Clinical application of a terrain centered approach to Cancer through the lens of a Functional Medicine Practitioner

29.06.23

Jo Gamble

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& Fellow in Integrative Oncology

ICT FELLOWSHIP

PRACTITIONER METABOLIC APPROACH TO CANCER GRADUATE MTIH.ORG

THE INSTITUTE FOR FUNCTIONAL MEDICINE® 2013 CERTIFIED PRACTITIONER

Embracing Nutrition & Functional Medicine


LET'S
GO!

Meet Liam

A 49 year old man, father of 5 girls

Described as being a previously healthy business man working as a CEO in finance

Never smoked
Very minimal alcohol intake prior to diagnosis
Was cycling daily

Tonsillectomy as a child

Presented March 22 with a 4 month history of digestive symptoms: meals not sitting as well, less interested in food, reflux.

GP suggested IBS and suggested Rennie and Gaviscon and cut out milk
Coeliac negative

6 months before back pain, bone scan, MRI, bloods all clear

Had increased pain meds so thought this was the cause of the GI symptoms

Pain was only 2/10, worse at night

By February 22, every now and then vomiting if food too rich and increasing nauseousness
Still traveling and went on a ski holiday and skid daily

More tired, started going to bed at 9 pm
Loose stools

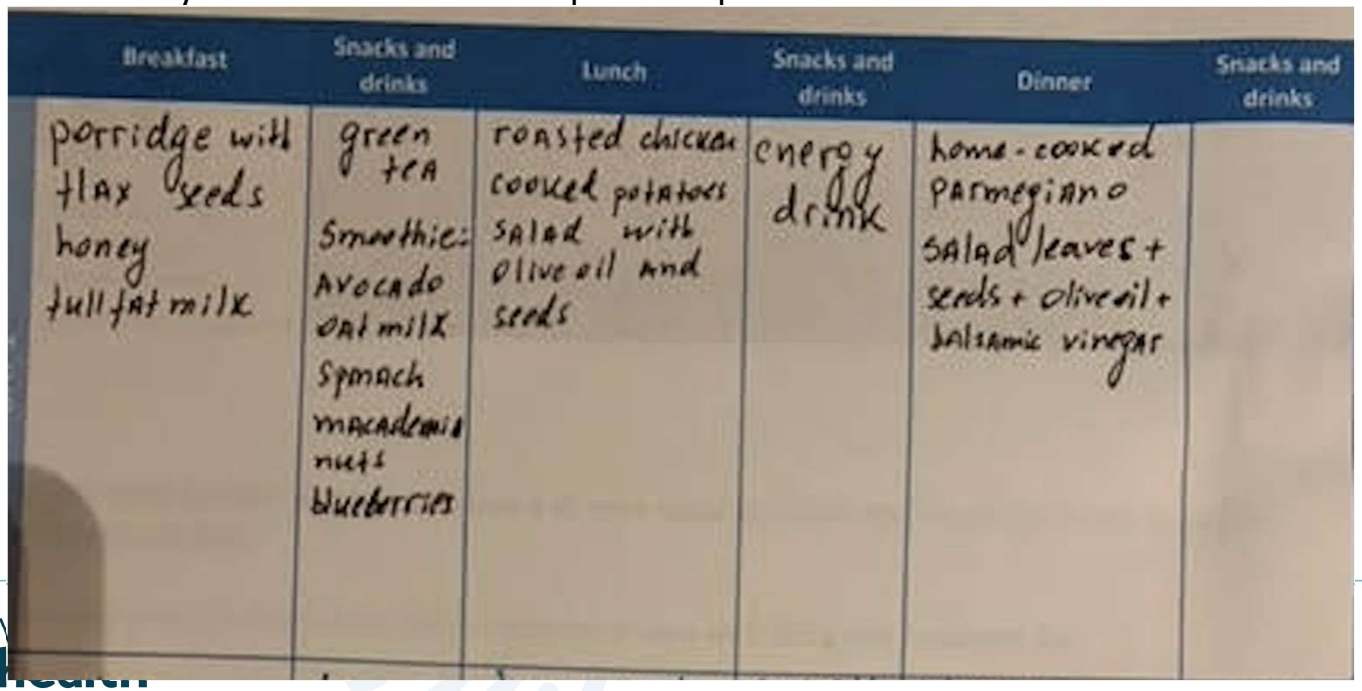
2-3 week history of more vomiting episodes
Presented to hospital

CT scan confirmed:

Body of pancreas adenocarcinoma with lung, liver, and peritoneal metastases.
BRCA2 mutation and KRASG12R mutation.

10.03.22 Gastrojejunostomy for gastric outlet obstruction
04.04.22: Commenced 2 weekly FOLFIRINOX x 12.

Presented to me on 21st March 2022:
Weight dropped from 78 kg to 68 kg
Current meds: Creon, Paracetamol, blood pressure meds
Current nutrition: Ensure 3-4 daily
Currently able to eat 50-75% off previous portion size



Breakfast	Snacks and drinks	Lunch	Snacks and drinks	Dinner	Snacks and drinks
porridge with flax seeds honey full fat milk	green tea Smoothie: Avocado oat milk Spinach macadamia nuts blueberries	roasted chicken cooked potatoes salad with olive oil and seeds	energy drink	home-cooked Parmegiano salad leaves + seeds + olive oil + balsamic vinegar	

Family history: Mum cervical cancer
Dad Prostate cancer

Other key points: Diet already 80-90% organic

Very supportive wife
Private medical cover
Financially able to do everything suggested

Bloods at diagnosis 15th March :

HB: 126
WBC: 8.11
Neutrophils: 5.44
Lymphocytes: 1.62
Alk Phos: 84
Gamma GT
ALT:81
AST: 66
Vitamin D: 53
CRP: 43
ESR:
LDH:
Homocysteine:

BP 146/94
02 96
Heart Rate 83

Plan :

- Ascertain Genomics
  - Lifecode detox and methylation

- Increase fats, and decrease carbohydrates
- Increase anti-oxidants through food
- Intermittent fasting
- Detox: FIR sauna, detox baths,

- Healing foods:
  - Bone Broth
  - Greens
  - Cruciferous vegetables
  - Ghee
  - Oily fish
  - Berries
  - Olives and olive oil
  - Nuts and seeds (avoid peanuts and cashews)
  - Avocado
  - Grass fed/wild meat
  - Coconut oil/coconut milk

- Herbs and spices
  - Turmeric
  - Ginger
  - Cumin
  - Cacao
  - Parsley
  - Coriander
  - Cinnamon

BIOLOGY

Fasting Might Boost Chemo's Cancer-Busting Properties

A new animal study suggests that short-term starvation might improve outcomes for cancer

Fasting Cycles Retard Growth of Tumors and Sensitize a Range of Cancer Cell Types to Chemotherapy

Changhan Lee[1,*], **Lizzia Raffaghello**[2,*], **Sebastian Brandhorst**[1,3], **Fernando M. Safdie**[1], **Giovanna Bianchi**[2], **Alejandro Martin-Montalvo**[4], **Vito Pistoia**[2], **Min Wei**[1], **Saewon Hwang**[1], **Annalisa Merlino**[1], **Laura Emionite**[5], **Rafael de Cabo**[4], and **Valter D. Longo**[1,†]

[1]Andrus Gerontology Center, Department of Biological Sciences and Norris Cancer Center, University of Southern California, 3715 McClintock Avenue, Los Angeles, CA 90089-0191, USA

[2]Laboratory of Oncology, Giannina Gaslini Institute, Genova 16145, Italy

[3]Centre for Medical Biotechnology, Faculty of Biology, University Duisburg-Essen, Essen 45117, Germany

[4]Laboratory of Experimental Gerontology, National Institute on Aging, National Institutes of Health, Baltimore, MD 21224, USA

[5]Animal Research Facility Istituto Tumori, Genova 16145, Italy

Abstract

Short-term starvation (or fasting) protects normal cells, mice, and potentially humans from the harmful side effects of a variety of chemotherapy drugs. Here, we show that treatment with starvation conditions sensitized yeast cells (*Saccharomyces cerevisiae*) expressing the oncogene-

Plan :

- Lifestyle recommendations:
  - Daily mindfulness
  - Time in Nature
  - Barefoot walking
  - Wim Hoff breathing
  - Reduce EMF exposure
  - Sleep
  - Reduce toxic exposure
  - Clean air
  - Gentle exercise

Vagal nerve activity predicts overall survival in metastatic pancreatic cancer, mediated by inflammation

Marijke De Couck [1], Raphaël Maréchal [2], Sofie Moorthamers [3], Jean-Luc Van Laethem [2], Yori Gidron [3]

Affiliations + expand

PMID: 26618335 DOI: 10.1016/j.canep.2015.11.007

Abstract

Recent research findings suggest neuro-modulation of tumors. Finding new modifiable prognostic factors paves the way for additional treatments, which is crucial in advanced cancer, particularly pancreatic cancer. This study examined the relationship between vagal nerve activity, indexed by heart rate variability (HRV), and overall survival (OS) in patients (N=272) with advanced pancreatic cancer. A "historic
confounders were
examined. HRV wa
were measured as
and the Belgian na
than double the da
higher initial HRV v
including age and
by CRP levels. Imp
unrelated to CRP, v
(r=-0.20, p<0.05).

