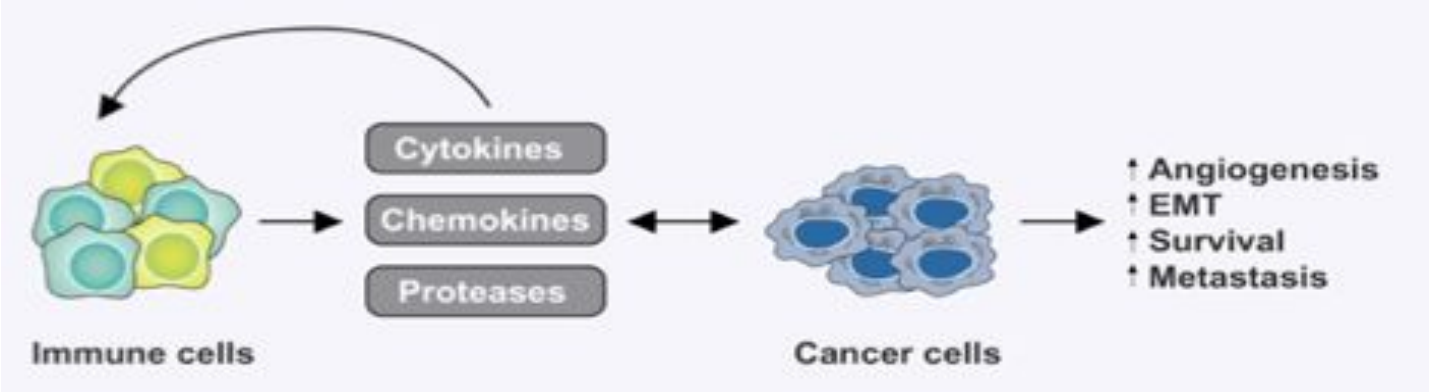
ONCO-INFLAMMATION

Targeting Tumor Promoting Inflammation with Selected Nutriceuticals and Phytochemicals

Dr. Nalini Chilkov, L.Ac., OMD, Founder
American Institute of Integrative Oncology
info@aiiore.com



FOUNDATIONS OF INTEGRATIVE ONCOLOGY

Online Professional Training

Deliver Health & Change Lives

Instant Access

SURVIVOR THRIVER CARE PLANNER

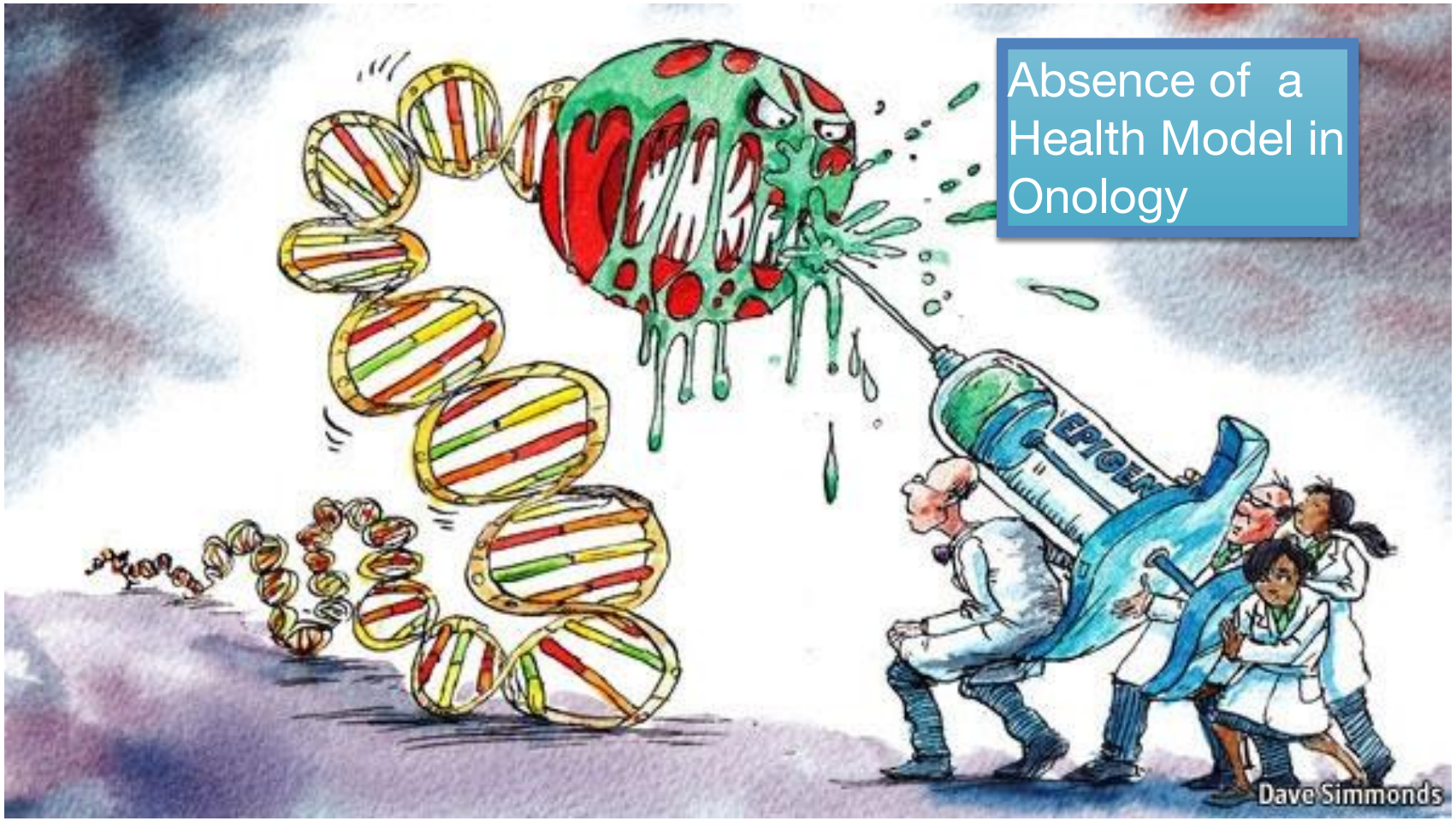
Support the Health of Cancer Patients
and Watch Your Practice Grow

OUTSMART CANCER SYSTEM®

OUTSMART CANCER®
SYSTEM

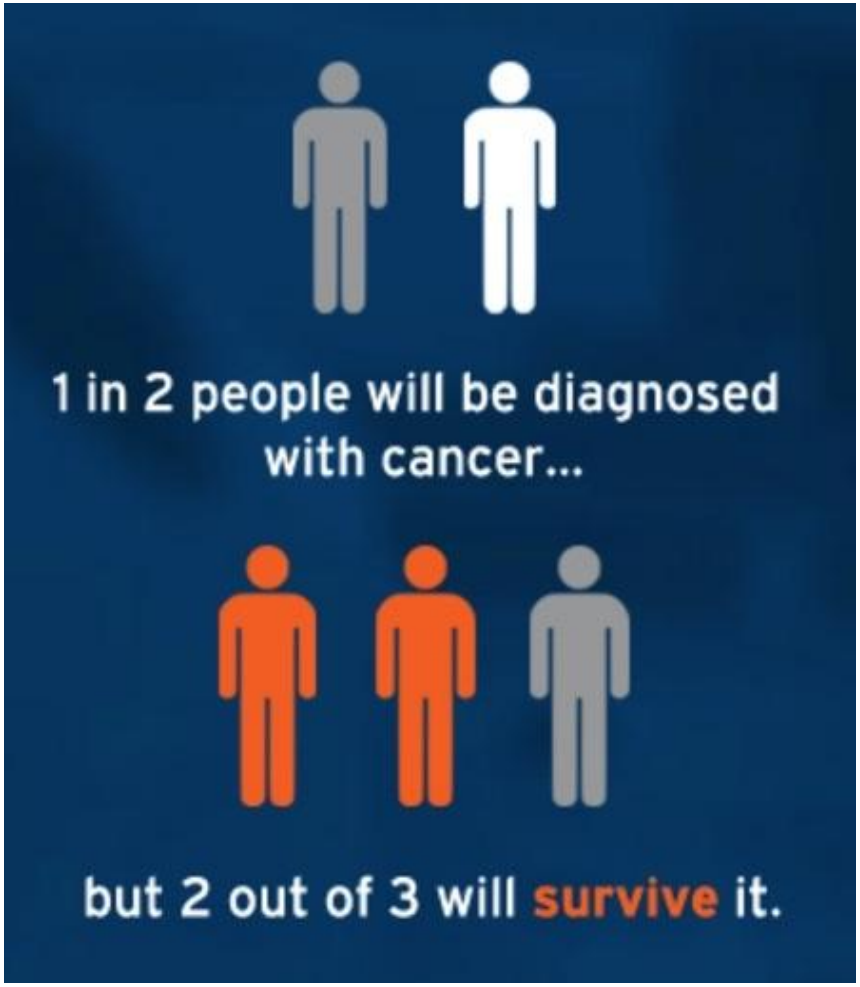
THE LANDSCAPE OF CANCER

What If Every Cancer Patient Had a HEALTH PLAN and not just a disease plan???

