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Cancer can strike everyone

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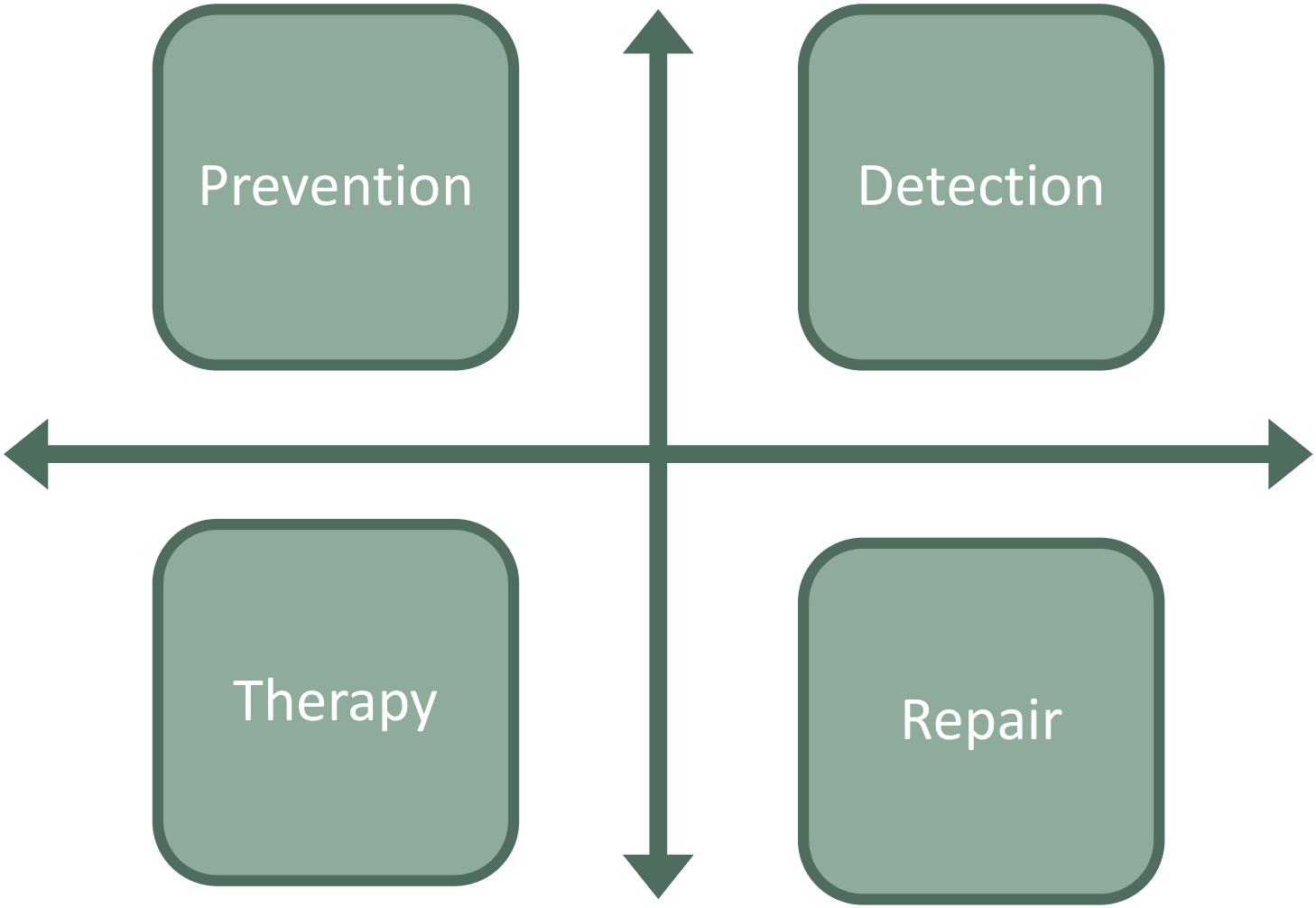
MICC Miskawaan Individualised Cancer Concept



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Prevention

- Lifestyle: sports, smoking, alcohol
- Food: low carb , phytoprevention, microbiome, probiotics
- Genetics: Whole exome sequencing
- Heavy metal screening (hormone disruptors)
- Immune surveillance
- **SLEEP**

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Phytoprevention

nature OUTLOOK

CANCER PREVENTION

24 March 2011 / Vol 471 / Issue No. 7339

COVER ART:

Ask many people what they are afraid of, and cancer — the big C — will often top the list. Some forms of cancer have become easily treatable. But in many cases, by the time doctors deploy the weapons of surgery, chemotherapy or radiation, the cancer has already progressed past the point where medical intervention can cure the condition.

Many cancer specialists now contend that the best way to deal with cancer is to ensure it doesn't develop in the first place.

CONTENTS

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Phytoprevention

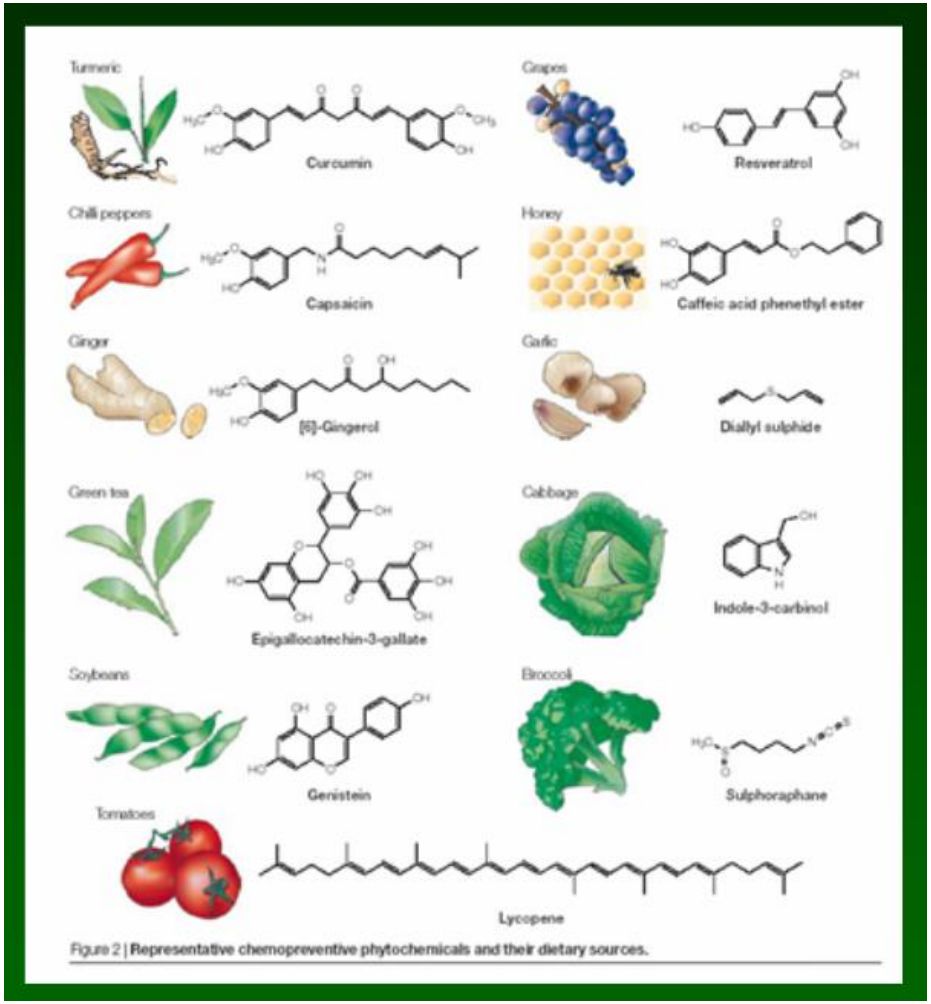

Figure 2 | Representative chemopreventive phytochemicals and their dietary sources.

Arch. Pharm. Chem. Life Sci. 2010, *9*, 489–499

Review Article

Curcumin in Cancer Chemoprevention: Molecular Targets, Pharmacokinetics, Bioavailability, and Clinical Trials

Adeeb Shehzad, Fazli Wahid, and Young Sup Lee

"Sufficient data has been shown to advocate phase II and phase III clinical trials of curcumin for a variety of cancer conditions including multiple myeloma, pancreatic and colon cancer…"

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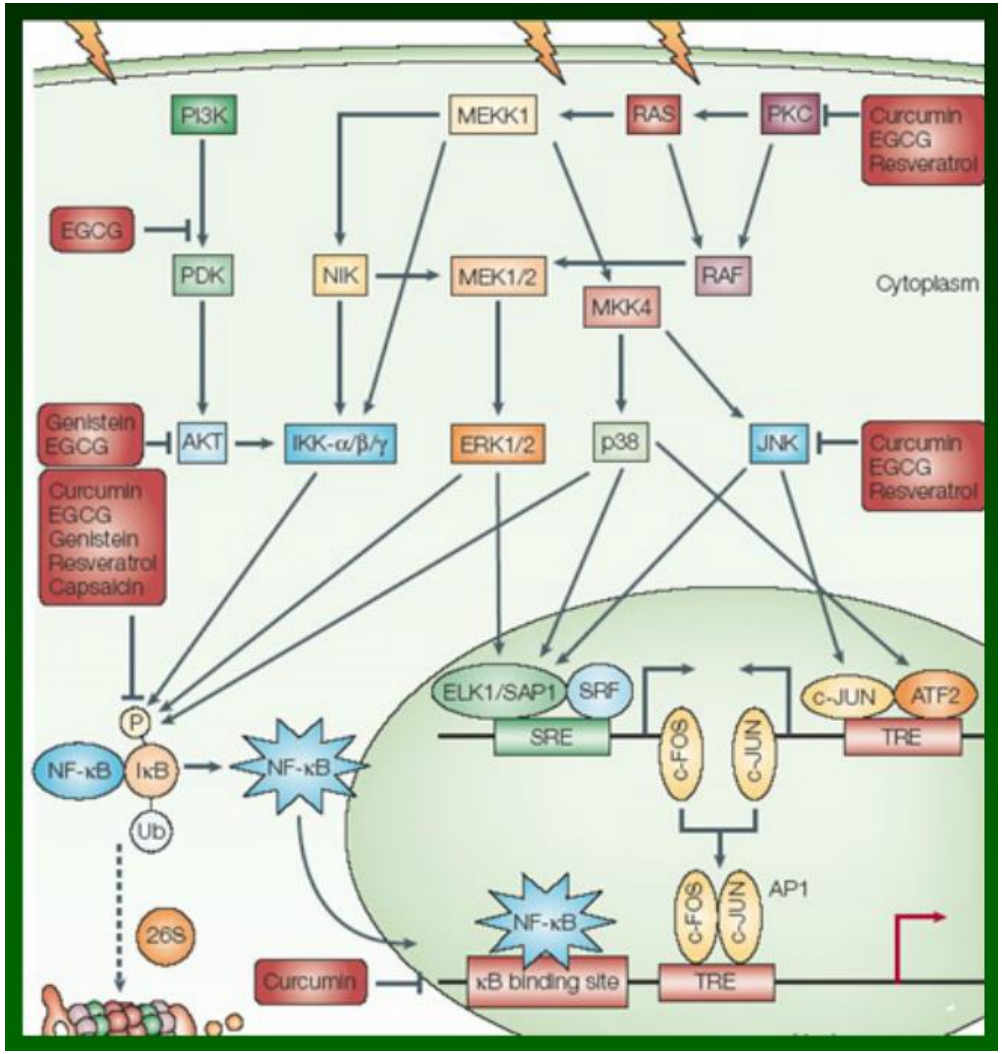
Phytotherapy



www.nature.com/reviewrs/cancer

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The Role of Probiotics

Gastroenterology 2017;152:1889–1900

Timely Use of Probiotics in Hospitalized Adults Prevents *Clostridium difficile* Infection: A Systematic Review With Meta-Regression Analysis

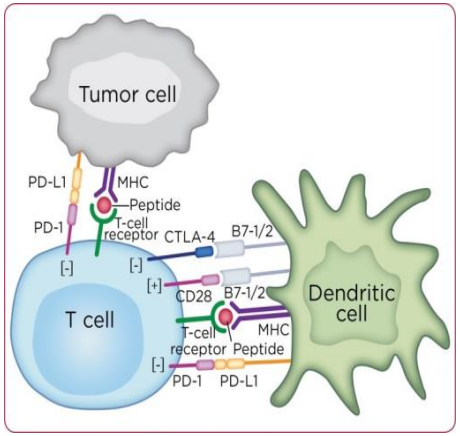
Nicole T. Shen,[1] Anna Maw,[2] Lyubov L. Tmanova,[3] Alejandro Pino,[4] Kayley Ancy,[4] Carl V. Crawford,[1] Matthew S. Simon,[5,6] and Arthur T. Evans[5]

"… the role of probiotics is clear

- in getting rid of mutagens,
- delaying the onset of tumors,
- alleviating the side effects of chemotherapy,
- pepping up chemotherapy,
- easing the postoperative complications,
- foiling remission and
- lifting the spirit of survivors."

Patel, 2013

Probiotics and Antimicrobial Proteins Volume 5, Issue 1 , pp 59-67



Gopalakrishnan V, Spencer CN, Nezi L, et al. Gut microbiome modulates response to anti-PD-1 immunotherapy in melanoma patients. *Science*. 2018; 359(6371):97-103. doi: 10.1126/science.aan4236.

