targeting cancer signaling pathways by natural products: Exploring promising anti-cancer agents

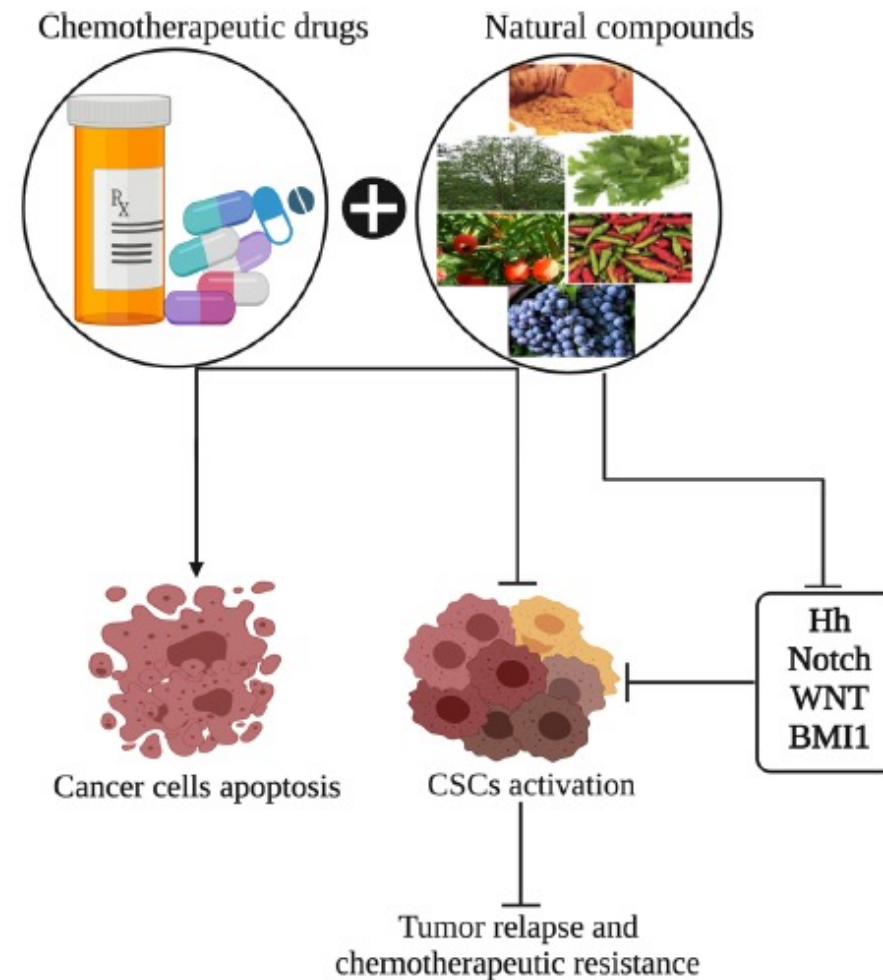
Sheema Hashem^{a,1}, Tayyiba Akbar Ali^{a,1}, Sabah Akhtar^{a,1}, Sabah Nisar^a, Geetanjali Sageena^b, Shahid Ali^c, Sharefa Al-Mannai^d, Lubna Therachiyil^{e,f}, Rashid Mir^g, Imadeldin Elfaki^h, Mohammad Muzaffar Mirⁱ, Farrukh Jamal^j, Tariq Masoodi^a, Shahab Uddin^e, Mayank Singh^k, Mohammad Haris^{a,l,m}, Muzafar Macha^{n,*}, Ajaz A. Bhat^{a,**}