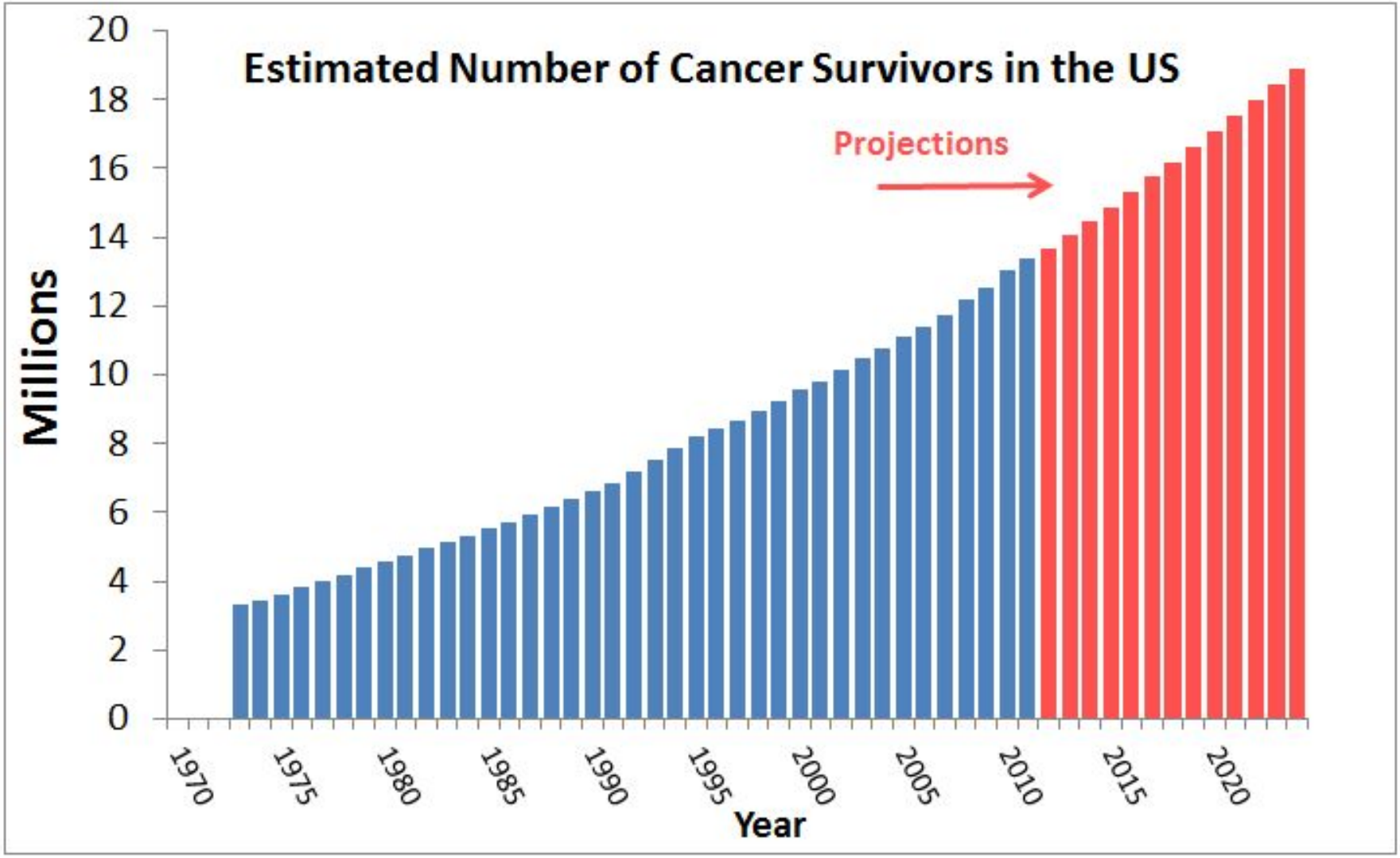


…**the number of new cases of cancer is set to nearly double by the year 2050** from 1.36 million in 2000 **to almost 3 million in 2050** due to aging & the growing US population.

Much of this increase in the number of new cancers will be in the 65-to-84-year age group, and this will reach a peak at 2030, as the baby-boomer generation ages…



Surveillance Epidemiology and End Results (SEER) National Cancer Institute



[1] DeSantis C, Chunchieh L, Mariotto AB, et al. (2014). Cancer Treatment and Survivorship Statistics, 2014. CA: A Cancer Journal for Clinicians. In press.

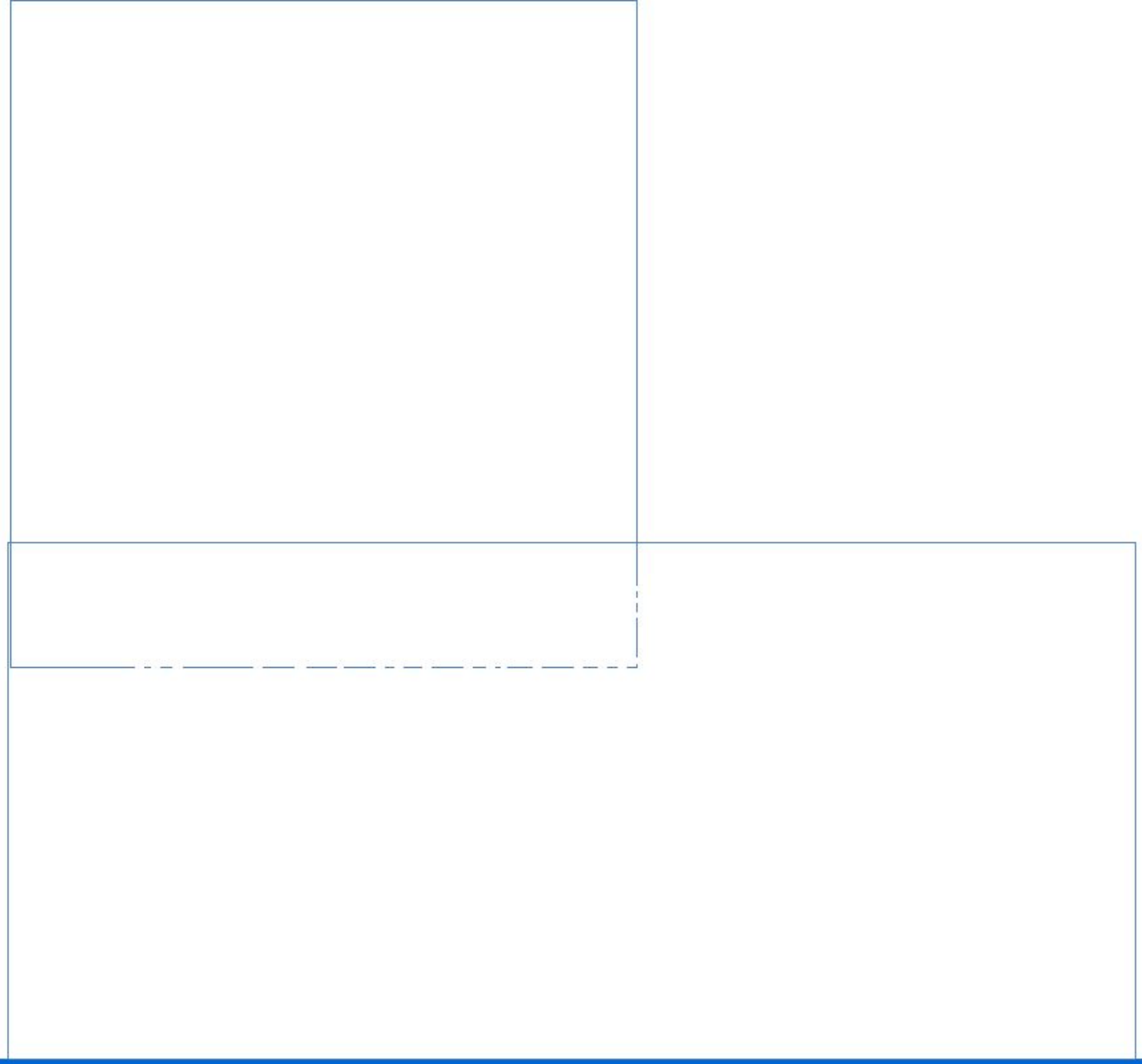
Oncologists' and Primary Care Physicians' Awarenessof Late and Long-Term Effects of Chemotherapy:

Implications for Care of the Growing Population of Survivors

J Oncol Pract Mar 1, 2014:e29-e36

Primary Care Providers **awareness** of late and long term effects of chemotherapy **was limited.**

Education for all providers caring for the growing population of cancer survivors **is needed."**



OUTSMART CANCER®

CONTROL THE TUMOR
NOURISH THE PATIENT

Cancer Journey & Cancer Survivorship

- Transforming Outcomes & Prognosis
- Enhancing Oncology Treatments
- Managing Short Term and Long Term Adverse Effects
- Providing A Health Model

The Tumor Microenvironment Contributes to Every Aspect of Carcinogenesis

Current Cancer Drug Targets, 2014, 14, 30-45

Role of Inflammation-Associated Microenvironment

Let the Oncologist
be the
Disease Expert

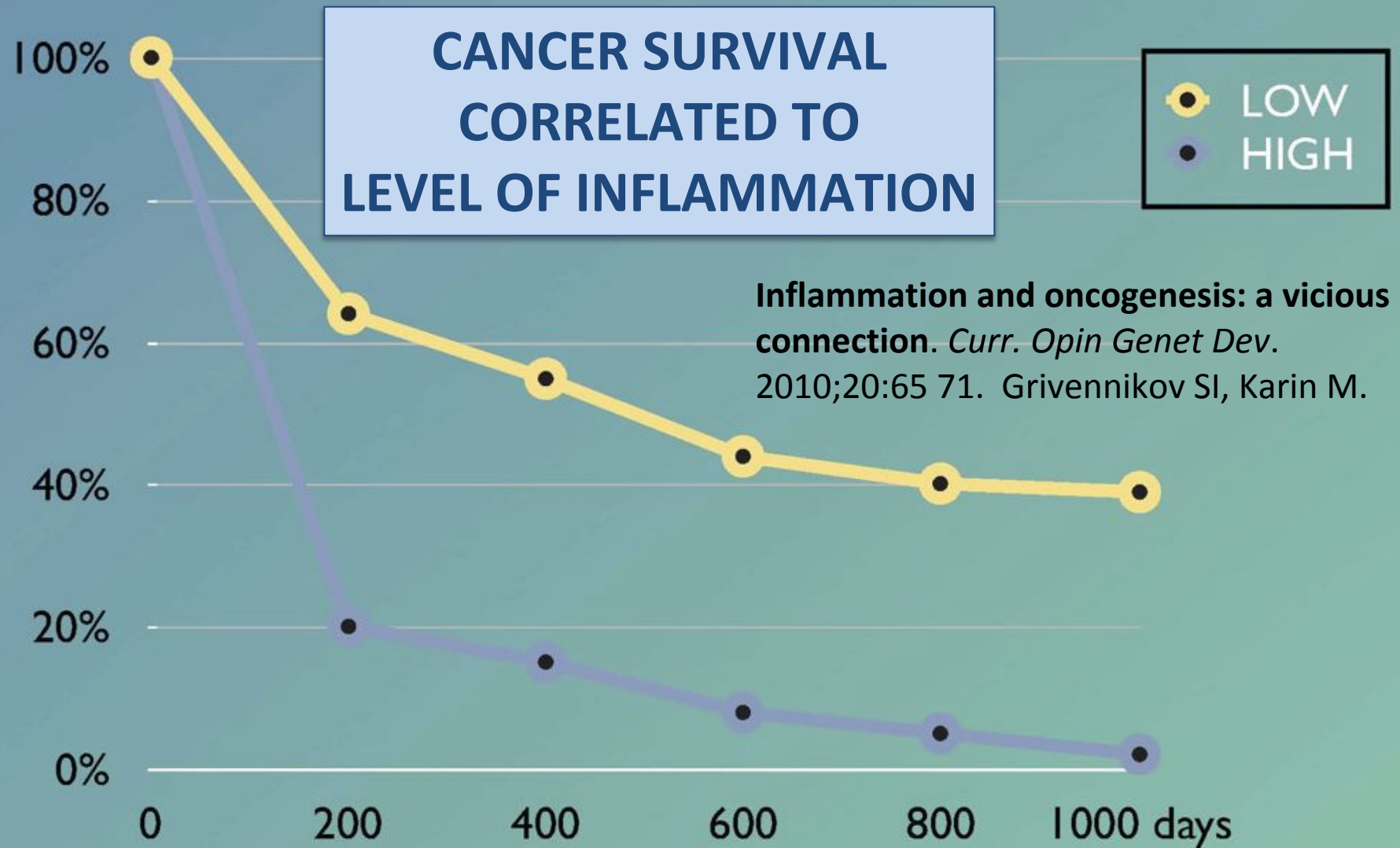
You Can be the
HEALTH EXPERT
Cancer Patients
Are Searching For

OUTSMART CANCER®
SYSTEM

ONCO
INFLAMMATION

AMERICAN INSTITUTE OF
INTEGRATIVE ONCOLOGY
RESEARCH & EDUCATION™

CHRONIC INFLAMMATION
TUMOR ASSOCIATED INFLAMMATION
THERAPY INDUCED INFLAMMATION



Inflammation and oncogenesis: a vicious connection. *Curr. Opin Genet Dev*. 2010;20:65 71. Grivennikov SI, Karin M.

AMERICAN INSTITUTE OF INTEGRATIVE ONCOLOGY
RESEARCH & EDUCATION

THE HALLMARKS of CANCER

Hallmarks of Cancer: The Next Generation

Hanahan, Douglas et al.
Cell , Volume 144
Issue 5 , 646 – 674

INCREASED CANCER RISK

INFLAMMATORY SYNDROMES	INFECTIONS
Cervicitis, Pharyngitis	Human Papilloma Virus (Cervical & Head and Neck CA)
Inflammatory Bowel Syndrome, Colitis	Intestinal Dysbiosis (CRCA)
Hepatitis	Hepatitis Virus B and C (Hepatic CA)
Cholecystitis Pancreatitis, Endometriosis	Parasitic Infections Liver Flukes(Cholangiocarcinoma) Schistosoma (UBCA)
Diabetes, Obesity	Epstein Barr Virus (Lymphoma)
Gastritis, Esophagitis	H.Pylori (Burkitt's Lymphoma)

Integr Cancer Ther. 2005 Mar 4(1)3-4 Inflammation, COX2 Inhibitor & Cancer. Block,K et al

INFLAMMATION and TUMORIGENESIS

Bio Pharm
Vol. 72, Issue
11 30 Nov 2006
1605–1621
Inflammation
and cancer:
How hot is the
link?
Bharat B.
Aggarwal