Matson V, Fessler J, Bao R, et al. The commensal microbiome is associated with anti-PD-1 efficacy in metastatic melanoma patients. *Science*. 2018; 359(6371):104-8. doi: 10.1126/science.aao3290.

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Yesterday's Immune

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Immune Stimulation

- Mistletoe (different kinds after testing)
- Peptides (from thymus, spleen)
- Arabinoxylan
- Cimetidin

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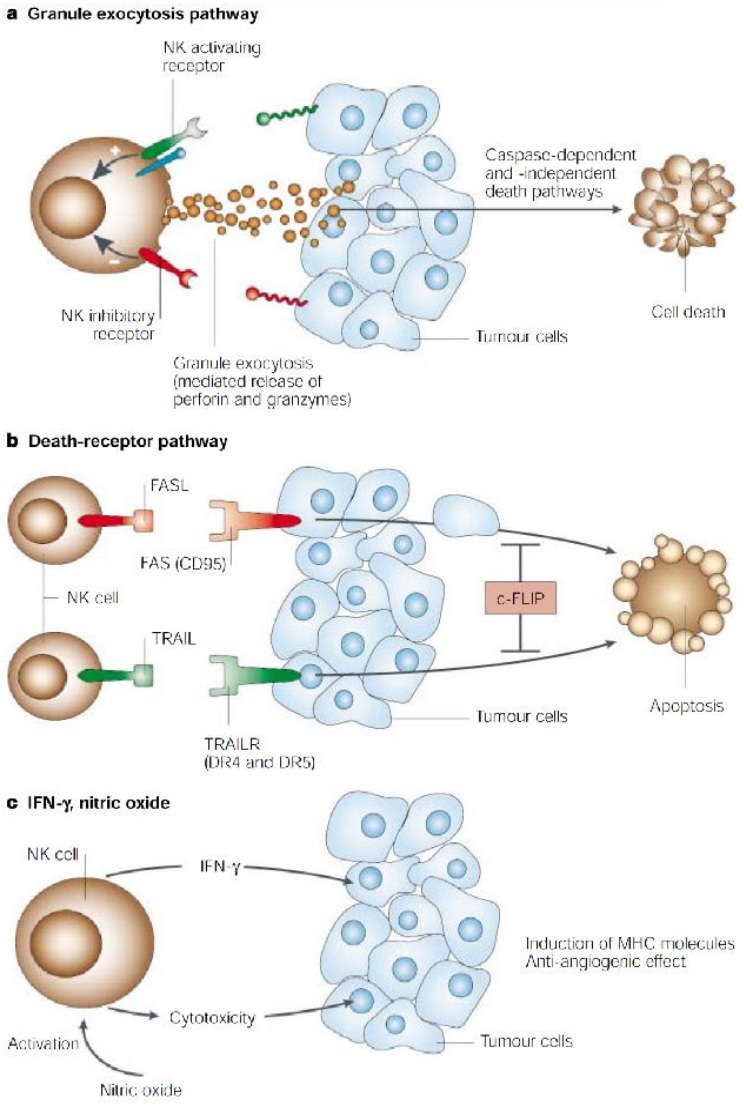
NK cell function

NK cells eliminate target cells by 2 major effector functions.

The direct cytotoxicity mechanism

- Granule exocytosis pathway:
  - Perforin and Granzymes
- Death-receptor pathway : FasL / TRAIL
- ADCC : Antibody-Dependent
- Cellular Cytotoxicity
  - Cytokines secretion
- IFN-gamma, TNF-α, TNF-β, GM-CSF etc.

Mark J. Smyth et al, 2002



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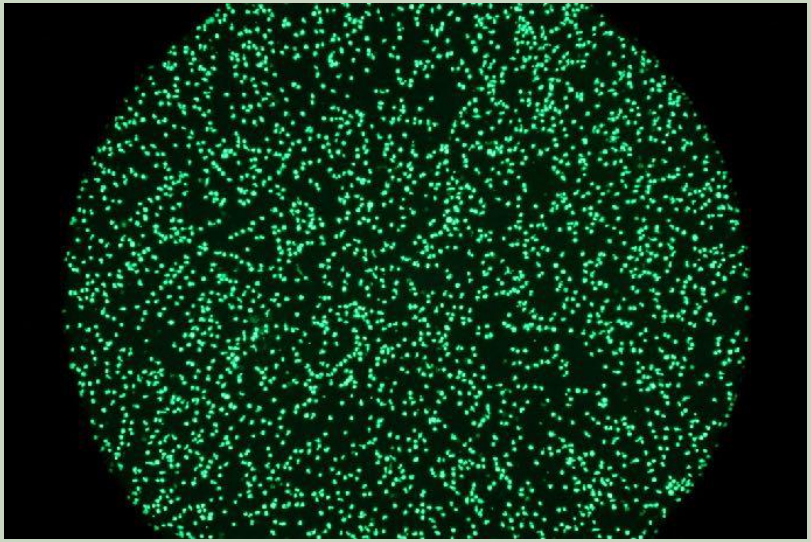
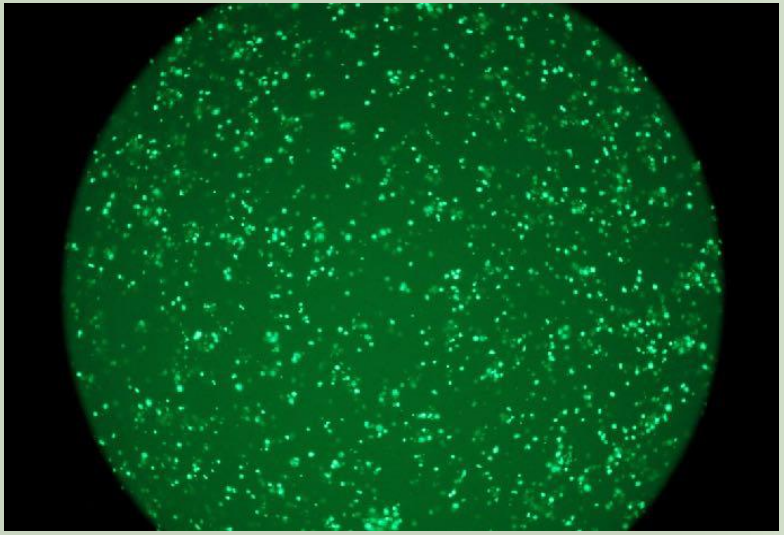
NK Activity Test - WinCell

Before (0 hour)	After (4 hours)





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NK Activity Test - WinCell

Volker K. 45J. **02.2010**
Labor **10.2010**

NK-Zellfunktion				
NK-SELECT®				
NK-Check®				
NK/Ctx: basal	12	19	% K562	> 20
NK/Ctx: IL-2 stim	15	19	% K562	> 35
NK-Zellen CD69 basal	17	14	% NK	
NK-Zellen CD 69 IL2	36	36	% NK	
MODULATOR 1	**Iscucin Abiet**			
NK-Zellen CD 69 Mod 1	14		% NK	
MODULATOR 2	**Pini**			
NK-Zellen CD 69 Mod 2	15		% NK	
MODULATOR 3	**Populi**			
NK-Zellen CD 69 Mod 3	15		% NK	
MODULATOR 4	**MGN3**			
NK-Zellen CD 69 Mod 4	12		% NK	
MODULATOR 5	**Resveratrol**			
NK-Zellen CD 69 Mod 5	13		% NK	
MODULATOR 6	**Vitamin C**			
NK-Zellen CD 69 Mod 6	17		% NK	
MODULATOR 7	**Quercus**			
NK-Zellen CD 69 Mod 7	16		% NK	
MODULATOR 8	**Abnoba Visc**			
NK-Zellen CD 69 Mod 8	16		% NK	
MODULATOR 9	**Immuherbs**			
NK-Zellen CD 69 Mod 9	16		% NK	
MODULATOR 10	**Lektinol**			
NK-Zellen CD 69 Mod 10	22		% NK	
MODULATOR 11	**Iscador mali**			
NK-Zellen CD 69 Mod 11	4		% NK	

NK-Zellfunktion				
NK-SELECT®		...		
NK-Check®		...		
NK/Ctx basal	46	20	% K562	> 20
NK/Ctx IL-2 stim	46	21	% K562	> 35
NK-Zellen CD69 basal	22	7	% NK	
NK-Zellen CD 69 IL2	68	35	% NK	
MODULATOR 1	**Lektinol**	Immunpil		
NK-Zellen CD 69 Mod 1	25	15	% NK	
MODULATOR 2	**Abnoba Mali**	MGN3		
NK-Zellen CD 69 Mod 2	30	17	% NK	
MODULATOR 3	**Iscucin Abietis**	Mistel		
NK-Zellen CD 69 Mod 3	24	10	% NK	
MODULATOR 4	**Abnoba Pini**	Vitamin C		
NK-Zellen CD 69 Mod 4	30	6	% NK	
MODULATOR 5	**Iscucin Populi**			
NK-Zellen CD 69 Mod 5	34		% NK	
MODULATOR 6	**Iscador ercus**			
NK-Zellen CD 69 Mod 6	26		% NK	
MODULATOR 7	**Abnoba Viscum**			
NK-Zellen CD 69 Mod 7	31		% NK	
MODULATOR 8	**MGN3**			
NK-Zellen CD 69 Mod 8	69		% NK	
MODULATOR 9	**Thymuvocal**			
NK-Zellen CD 69 Mod 9	24		% NK	
NK-Zellen (relativ)	12	12	% Lympho	6 - 29

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Melatonin Reduces Cancer Progression and Metastasis

Russel J. Reiter, Ph.D., M.D (*h.c.*), D.Sc. (*h.c.*)
Professor of Cell Biology
UT Health San Antonio
San Antonio, Texas USA

Vienna, Austria: December 2019

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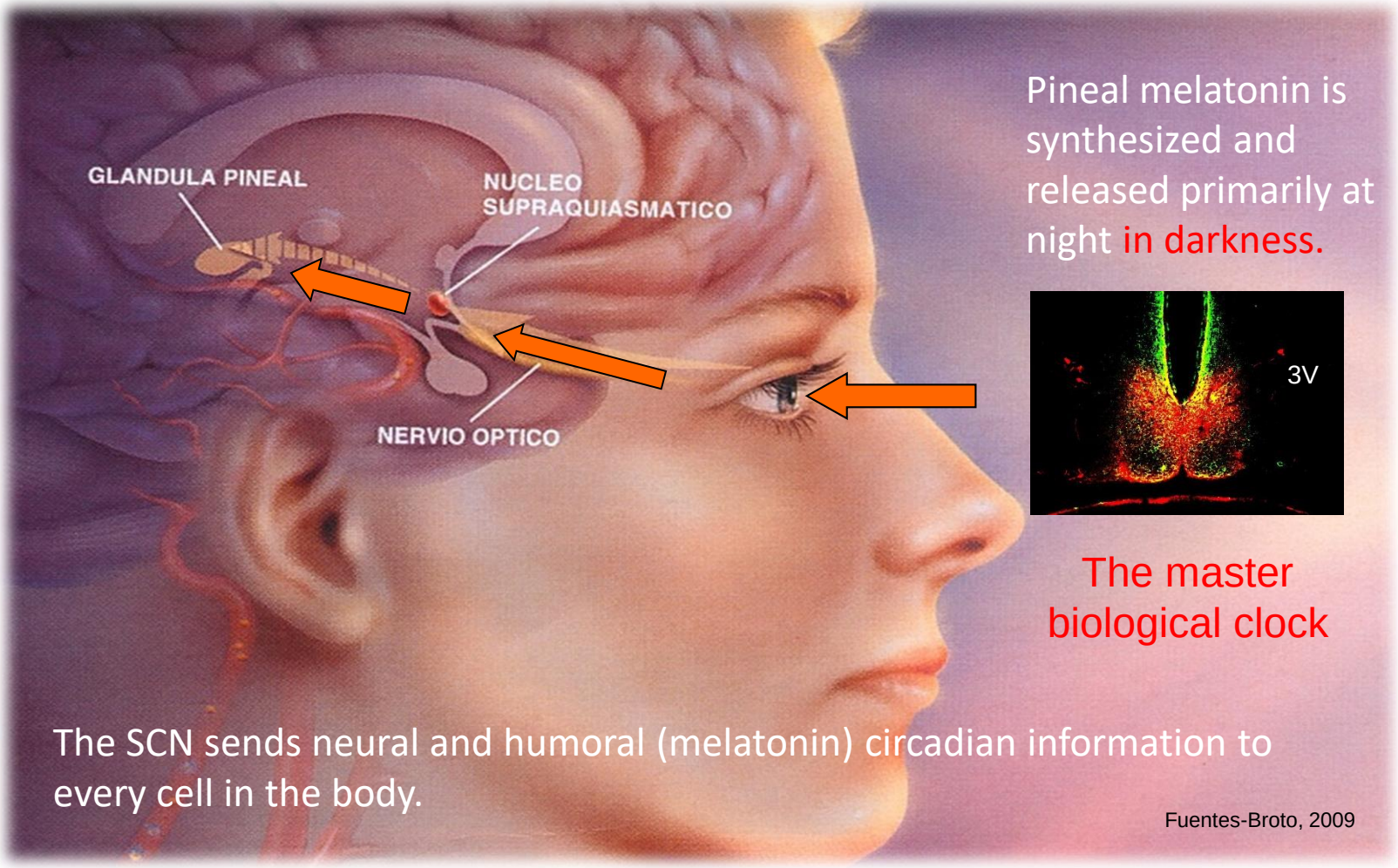
Melatonin – The Biological Clock



Pineal melatonin is synthesized and released primarily at night in darkness.