^a Laboratory of Molecular and Metabolic Imaging, Sidra Medicine, Doha, Qatar

^b Keshav Mahavidyalaya, University of Delhi, New Delhi 110034, India

^c International Potato Center (CIP), Shillong, Meghalaya, India

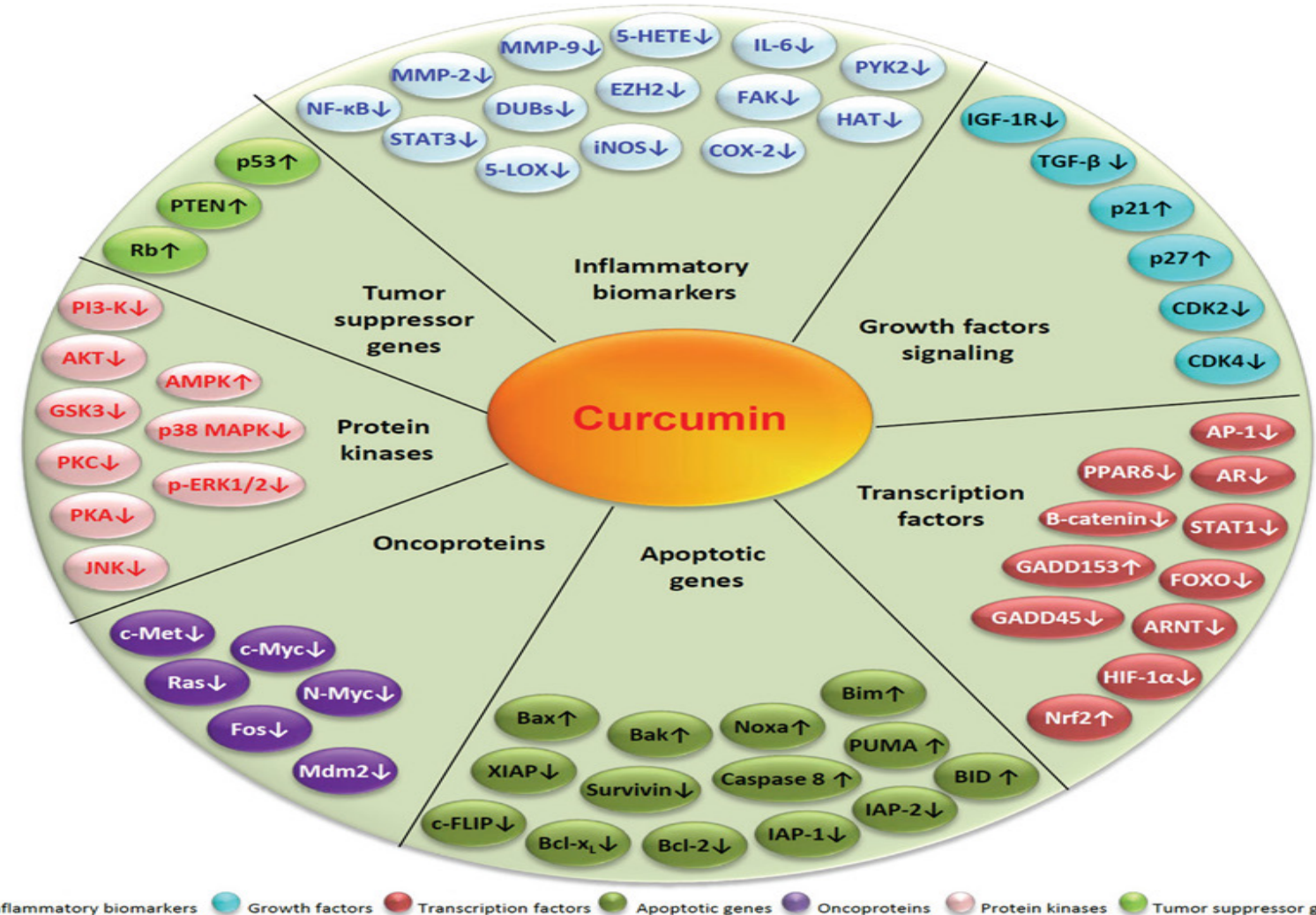
^d Division of Translational Medicine, Research Branch, Sidra Medicine, Doha 26999, Qatar





Nature is here to Help...

