Cancer through another lens

Fresh thoughts on the origin and mechanisms of cancer

Post-event presentation references and synopsis, for:

Professional delegates

Event: Online discussion regarding the origins of cancer
Event date: February 12th 2023
Hosted by: Yes to Life, registered charity 1112812
Supported by: Love *from* Margot FOUNDATION & Mike Murphy, Academy of Nutritional Medicine and the Alliance for Natural Health International

YES TO LIFE YOUR OPTIONS FOR CANCER

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&

Mike Murphy

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By
Mark Lintern, in partnership with Yes to Life

Presentation references & synopsis:
Recipient: Event delegates **Event Date:** February 12th 2023

SYNOPSIS:

While scientists have made great progress against many diseases, cancer has not fared so well. Despite a monumental effort to understand the disease the mainstream *Somatic Mutation Theory* (SMT) hasn't delivered the results we were hoping for. As it stands the underlying cause of cancer remains unknown, which is why at least eight different theories of cancer co-exist. While researchers are working hard to find a solution, it should be noted that their efforts are being hindered by an incomplete understanding of the disease. Surely an effective treatment can only be realised once the underlying cause has been successfully identified. To that end we must continue to question what we think we know and remain open to new perspectives if we are to conquer this complex disease.

At present, the *Metabolic Theory* stands as the most accurate cancer theory currently available when evaluated against the Hanahan and Weinberg hallmarks of cancer. These are officially recognised as the main traits of the disease and are arguably the parameters most suited to assessing the validity of any theory – the more hallmarks that can be explained the more accurate a theory is deemed to be. To put this in context, the Metabolic Theory can explain nine of these 10 hallmarks and is close to explaining the remaining hallmark, whereas the mainstream Somatic Mutation Theory, also known as the *DNA Theory*, struggles to explain more than two. This indicates that DNA mutations are a symptom of the disease as opposed to the mechanism driving it, and that cancer is a metabolic disease driven by abnormal energy respiration. Given this, there is a strong case for offering metabolic treatments as standard care. The concern is that many in the field continue to claim that the DNA Theory is correct even though it remains an unproven theory, and that this will result in a continued reliance on DNA-based treatments that have been shown to be largely ineffective.

Recognising the shortcomings of placing all our faith in one unproven theory, leaders in the field continue to develop other theories to address the remaining aspects of the disease that the DNA Theory is struggling to account for. For instance, the Metabolic Theory has been complemented in recent years by the *Atavistic Theory* and the *Tissue Organisation Field Theory* (TOFT). The former seeks to explain why cancer cells revert to an old evolutionary form of metabolism (aerobic glycolysis) and how this results in an *epithelial-mesenchymal transition* (EMT) leading to an embryonic stem-cell-like phenotype. The latter asserts that carcinogenic insult results in the loss of suppressive growth signals in surrounding tissue leading to abnormal, invasive tumour growth.

Together these theories have greatly advanced our understanding and provide new treatment avenues that appear more successful than current standard-of-care treatments. However, there is a caveat. While the Metabolic

Theory acknowledges the Warburg effect and it's clear that abnormal metabolism plays a pivotal role, there seems to be contention over the mechanism purported to be driving this condition. Professor Seyfried cites defective Oxidative Phosphorylation (OXPHOS) as the origin of cancer, however, OXPHOS has been shown to be operational to varying degrees in many cancers, while cells of the body such as endothelial cells, that rely heavily on glycolysis, do not become cancerous as a matter of normal function – indicating that some additional factor is required for cancer to form over and above a reliance upon glycolysis. Oncocytomas, which have defective OXPHOS, generate benign tumours as opposed to malignant cancers.

Regardless, Hallmark 7 (abnormal metabolism) is a crucial hallmark to account for because it appears to be the gateway to explaining the other nine hallmarks of cancer, all of which appear to result from the Warburg effect. This is why Professor Seyfried places so much emphasis on this aspect of the disease, he recognises that the Warburg effect is pivotal to explaining cancer. Determining the potential causes of the Warburg effect then, will likely lead to the identification of the underlying mechanism(s) responsible for driving the disease.