The master biological clock

The SCN sends neural and humoral (melatonin) circadian information to every cell in the body.

Fuentes-Broto, 2009

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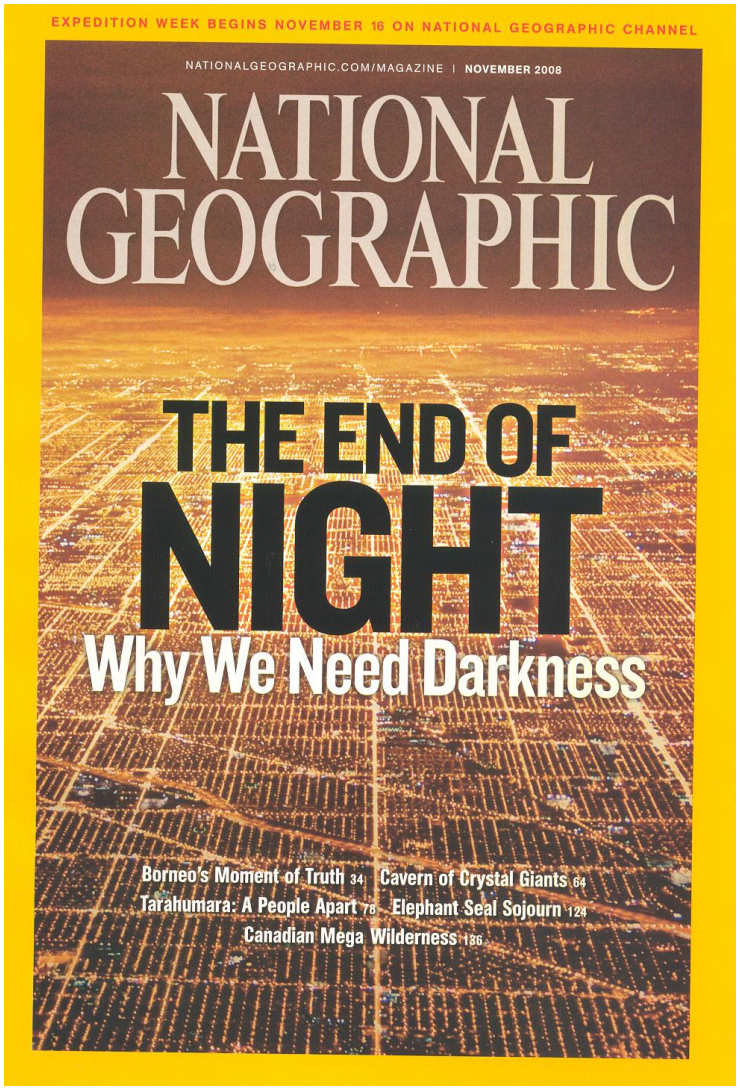
Melatonin



The "end of night" means the loss/suppression of the melatonin rhythm

World Health Organization has classified light-at-night as a class 2A carcinogen

Significant consequences in terms of circadian misalignment (chronodisruption) and melatonin suppression

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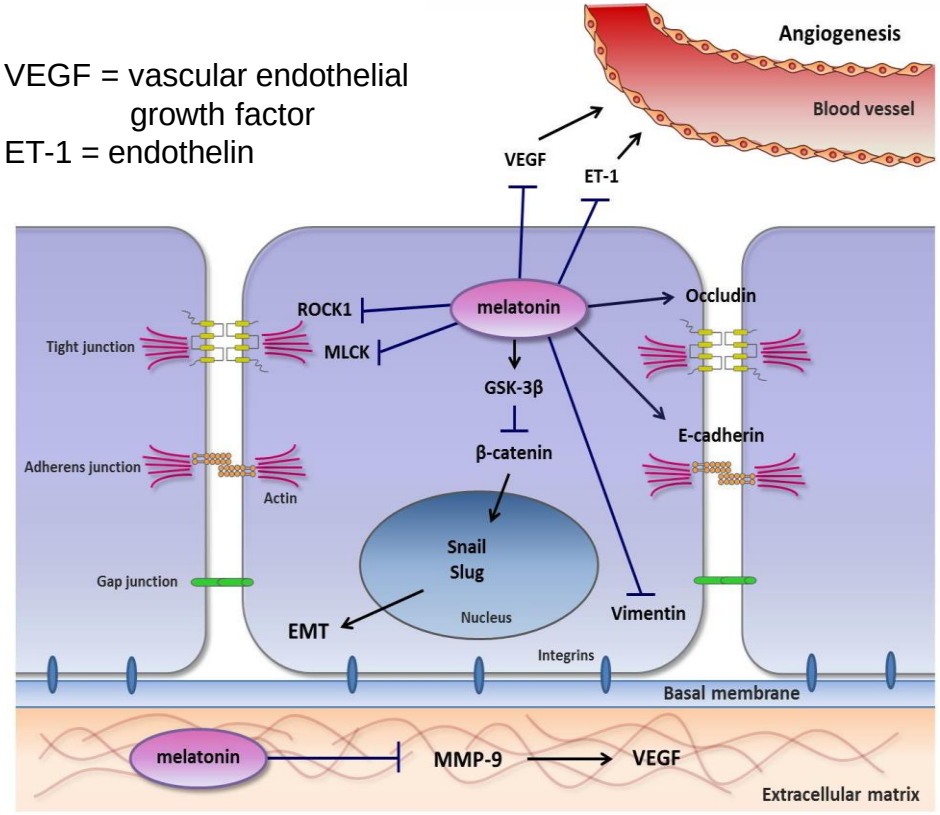
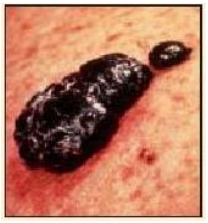
Melatonin is a Potent Inhibitor of Cancer Metastasis

VEGF = vascular endothelial growth factor
ET-1 = endothelin



Reiter, 2017



Google image

Metastatic cancer is almost always worse than primary cancer.

Metastatic melanoma is an example of the increased danger of metastases.

Melatonin downregulates vimentin, ROCK & MLCK to reduce cytoskeletal reorganization.

Melatonin reduces cancer cells to a less invasive state by upregulating adhesion molecules.

Melatonin reduces angiogenesis by inhibiting VEGF and ET-1.

Melatonin activates GSK-β to decrease EMT transcription factors, snail and slug.

Melatonin inhibits MMP-9 in ECM to prevent invasion.

Yang et al, 2015

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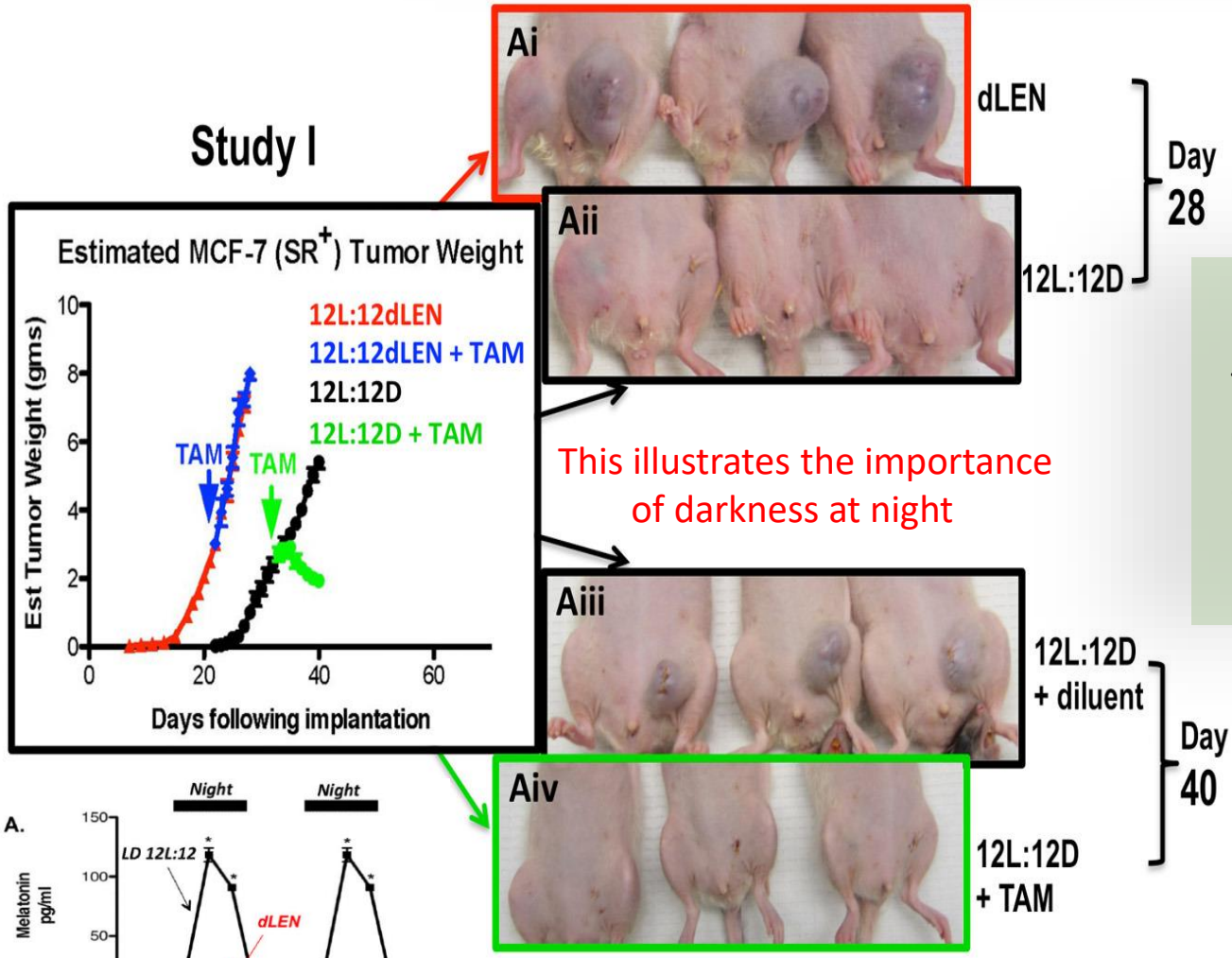
Cancer and Melatonin



Melatonin renders treatment resistance cancers sensitive to chemotherapies (tamoxifen)

Dauchy et al, 2014

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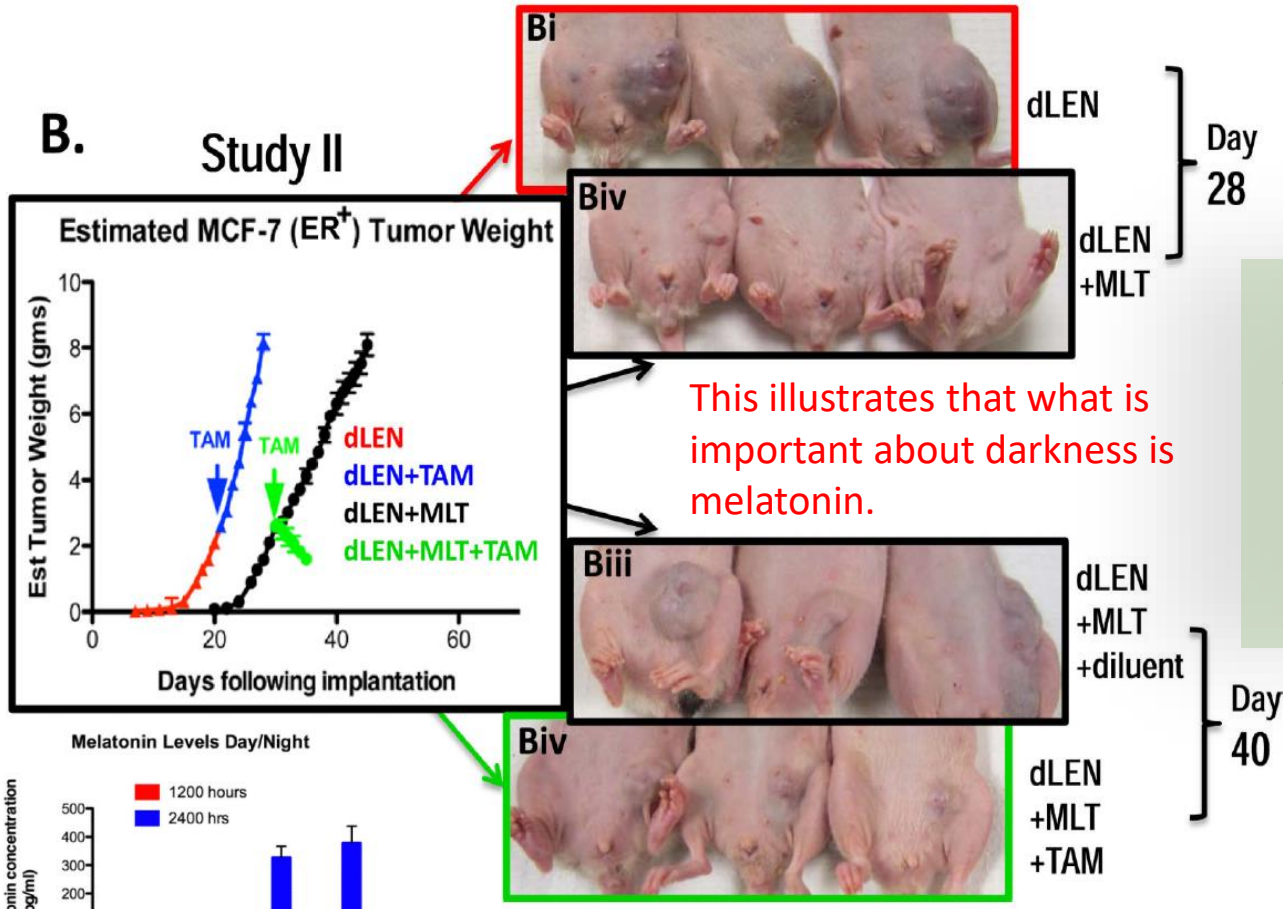
Cancer and Melatonin