Curcumin



Targets CSC

- Optimizes Chemotherapy
- Targets CSCs
- Prevents invasion & metastases

Ramasamy et al. Cancer Cell Int (2015) 15:96

Combined with 5-FU or FOLFOX proved a superior therapeutic strategy for chemoresistant colon cancer

Curr Colorectal Cancer Rep (2014) 10:62–67

Curcumin & Resveratrol synergistically inhibit the growth of transformed cells & colon carcinogenesis.

Nutr Cancer 2009, 61(4): 544-53



Nature is here to Help...

Sulforaphane:

Targets CSC

TABLE 1: The epigenetic regulation of sulforaphane (SFN) in cancer.

Epigenetic mechanisms	Cancer types	Epigenetic functions	Target genes/ proteins	Anticancer effects	References
Histone acetylation	Prostate cancer cells (LnCaP and PC-3) and PC-3 cell xenografts	Inhibition of class I and II HDACs	Reactivation of p21 and Bax	Cell cycle arrest and apoptosis↑	[42, 45, 49]
	Colon cancer cells (HCT116)	Inhibition of HDAC3	CtIP: a critical DNA repair protein Acetylation of CtIP and its degradation	DNA damage and apoptosis↑	[43]
	Lung cancer cells (A549 and H1299) and A549 cell xenografts	Inhibition of HDAC activity	Reactivation of p21 and Bax	Cell growth↓ Apoptosis↑	[44]
Histone phosphorylation	Bladder cancer cells (RT4, J82, and UMUC3) and UMUC3 cell xenografts	Inhibition of histone H1 phosphorylation	Increased PP1β and PP2A phosphatase	Carcinogenesis and progression↓	[55]
DNA methylation	Prostate cancer cells (LNCap)	Decreased expression of DNMT1 and 3b	Restoration of cyclin D2	Cancer cell death↑	[59]
	Human breast cancer cells (MCF-7 and MDA-MB-231)	Inhibition of DNMT1 expression	Restoration of P21, PTEN, and RARbeta2	Cell growth arrest and apoptosis↑	[61]
	Human breast cancer cells (MCF-7 and MDA-MB-231)	Decrease in DNMT1 and 3a expression and activity	Downregulation of hTERT expression	Apoptosis↑	[58]
	Cervical cancer cells (HeLa)	Inhibition of DNMT3b activity	Upregulation of RARβ, CDH1, DAPK1 and Bax	Cell cycle arrest and apoptosis↑	[60]

Anticancer Activity of Sulforaphane: The Epigenetic Mechanisms and the Nrf2 Signaling Pathway. Oxidative Medicine and Cellular Longevity. Volume 2018, Article ID 5438179