To this end, I have spent the last eight years investigating this link and collating the evidence for a plausible mechanism. The sum of this evidence suggests that carcinogenesis can be interpreted through a different lens entirely. I have documented my findings in a way that not only compliments the theories that already exist, but also provides an alternative explanation for the Warburg effect, as well as all nine other Hanahan and Weinberg hallmarks of cancer. In addition, this new interpretation of the science provides a unique explanation of at least 20 other cancer-related conditions, such as arginine auxotrophy, the reverse Warburg effect and chemotherapy resistance (see the RESULTS section below). This indicates that an entirely different mechanism is at play.

Intriguingly, this new perspective does not rewrite how we treat the disease from a metabolic point of view, far from it. In fact, it encompasses all the very same treatments advocated for by the Metabolic Theory, but it also highlights the need to consciously target an additional factor that many metabolic treatments are often inadvertently targeting. All that may be needed to treat cancer more effectively is to make minor adjustments to the metabolic approach.

To explain, I would like to shift your perspective of the disease momentarily. Nearly all mainstream theories view cancer through the same lens – the notion that it arises from a malfunction within the cell due to damage. Such a malfunction is thought to develop within the genome, within mitochondria, or within the surrounding tissue leading to a loss of suppressive growth signals. It is this breakdown in cell functionality that allegedly drives the disease. For instance, the DNA Theory claims that mutated DNA genes are responsible, the *Aneuploid Theory* asserts that abnormal chromosome formation is the driver, whereas the Metabolic Theory claims that faulty mitochondria trigger an energy switch that results in the conditions of cancer. All data is interpreted through this cell-malfunction lens where the cell itself is ultimately to blame. One could argue that currently only one overall theory of cancer exists – the *Cell Malfunction Theory* if you will, and that all mainstream theories are sub-theories within this paradigm. The contention between these theories lies in which part of the cell is faulty and therefore

responsible. The problem for all these theories has been an inability to identify a pattern of damage that can account for the consistency of the disease.

What if the abnormal behaviour of a cancer cell is not a result of malfunction, but of suppression, where an external factor foreign to the cell influences cell death and growth mechanisms, leaving the cell no longer in full control?

In support of this concept, Ravid Straussman's pioneering work has illustrated that tumours used in laboratory experiments, which were previously thought to be sterile, harbour intracellular micro-organisms and a tumour-specific microbiome that interfere with cell functionality and drug effectiveness. Significantly, studies analysing the microbiome of oral cancer patients show that a particular type of micro-organism dominates, and that it can instigate most of the hallmarks we see in cancer. Recent evidence highlighting the direct influence of these micro-organisms in driving the disease has prompted Douglas Hanahan to update the hallmark list to include a 'Polymorphic microbiome' as part of the equation. And when searching for an answer to arguably the most pressing question in cancer research: '*What's the underlying cause of hallmark 7*?' studies confirm that, upon infection, pathogens instigate the Warburg effect – the Warburg effect is a natural anti-infection response.[01 – 08]

Here, hiding in plain sight is a known cause for the Warburg effect, ignored up until now due to the common assertion that cancer results from faulty cell machinery. While the notion of cancer resulting from infection is not new, this cell suppression concept is unique and has yet to be explored by scientists. Currently, around 20% of cancers are associated with infection, but not in a suppressive capacity; rather, micro-organisms are thought to damage the cell leading to malfunction – and it is this malfunctioning cell machinery that is ultimately thought to be driving the disease, rather than the micro-organism per se.

Challenging this perspective, I'm proposing that it's the suppressive nature of the pathogen and it's control over specific cell functions, such as cell death and cell growth mechanisms, that's driving the disease, not the random damage inflicted by infection or carcinogens. We now know that intracellular micro-organisms exist within tumours, that pathogens actively suppress tumour-specific cell functions in order to keep the cell alive so long as it's beneficial for their survival, and we know that the Warburg effect is triggered as part of an anti-microbial defence mechanism. During the infectious process the Warburg effect is actively sustained until the infection is eradicated regardless of oxygen availability. Failure to eradicate the infection provides an explanation for cancer's sustained reliance on glycolysis even in the presence of oxygen – the condition known as the Warburg effect. Ongoing damage to mitochondria results in an epithelial-mesenchymal transition that explains the reversion of regular cancer cells to one of a cancer stem-cell-like phenotype and accounts for unlimited growth. Latent survival within macrophages and lateral transfer of the pathogen between these immune cells also helps to explain metastasis, immune evasion, the ability of cancer to cross the blood brain barrier and why macrophages appear to play a dominant role in cancer progression.