The effect of the vagus nerve on inflammation was suggested as the main factor. It is known as the 'Inflammatory Reflex'. The vagus nerve basically turns off inflammation at the genetic level by turning down a gene that produces TNF-alpha (Tumour Necrosis Factor), which is an inflammatory protein in the body that sets off a cascade of inflammation. Thus, the vagus nerve can effectively control inflammation in this way. Therefore, higher vagus nerve activity usually means lower inflammation.

In one study of patients with advanced pancreatic cancer, for example, patients with high HRV (or vagus nerve activity) survived longer and had lower inflammation levels than patients with low HRV (vagus nerve activity).

Detoxification Summary

Phase 1 reactions

Cytochrome P450s

- CYP1A1
- CYP1A2
- CYP1B1
- CYP2A6
- CYP2C19
- CYP2C9
- CYP2D6
- CYP2E1
- CYP3A4

Alcohol

- ADH1B
- ADH1C
- ALDH2

Pesticides, Lipids

- PON1

ROS detoxification

- GPX1
- NQO1
- SOD2

Phase 2 conjugation

Glucuronidation

- UGT1A1
- UGT1A6

Sulphonation

- SULT1A1
- SULT1E1
- SULT2A1

Acetylation

- NAT1
- NAT2

Glutathione conjugation

- GSTM1
- GSTP1
- GSTT1

Methylation

- COMT
- TPMT

Phase 3 antiporter

Antiporter

- ABCB1

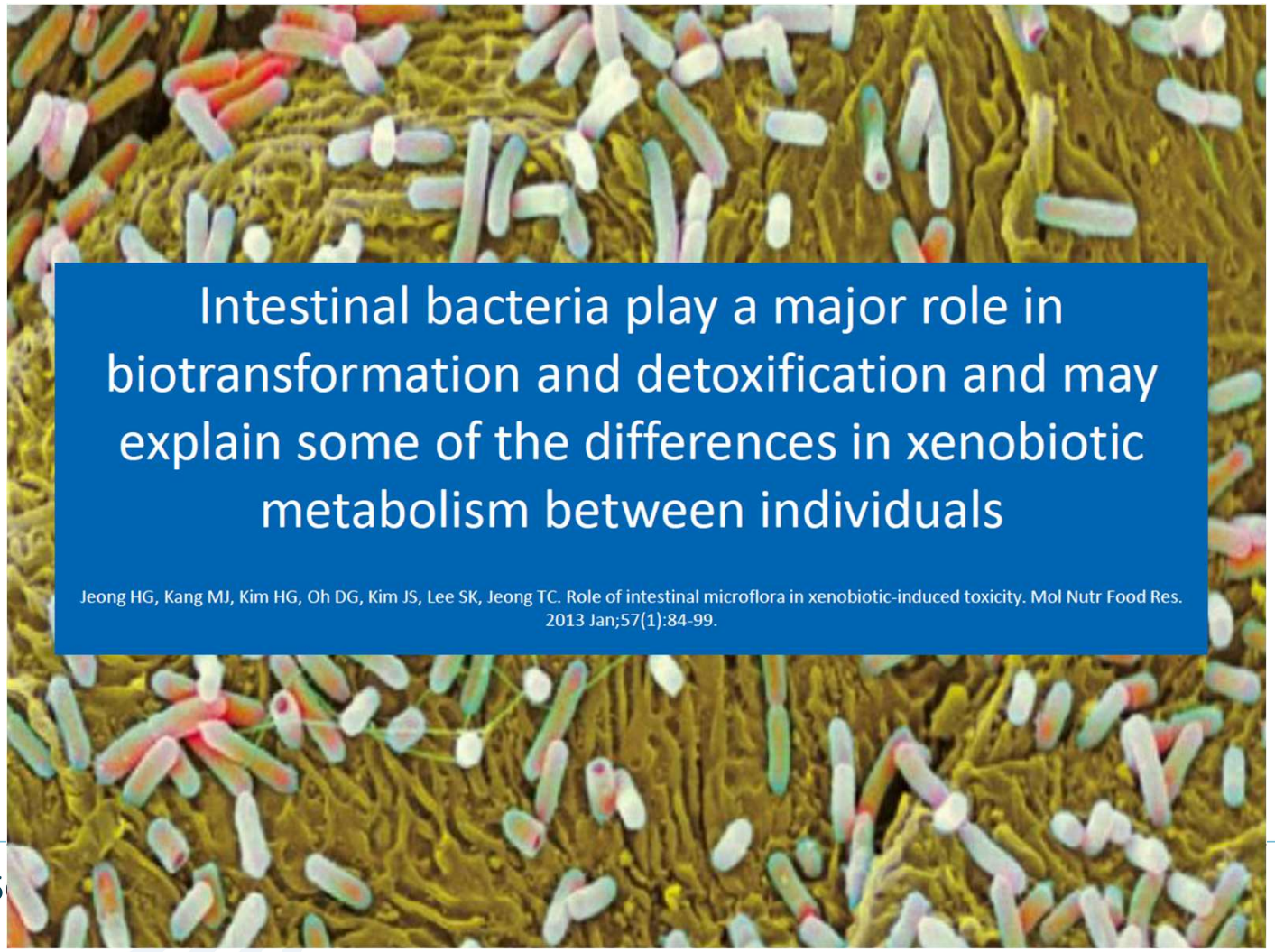
The critical roles of glutathione

- Direct chemical neutralization of singlet oxygen, hydroxyl radicals and superoxide radicals
- Cofactors for several antioxidant enzymes
- Regeneration of vitamins C and E
- Neutralization of free radicals produced by Phase I liver metabolism of chemical toxins
- One of the liver phase II reactions, which conjugate the activated intermediates produced by phase I to make them water soluble for excretion by the kidneys
- Transportation of mercury out of cells and the brain
- Regulation of cellular proliferation and apoptosis
- Vital to mitochondrial function and maintenance of mitochondrial DNA (mtDNA)

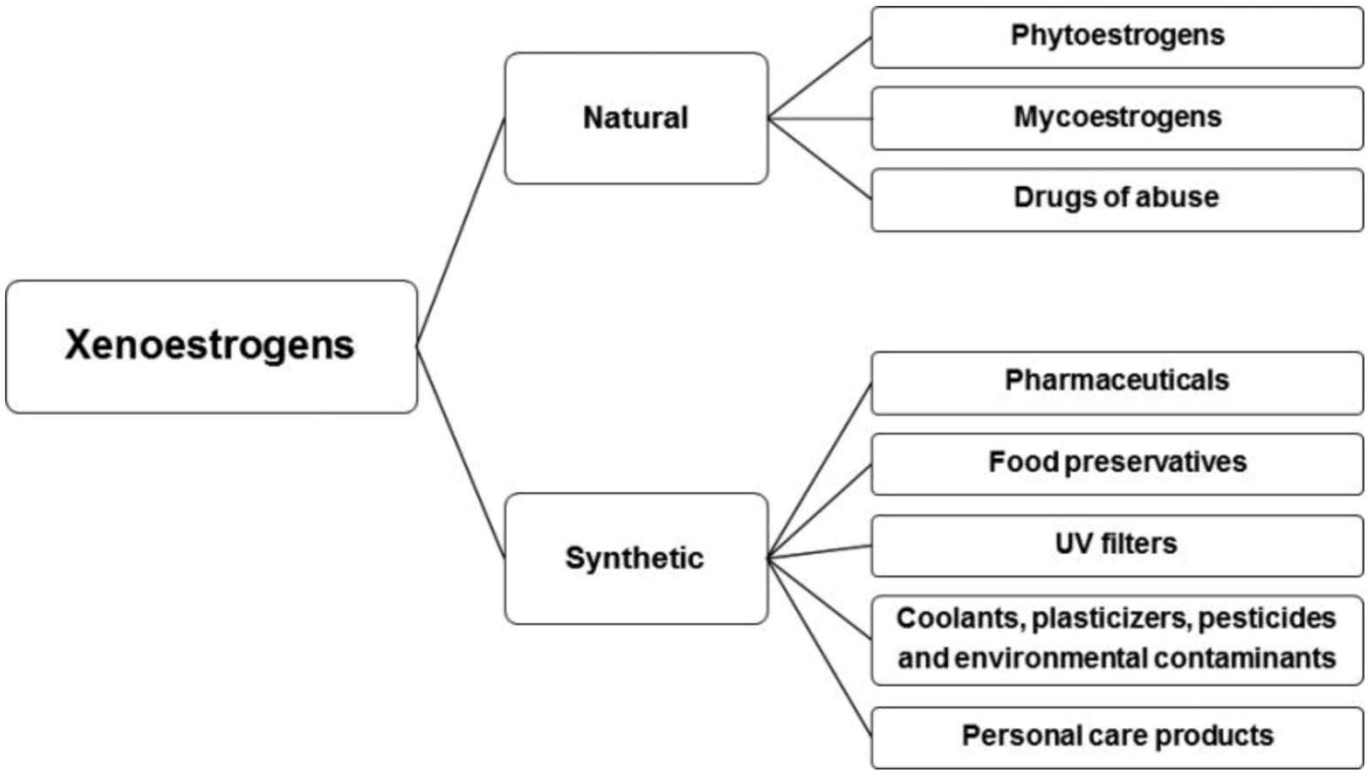
Glutathione: Whole Body Homeostasis

- Gene expression
- DNA and protein synthesis
- Cell proliferation and apoptosis
- Signal transduction
- Cytokine production
- Immune response
- Reduction-Oxidation
- Protein glutathionylation