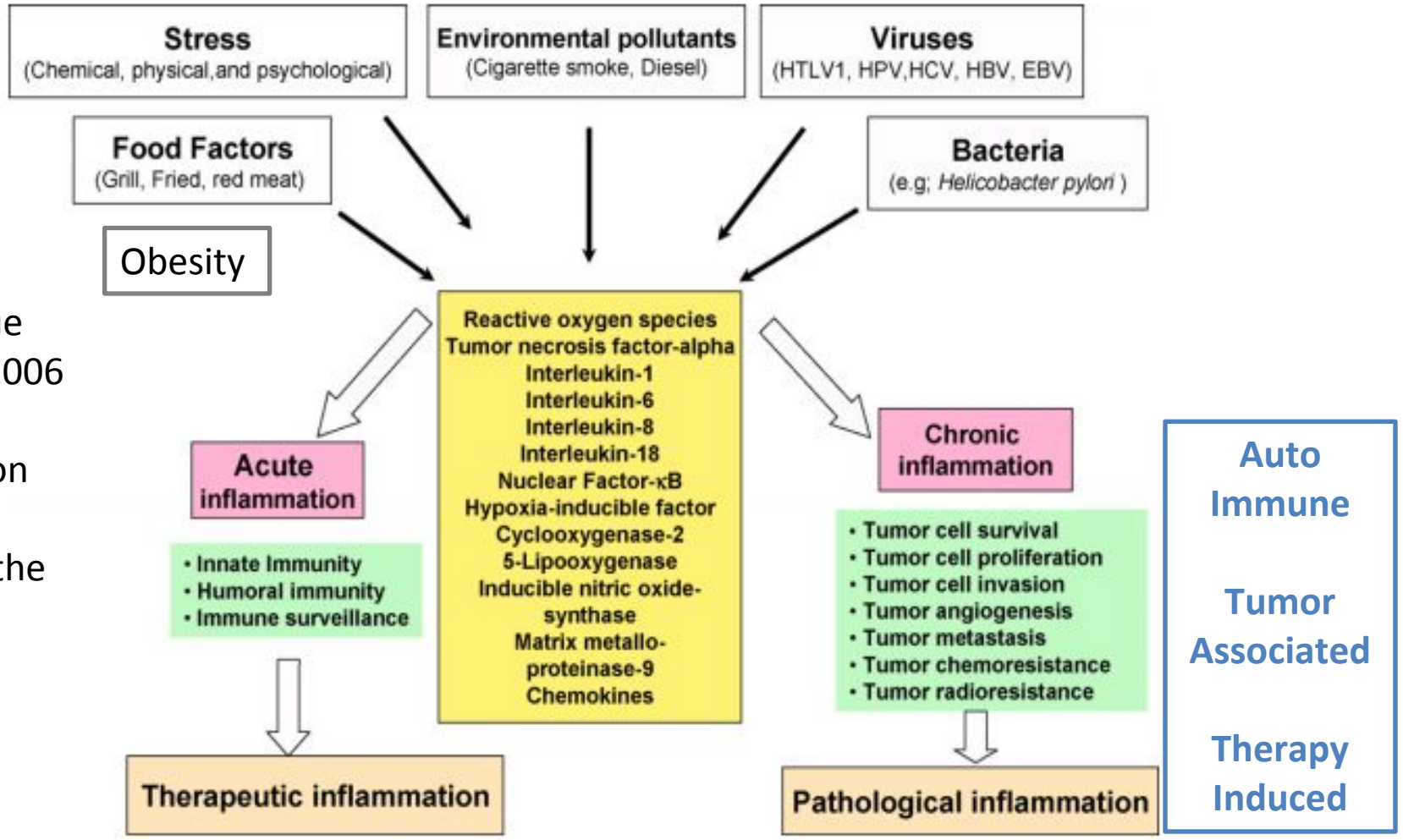
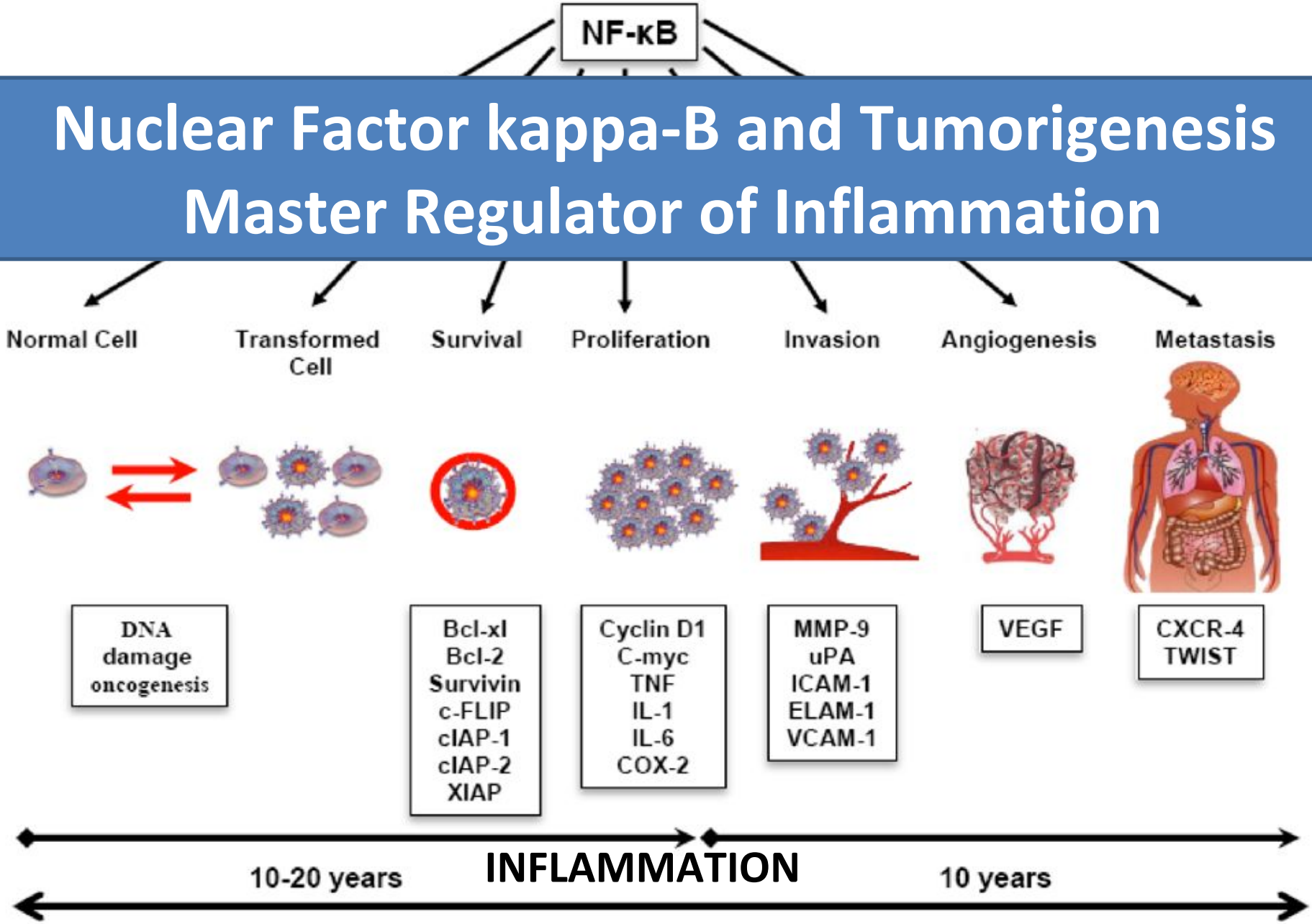


Fig. 1 – Different faces of inflammation and its role in tumorigenesis.