When viewed through this suppressive lens all major aspects of the disease can be explained. For example, in terms of understanding carcinogenesis, scientists are struggling to explain how the random DNA damage caused by so many

different toxic carcinogens could lead to the consistency of cancer. This is certainly an impossible task given that randomness cannot generate consistency. To explain how the consistency of cancer can develop from the apparent randomness of carcinogen damage, we have to consider that there must be other consistent conditions generated by all carcinogens – and that these conditions have been overlooked. When we investigate further, this is indeed what we find. All carcinogens generate at least four consistent conditions: a weakened immune response, chronic inflammation, overproduction of lactic acid and iron overload. This is a crucial point to acknowledge because these conditions shed light on the underlying cause:

- A weakened immune system offers less resistance to infection.
- Inflammation renders cells more vulnerable to pathogen invasion.
- Lactic acid overproduction and iron overload feeds the infectious process and has the adverse effect of suppressing immune cells at the site of injury.

Essentially, carcinogens generate favourable conditions that facilitate infection – this toxic niche feeds these pathogens and provides a protective environment within which the efficacy of the immune response is greatly reduced. Add in the Warburg effect and suppression of cell death mechanisms, and we have the promotion of a proliferative state that can explain the initial stages of carcinogenesis.

As the infection is slow-growing and encased within the protective boundary of the tumour, the patient won't be aware of the infection until the tumour grows large enough to be noticed. Assuming that cell malfunction is driving these conditions has meant we've overlooked another possibility – that sustained infection by particular pathogens is stimulating this abnormal cell expansion. Naturally, the increased absorption of glucose feeds the pathogen while depleting glucose within the surrounding tissue. This further suppresses the immune response at the tumour site because immune cells require glucose to operate. This provides an alternative explanation for why glucose feeds the disease – in sustaining the voracious demand of the pathogen, the monopolising of available glucose simultaneously depletes and weakens the immune response, all while the proliferative state of aerobic glycolysis stimulates cell proliferation.

Acquisition of nutrients by the pathogen, such as pyrimidines, purines, methionine and arginine, forces the cell to absorb higher quantities of these nutrients to replenish those that are lost. In effect, the cell is operating on autopilot having lost control of cell growth and cell death mechanisms. As with glucose, glutamine receptors are also stimulated because glutamine is converted into many essential nutrients that need replenishing – incidentally, the pathogen in question utilises this glutamine by converting it to glucose in situations where glucose availability is scarce. The consumption of methionine by the pathogen explains why hypomethylation is a condition of pre-cancerous tissue and accounts for the random DNA damage that occurs in early-stage tumour development. Acquisition of arginine explains arginine auxotrophy and why arginine starvation therapy can be effective but can also render the tumour more aggressive.

Inhibiting these fuels has been shown to inhibit cancer cells. This alternative perspective proposes that this is not just because the cell requires them to survive,

but because the pathogen also requires these same fuels to sustain the infection. This explains why the mechanism of apoptosis – which is currently thought to be broken – is once again initiated when anti-microbial drugs or anti-microbial plant compounds (bromelain, sulforaphane) are introduced to cancer cells. The pathogen is killed allowing mitochondria to regain control of cell death mechanisms, resulting in apoptosis. The apoptotic pathway was never faulty, just suppressed by the pathogen.