Melatonin renders treatment resistance cancers sensitive to chemotherapies (tamoxifen)

Dauchy et al, 2014

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Early Detection

- Pantum (EDIM Technology)
- Prescan (Whole Body MRI/CT)
- Metavectum (Liquid biopsy, drug test)

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Visualisation of Glucose Metabolism

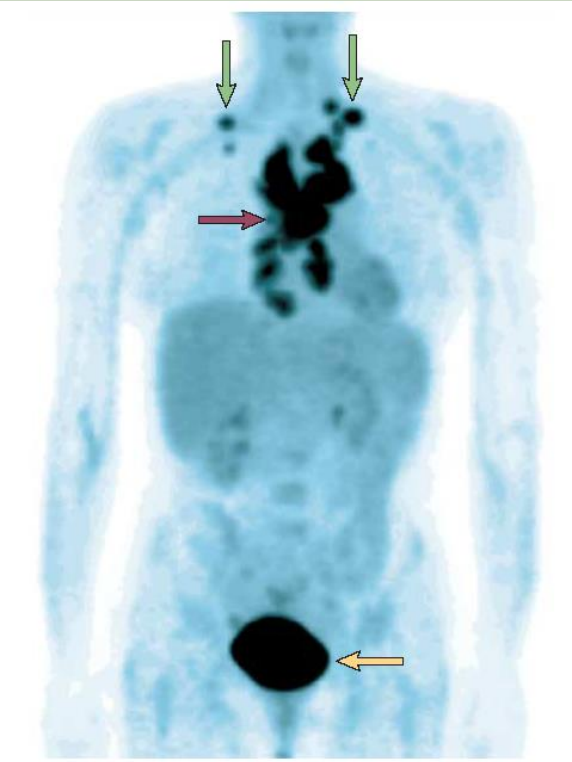

Figure 2 | **Positron-emission tomography imaging with ^{18}fluorodeoxyglucose of a patient with lymphoma.** The mediastinal nodes (purple arrow) and supraclavicular nodes (green arrows) show high uptake of ^{18}fluorodeoxyglucose (FdG), showing that tumours in these nodes have high levels of FdG uptake. The bladder (yellow arrow) also has high activity, because of excretion of the radionuclide.

Through ^{18}F-FDG-PET

a) Cancer ↑

b) Alzheimer ↓

Gatenby and Gillies, Nature Reviews Cancer 2004

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Warburg Effect

Fermentation of glucose despite the availability of oxygen

Über den Stoffwechsel der Carcinomzelle[1]).

Von

Otto Warburg, Karl Posener und Erwin Negelein.

(Aus dem Kaiser-Wilhelm-Institut für Biologie, Berlin-Dahlem, und aus der chirurgischen Universitätsklinik der Charité, Berlin.)

(Eingegangen am 10. September 1924.)

Mit 6 Abbildungen im Text.

Greift man das Carcinomproblem von der Seite der Stoffwechselphysiologie an, so ist die erste Frage: wodurch unterscheidet sich der Stoffwechsel wachsenden Gewebes von dem Stoffwechsel ruhenden Gewebes? Die Aussichten, eine Antwort auf diese Frage zu finden, sind groß. Ob ein Gewebe seine Substanz konstant hält oder ob es

Winner of the Nobel Price Otto Warburg 1924

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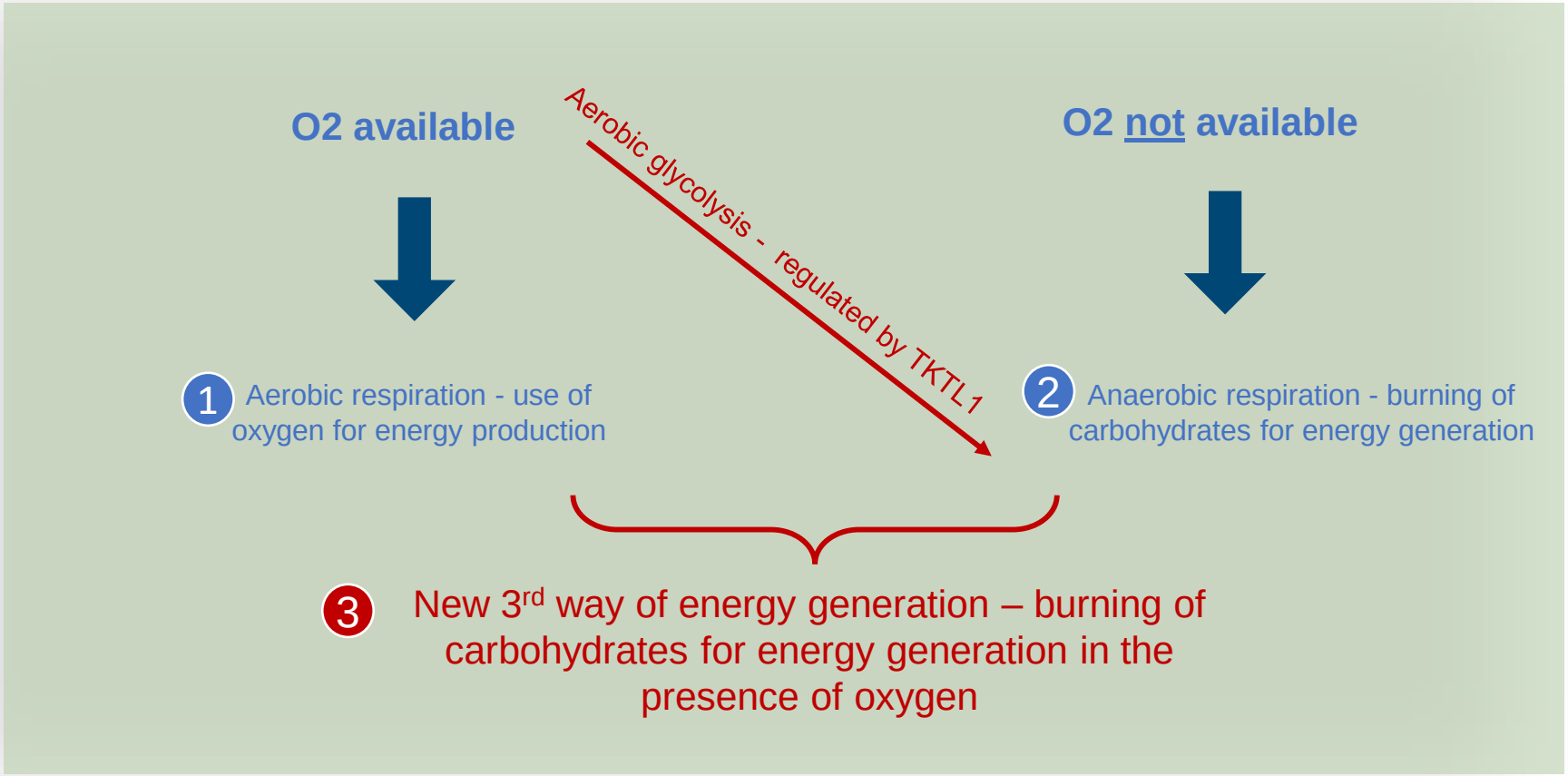
Metabolism – Energy Generation in Cells

TKTL1-protein regulates aerobic glycolysis – a new, 3rd way of energy metabolism



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TKTL1 (Transketolase-like 1)

An increased TKTL1-Score is an indication of an aggressive tumour.

- TKTL1-gene discovered in 1995 by Dr Coy during his research at German Centre of Cancer Research (DKFZ), Heidelberg.
- TKTL1-metabolism describes long unknown **third way of energy generation** in the cell.
- TKTL1-protein regulated the **aerobic glycolysis** = fermentation process of glucose even in presence of oxygen.
- Tumour cells make use of this TKTL-1 metabolism as **growth becomes invasive/ aggressive**.
- Confirmed by analysis of more than 50 tumour entities in more than 110,000 blood samples.

Grimm et al. BMC Cancer 2013, 13:569
http://www.biomedcentral.com/1471-2407/13/569

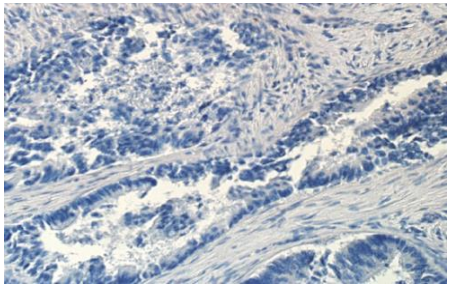
BMC Cancer

RESEARCH ARTICLE Open Access

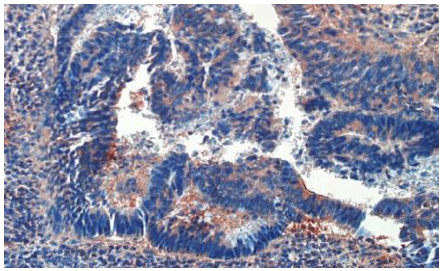
A biomarker based detection and characterization of carcinomas exploiting two fundamental biophysical mechanisms in mammalian cells

Martin Grimm[1*], Steffen Schmitt[2], Peter Teriete[3], Thorsten Biegner[4], Amulf Stenzl[5], Jörg Hennenlotter[5], Hans-Joachim Muhs[6], Adelheid Munz[1], Tatjana Nadtotschi[1], Klemens König[7], Jörg Sänger[8], Oliver Feyen[9], Heiko Hofmann[9], Siegmar Reinert[1] and Johannes F Coy[9]

TKTL1-negative tumor material



TKTL1-positive tumor material



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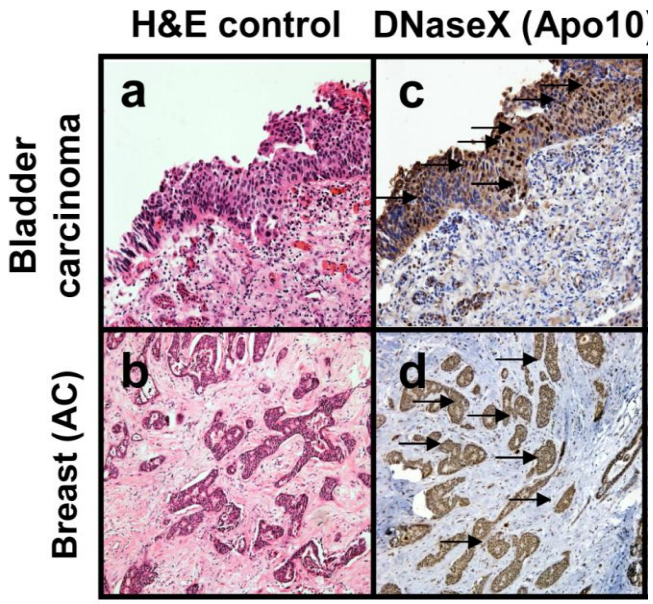
Apo10 (DNAseX)

An increased Apo10-Score is an indication of a proliferative disorder / tumor.

- Apo10 accumulates in cells due to **disordered apoptosis.**
- Independent from the type of tumour.
- Confirmed by analysis of more than 50 tumour entities in more than 90,000 blood samples.
- Disordered apoptosis is the **origin of malign degeneration** respectively a tumour.