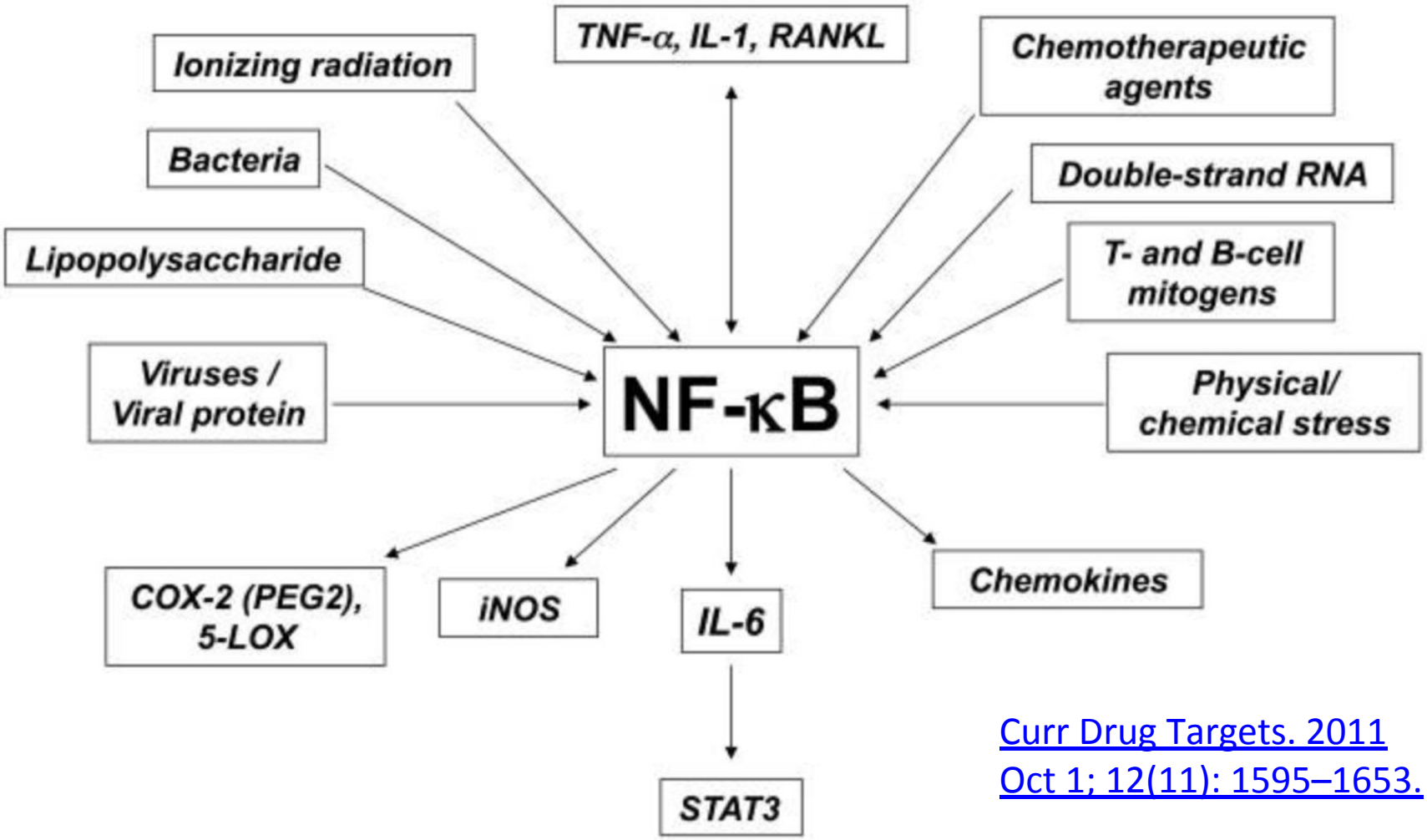
ELIMINATION **EQUILIBRIUM** **ESCAPE**

Nuclear Factor kappa-B and Tumorigenesis
Master Regulator of Inflammation



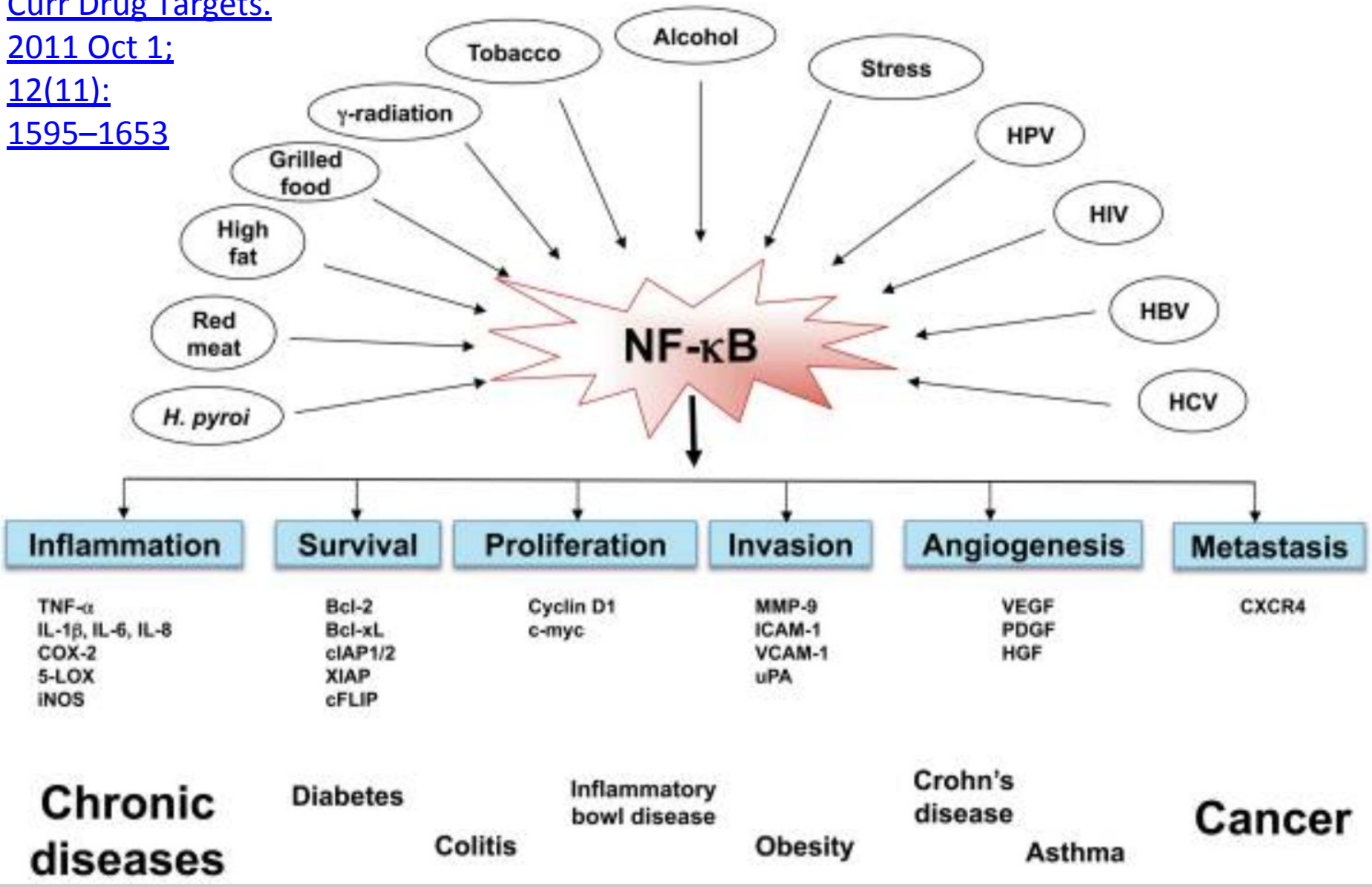
Curr Opin Pharmacol. 2009 Aug ; 9(4): 351–369. Aggarwal.B et al