Viewing cancer through the lens of cell suppression enables us to re-interpret why certain treatments appear effective, and why the survival rate is so low with current standard of care. For instance: three of the four drugs used by the Care Oncology Clinic aimed at inhibiting metabolic pathways, are also strong anti-microbial drugs. Metformin, Atorvastatin and Mebendazole are all effective at killing the common pathogens involved, not to mention that the first two inhibit the fuels that these pathogens also require to sustain the infection. Hyperbaric oxygen therapy is also anti-microbial, as is 3BP (3-Bromopyruvate), Tamoxifen, Arimidex, Lovastatin and many more besides. Regarding chemotherapy, while the free radicals generated by initial chemotherapy treatment can eradicate a large portion of the infection and reduce initial tumour size, chemotherapy often fails because it generates the same inflammatory conditions that go on to feed the infection – namely, immune weakness, chronic inflammation, overproduction of lactic acid and iron overload. Not to mention that the cell's free-radical-producing capacity is diminished over time due to the damage inflicted, which incapacitates mitochondria. The stimulation of cancer stem cells also plays a key role too. This explains why chemotherapy treatment can initially have a dramatic effect at reducing a tumour, but wanes substantially over time, and can become detrimental in the latter stages of treatment.

For the first time it is possible to explain why natural-based compounds such as bromelain, sulforaphane, honey and even silver can selectively kill cancer cells – all are highly anti-microbial. This new perspective has enabled the explanation of many key aspects of the disease, which are listed below.

RESULTS – Aspects of cancer explained by cell suppression:

- All 10 Hanahan and Weinberg hallmarks
- Carcinogenesis

An alternative explanation is also provided for:

- Glucose, glutamine, lactate, fat, methionine, and arginine used as fuel by cancer cells.
- The Reverse Warburg effect
- Arginine auxotrophy
- Methionine auxotrophy – methionine dependence
- Hypomethylation
- Aneuploidy
- Chemotherapy resistance
- Iron's role in carcinogenesis
- The role of estrogen
- The role of nagalase

- The role of galectin-3
- Why antioxidant supplementation aids tumour development
- The role of CYP1B1 and the reason for its upregulation
- The role of macrophages in tumour progression
- The role of myeloid-derived suppressor cells in tumour progression
- The reason for T-cell suppression
- Why cancer is primarily a disease of old age
- Why cancer incidence is increasing
- Why childhood cancers exist
- Why cancer appears to run in the family

An alternative explanation can be made for the effectiveness of particular treatments:

- The Care Oncology Clinic treatment protocol
- Metformin
- 3BP
- Statins – Lovastatin, Atorvastatin, Fluvastatin
- Tamoxifen
- Gleevec
- Herceptin
- Artemisinin
- Melatonin supplementation
- Hyperbaric oxygen therapy
- Ketogenic diet
- Fasting
- Salvestrols and other plant antibiotic compounds
- Restriction of glucose, glutamine, fat, methionine, arginine, and estrogen

Abundant evidence supports a metabolic approach to treatment, detoxification of the cellular terrain, and re-balancing of the microbiome in conjunction with the addition of a targeted anti-microbial solution. Data indicates that such a solution would work synergistically to target the dominant infection, which is protected within the inflamed toxic environment of the tumour. This would allow mitochondria to re-instigate apoptosis, resulting in regression of the disease.

OBJECTIVES:

In partnership with the integrative cancer care charity Yes to Life, we are hosting an online debate with the aim of evaluating this new perspective. A select group of expert cancer scientists, clinicians and cancer survivors will be present and taking part directly in the discussion – as will an invited audience of hundreds of scientists, clinicians and other cancer specialists. The merit of this new perspective will be discussed and carefully evaluated in a non-combative, constructive scientific manner.

The objective is to generate awareness of this cell-suppression concept, while subjecting it to a high level of scrutiny to assess its validity. The event will stimulate debate within the cancer community, highlight the serious flaws within the accepted paradigm and its approach to treatment and draw attention to the

Metabolic Theory and metabolic treatments. The intention is to stimulate a shift in perspective that is hoped will lead to improved survival outcomes for people with cancer, as well as more robust prevention strategies.