Immunohistochemistry of tumor material

Grimm *et al. BMC Cancer* 2013, **13**:569
http://www.biomedcentral.com/1471-2407/13/569

BMC Cancer

RESEARCH ARTICLE Open Access

A biomarker based detection and characterization of carcinomas exploiting two fundamental biophysical mechanisms in mammalian cells

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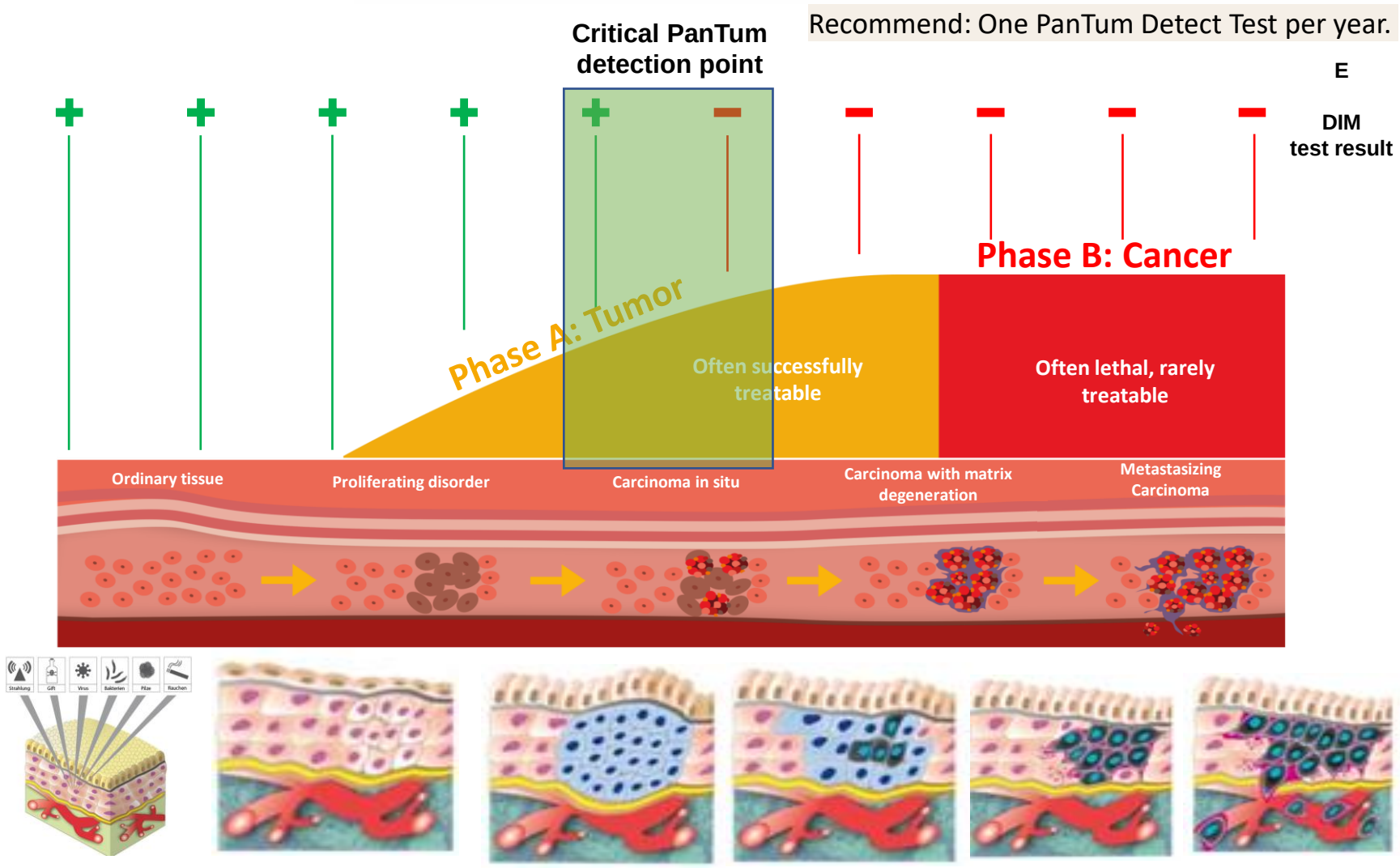
PanTum Application in Screening



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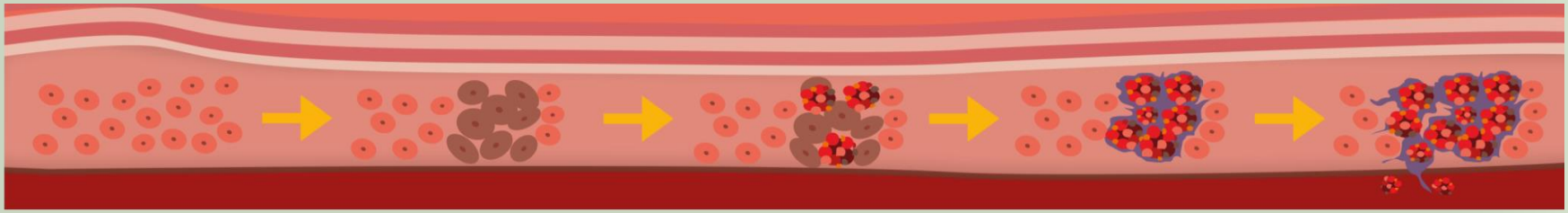
PanTum Detect can detect all tumour stages

The combination of Apo10 and TKTL1 allows the detection of all tumor stages.



Ordinary tissue	Proliferating disorder	Carcinoma in situ	Carcinoma with matrix degeneration	Metastasizing carcinoma
Apo 10 -ve	Apo 10 +ve	Apo 10 +ve	Apo 10 +ve	Apo 10 +ve/ -ve
TKTL1 -ve	TKTL1 -ve	TKTL1 -ve/ +ve	TKTL1 +ve	TKTL1 +ve
Cum. PanTum -ve	**Cum. PanTum** -ve	**Cum. PanTum** +ve	**Cum. PanTum** +ve	**Cum. PanTum** +ve

-ve = Negative
+ve = Positive

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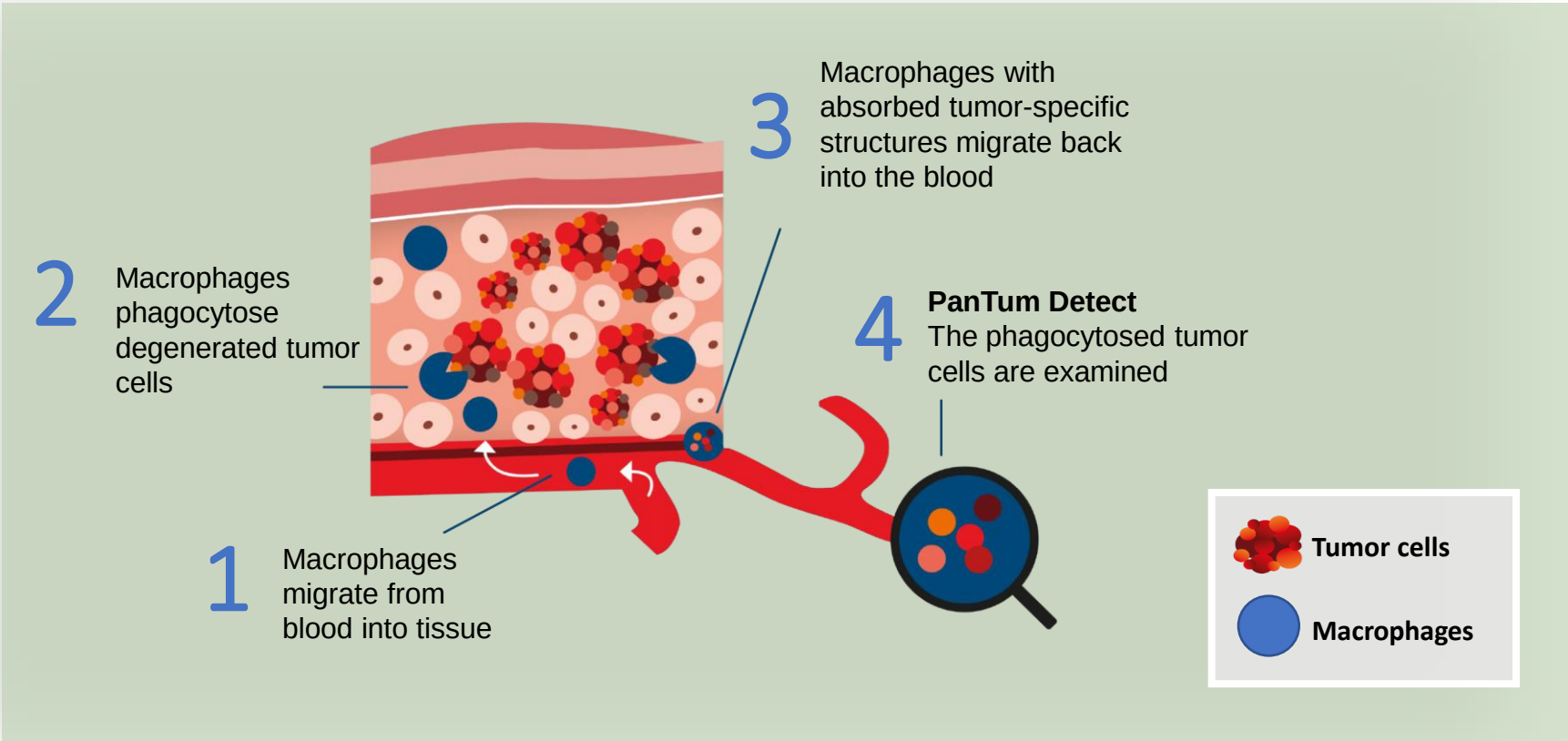
Biological Biopsy – Leveraging the immune system

Highest test accuracy achieved by making use of the body's own immune system.



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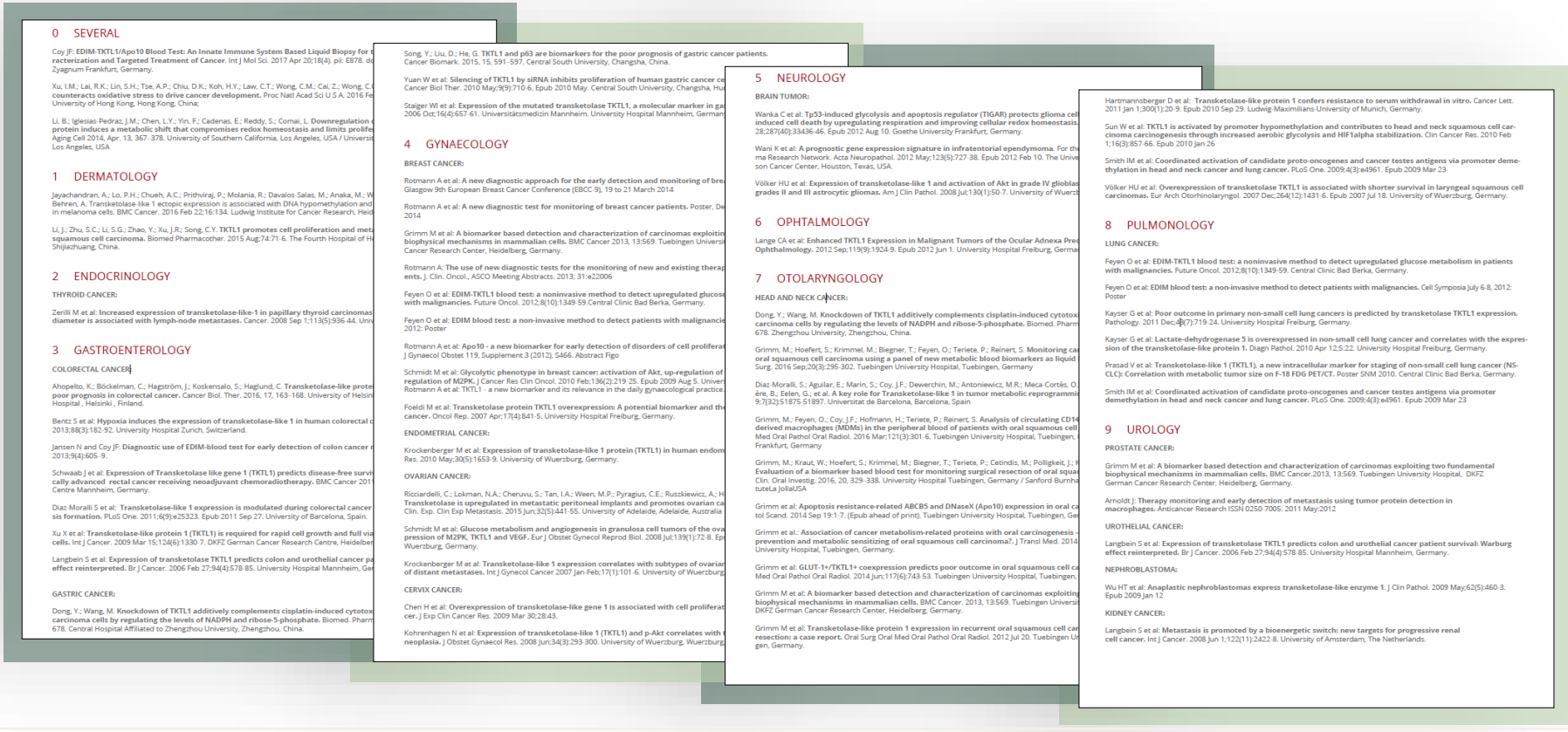
PanTum Test - Supporting Studies

Supporting Studies in:

Dermatology, Endocrinology (thyroid cancer), Gastroenterology (colorectal & gastric cancer), Gynaecology (breast, ovarian, cervix cancer), Neurology (brain tumour), Ophtalmology, Otolaryngology (head & neck cancer), Pulmonology (lung cancer), Urology (prostate, urothelial & kidney cancer)



0 SEVERAL

1 DERMATOLOGY

2 ENDOCRINOLOGY

THYROID CANCER:

3 GASTROENTEROLOGY

COLORECTAL CANCER:

GASTRIC CANCER:

4 GYNAECOLOGY

BREAST CANCER:

ENDOMETRIAL CANCER:

OVARIAN CANCER:

CERVIX CANCER:

5 NEUROLOGY

BRAIN TUMOR:

6 OPHTALMOLOGY

7 OTOLARYNGOLOGY

HEAD AND NECK CANCER:

8 PULMONOLOGY

LUNG CANCER:

9 UROLOGY

PROSTATE CANCER:

UROTHELIAL CANCER:

NEPHROBLASTOMA:

KIDNEY CANCER:

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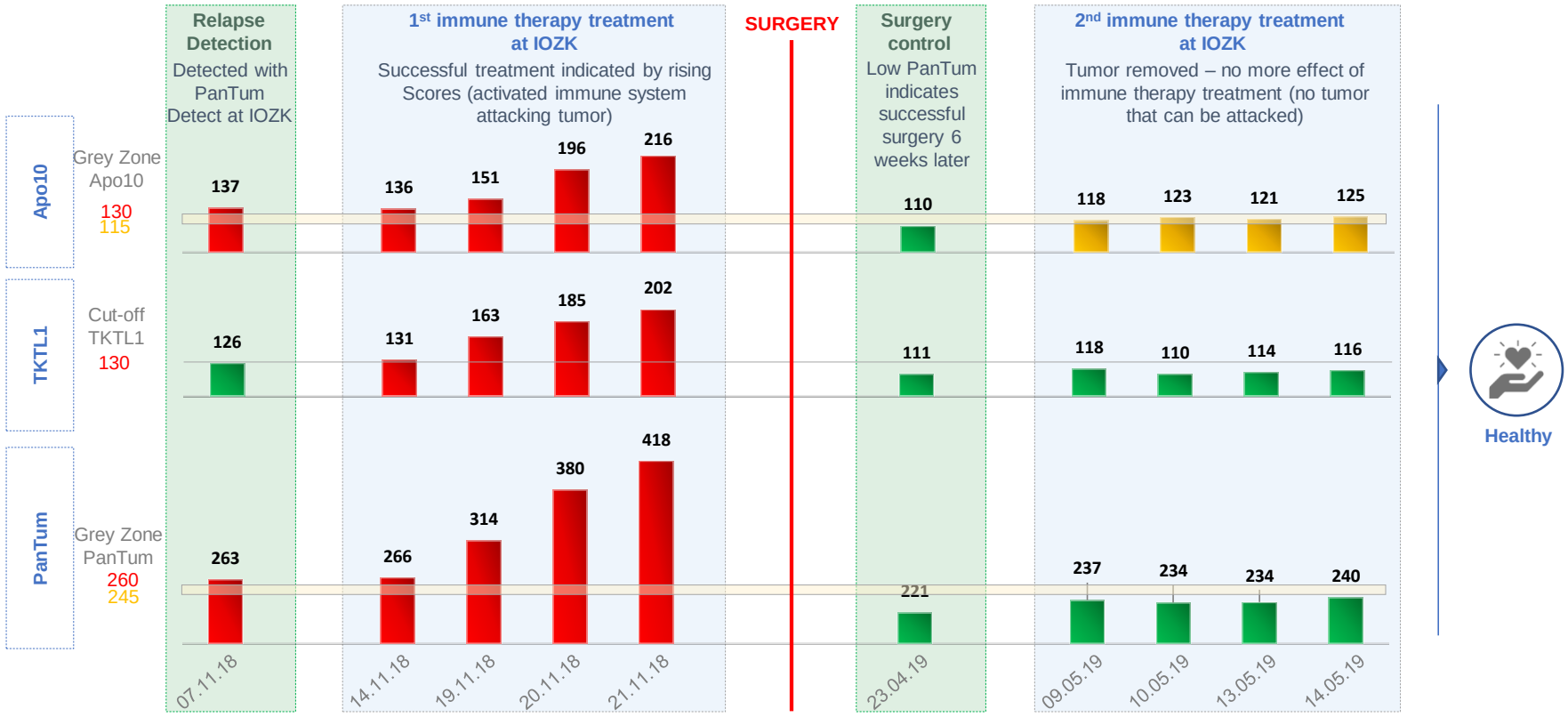
Patient Case Example – PanTum Surveillance



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Cancer therapy approach

Cancer Therapy Approach

FOOD & MICROBIOME	IMMUNE THERAPY	LIQUID BIOPSY	INFUSION	COMBINATION OF CHEM, BIOLOGICAL, HYPERTHERMIA

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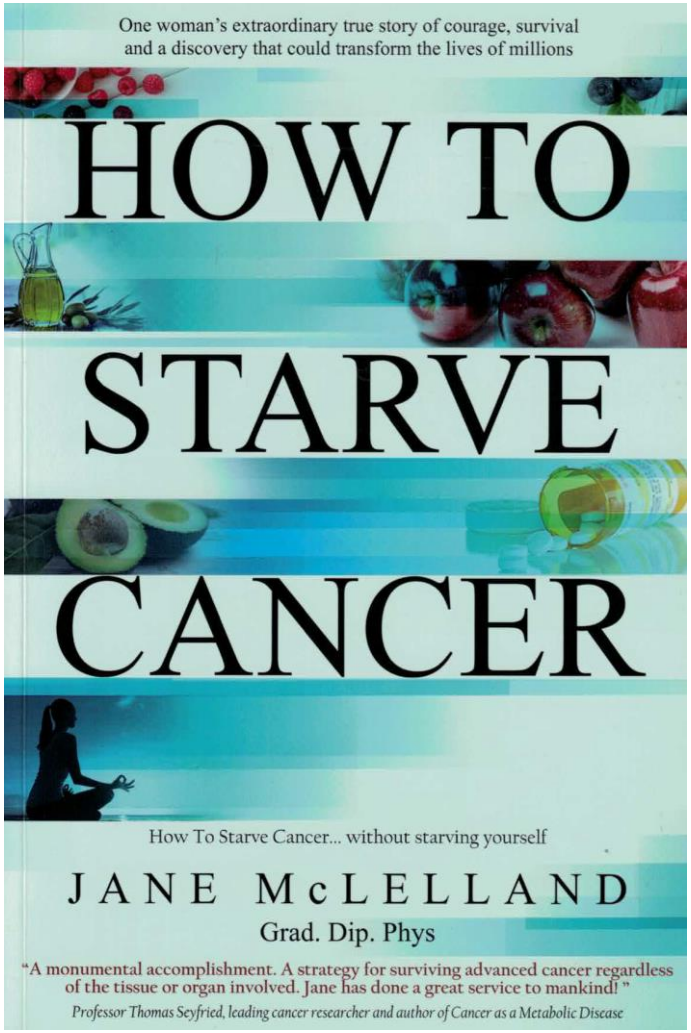
Stem Cell Metro Map



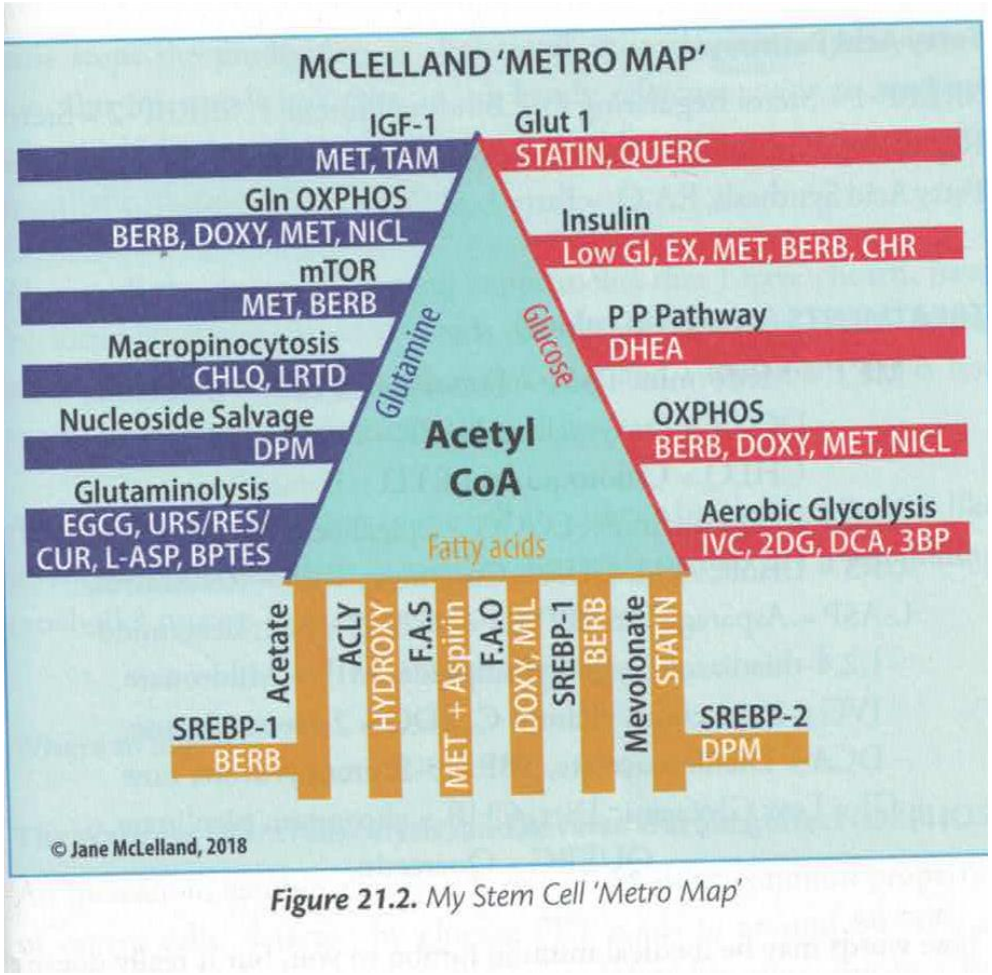


Figure 21.2. My Stem Cell 'Metro Map'

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Janus-faced Character of Sugar

Role in Healthy cells:

- Prevents and neutralizes radicals
- Fast glucose degradation
- Protection from glucose-associated cell- damages / advanced glycation end products (AGEs) in endothelial cells nerves retina.

Role in Cancer cells:

- Energy realease without oxygen
- Degradation of surrounding matrix
- Invasion and metastasis
- Resistence towards radio and chemotherapy

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Otto Warburg 1924

8. Andere Kohlehydrate. α- und β-Glucose.

In den bisher beschriebenen Versuchen war der Zucker der Ringerlösung eine im Gleichgewicht befindliche Mischung von α- und β-Glucose. Wir haben uns gefragt, wie spezifisch die Zelle auf ihr natürliches Substrat eingestellt ist, und verschiedene Kohlehydrate auf ihre glykolytische Spaltbarkeit geprüft. Es zeigte sich, daß nur Hexosen angegriffen werden und von ihnen außer Glucose nur Mannose, Fructose und Galaktose. Dabei waren die Geschwindigkeiten

	$Q_{CO_2}^{N_2}$
für d-Glucose	23,9
„ d-Mannose	21,6
„ d-Fructose	3,3
„ d-Galaktose	1,3

Was die beiden Formen der Glucose, ihre α- und β-Form, anbetrifft, so haben wir einen wesentlichen Unterschied der glykolytischen Spaltbarkeit nicht gefunden. Da sich beide Formen, in Wasser gelöst,

Carcinomas are fermenting GALACTOSE much more slowly than GLUCOSE.

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PanTum Application in Screening

Elimination of TKTL1 leads to lower cisplatin-induced cytotoxicity.

Knockdown of TKTL1 additively complements cisplatin-induced cytotoxicity in nasopharyngeal carcinoma cells by regulating the levels of NADPH and ribose-5-phosphate

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Cisplatin
Cytotoxicity
Pentose phosphate pathway
Nasopharyngeal carcinoma

ABSTRACT

Background: Transketolase-like 1 (TKTL1) plays an important role in pentose phosphate pathway (PPP) branch, the main pathway generating nicotinamide adenine dinucleotide phosphate (NADPH) and nucleotides for DNA synthesis. TKTL1 is closely related to DNA damage and has a close relationship with incidence and progression of cancers. Cisplatin is the main chemotherapeutic drug by inducing DNA damage. Whether TKTL1 knockdown additively complements cisplatin-induced cytotoxicity in nasopharyngeal carcinoma cells, however, remains largely undefined.

Methods: Lipofectamine 2000 was used to transfect si-TKTL1s with different sequences into the CNE2 and HONE1 cells. The mRNA and protein levels of TKTL1 were determined by qRT-PCR and western blot, respectively. MTT assay and flow cytometry were used to access the viability and apoptosis of CNE2 and HONE1 cells. The NADPH and ribose-5-phosphate levels in both CNE2 and HONE1 cells were determined by NADPH examination kit and HPCE analysis, respectively. The effect of TKTL1 knockdown and NADPH/ribose-5-phosphate supplement on DNA damage was assessed by using Comet assay.

Results: TKTL1 knockdown significantly decreased TKTL1 level in CNE2 and HONE1 cells. A significant decrease in cell viability and an obvious increase in cell apoptosis rate were found in si-TKTL1 + cisplatin group compared with si-TKTL1 group or si-control + cisplatin group. The levels of NADPH and ribose-5-phosphate in CNE1 and HONE1 cells were dramatically decreased in si-TKTL1 group compared with si-control group. TKTL1 knockdown additively complemented cisplatin-induced cytotoxicity, which was partly reversed by the supplements of NADPH and ribose-5-phosphate, including the increased survival rate, decreased apoptosis and DNA damage.

Conclusions: Knockdown of TKTL1 additively complements cisplatin-induced cytotoxicity in the nasopharyngeal carcinoma cells by inhibiting the levels of NADPH and ribose-5-phosphate, indicating that TKTL1 may be a promising target to improve the therapeutic effect combining with cisplatin for the patients with nasopharyngeal carcinoma.

Biomedicine & Pharmacotherapy. 2017 85:672-678

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PanTum Application in Screening

TKTL1 leads to resistance to paclitaxel.