Inflammatory Network

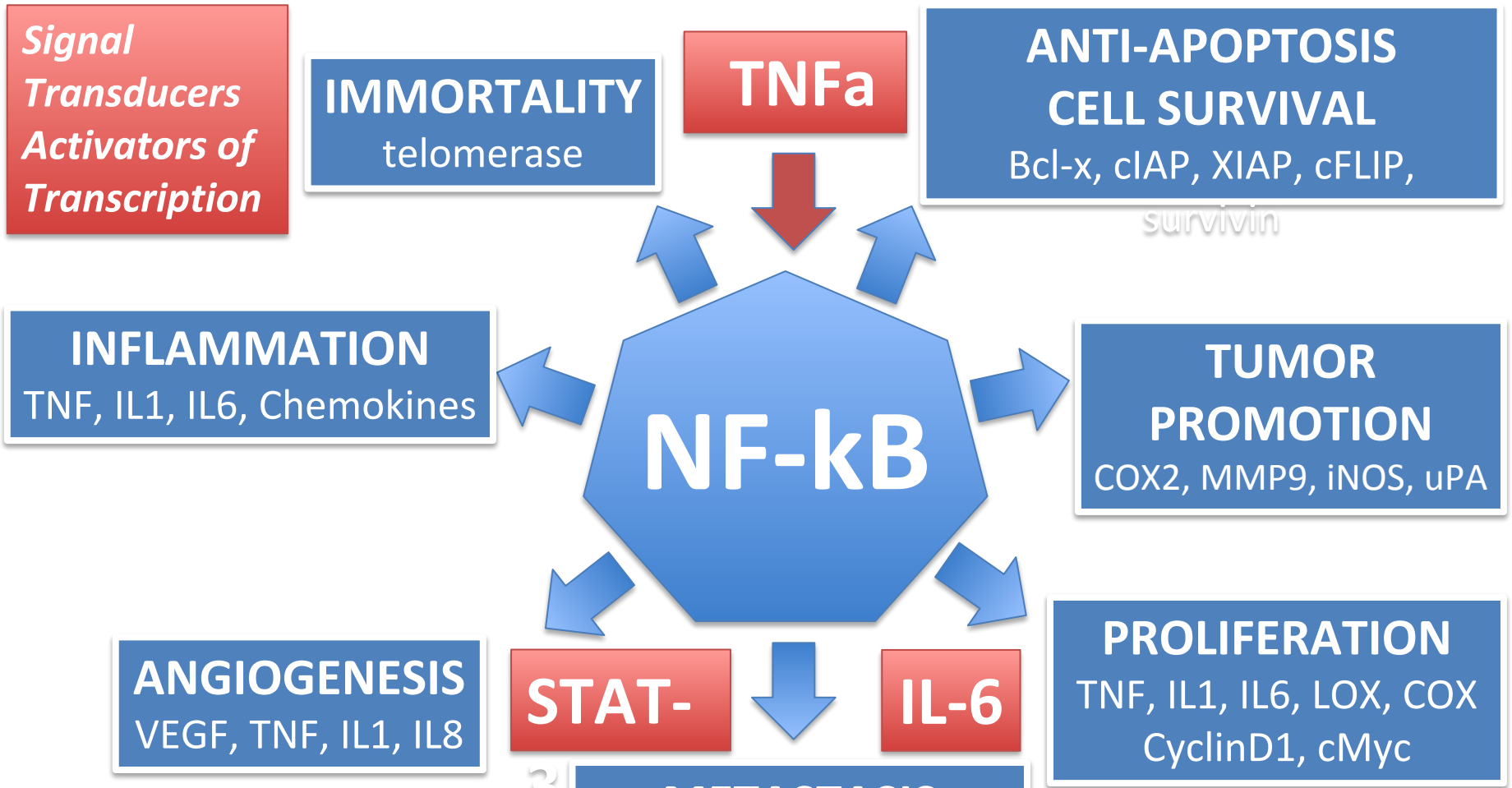


Curr Drug Targets. 2011 Oct 1; 12(11): 1595–1653.

[Curr Drug Targets. 2011 Oct 1; 12(11): 1595–1653]



Nuclear Factor kappa-B and Tumorigenesis
Master Regulator of Inflammation



Bio PharmVol 72, Issue 11 30 Nov 2006 1605–1621 Bharat B. Aggarwal

OUTSMART CANCER®
SYSTEM

PROGNOSTIC BIOMARKERS

SYSTEMIC IMMUNE INFLAMMATION PROGNOSTIC BIOMARKERS

 Risk | Mortality

 Overall Survival | Progression Free Survival

	HIGH RISK LEVEL
• C-Reactive Protein	≥1.0-3.0 mg/L
• Neutrophil : Lymphocyte Ratio	≥1.7-4.0
• Platelet : Lymphocyte Ratio	≥120-170
• Albumin: Globulin Ratio	≤1.1

Other Contributors to Systemic Inflammation

- Diabetes-Hyperinsulinsim HgbA1c ≥5.2 IL6 IL8 IL1
- Obesity- Body Mass Index ≥30 Cp CA-125 Ferritin
- Autoimmune Syndromes Vitamin D3 ≤ 55mg/ml

CBC + CMP
Prognostic Biomarkers

POOR PROGNOSIS

NLR NEUTROPHIL:LYMPHOCYTE RATIO	**> 2.4**
PLR PLATELET:LYMPHOCYTE RATIO	**>118**
MLR MONOCYTE:LYMPHOCYTE RATIO	**> 0.26**
TRL TUMOR RELATED LEUCOCYTOSIS	
Absolute Leukocyte (WBC)Count	**>9000**
CRP/ALB CRP:ALBUMIN RATIO	**>0.095**
SII SYSTEMIC IMMUNE INDEX	**> 475**

CRP : ALBUMIN RATIO

CRP/Alb >0.095 POOR PROGNOSIS

Higher levels are associated with

- Larger tumor size
- Poorer differentiation
- Deeper tumor invasion
- More lymph node metastasis
- More distant metastasis
- More advanced TNM stage
- Early identification of cachexia

J Palliat Med. 2019 Jun 12. doi: 10.1089/jpm.2019.0102. **C-Reactive Protein/Albumin Ratio Is an Independent Prognostic Predictor of Survival in Advanced Cancer Patients Receiving Palliative Care.** Zhang J

Systemic Immune Index

PRE-TREATMENT PROGNOSIS

OS Overall Survival

PFS Progression Free Survival

PFMS Progression Free Metastatic Free Survival

> 475 Poor Prognosis

higher = more inflammation

SII= platelet count x NLR count

Curr Opin Pharmacol. 2009 August ; 9(4): 351 369.

Inflammation and Cancer: How Friendly Is the Relationship For Cancer Patients? B.B. Aggarwal

CRP is emerging as an important prognostic marker in a wide variety of cancers.

C-reactive protein (CRP), an NF-κB-regulated gene product has been **linked with prognosis of cancers of the breast, colon, kidney , ovary, lung and stomach, and multiple myeloma, melanoma, and non-Hodgkin's lymphoma.**

Prognostic Role of Neutrophil-to-Lymphocyte Ratio in Solid Tumors: A Systematic Review and Meta-Analysis

JNCI J Natl Cancer Inst (2014) 106(6): dju124 doi:10.1093/jnci/dju124

Prognostic
Progression Free Survival
Overall Survival
NLR>4 Poor Prognosis

OUTSMART CANCER®
SYSTEM

ONCO-INFLAMMATION MATERIA MEDICA

ONCO INFLAMMATION

2-4 g/d

Green Tea Catechins (EGCG)	NFkB,TNFa,IL1B,COX-2
Rz.Curcuma longa	COX 2, NFkB, TNFa
Curcuminoids	IL6, IL1,CRP, IL8,LOX5
O-3 FA EPA DHA	COX 2, LOX5, PGE2, IL1, IL6, TNFa, CRP
Probiotics	TNFa, IL6, IL 10, NFkB
Rdx. Scutellaria baicalensis	TNFa IL-6 IL-1 NFkB
Baicalein polyphenol	COX-2
Berberine alkaloid	IL-6 TNFa IL1
Ganoderma polysaccharide	TNFa, IL1B1,IL6
Resveratrol	COX1, COX2, NFkB, IL1, IL6, IL8
Andrographis paniculata	NF-κB TNF-α IL-6 iNOS
andrographolide	COX-2 nrf2