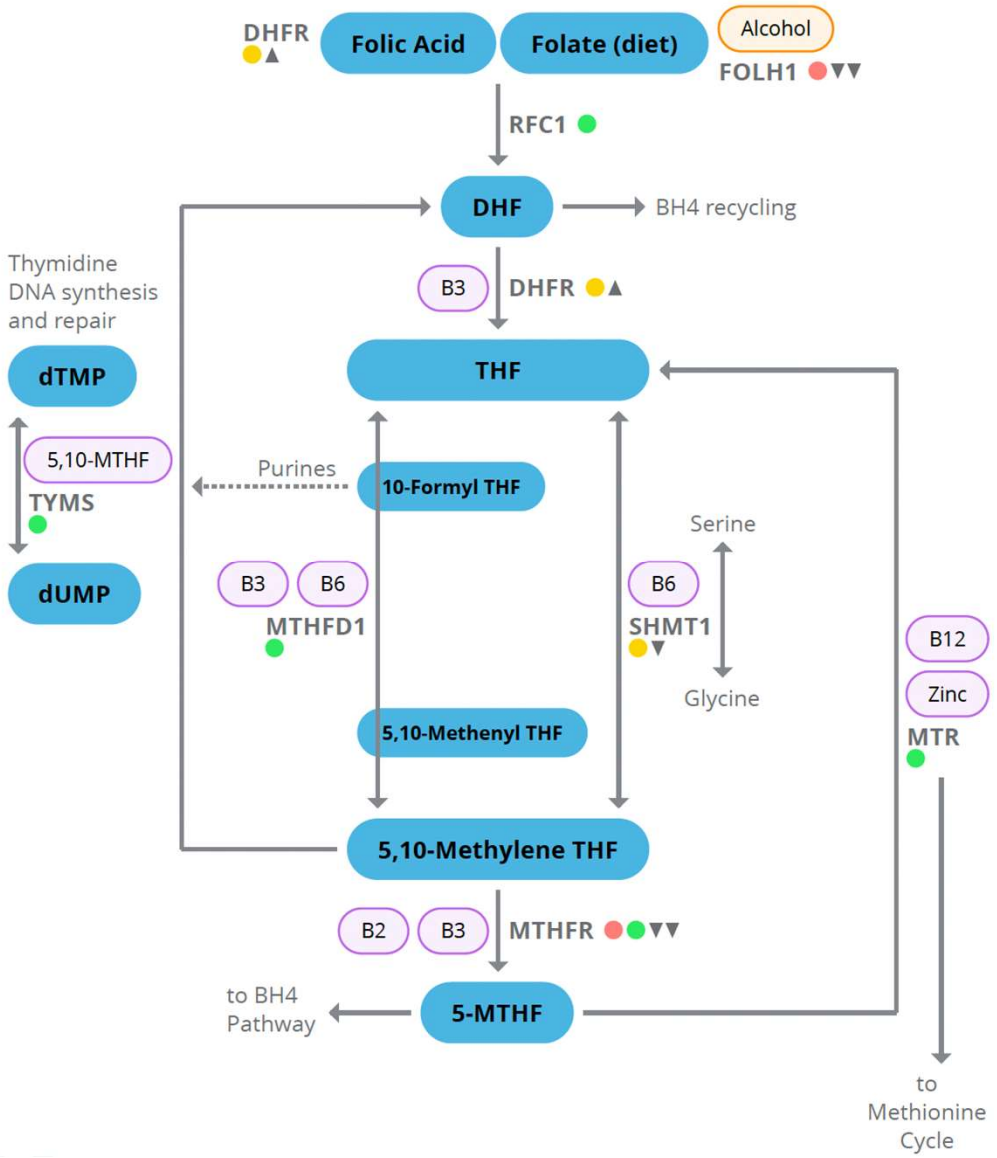
To date there are over 177,194 citations in PubMed that reference glutathione

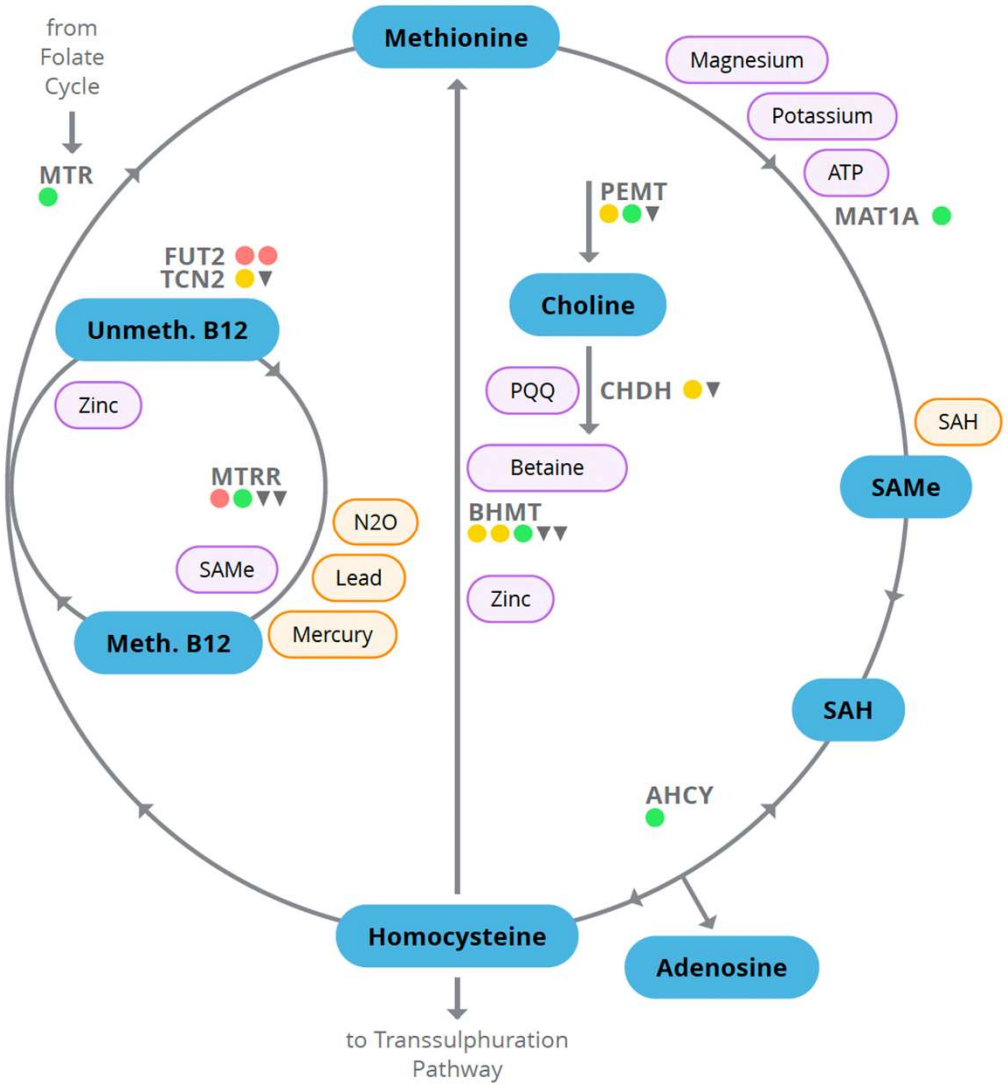

Intestinal bacteria play a major role in biotransformation and detoxification and may explain some of the differences in xenobiotic metabolism between individuals
Jeong HG, Kang MJ, Kim HG, Oh DG, Kim JS, Lee SK, Jeong TC. Role of intestinal microflora in xenobiotic-induced toxicity. Mol Nutr Food Res. 2013 Jan;57(1):84-99.