TKTL1 modulates the response of paclitaxel-resistant human ovarian cancer cells to paclitaxel

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RNA interference
Redox

ABSTRACT

Transketolase-like 1 (TKTL1) plays an important role in the pentose phosphate pathway (PPP) branch. The main obstacle of ovarian cancer treatment is chemotherapeutic resistance. We investigated whether inhibiting TKTL1 in OC3/TAX300 cells could re-sensitize paclitaxel-resistant cells to paclitaxel and proposed a mechanism of action. Western blotting revealed that TKTL1 expression levels in OC3/Tax300 cells were significantly higher than those in OC3 cells. Inhibition of TKTL1 significantly decreased the cellular proliferation rate and IC50 for paclitaxel. Metabolomics revealed that NADPH levels were reduced in the si-TKTL1 group, whereas $NADP^+$ was increased compared with the level in the negative si-TKTL1 group. A 2.2-fold increase in the ROS level and an obvious increase in the cell apoptosis rate were observed in the si-TKTL1+paclitaxel group compared with those in the negative si-TKTL1+paclitaxel and OC3/Tax300 + paclitaxel groups. Western blotting revealed that Bax and Caspase 3 proteins were up-regulated, whereas Bcl-2 expression was down-regulated. Quantitative RT-PCR revealed no changes in gst-π or mrp1 gene expression in the three groups, whereas GSH levels were reduced in the si-TKTL1 group as verified by metabolomics. TKTL1 inhibition also reduced tumor growth in *vivo*. Collectively, TKTL1 down-regulation sensitized paclitaxel-resistant OC3/Tax300 ovarian cancer cells to paclitaxel.

Biochem Biophys Res Commun. 2018 Sep5;503(2):572-579

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PanTum Application in Screening

TKTL1 association with carcinoma carcinogenesis.

Published Online First on January 26, 2010 as 10.1158/1078-0432.CCR-09-2604

Clinical Cancer Research

Human Cancer Biology

TKTL1 Is Activated by Promoter Hypomethylation and Contributes to Head and Neck Squamous Cell Carcinoma Carcinogenesis through Increased Aerobic Glycolysis and HIF1α Stabilization

Wenyue Sun[1], Yan Liu[2], Chad A. Glazer[1], Chunbo Shao[1], Sheetal Bhan[1], Semra Demokan[1], Ming Zhao[3], Michelle A. Rudek[3], Patrick K. Ha[1], and Joseph A. Califano[1,4]

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TKTL1 and Phytotherapy

RESVERATROL INHIBITS EXPRESSION OF CANCER-SPECIFIC PENTOSE PHOSPHATE PATHWAY ENZYME TKTL1

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Received: 30 January 2018, Revised and Accepted: 19 March 2018

Resveratrol treatment in HeLa cells inhibited proliferation, promoted ROS, and reduced intracellular GSH levels. In TKTL1 promoter activity assay, resveratrol treatment was found to directly inhibit promoter activity of TKTL1.

Resveratrol inhibited both mRNA and protein expression of TKTL1 in a dose-dependent manner.

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TKTL1 and Oxythiamin (OT)

PNAS

Transketolase counteracts oxidative stress to drive cancer development

Iris Ming-Jing Xu[a], Robin Kit-Ho Lai[a], Shu-Hai Lin[b,c], Aki Pui-Wah Tse[a], David Kung-Chun Chiu[a], Hui-Yu Koh[a], Cheuk-Ting Law[a], Chun-Ming Wong[a,d], Zongwei Cai[b,c], Carmen Chak-Lui Wong[a,d,1], and Irene Oi-Lin Ng[a,d,1]

[a]Department of Pathology, The University of Hong Kong, Hong Kong, SAR, China; [b]Department of Chemistry,Hong Kong Baptist University, Hong Kong, SAR, China; [c]State Key Laboratory of Environmental and Biological Analysis, Hong Kong Baptist University, Hong Kong, SAR, China; and [d]State Key Laboratory for Liver Research, The University of Hong Kong, Hong Kong, SAR, China

Edited by Tak W. Mak, The Campbell Family Institute for Breast Cancer Research at Princess Margaret Cancer Centre, University Health Network, Toronto, ON, Canada, and approved December 24, 2015 (received for review May 5, 2015)

We next examined the sensitization effect of the TKT inhibitor oxythiamine (OT), a thiamine antagonist, for Sorafenib.

Cell proliferation assay revealed that OT drastically sensitized SMMC and MHCC97L cells to Sorafenib treatment in vitro and increased ROS accumulation in the Sorafenib-treated HCC cells.

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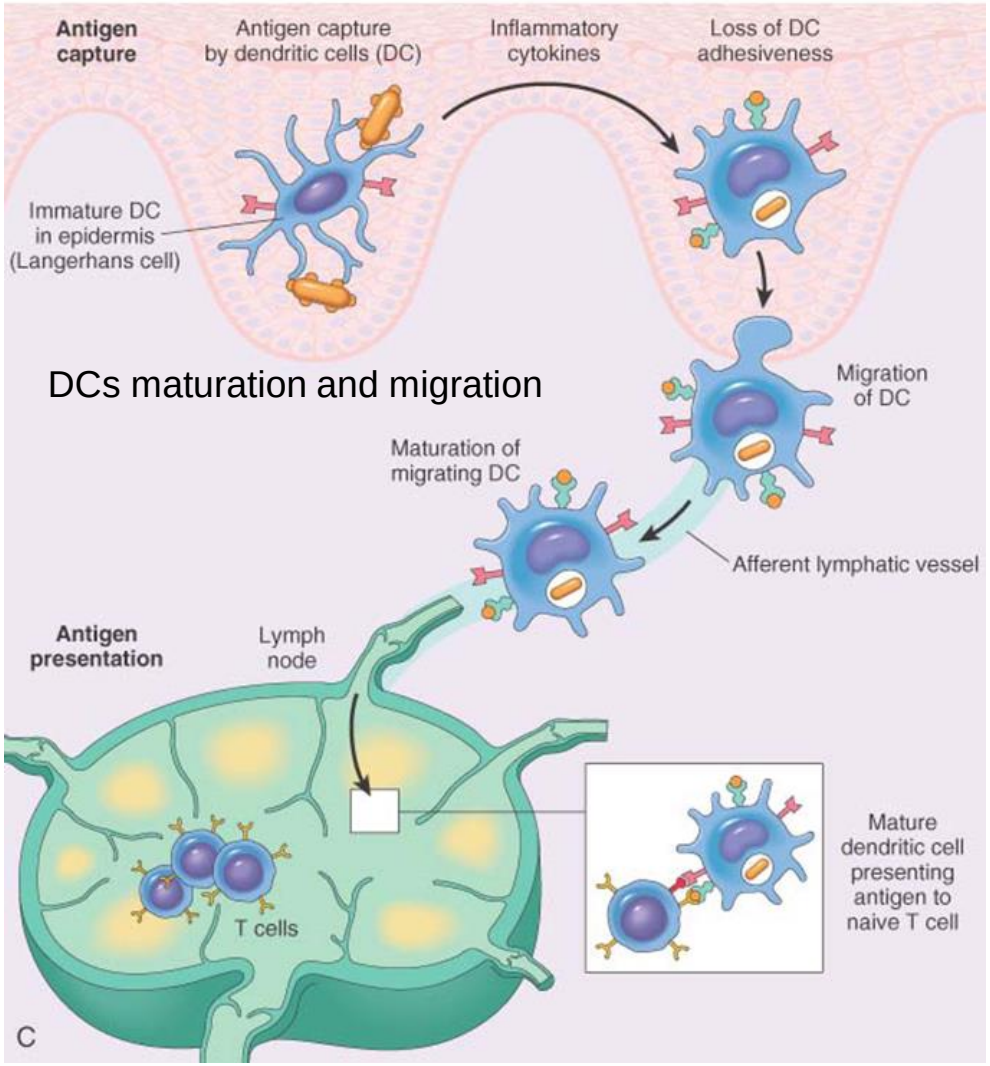
Dendritic Cells (DC)



Immature DCs

- Residing in tissue and unable to stimulate naïve T-cells.
- The functions of immature DCs are antigen uptake and processing.

Mature DCs

- Residing in Lymphoid organs and able to stimulate naïve T-cells.
- The functions of mature DCs are presenting antigen to naïve T-cells.

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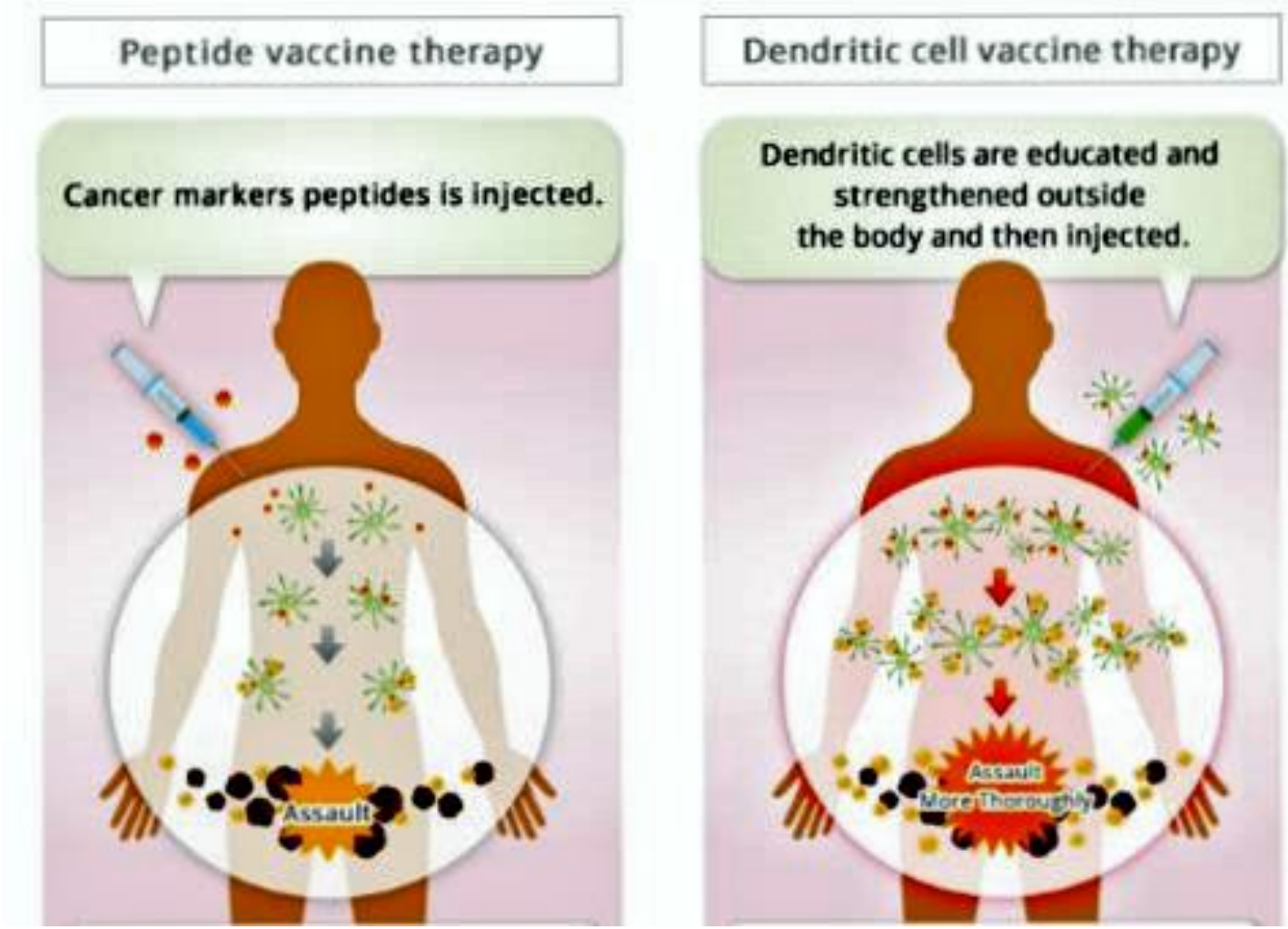
Peptide Vaccine VS DC Vaccine Therapy