ONCO INFLAMMATION

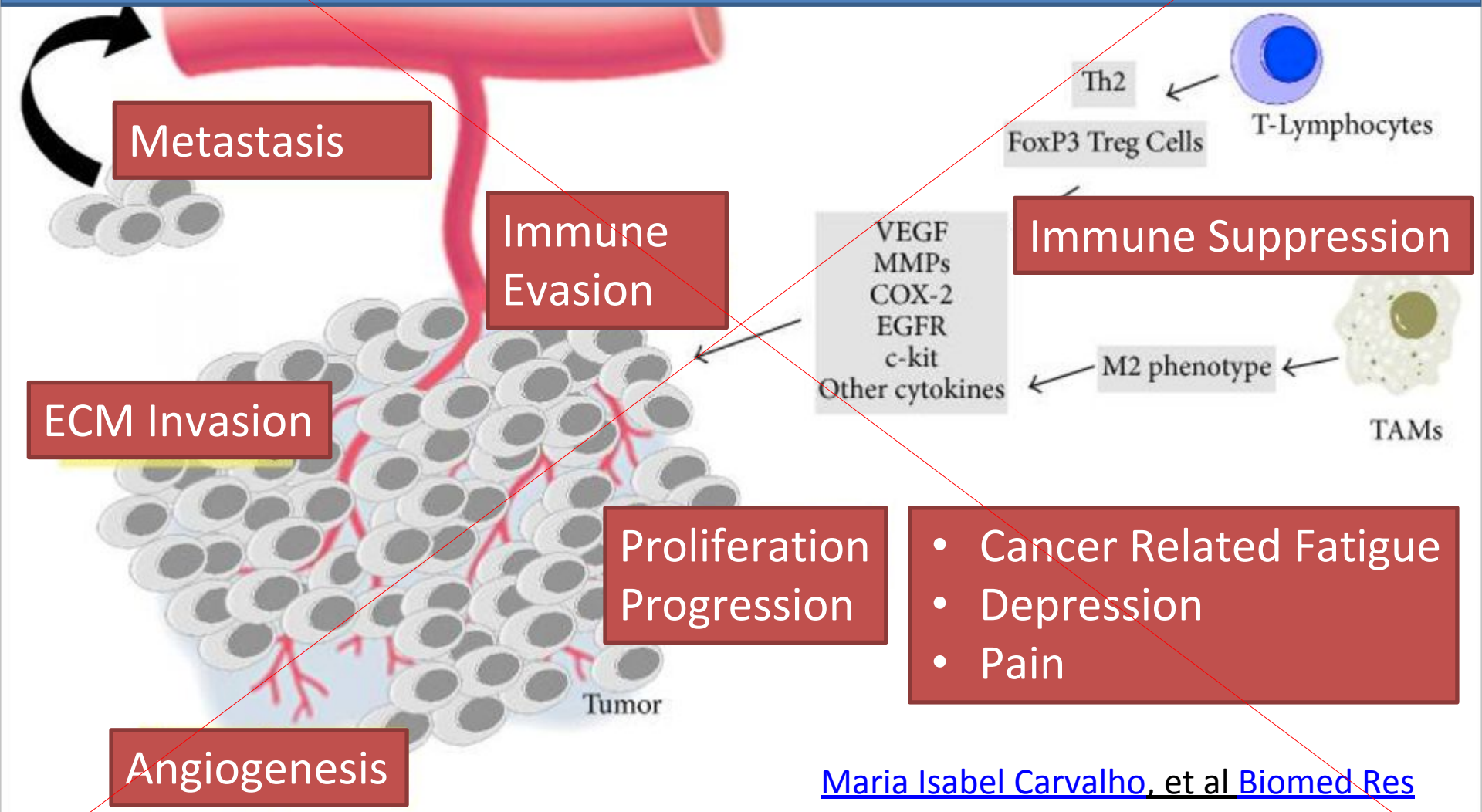
2-4 g/d

Bosewellia serrata (Alpha Keto Boswellic Acids)	LOX 5 Leukotrienes
Sulphoraphanes (Cruciferae) (Di-IndoleMethane, Glucoraphannin)	nrf2 NFkB
Rz. Zingiber officinalis (gingerols, zerumbone)	COX1 COX2 IFNg
H.Andrographis paniculata (andrographolide)	NFkB nrf2
Fl.Tanacetum parthenium (parthenolide)	NFkB TNFa IL1B
Rdx. Panax ginseng (ginsenosides)	NFkB TNFa IL1 IL6 IL8 IFNg






Cancer Related Inflammation: Carcinogenesis, Evasion of Immune Surveillance, ECM Remodeling, Angiogenesis, Metastasis, Proliferation and Progression.



Maria Isabel Carvalho, et al Biomed Res Int. 2016; 2016: 4917387.

ANDROGRAPHIS PANICULATA
Chuan Xin Lian
Andrographolide

Andrographolide, a diterpenoid lactone, and the major active principle isolated from the plant *A. paniculata*, has been shown to possess a **strong anti-inflammatory activity through suppression of inflammatory mediators such as NF-κB, TNF-α, IL-6, MIP-2, iNOS and COX-2**

Curr Drug Targets. 2011 Oct 1; 12(11): 1595–1653. Identification of Novel Anti-inflammatory Agents from Ayurvedic Medicine for Prevention of Chronic Diseases"Reverse Pharmacology" and "Bedside to Bench" Approach
Bharat B. Aggarwal,* Sahdeo Prasad, et al

Grape Resveratrol Increases Serum Adiponectin and Downregulates Inflammatory Genes 1000-5000mg/day

Significantly decreases inflammatory factors

High-sensitivity C-reactive protein (-26%,p = 0.03),
Tumor necrosis factor-α (-19.8%, p = 0.01),
Plasminogen activator inhibitor type 1 (-16.8%, p = 0.03)
Interleukin-6/interleukin-10 ratio (-24%, p = 0.04)
Decreases fasting glucose, insulin, A1C and insulin resistance

Increases anti-inflammatory

Interleukin-10 (19.8%, p = 0.00)
Adiponectin (6.5%, p = 0.07)

World J Diabetes 2016 April 10; 7(7): 142-152 **Novel nutraceutic therapies for the treatment of metabolic syndrome** Esperanza Martínez-Abundis
Cardiovasc Drugs Ther. 2013 Feb;27(1):37-48 Tomé-Carneiro J.et al

Trends Pharmacol Sci. 2009 Feb;30(2):85-94.

Pharmacological basis for the role of curcumin in chronic diseases: an age-old spice with modern targets.

Aggarwal BB1, Sung B.

Curcumin mediates its anti-inflammatory effects through the **downregulation of inflammatory transcription factors (such as nuclear factor kappaB), enzymes (such as cyclooxygenase 2 and 5 lipoxygenase) and cytokines (such as tumor necrosis factor, interleukin 1 and interleukin 6**

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Risk | Mortality

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- Obesity- Body Mass Index ≥30 Cp CA-125 Ferritin
- Autoimmune Syndromes Vitamin D3 ≤ 55mg/ml

OMEGA-3 FATTY ACIDS EPA DHA

Down-regulate Inflammation

IL1 IL6 TNFa CRP

COX 2 LOX5 PGE2

2g-6g/day

Adv Food Nutr Res. 2012;65:211-22

Health benefits of n-3 polyunsaturated fatty acids: eicosapentaenoic acid and docosahexaenoic acid.

Siriwardhana N et al

…ω-3 polyunsaturated fatty acids could improve plasma fatty acid profile, CRP/Alb status, and immune function and prevent weight loss during treatment in cancer patients

Mocellin MC, Pastore ESJA, Camargo CQ, Fabre ME, Gevaerd S, Naliwaiko K, et al. **Fish oil decreases C-reactive protein/albumin ratio improving nutritional prognosis and plasma fatty acid profile in colorectal cancer patients.** Lipids. 2013;48(9):879–88.

Long H, Yang H, Lin Y, Situ D, Liu W. **Fish oil-supplemented parenteral nutrition in patients following esophageal cancer surgery: effect on inflammation and immune function.** Nutr Cancer. 2013;65(1):71–75

Tocotrienols exhibit stronger antioxidant and anti-inflammatory activities compared to alpha-tocopherol

TOCOTRIENOLS SUPPRESS

125-250mg bid

- **Expression of Mediators of Inflammation:**
  TNFa, NFkb, IL1, IL6, IL8 ,COX2, 12-LOX PGE-2
- STAT 3 Signaling
- Glutamate induced neurotoxicity
- Arachidonic Acid induced inflammation and oxidative stress

Ann N Y Acad Sci. 2011 Jul;1229:18-22. doi: 10.1111/j.1749-6632.2011.06088.x.
Tocotrienols: inflammation and cancer.
J Neuroinflammation. 2016 Jun 14;13(1):148. doi: 10.1186/s12974-016-0615-6.
Rice bran derivatives alleviate microglia activation: possible involvement of MAPK pathway. Bhatia HS[1,2], Baron J[3], Hagl S[4], et al

Diabetes and Inflammation

Both type 1 and type 2 diabetes are associated with increased blood concentrations of several inflammatory biomarkers

- C-reactive protein (CRP)
- Interleukin 2 IL-2
- Interleukin-6 IL-6
- Tumour Necrosis Factor-alpha (TNF-α)