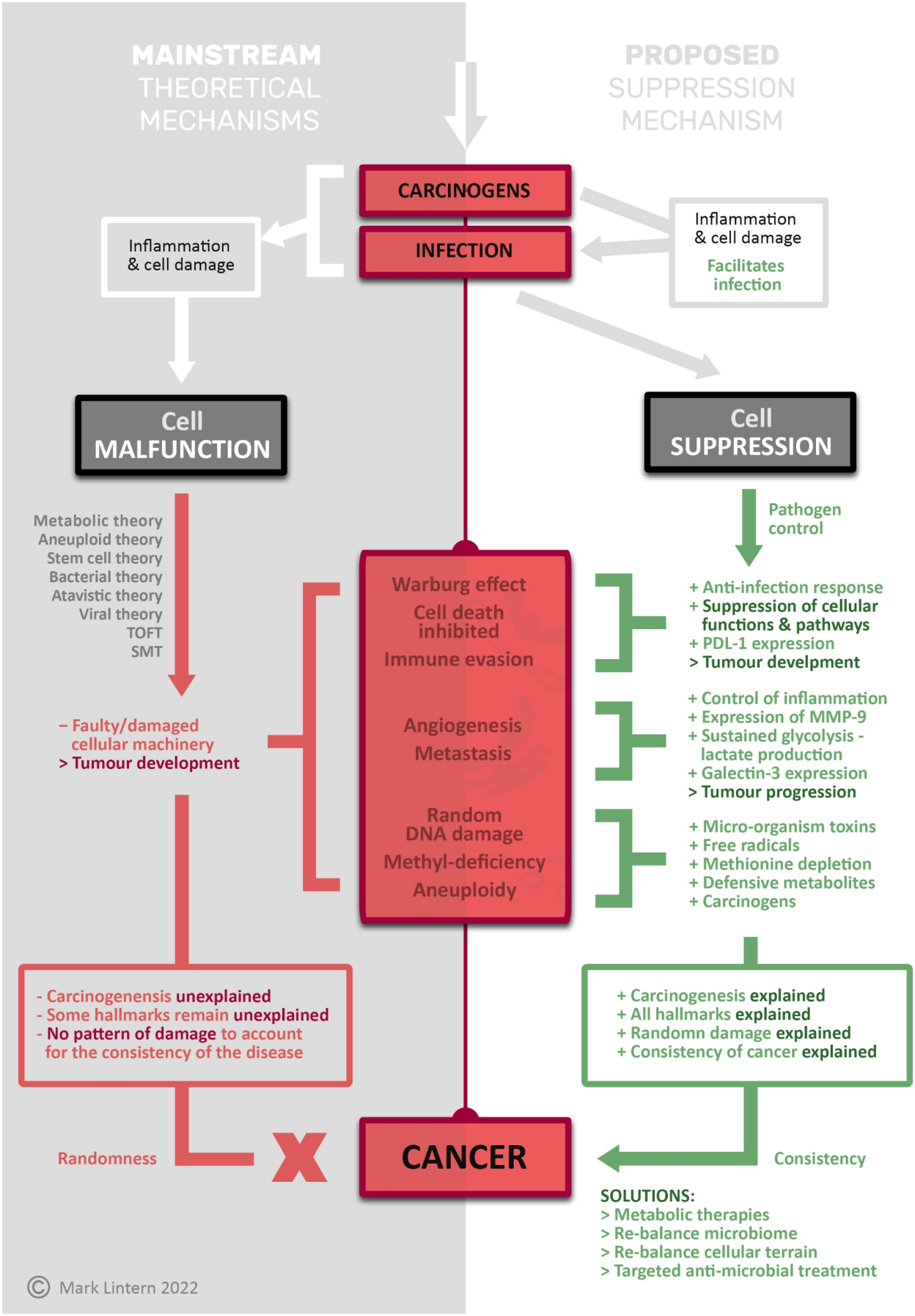
CONCLUSION:

Abundant evidence supports the proposition that cancer is a cell-suppression disease caused by an opportunistic pathogen that takes advantage of the conditions arising from chronic inflammation. Emerging data confirms the presence of a dysbiotic tumour-associated microbiome dominated by common pathogens.