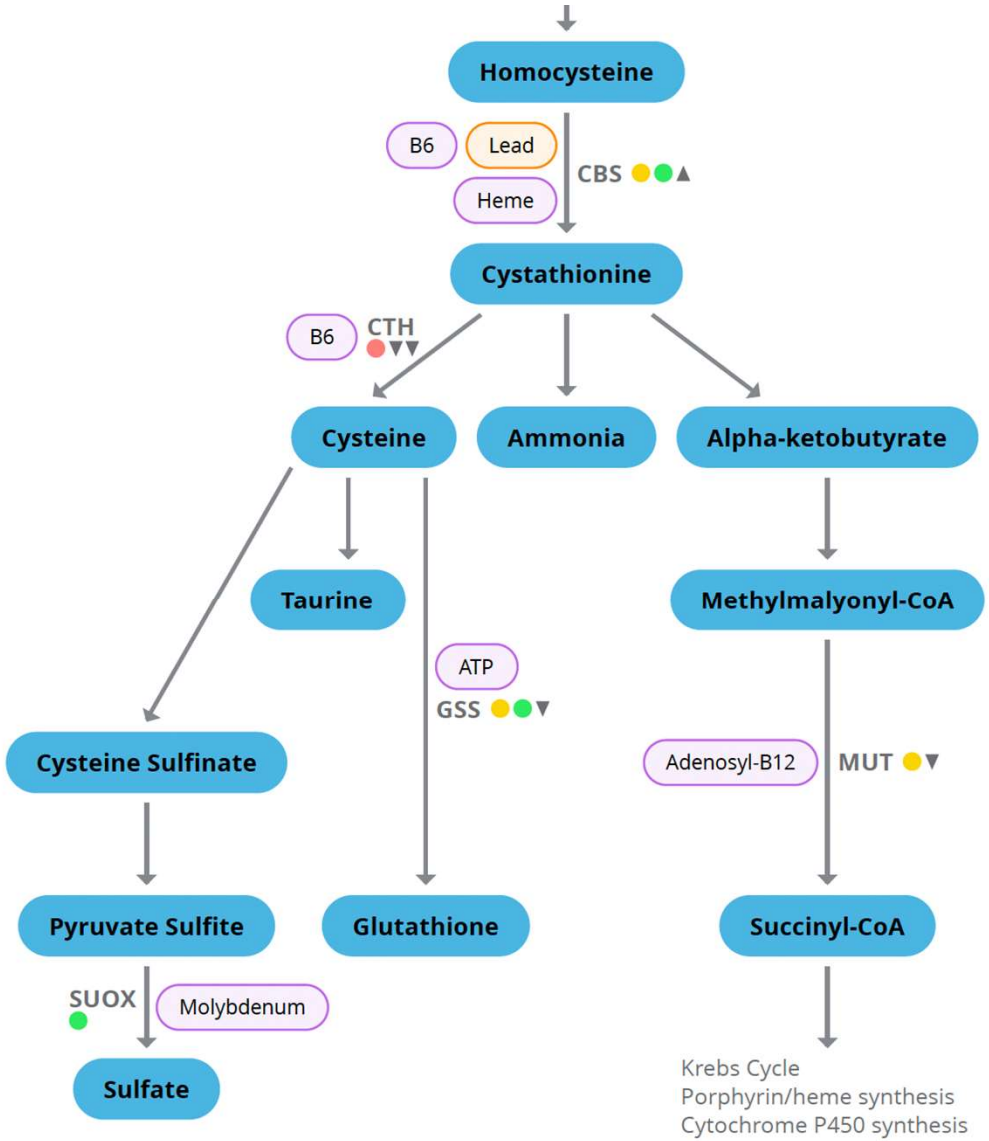
Classification of xenoestrogens



https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6104637/

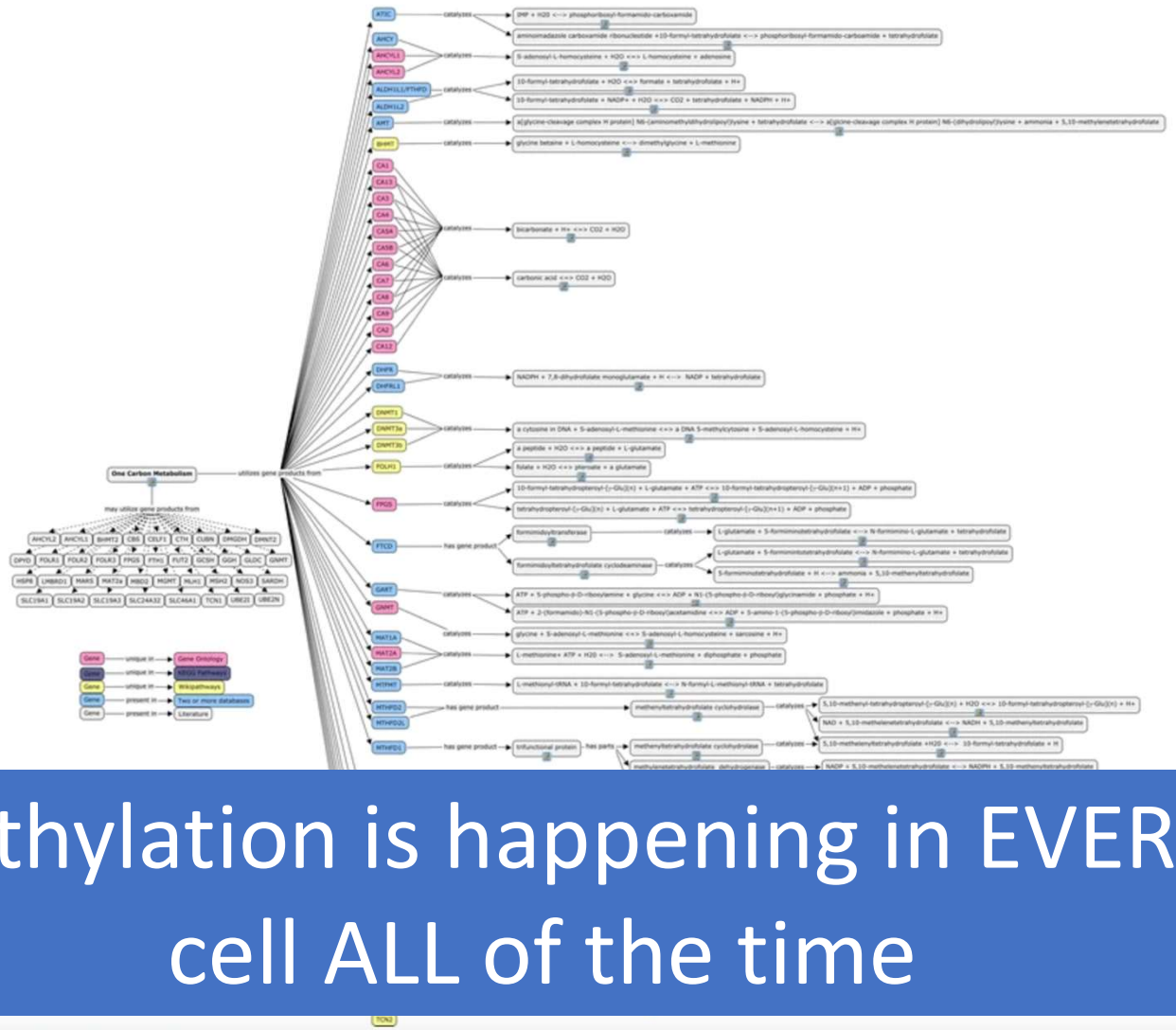

DHFR
Folic Acid
Folate (diet)
Alcohol
FOLH1
RFC1
DHF
BH4 recycling
Thymidine
DNA synthesis
and repair
B3
DHFR
dTMP
THF
5,10-MTHF
TYMS
Purines
10-Formyl THF
dUMP
B3
B6
MTHFD1
Serine
B6
SHMT1
Glycine
B12
Zinc
MTR
5,10-Methenyl THF
5,10-Methylene THF
B2
B3
MTHFR
to BH4
Pathway
5-MTHF
to
Methionine
Cycle


from
Folate
Cycle
MTR
Methionine
Magnesium
Potassium
ATP
MAT1A
PEMT
Choline
PQQ
CHDH
Betaine
BHMT
Zinc
FUT2
TCN2
Unmeth. B12
Zinc
MTRR
N2O
Lead
Mercury
SAMe
Meth. B12
SAH
SAMe
SAH
AHCY
Homocysteine
Adenosine
to Transsulphuration
Pathway


Homocysteine
B6
Lead
Heme
CBS
Cystathionine
B6
CTH
Cysteine
Ammonia
Alpha-ketobutyrate
Taurine
Methylmalyonyl-CoA
ATP
GSS
Cysteine Sulfinate
Adenosyl-B12
MUT
Pyruvate Sulfite
Glutathione
Succinyl-CoA
SUOX
Molybdenum
Sulfate
Krebs Cycle
Porphyrin/heme synthesis
Cytochrome P450 synthesis
Nucleotide synthesis

Methylation Uses

- Cell division (DNA, RNA synthesis and repair)Early CNS development (neural tube defects)
- Immune cell differentiation
- Neurotransmitter biosynthesis and metabolism (dopamine, adrenaline, neuroadrenaline, acetylcholine, melatonin)
- Histamine clearance
- Detoxification and hormone biotransformation
- Cellular energy metabolism
- Phospholipid synthesis
- Myelination of peripheral nerves
- Epigenetic regulation of gene expression (especially gene silencing)



Methylation is happening in EVERY cell ALL of the time

https://genesandnutrition.biomedcentral.com/articles/10.1007/s12263-014-0419-1/figures/3

Methylation Impacts

When we have a healthy methylation process, we have health.