Annu Rev Nutr. 2010 Aug 21; 30: 173–199. Bharat B. Aggarwal

Targeting Inflammation-Induced Obesity and Metabolic Diseases by Curcumin and Other Nutraceuticals

- Curcumin-induced alterations reversed insulin resistance, hyperglycemia, hyperlipidemia, and other symptoms linked to obesity.
- Other structurally homologous nutraceuticals derived from red chili, cinnamon, cloves, black pepper, and ginger, also exhibit effects against obesity and insulin

Anti-Diabetic & Anti-Obesogenic Effects of Polysaccharides from Aqueous Extract **Ganoderma lucidum (Reishi Mushroom)**

2 - 6 grams per day

- Reduction of Body Weight and Fat Accumulation
- **Modulation of Gut Bacteria**
- Maintenance of Intestinal Integrity & Tight Junctions
- Increased Production of SCFA in Intestines
- Delayed Gastric Emptying>Reduced Appetite
- **Reduced expression of TNFa, IL1B1, IL6**
- Improved Glucose Tolerance & Insulin Sensitivity

Omega-3 fatty acids 2-6 g/day reduce obesity-induced tumor progression

Obesity and inflammation are both risk factors for a variety of cancers, including breast cancer in postmenopausal women.

Intake of omega-3 polyunsaturated fatty acids (ω-3 PUFAs) decreases the risk of breast cancer, and also reduces obesity-associated inflammation and insulin resistance

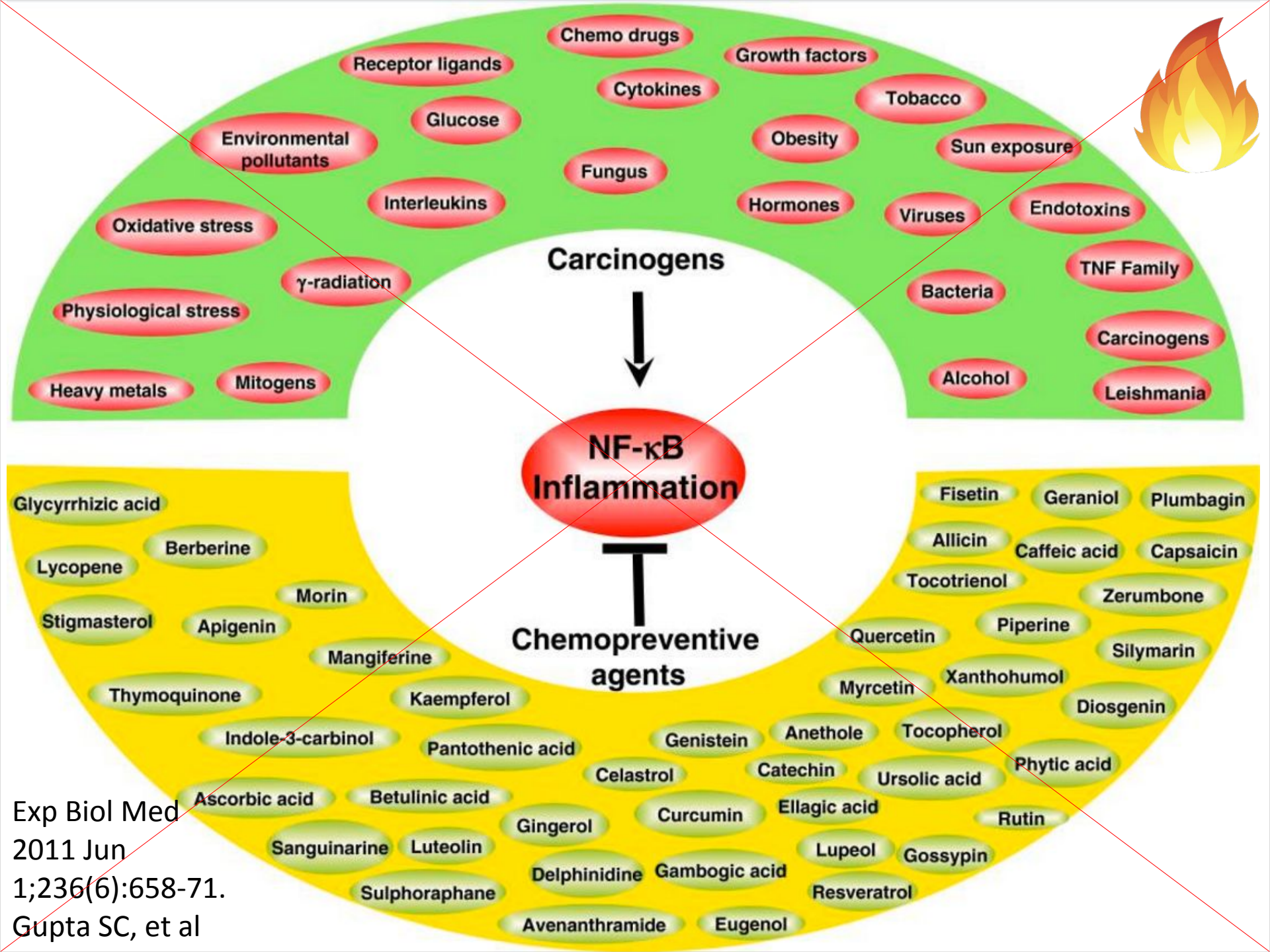
Oncogene. 2015 Jul; 34(27): 3504–3513. Heekyung Chung,et al

Omega-3 Fatty Acids Lower Diabetes Associated Inflammation

Study doses: 2.7 - 4.0 grams/day

Biochim Biophys Acta. 2015 Apr;1851(4):469-84
Marine omega-3 fatty acids and inflammatory processes: Effects, mechanisms and clinical relevance. Calder PC

Lipids Health Dis. 2016 Aug 20;15:133.
What is the impact of n-3 PUFAs on inflammation markers in Type 2 diabetic mellitus populations?: a systematic review and meta-analysis of randomized controlled trials. Lin N, et al



Exp Biol Med 2011 Jun 1;236(6):658-71. Gupta SC, et al

Arch Biochem Biophys. 2014 Oct 1;559C:91-99
Downregulation of TNF tumor necrosis factor and other proinflammatory biomarkers by polyphenols. Gupta SC,, Aggarwal BB. et al

Endocrine. 2008 Jun;33(3):331-7 **Berberine inhibits the expression of TNFalpha, MCP-1, and IL-6 in AcLDL-stimulated macrophages through PPARgamma pathway.**
Chen FL et al

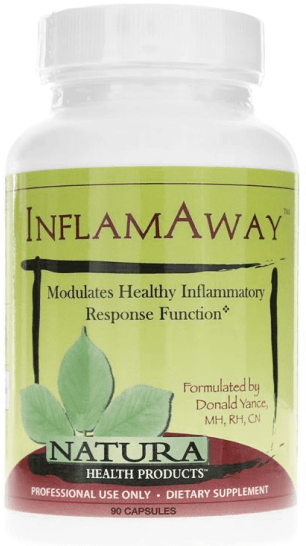
American Journal of Physiology - Endocrinology and Metabolism 1 April 2009 **Vol.** 296 **no.** 4,E955-E964 **Berberine suppresses proinflammatory responses through AMPK activation in macrophages**
Hyun Woo et al

OUTSMART CANCER®
SYSTEM

DR. NALINI RECOMMENDS

Dr. Nalini Recommends

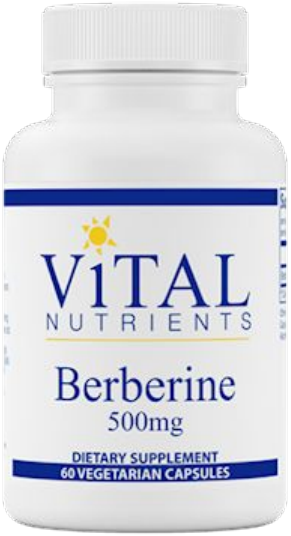
Available on: Fullscript™



Available On: Fullscript™

Dr. Nalini Recommends

Huang Qin



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Support the Health of Cancer Patients
and Watch Your Practice Grow

OUTSMART CANCER SYSTEM®

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