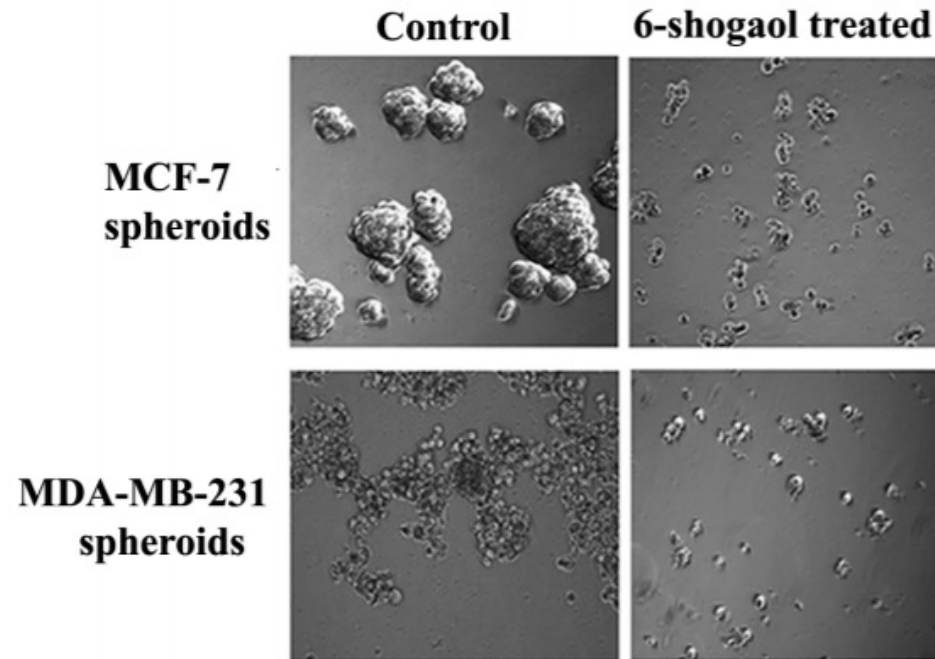


Nature is here to Help...

6 Shoagal (GINGER)

Targets CSC

A



6-Shogaol Inhibits Breast Cancer Cells and Stem Cell-Like Spheroids by Modulation of Notch Signaling Pathway and Induction of Autophagic Cell Death. PLoS One. 2015 Sep 10;10(9):e0137614.

Nature is here to Help...