Methylation impacts

- Cellular activities
- Genetic expression
- Cellular healing
- Aging Process
- Detoxification
- Stress response

Promote methylation balance

- Optimize Microbiome
- Optimize Mitochondrial function
- Reduce Toxic burden
- Reduce oxidation and inflammation
- Stress management
- Exercise
- Methylation Adaptogens

Dietary optimization

- Anti-inflammatory
- Low-glycemic
- Antioxidant rich
- Phytonutrients as enzyme modulators and antioxidants
- Optimal hydration
- Support detox processes
- Calorific restriction/Intermittent fasting
- Avoid folic acid fortification
- Avoid minimize alcohol
- Minimize Advanced Glycation End products
- Avoid processed meats
- Avoid high mercury fish
- Avoid plastic containers

The metabolic, microbiome and hormonal milieu need to be addressed here.

Pancreatic cancer cells over express cox-2 by as much as 60 times normal
Pancreatic cancer cells have testosterone receptors and aromatase enzyme to convert testosterone to oestogen

I3C
Reishi
Genistein
Pancreatic enzymes
Berberine
Milk Thistle
Vitamin D3
Curcumin C3
Butyrate

Stress management
Supporting Vagal tone
Castor oil packs over liver

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3469770/

> Anticancer Res. 2011 Oct;31(10):3171-80.

Enhanced efficacy of gemcitabine by indole-3-carbinol in pancreatic cell lines: the role of human equilibrative nucleoside transporter 1

Honggang Wang [1], Beverly R Word, Beverly D Lyn-Cook

Affiliations + expand

PMID: 21965724

Abstract

Pancreatic cancer patients treated with gemcitabine (2',2'-difluorodeoxycytidine) can eventually develop resistance. Recently, published data from our laboratory demonstrated enhanced efficacy of gemcitabine with the dietary agent, indole-3-carbinol (I3C). The current study examined the possible mechanism for this I3C-enhanced efficacy. Several pancreatic cell lines (BxPC-3, Mia Paca-2, PL-45, AsPC-1 and PANC-1) were examined for modulation of human equilibrative nucleoside transporter 1 (hENT1) expression, the major transporter for gemcitabine, by I3C alone

Bloods 4th April day 1 of chemo:

HB: 116
WBC: 10.8
Neutrophils: 7.9
Lymphocytes: 1.9
Alk Phos:111
Gamma GT 28
ALT: 34
AST: 23
Vitamin D:
CRP: 8.8
ESR:
LDH: 157
Homocysteine: CEA
CA19-9

Bloods 19th April: Chemo 2

HB: 111
WBC: 4.6
Neutrophils: 2.4
Lymphocytes: 1.4
Alk Phos: 121
Gamma GT 36
ALT: 37
AST: 26
Vitamin D:
CRP: 25.4
ESR:
LDH: 203
Homocysteine:

Bloods 30th April: Chemo 3

HB: 98
WBC: 6.8
Neutrophils: 4.1
Lymphocytes:1.6
Alk Phos:
Gamma GT: 29
ALT: 53
AST: 40
Vitamin D:
CRP: 89.9
ESR: 40
LDH: 246
Homocysteine:
TOTAL PROTEIN

Bloods 1st May:

HB: 82
WBC: 4.8
Neutrophils: 2.4
Lymphocytes: 1.6
Alk Phos:79
Gamma GT 23
ALT: 48
AST: 33
Vitamin D:
CRP: 99.4
ESR: 28
LDH: 193
Homocysteine: 30.2
CEA: 6
CA19-9: 7455

Bloods 4th May

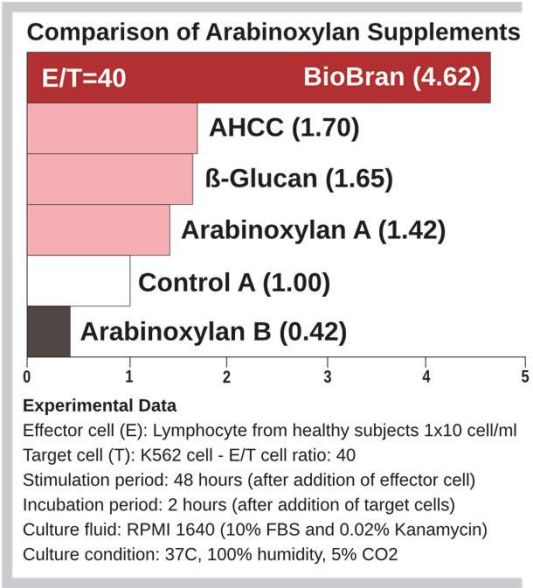
HB: 102
WBC: 5.9
Neutrophils: 2.3
Lymphocytes: 2.6
Alk Phos:109
Gamma GT: 31
ALT: 49
AST: 32
Vitamin D:
CRP: 44.3
ESR:
LDH: 223
Homocysteine:

Bloods 5th May

HB: 98
WBC: 6.8
Neutrophils: 4.1
Lymphocytes:1.6
Alk Phos:85
Gamma GT: 29
ALT: 53
AST: 40
Vitamin D:
CRP: 89.9
ESR: 28
LDH: 246
Homocysteine:
TOTAL PROTEIN

IV ALA and LDN
IV vitamin C
Bio Bran
Methyl B complex

- Biobran is MGN-3 Arabinoxylan Compound formed by breaking down rice bran with Shiitake enzymes. (Mycelia removed)
- Very powerful immunomodulator backed by 64 peer-reviewed research papers and 25 years of clinical data.
- Can modulate NK-cell activity by up to 300%, and T and B-cell activity by up to 200% and 150%.
- Anti-inflammatory effect and antioxidant scavenging activity, as well as the ability to improve glucose tolerance, and enhance pancreatic and liver function.
- Upregulates TNF-alpha and IFN-gamma.
- Safe, non-toxic and non-hyporesponsive.



Lippincott Williams & Wilkins Open Access

ANTI-CANCER DRUGS

Anticancer Drugs. 2018 Apr; 29(4): 373–379.
Published online 2018 Mar 15. doi: 10.1097/CAD.0000000000000603

PMCID: PMC5882293
PMID: 29438178

Treatment of pancreatic cancer with intravenous vitamin C: a case report

Jeanne A. Drisko,[a] Oscar K. Serrano,[c] Lisa R. Spruce,[d] Qi Chen,[b] and Mark Levine[e]

Author information · Article notes · Copyright and License information Disclaimer

Abstract

Go to:

Pancreatic ductal adenocarcinoma (PDA) has a dismal prognosis and is often discovered at an advanced stage with few therapeutic options. Current conventional regimens for PDA are associated with significant morbidity, decreased quality of life, and a considerable financial burden. As a result, some patients turn to integrative medicine therapies as an alternate option after a diagnosis of PDA. Intravenous pharmacologic ascorbic acid (PAA) is one such treatment. The use of PAA has been passionately debated for many years, but more recent rigorous scientific research has shown that there are significant blood concentration

We believe that a new treatment agent that shows robust laboratory and animal evidence, coupled with minimal patient toxicity, deserves rigorous clinical investigation without concern that clinical trials might not be supported by industry or have potential to generate profits. Indeed, patients deserve no less. It is our opinion that the current evidence is sufficient to encourage both private and public funding agencies to evaluate support for targeted phase I and II clinical trials of PAA as a complement to standard therapies in the treatment of metastatic PDA.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5882293/

Case Reports > Integr Cancer Ther. 2009 Dec;8(4):416-22. doi: 10.1177/1534735409352082.

Revisiting the ALA/N (alpha-lipoic acid/low-dose naltrexone) protocol for people with metastatic and nonmetastatic pancreatic cancer: a report of 3 new cases

Burton M Berkson [1], Daniel M Rubin, Arthur J Berkson

Affiliations + expand

PMID: 20042414 DOI: 10.1177/1534735409352082

Free article

Erratum in

long-term survival of a man with pancreatic cancer and metastases to the liver, treated with intravenous alpha-lipoic acid and oral low-dose naltrexone (ALA/N) without any adverse effects. He is alive and well 78 months after initial presentation.

Korean J Thorac Cardiovasc Surg. 2013 Apr; 46(2): 162–163.
Published online 2013 Apr 9. doi: 10.5090/kjtcs.2013.46.2.162
PMCID: PMC363179
PMID: 2361410

The Anti-neoplastic Effects of Alpha-Lipoic Acid: Clinical Benefits in System Tumors besides Lung Carcinomas

Shailendra Kapoor, M.D.

I read with great interest the recent article by Kim et al. [1]. Interestingly, alpha-lipoic acid has recently been shown to exert anti-neoplastic effects in a number of systemic tumors other than lung carcinomas. For instance, alpha-lipoic acid exerts anti-neoplastic effects in colon carcinomas. DHL-HisZnNa is a newer alpha-lipoic acid derivative that has shown similar anti-neoplastic effects in colon cancer cell lines [2]. Levels of retinoblastoma protein are attenuated by DHL-HisZnNa while a simultaneous accentuation of p21 levels is seen. Similarly, anti-proliferative effects have been seen in hepatocellular carcinomas following the administration of alpha-lipoic acid in conjunction with caffeic acid and a new synthesized lipoyl-caffeic conjugate. This combination results in enhanced interleukin 10 levels and attenuated tumor necrosis factor-α levels.