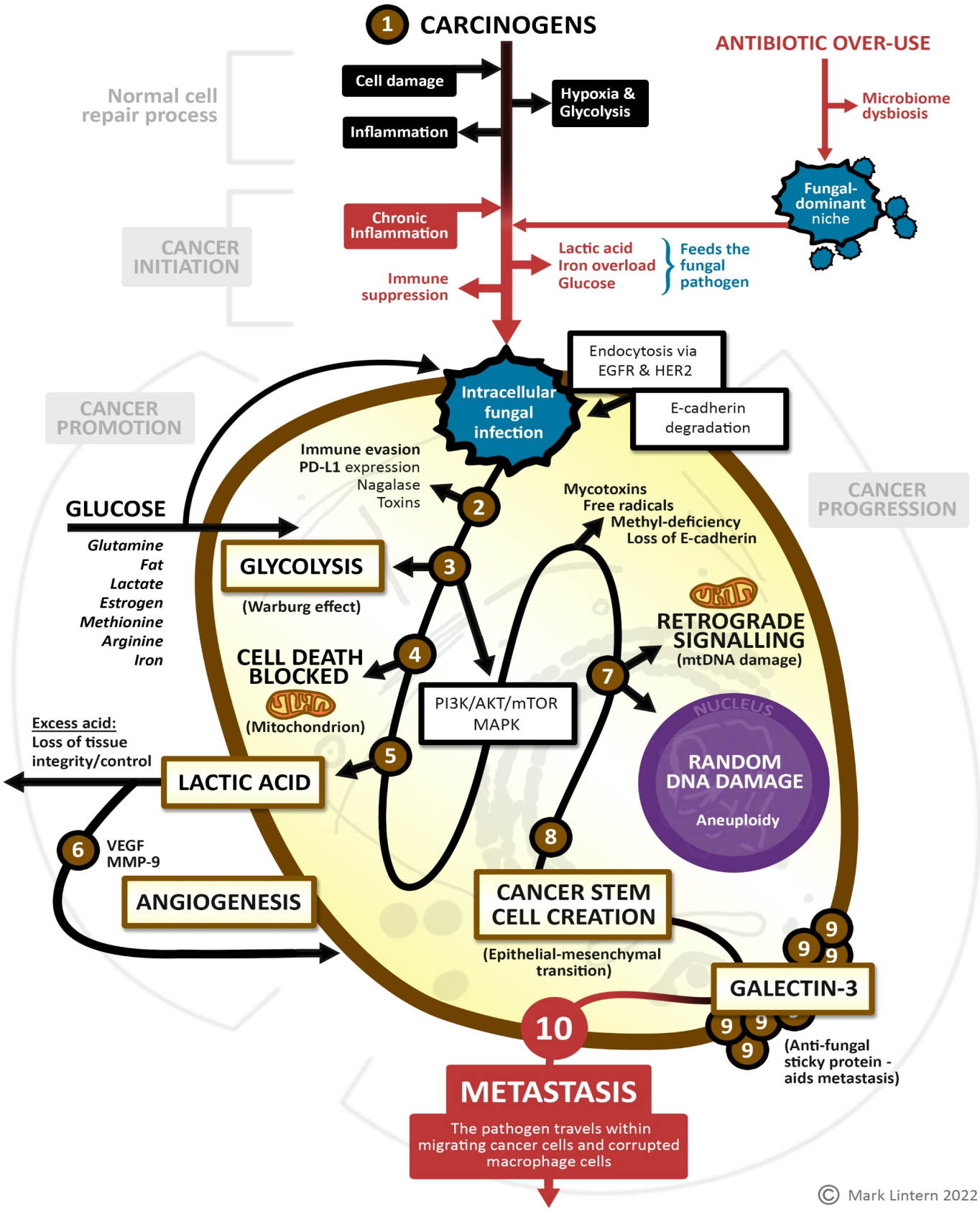
When viewed through the traditional 'cell malfunction' lens, it becomes impossible to identify the cellular mechanism(s) responsible for the odd behaviour expressed by the cancer cell because the cell itself is not at fault. This explains why the Somatic Mutation Theory cannot identify cancer-specific mutations, and why the Cancer Genome Atlas data shows that mutations appear random – these mutations are symptoms resulting from the infectious process and the initial toxin exposure. Cell suppression also explains why mitochondria appear to re-instigate apoptosis when supplied with plant antibiotic compounds, honey or silver. This cell death mechanism is suppressed rather than faulty.