Targets CSC

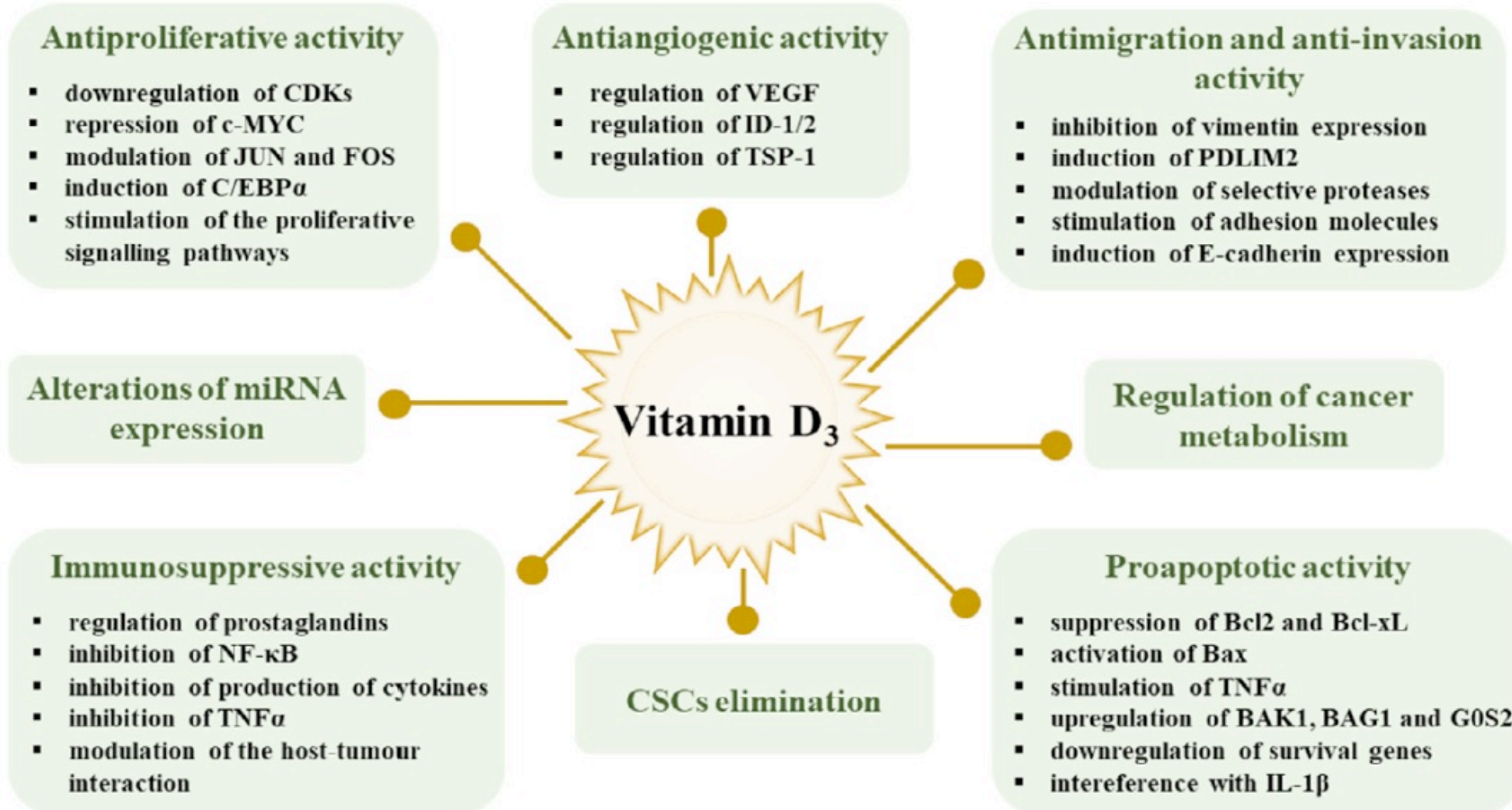


Fig. 1. Anticancer activity of vitamin D₃ in solid tumors.



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Flaxseed

Clinical Cancer Research

Advanced

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Cancer Therapy: Clinical

Dietary Flaxseed Alters Tumor Biological Markers in Postmenopausal Breast Cancer

Lilian U. Thompson, Jian Min Chen, Tong Li, Kathrin Strasser-Weippl, and Paul E. Goss

DOI: 10.1158/1078-0432.CCR-04-2326 Published May 2005

- Dietary flaxseed has the potential to reduce tumor growth in patients with breast cancer.
- Reductions in Ki-67 labeling index (34.2%; $P = 0.001$)
- Reductions in c-erbB2 expression (71.0%; $P = 0.003$)
- Increase in apoptosis

Anti- Her2-neu!



The Effect of Flaxseed in Breast Cancer: A Literature Review

Ana Calado^{1*}, Pedro Miguel Neves², Teresa Santos^{3,4,5} and Paula Ravasco²







¹Instituto de Ciências da Saúde, Universidade Católica Portuguesa, Lisbon, Portugal, ²Faculdade de Medicina da Universidade de Lisboa, Hospital Universitário de Santa Maria and Centro de Investigação Interdisciplinar em Saúde da Universidade Católica Portuguesa, Lisbon, Portugal, ³Faculdade de Motricidade Humana (FMH) (Projecto Aventura Social-Social Adventure Team), Universidade de Lisboa, Lisbon, Portugal, ⁴Instituto de Saúde Ambiental (ISAMB)

- α -linolenic acids in flaxseed have been shown to be able to suppress growth, size, and proliferation of cancer cells & also to promote breast cancer cell death
- The intake of **flaxseed combined with tamoxifen** can **reduce tumor size to a greater extent than taking tamoxifen alone.**



Review

Mechanistic Insights into the Pharmacological Significance of Silymarin

Karan Wadhwa ¹, Rakesh Pahwa ², Manish Kumar ³, Shobhit Kumar ⁴, Prabodh Chander Sharma ⁵, Govind Singh ¹, Ravinder Verma ⁶, Vineet Mittal ¹, Inderbir Singh ⁷, Deepak Kaushik ^{1,*} and Philippe Jeandet ^{8,*}

¹ Department of Pharmaceutical Sciences, Maharshi Dayanand University, Rohtak 124001, Haryana, India

² Institute of Pharmaceutical Sciences, Kurukshetra University, Kurukshetra 136119, Haryana, India

³ M.M. College of Pharmacy, Maharishi Markandeshwar (Deemed to be University), Ambala 133207, Haryana, India

⁴ Department of Pharmaceutical Technology, Meerut Institute of Engineering and Technology (MIET), Meerut 250005, Uttar Pradesh, India