Similarly, alpha-lipoic acid derivatives such as CPI-613 demonstrate anti-neoplastic effects in pancreatic

Bloods 18th may :

HB: 106
WBC: 6.6
Neutrophils: 2.0
Lymphocytes: 3.8
Alk Phos:151
Gamma GT 42
ALT: 57
AST: 53
Vitamin D:
CRP: 9
ESR: 28
LDH: 247
Homocysteine: 13.8
CEA:
CA19-9: 5793

Scan 26th May after 4 cycles of chemo:

Lesions in segment 6 are also smaller, a previously ill-defined metastasis which measured 14 mm is now barely visible and similarly a more posterior lesion is also difficult to identify/measure.

The infiltrative pancreatic mass has reduced in size. Measured at a similar axial level to the previous examination, it was 6.4 x 4.9 cm and is currently 3.9 x 4.5 cm. As before, there is encasement of the celiac axis and its branches with compression of the splenic artery, the SMA and SMV are encased, the portal vein is patent.
There are multiple collateral vessels seen within the abdomen/pelvis (stable).

There was previously a large plaque of low-density disease on the right posterior diaphragm measuring approximately 6.3 cm, this has significantly reduced in size now approximately 3.1 cm.

Bloods 31st May: Chemo 5

HB: 100
WBC: 6.1
Neutrophils: 1.7
Lymphocytes: 3.4
Alk Phos: 131
Gaamma GT 47
ALT: 60
AST: 44
Vitamin D:
CRP: 8.3
ESR:
LDH: 249
Homocysteine:
CEA: 8
CA19-9: 3777

Bloods 28th June Chemo 6

HB: 96
WBC: 5.4
Neutrophils: 2.1
Lymphocytes: 2.4
Alk Phos:135
Gamma GT: 56
ALT: 62
AST: 53
Vitamin D: 82
CRP: 11.9
ESR:
LDH: 315
Homocysteine:
CEA: 6
CA19-9: 2109

Bloods 28th June Chemo 8

HB: 105
WBC: 7.2
Neutrophils: 2.4
Lymphocytes: 3.9
Alk Phos:135
Gamma GT: 67
ALT: 59
AST: 50
Vitamin D:
CRP: 3.9
ESR:
LDH: 279
Homocysteine:
CEA: 7
CA19-9: 1367

PET Scan after 9 cycles

The results are excellent! Mets are non measurable and the main tumour shrunk further.
It's an enormous relief but I am thinking what's next.

The next steps are three more chemo sessions to total 12, followed by another scan and then Olaparib

08.08.22: CT CAP and PET show very good partial response and near complete metabolic response after 9 cycles of FOLFIRINOX. CA19-9 1075

PET Scan after 12 cycles

last pet scan are even better than the previous ones! The mets are gone and the tumour shrank in size with very little activity. The cat numbers reduced from 830 to 300.

Next step from the oncologist is Olaparib. Planned to start the week of 3october.

CT CAP and PET show complete metabolic response at all metastatic sites. Mild FDG update in pancreatic primary SUV 4.2. CA19-9 353 after 12 x FOLFIRINOX.

Bloods 3rd October (After cycle 12) :

HB: 113
WBC: 6.4
Neutrophils: 2.0
Lymphocytes: 3.2
Alk Phos: 182
Gamma GT: 70
ALT:64
AST: 61
Vitamin D: 57
CRP: 1.9
ESR:
LDH: 292
Homocysteine:
CEA 8
CA19-9: 330

Mistletoe therapy commenced

Vitamin D increased to 5000 iu daily
ALA switched to nebulized
Black seed oil
CoQ10
Genistein
Selenium
PHGG

Oncology

The efficacy of tyrosine kinase inhibitors on human pancreatic cancer cell lines[1]

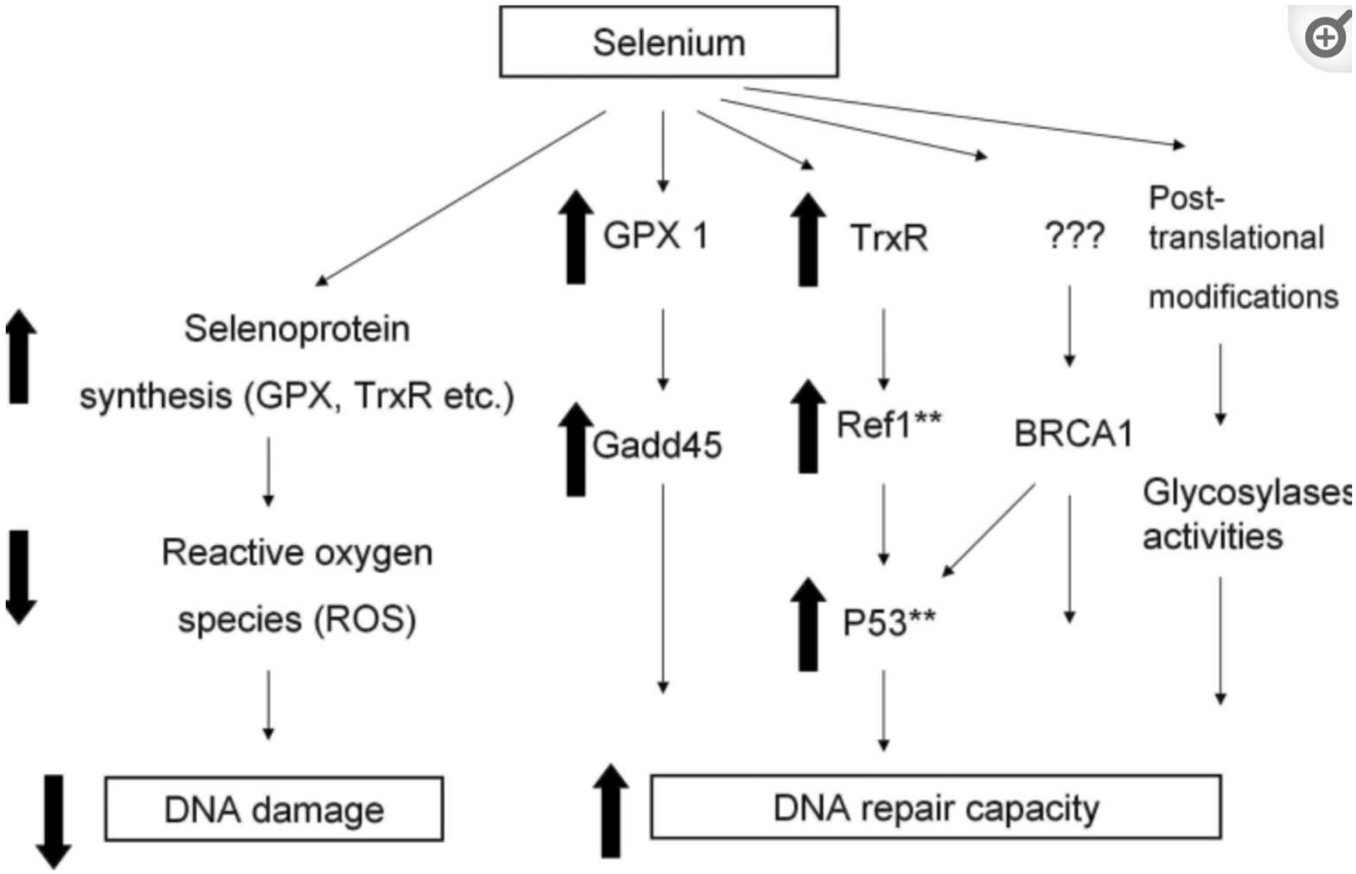
[1]This paper was presented at the Annual meeting of the Association for Academic Surgery, November 7–9, 2002, Boston, MA.

Robert Saeid Farivar M.D., Ph.D., James Gardner-Thorpe M.D. *, Hiromichi Ito M.D. *, Hassan Arshad M.S. *, Michael J Zinner M.D. *, Stanley W Ashley M.D. *, Edward E Whang M.D. *

https://doi.org/10.1016/S0022-4804(03)00246-4

Abstract

Genistein-based kinase inhibitors may offer potential and should be tested in other in vivo models for their ability to inhibit the growth of pancreatic cancer.



Possible mechanisms by which selenium might influence DNA damage repair (arrows indicate up-regulation or down-regulation and asterisk indicates activation of respective proteins).

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3570792/

Genistein induced anticancer effects on pancreatic cancer cell lines involves mitochondrial apoptosis, G_0/G_1cell cycle arrest and regulation of STAT3 signalling pathway

Yi-Liang Bi [1], Min Min [1], Wei Shen [1], Yan Liu [2]

Affiliations + expand

PMID: 29433670 DOI: 10.1016/j.phymed.2017.12.001

Abstract

Background: Genistein is a natural flavonoid that has been reported to exhibit anticancer effects against different types of cancers which include, but are not limited to, breast and oral squamous cell carcinoma.