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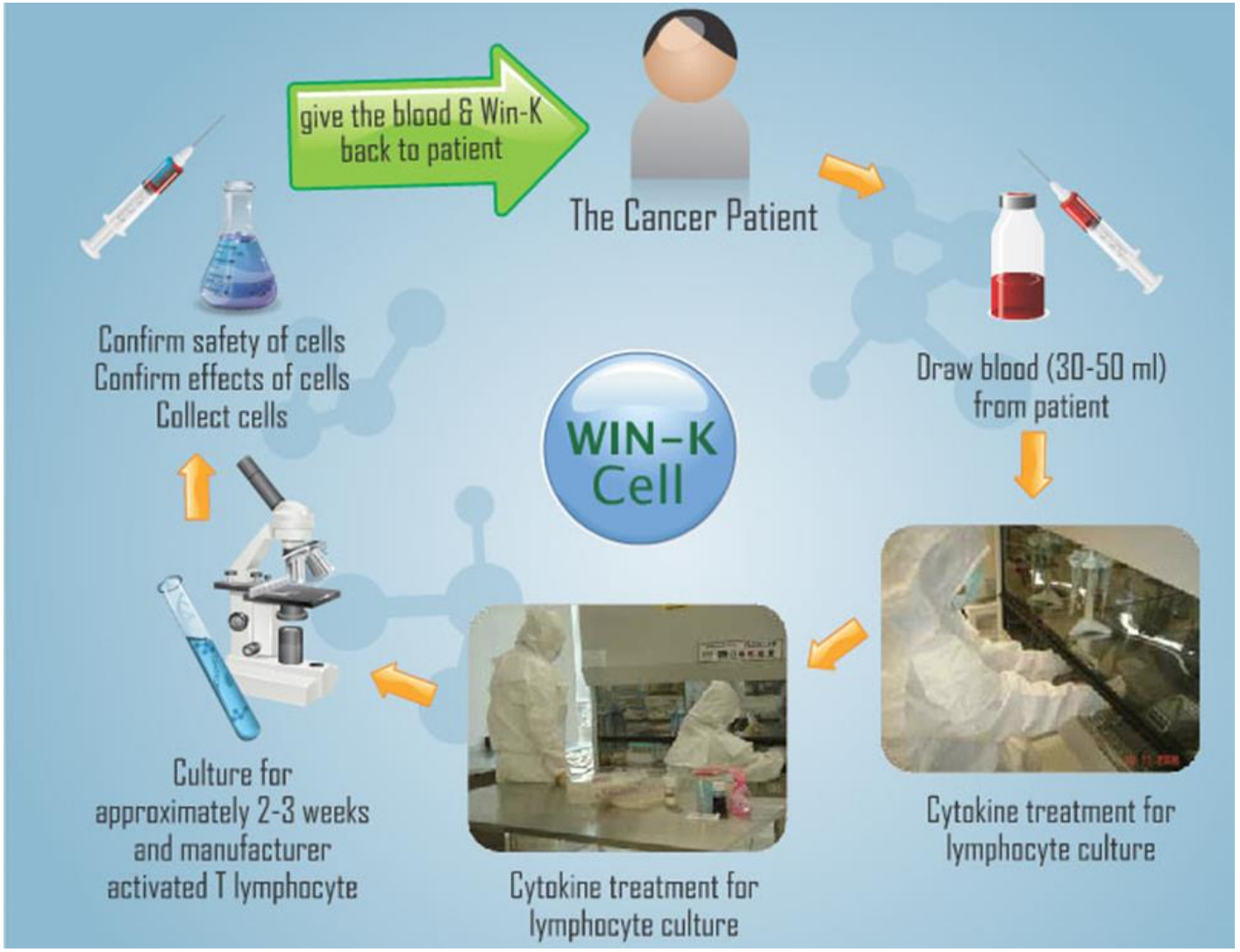
Immune Therapy with NK cells



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Liquid Biopsy

The **Metavectum Tumour-Therapy Test** pinpoints the "Achilles' heel" of the tumor on a genomic, proteomic and metabolomic level and based on the results a therapy proposal is submitted.

Tumors develop a unique individual profile which differs from person to person. Consequently the medical treatment for tumor must be carried out individually.

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Therapy: IV or Orally

I.V. Infusions

+

Oral Supplements

- Curcumin
- DCA
- Amygdalyn
- Artesunate
- Vitamin C
- ECGC
- Germanium
- Procain
- **Silibinin, Apigenin, Berberin in progress**
- Phytotherapy
- Salvestroles
- Cannabis
- Methadon
- Metformin
- Melatonin

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Metavectum Report (Part I)

Anti-Cancer Agent	Gene Profile (+)	Gene Profile (-)	Gene Profile normal
5-FU	TS +	TP (-), DPD (-)	
Adriamycin, Epirubicin	TOPOIIA1 ≈+		
Alkylators (Ifosphamid, Cyclophosphamid etc.)	GCS +, GSTpi +		
Apigenin			STAT1 n
Aromatase-Inhibitoren			CYP19A1 n
Artesunate			TF n
Atezolizumab etc.	PDL-1 +		
Avastin	VEGFA ≈+		
Berberin	TOPOIIA1 ≈+		
Busulfan, Treosulfan	GCS +, GSTpi +		
Carmustin, Lomustin etc. Nitrosoharnstoffe	GCS +, GSTpi +		
Capecitabin, Xeloda		TP (-)	
Cabozantinib, Cometriq	MET ≈+, MDM2 +		MET ≈+
Crizotinib, Alectinib	MET ≈+, ALK +		
Celebrex etc.			COX2 n
Curcumin	NFKB +		
Dabrafenib, Trametinib	MEK ≈+		
Dacarbazin	CD133 +		MGMT n
Denosumab	RANKL +		
Digogxin	HIF +		
Enzalutamid, Bicalutamid	ARFL + <> ARV7 +		
Enzalutamid, plus Niclosamid	ARFL + <> ARV7 +		

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Metavectum Report (Part II)

Erlotinib, Gefitinib etc.	EGFR ≈+		
Estramustin	BCL2 +		
Etoposid	TOPOIIA1 ≈+		
Everolimus	mTOR +		
Glivec, Imatinib	C-KIT +, MDR1 +		
Gemcitabine, Cytarabin	RRM1 ≈+, DCK ≈+		
Herzeptin, Lapatinib			ERBB2 n
Hydroxyharnstoff	RRM1 ≈+		
Hyperthemie			HSP27 n
IFN-alpha, IL2			IFNAR1 n, IFNGR1 n
IP-6	TERT +		
Methotrexat, Pemetrexed	DHFR +, MSH2 +		
Mitomycin C	GCS +, GSTpi +		
Mitoxantron	TOPOIIA1 ≈+		
Niclosamid	AEV7 +		
Nivolumab, Pembrolizumab	PD1 +, CYP3A4 ≈+		
Palbociclib			CDK4/6 n
Platinverbindungen	CD133 +, CD44+, GSTpi +	ERCC1 (-)	
Quercetin, Sulforaphan	CD133+		
Salinomycin etc.	CD133+		
Sorafenib, Sunitinib	PDGFRbeta +, C-KIT +		
Tamoxifen, Raloxifen			ER1 n
Taurolidin	TNF ≈+		
Taxane	MDR1 +		
Temozolomid			
Topo-, Irinotecan	TOPOI ≈+, MDR1 +		
Vinca-Alkaloide	GCS +, GSTpi +		
Vitamin C Hochdosis	SVCT-2 +, HIF +		

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Metavectum Report (Part III)

META-V-20181932325-R1

Natural Product	Gene Profile (+)	Gene Profile (-)	Gene Profile normal
Amygdalin			Beta-Glucosidase n
Apigenin			STAT1 n
Artesunate			TF n
Berberin	TOPOIIA1 ≈+		
Cannabinoide	CB2 +		
Celebrex etc.			COX2 n
Curcumin	NFKB +		
DCA			LDHA n
Digoxin	HIF +		
Genistein			uPAR n
Hyperthermia			HSP27 n
IFN-alpha, IL2			IFNAR1 n, IFNGR1 n
IP-6	TERT +		
Isoflavone, Estriol			ER1 n
Niclosamid	ARV7 +		
Quercetin/Sulforaphan	CD133 +		
Resveratrol	BIRC5 +		
Salinomycin	CD133 +		
Silibinin	CD44 +		
Taurolidin			TNF n
Vitamin C	HIF +, SVCT-2 +		
Zileuton			5LOX n

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Metavectum Report (Part IV)

CD133/CD44: "…CD133+CD44+ cancer stem cells previously isolated from laryngeal squamous cell carcinoma (LSCC) cell lines showed strong malignancy and tumorigenicity…" [Lit.: Whole-Transcriptome Analysis of CD133+CD144+ Cancer Stem Cells Derived from Human Laryngeal Squamous Cell Carcinoma Cells. Yongyan Wu et al., Cell Physiol Biochem (2018) 47 pp 1696-1710; Identification of molecular signature of head and neck cancer stem-like cells. S. Shrivastava et al., Nature SCIENTIFIC REPORTS (2015) 5:7819].

Salinomycin >> CD133: "…The combination of salinomycin targeting stem cells with current chemotherapeutic drugs i.e., doxorubicin or paclitaxel directed to cancer cells…" [Lit.: Targeting breast cancer stem cells in triple-negative breast cancer using a combination of LBH589 and salinomycin. M. Kai, et al., Breast Cancer Res. Treat. (2015) 151, 281–294; Targeting Breast Cancer Stem Cells to Overcome Treatment Resistance. Sònia Palomeras et al., Molecules (2018) 23(9): 2193].

Silibinin >> CD44 >: [Lit.: Anti-metastatic Efficacy of Silibinin: Molecular Mechanisms and Therapeutic Potential against Cancer. G. Deep et al., Cancer Metastasis Rev. (2010) 29(3): 447–463].

Atezolizumab / Nivolumab: It was shown in the literature, that the combination of Atezolizumab (>PDL-1) and Nivolumab (>PD1) is more effective than the respective monotherapy. Therapy should be started with low dose to evaluate possible side effects.

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Circulating Tumour Cells Detection Case Study

Patient: FEMALE - 69 years old
Primary Tumour: Head and neck squamous cell carcinoma

1 Isolation of circulating tumour cells (CTC) / micrometastases

Epithelial cells were isolated from the patient's peripheral blood. Mononuclear cells (MNC) served as a control. mRNA was isolated from all cell isolates and the expression of the tumour-relevant genes and chemo sensitivity markers was measured using RT-PCR.

Conclusion: Proof of the increased expression of TERT, C-MYC, BIRC5, EpCAM, CD44, CD133 and CK8/18 refers to the presence of circulating tumor cells (CTC) in the examined blood sample.

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Therapy D.F.

I.V. Infusions

+

Oral Supplements

I.V.
- Curcumin
- ECGC
- Vitamin C
- Hyperthermia

Oral
- Niclosamid
- **Salinomycin**
- **Possible combination: Atezolizumab, Nivolumab**

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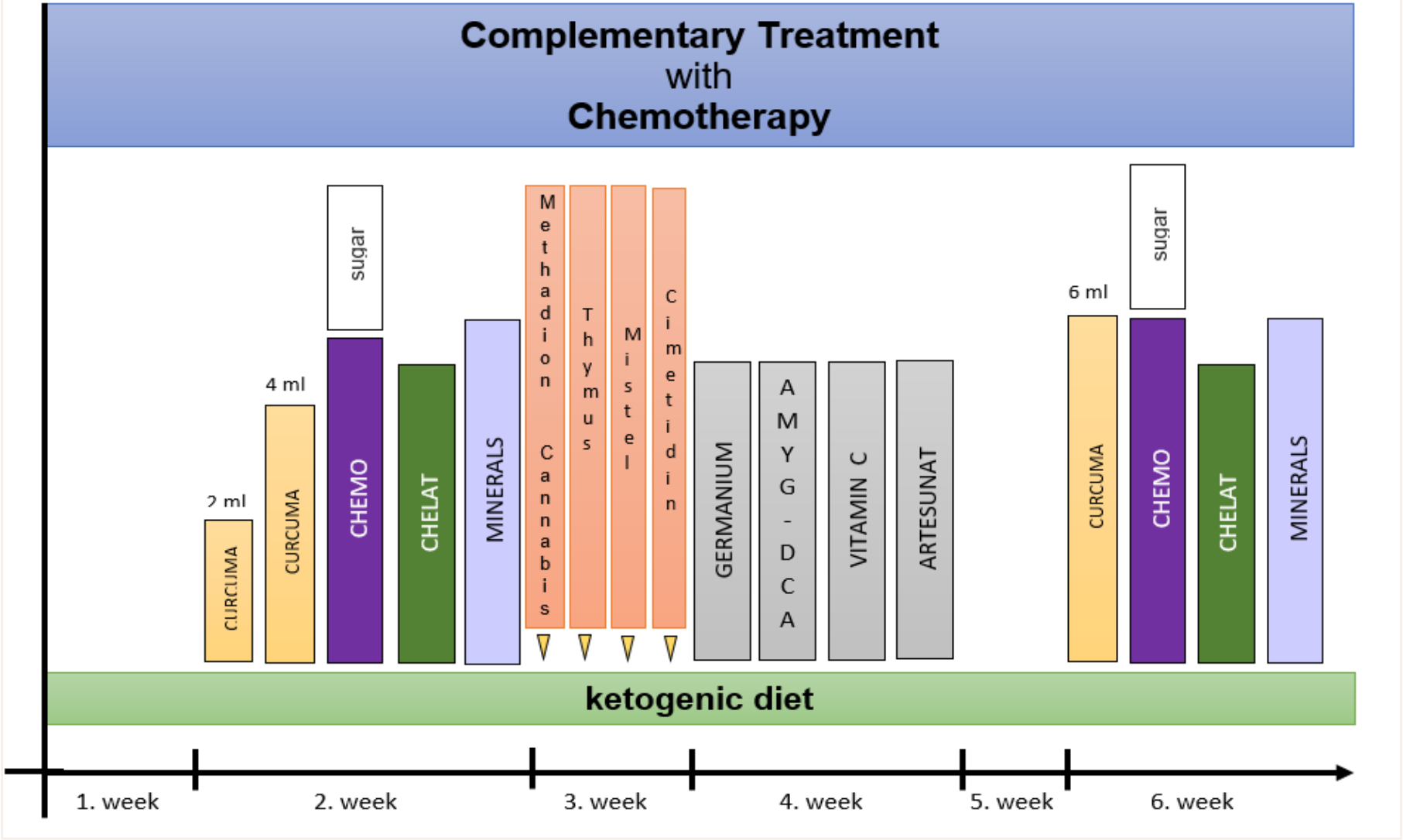
Complementary Treatment with Chemotherapy



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Thank you for your attention.