⁵ Department of Pharmaceutical Chemistry, Delhi Pharmaceutical Sciences and Research University, New Delhi 110017, Delhi, India

⁶ Department of Pharmacy, G.D. Goenka University, Sohna Road, Gurugram 122103, Haryana, India

⁷ Chitkara College of Pharmacy, Chitkara University, Rajpura 140401, Punjab, India

⁸ Research Unit-Induced Resistance and Plant Bioprotection, University of Reims, EA 4707-USC INRAe 1488, SFR Condorcet FR CNRS 3417, 51687 Reims, France

* Correspondence: deepkaushik1977@gmail.com (D.K.); philippe.jeandet@univ-reims.fr (P.J.)



Tablet/ Supplement	Amount	Breakfast	Lunch	Dinner	Bedtime	Notes
10% in 400iu gamma tocopherol vit E			yes			Protect Liver if using high dose green tea (EGCG)
Asprin	75 mg		Yes			Synergistic with Omega 3
Berberine	500mg					. Stop 3 days b4 scan and 2 days after
Black seed Oil	1000mg	Yes	Yes	Yes		
Broccoli Ultra (sulforaphane)	600 mg	Yes		Yes		
Chaga Mushrooms	2 capsules	Yes		Yes		Take magnesium citrate to stop kidney stones
Coq 10 ubiquinol	100 mg					
Curcumin	500 mg	Yes		Yes		
Ellagic Acid			Yes			Take approx. 4 hours
Garcinia (hydroxy citrate)	1000 mg	Yes				
EGCG	400mg	Yes	Yes	Yes		
Indole – 3 Carbinol 13c (DIM)	300 mg		Yes	Yes		
Lions' mane	400 mg		Yes			
Loratadine	10mg		Yes			
Magnesium citrate	300 mg	Yes				
Melatonin	120 mg					
Milk thistle	500mg x 2	Yes				
Omega 3 EPA	700mg x2	yes				
Pectasol power I teaspoon						each up to three times a day
Quercetin	1000 mg					with resveratrol
R alpha lipoic acid	300 mg					Stop 24 hour before chemo
Reishi						
Resveratrol 500mg						
Vit d3 K2	3000 IU					
Wheat germ (metatrol)	2 ta					One month on one month off expensive not currently taking
Bio. Me Prebio PHGG	1 teasp					Take first thing
Block buster all clear	2 Tablet	yes		yes		Take on empty stomach
Zinc	60mg	Yes				
Vitamin C	30000mg	Yes		Yes		Pulse weekly
Lactoferrin	250mg	yes				
Seabuck thorn oil omegs 7	300 mg	yes				Stopped taking this week
Pysllum husk	1400 mg			yes		
Haritaki	1000 mg	Yes	Yes	Yes		Take on empty stomacj
Fucoidia	500mg	yes		tes		
Bio Kult		yes				
Atresimin	500mg		Yes			
Akermansia	400mg		yes			

What to take?... Why?...
When?... The right dose!

• I have metformin /LDN /propranolol /simvastatin/ mebendazole / doxycycline here at home but currently not taking any.

Nature is here to Help...



Seminars in Cancer Biology 73 (2021) 45–57



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journal homepage: www.elsevier.com/locate/semcancer



Effects of caloric restriction on immunosurveillance, microbiota and cancer cell phenotype: Possible implications for cancer treatment