Purpose: The present study was designed to evaluate the anticancer effects of the natural flavonoid genistein against pancreatic cancer cell lines and to explore the underlying mechanism.

Methods: Antiproliferative activity was investigated by MTT assay. Apoptosis was detected by DAPI and annexin V/PI staining. DNA damage was assessed by comet assay. Reactive oxygen

Ursolic Acid (glutamine inhibitor)
Avermar (fermented wheat)
Danshen
Bergamot
Luteolin
Lycopene

> Oncotarget. 2016 Mar 15;7(11):13182-96. doi: 10.18632/oncotarget.7537.

Ursolic acid inhibits the growth of human pancreatic cancer and enhances the antitumor potential of gemcitabine in an orthotopic mouse model through suppression of the inflammatory microenvironment

Sahdeo Prasad [1], Vivek R Yadav [1], Bokyung Sung [1], Subash C Gupta [1], Amit K Tyagi [1], Bharat B Aggarwal [1 2]

Affiliations + expand

PMID: 26909608 PMCID: PMC4914350 DOI: 10.18632/oncotarget.7537

Free PMC article

Abstract

The development of chemoresistance in human pancreatic cancer is one reason for the poor survival rate for patients with this cancer. Because multiple gene products are linked with chemoresistance, we investigated the ability of ursolic acid (UA) to sensitize pancreatic cancer cells to gemcitabine, a standard drug used for the treatment of pancreatic cancer. These investigations were done in AsPC-1, MIA PaCa-2, and Panc-28 cells and in nude mice orthotopically implanted with Panc-28 cells. In vitro, UA inhibited proliferation, induced apoptosis, suppressed

Oncol Lett. 2018 Feb; 15(2): 2673–2678.
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PMCID: PMC5777362
PMID: 29434991

Mechanism of the anti-angiogenic effect of Avemar on tumor cells

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Abstract

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Avemar, a derivative of fermented wheat germ extract, is a non-toxic and natural compound that is used as a dietary supplement by cancer patients undergoing chemotherapy and radiotherapy. Avemar has numerous biological activities, and several recent studies have reported that it may also have metastatic and anti-angiogenic effects. In the present study, the mechanism of the anti-angiogenic effect of Avemar on human cancer cells was investigated. The human cell lines NCI-N87 (gastric tubular adenocarcinoma), PC3 (prostate carcinoma), HeLa (endocervical adenocarcinoma) and A549 (lung adenocarcinoma) were treated with various doses (400, 800, 1,600 and 3,200 µg/ml) of Avemar, and the changes in mRNA and protein levels of two important markers of angiogenesis, vascular endothelial growth factor (VEGF) and cyclooxygenase-2 (Cox-2), were assessed by reverse transcription-quantitative polymerase chain reaction and ELISA. VEGF and Cox-2 protein and mRNA levels were significantly lower in Avemar-treated cells than in untreated cells. The data suggest that Avemar may exert an anti-angiogenic effect on cancer cells. Thus, it is suggested to medical doctors as a potential agent for the anti-angiogenic treatment of cancer.

Keywords: angiogenesis, Avemar, cyclooxygenase 2, vascular endothelial growth factor

Lycopene Induces Apoptosis in Pancreatic Cancer Cells

Yoonseon Jeong, Joo Weon Lim, Hyeyoung Kim

First published: 01 April 2016 | https://doi.org/10.1096/fasebj.30.1_supplement.691.23

Abstract

Pancreatic cancer is one of the most fatal human cancers, which has the lowest 5-year survival rate among all cancer types. Lycopene, a major carotenoid component in tomatoes, has a potential anticancer activity in many types of cancers. The inhibitors of apoptosis (IAPs) including survivin, cellular inhibitor of apoptosis 1(cIAP-1) and cellular inhibitor of apoptosis 2(cIAP-2) are a group of anti-apoptotic factors in the apoptotic pathway that cause cancer cells become insensitive to apoptotic stimulation. The purpose of this study is to investigate the anti-cancer mechanism of lycopene by determining the expression levels of inhibitors of apoptosis in human pancreatic cancer cells, PANC-1. The cells were treated with various concentrations of lycopene or caspase-3 inhibitor Z-VAD_FMK. Cell viability was examined by MTT assay. Expressions of survivin,

Comparative Study > Pharm Res. 2012 Jun;29(6):1595-608. doi: 10.1007/s11095-012-0670-3. Epub 2012 Jan 27.

Tanshinones from Chinese medicinal herb Danshen (Salvia miltiorrhiza Bunge) suppress prostate cancer growth and androgen receptor signaling

Yong Zhang [1], Suk-Hyun Won, Cheng Jiang, Hyo-Jeong Lee, Soo-Jin Jeong, Eun-Ok Lee, Jinhui Zhang, Min Ye, Sung-Hoon Kim, Junxuan Lü

Affiliations + expand

PMID: 22281759 DOI: 10.1007/s11095-012-0670-3

Abstract

Purpose: To test whether tanshinones inhibit prostate cancer (PCa) growth at least in part through inhibiting androgen receptor (AR) signaling.

Methods: We evaluated cell growth, survival and AR signaling parameters of PCa cells after exposure to tanshinones in in vitro models. We also tested the in vivo inhibitory efficacy of tanshinone IIA (TIIA) against LNCaP xenograft model in athymic nude mice.

Results: For androgen-dependent LNCaP cells, a colony growth assay showed strong inhibitory potency following the order of TIIA≈cryptotanshinone>tanshinone I, being 10-30 folds higher than

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Volume 1859, Issue 9, September 2018, Pages 984-996

Bergamot natural products eradicate cancer stem cells (CSCs) by targeting mevalonate, Rho-GDI-signalling and mitochondrial metabolism ☆

Marco Fiorillo [a b c], Maria Peiris-Pagès [a], Rosa Sanchez-Alvarez [a], Lucia Bartella [d], Leonardo Di Donna [d], Vincenza Dolce [c], Giovanni Sindona [d], Federica Sotgia [a b], Anna Rita Cappello [c], Michael P. Lisanti [a b 1]

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https://doi.org/10.1016/j.bbabio.2018.03.018

Highlights

> Food Funct. 2018 May 23;9(5):3018-3027. doi: 10.1039/c8fo00033f.

The dietary compound luteolin inhibits pancreatic cancer growth by targeting BCL-2

Zhimei Li [1], Yiyuan Zhang, Lixia Chen, Hua Li

Affiliations + expand

PMID: 29770817 DOI: 10.1039/c8fo00033f

Abstract

Overexpression of the prosurvival protein BCL-2 contributes to malignant cell initiation, progression and resistance to treatment. Agents that function as its natural antagonists targeting BCL-2 must provide therapeutic benefit. In SW1990 pancreatic cancer cells, amplified BCL-2 was observed, which was believed to offer advantages for malignant cell survival and lead to poor patient outcome. Using structure-based virtual ligand screening, luteolin was found to be a natural small-molecule inhibitor of BCL-2, which exhibited dose-response proapoptosis activity in a BCL-2 dependent manner in vitro. The cellular thermal shift assay (CETSA) and notably competitive binding assay by the microscale thermophoresis (MST) method provided the evidence that this flavonoid directly bound to BCL-2. Mechanistic studies revealed that luteolin (compound 1)

PLoS One. 2015 Aug 24;10(8):e0135637. doi: 10.1371/journal.pone.0135637. eCollection 2015.

The Flavone Luteolin Suppresses SREBP-2 Expression and Post-Translational Activation in Hepatic Cells

Tsz Yan Wong [1], Shu-mei Lin [2], Lai K Leung [3]

Affiliations + expand

PMID: 26302339 PMCID: PMC4547722 DOI: 10.1371/journal.pone.0135637

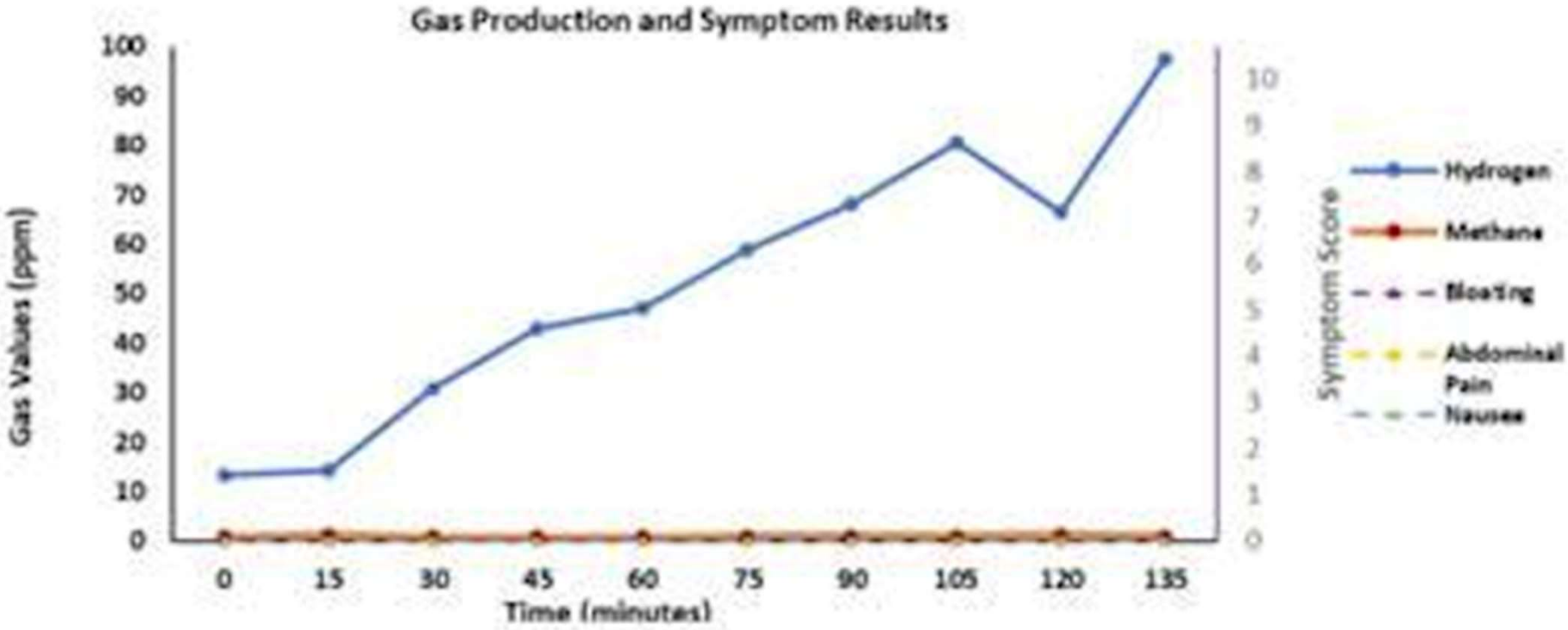
Free PMC article

Abstract

High blood cholesterol has been associated with cardiovascular diseases. The enzyme HMG CoA reductase (HMGCR) is responsible for cholesterol synthesis, and inhibitors of this enzyme (statins) have been used clinically to control blood cholesterol. Sterol regulatory element binding protein

Bloods 31st October (After Olaparib commenced) :

HB: 119
WBC: 5.9
Neutrophils: 2.6
Lymphocytes: 2.3
Alk Phos: 168
Gaamma GT: 58
ALT:85
AST: 67
Vitamin D: 57
CRP: 0.6
ESR: 6
LDH: 245
Homocysteine:
CEA 7
CA19-9: 204


Gas Production and Symptom Results
Gas Values (ppm)
100
90
80
70
60
50
40
30
20
10
0
0
15
30
45
60
75
90
105
120
135
Time (minutes)
Symptom Score
10
9
8
7
6
5
4
3
2
1
0
Hydrogen
Methane
Bloating
Abdominal Pain
Nausea

> Carcinogenesis. 2010 Oct;31(10):1813-21. doi: 10.1093/carcin/bgq157. Epub 2010 Aug 10.

Lycopene induces cell growth inhibition by altering mevalonate pathway and Ras signaling in cancer cell lines

Paola Palozza [1], Maria Colangelo, Rossella Simone, Assunta Catalano, Alma Boninsegna, Paola Lanza, Giovanni Monego, Franco O Ranelletti

Affiliations + expand

PMID: 20699249 DOI: 10.1093/carcin/bgq157

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Abstract

Several evidences suggest that cancer cells have abnormal cholesterol biosynthetic pathways and prenylation of small guanosine triphosphatase proteins. Tomato lycopene has been suggested to have beneficial effects against certain types of cancer, including that of prostate, although the exact molecular mechanism(s) is unknown. We tested the hypothesis that lycopene may exert its antitumor effects through changes in mevalonate pathway and in Ras activation. Incubation of the Ras-activated prostatic carcinoma LNCaP cells with a 24 h lycopene treatment (2.5-10 μM) dose dependently reduced intracellular total cholesterol by decreasing 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase expression and by inactivating Ras, as evidenced by its translocation from cell membranes to cytosol. Concomitantly, lycopene reduced the Ras-dependent activation of nuclear factor-kappaB (NF-κB). Such a reduction was parallel to an inhibition of reactive oxygen species production and to a decrease in the phosphorylation ofc-jun

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PMCID: PMC8471697
PMID: 34576078

The Human Microbiomes in Pancreatic Cancer: Towards Evidence-Based Manipulation Strategies?

Giovanni Brandi,[1,2,*] Silvia Turroni,[3] Florencia McAllister,[4,5] and Giorgio Frega[1,2,*]

Gaetano Santulli, Academic Editor

Abstract

Go to: ▸

Although being aware of the urgent need to conduct further studies to disentangle the contribution of the human microbiomes to PC and validate their potential for early diagnosis and risk stratification, we believe that their manipulation represents an attractive and promising way to modulate tumor immunosuppression and growth, to ultimately improve therapy responses and prolong survival. Given the anatomical position and physiological function of the pancreas, it is easy to speculate on the potential pivotal role of nutrition and the gut microbiota in the neoplastic lesions originating in this organ. Diet modulation, microbiota reshaping, alongside with intra-tumoral bacteria-mediated innovative therapies could probably constitute a novel attractive strategy of treatment for PC patients

dawning against pancreatic cancer: a neoplasm that arises in a central metabolic "hub" interfaced between the gut and the host.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8471697/

Ann Transl Med. 2020 Oct; 8(19): 1257.
doi: 10.21037/atm-20-2723

PMCID: PMC7607088
PMID: 33178789

Of fungi and men: role of fungi in pancreatic cancer carcinogenesis

Heling Wang, [1] Mjriam Capula, [2] Bastiaan P. Krom, [1] Dicky Yee, [3] Elisa Giovannetti,[# 2 , 3 , #] and Dongmei Deng[# 1 , #]

See the article "The Fungal Mycobiome Promotes Pancreatic Oncogenesis via MBL Activation" in *Nature*, volume 574 on page 264.

Associated Data

▸ **Supplementary Materials**

Another human microbiota worth mentioning is the oral microbiota. It has been suggested that part of the intestinal bacteria and fungi are of oral origin, with more than 45% overlap in the microbiota between oral cavity and gut (20,21). The increase of PDAC risk has been associated with a very common oral infection: periodontal disease (22). The levels of two periodontal pathogens, *Porphyromonas gingivalis* and *Aggregatibacter actinomycetemcomitans*, were elevated in PDAC patients (23). Oral bacteria are thought to reach the pancreas by swallowing or via the circulatory system after mastication and personal oral hygiene

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7607088/

Fungal invasion of pancreas creates cancer risk

Date: October 2, 2019

Source: NYU Langone Health / NYU School of Medicine

Summary: Certain fungi move from the gut to the pancreas, expand their population more than a thousand-fold, and encourage pancreatic cancer growth, a new study finds.

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Certain fungi move from the gut to the pancreas, expand their population more than a thousand-fold, and encourage pancreatic cancer growth, a new study finds.

Published online in *Nature* October 2, the study is the first to offer strong evidence that the mycobiome -- the local mix of fungal species in the pancreas -- can trigger changes that turn normal cells turn into pancreatic ductal adenocarcinoma or PDA. This form of cancer is usually deadly within two years.

Conducted in mice and in patients with pancreatic cancer, the study found that fungal species travel into the pancreas up the pancreatic duct, a tube through which digestive juices drain in the opposite direction into the intestines. The study authors say this exchange results in abnormal fungal populations in both the gut and pancreas in the presence of PDA.

Bloods 16th December:

HB: 126
WBC: 4.3
Neutrophils: 1.8
Lymphocytes: 1.8
Alk Phos: 139
Gaamma GT: 38
ALT:40
AST: 33
Vitamin D: 95
CRP: 4.9
ESR: 6
LDH: 181
Homocysteine: 9.2
CEA 6
CA19-9: 45

27 September 2021

The world's first pancreatic cancer research and treatment centre is born

The Botton-Champalimaud Pancreatic Cancer Centre was

Admitted on 12th April 2023 and submitted to distal pancreatectomy and splenectomy, portal vein resection (venous Goretex graft reconstruction), superior mesenteric artery divestment and segmental jejunal resection and duodenojejunal anastomosis. The procedure went without complications.

Champalimaud Foundation and Mauricio and Carlotta Botton, who contributed 50 million euros to its construction.

Bloods 20th April on discharge post surgery :

HB: 103
WBC: 17.91
Neutrophils: 13.13
Lymphocytes: 2.11
Alk Phos:
Gaamma GT: 168
ALT:187
AST: 34
Vitamin D:
CRP: 3.05
ESR:
LDH:
Homocysteine:
CEA
CA19-9:

Bloods 2/5/23:

HB: 98
WBC: 9.0
Neutrophils: 3.8
Lymphocytes: 3.1
Alk Phos: 209
Gaamma GT: 104
ALT:57
AST: 37
Vitamin D: 71
CRP: 12.9
ESR:
LDH: 201
Homocysteine:
CEA : 3
CA19-9: 45

Post surgery plan

Radiation for 5.5 weeks


Road Map
to Navigate
in Functional Medicine

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