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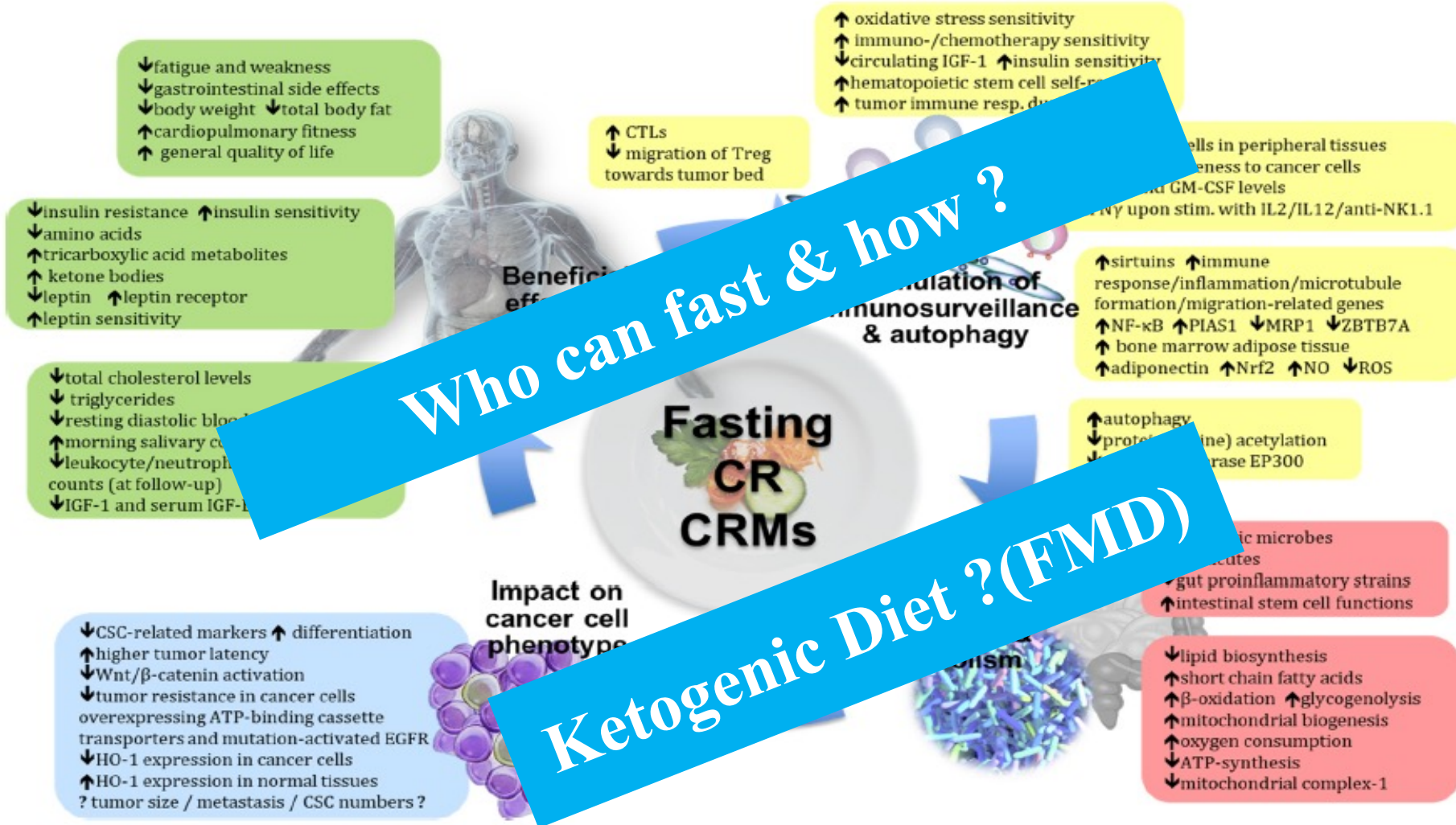
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F. Pistollato et al. Effects of caloric restriction on immunosurveillance, microbiota and cancer cell phenotype: Possible implications for cancer treatment. Seminars in Cancer Biology 73 (2021) 45–57

Nature is here to Help...

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What do you want to do exactly?!



G O - T O - I T

- **Individualized, Tailored & Integrative Cancer treatments are crucial.**
- **Analyzing Genes, how they are expressed in each patient.**
- **Optimizing their lifestyle modifiable factors.**
- **Looking at the Person & not the Tumor.**

More to come about Metabolic Health & Cancer Recovery



Thank you 😊 !

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