The abundant evidence supporting a cell-suppression mechanism for carcinogenesis, in combination with its ability to explain all major hallmarks of the disease, makes it clear that further investigation is warranted to determine the validity of this premise. Discussing its merits openly amongst experts in the field will allow it to receive the attention it deserves, and provides the opportunity for it to improve our understanding of cancer, and hopefully the survival outcomes for patients.

GRAPHICAL ABSTRACT – Cell Malfunction vs Cell Suppression:



GRAPHICAL ABSTRACT – Carcinogenesis explained:



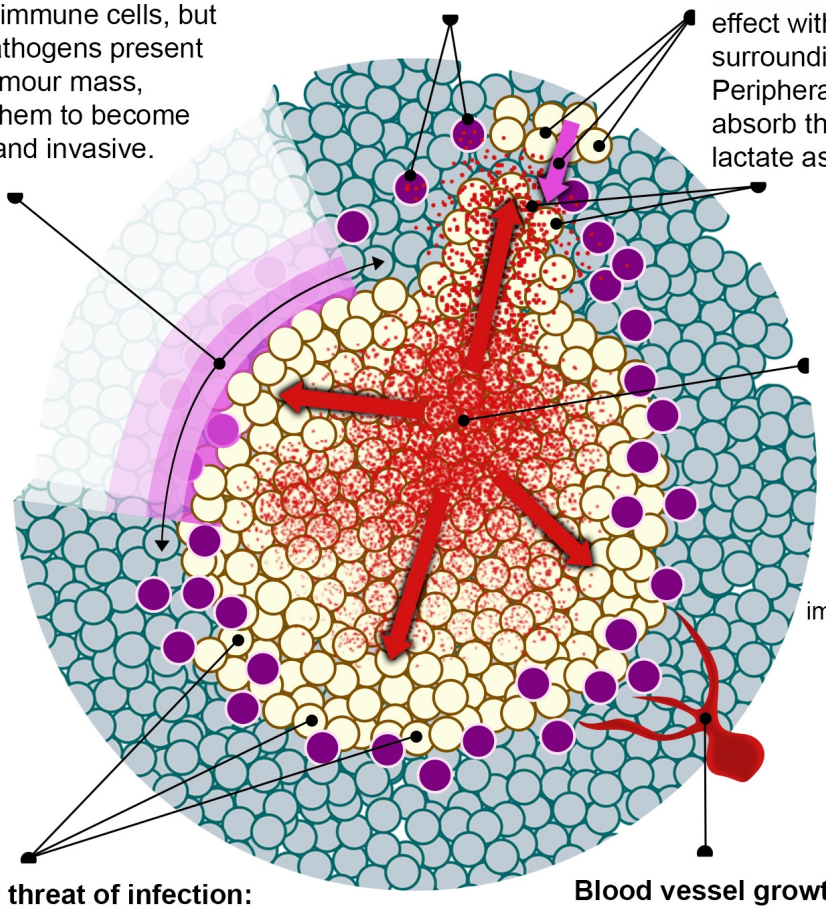
TUMOUR COMPOSITION

Cell suppression model

Lactic acid, iron overload, glucose depletion, chronic inflamation:
Creates a protective barrier around the tumour that suppresses immune cells, but feeds the pathogens present within the tumour mass, stimulating them to become aggressive and invasive.

Pathogen expansion:
Excess lactate fuels the infection which expands into surrounding tissue and dormant immune cells.

Reverse Warburg Effect:
Advancing infection stimulates the Warburg effect within the surrounding tissue. Peripheral tumour cells absorb the excess lactate as fuel.



Tumour-associated microbiome

Cell death inhibited, cell proliferation instigated, ineffective immune response
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Cancer

Hypoxia + threat of infection:
Results in cells close to the infection, but not yet infected, instigating glycolysis, stimulating proliferation. It's only a matter of time before they become infected, and added to the tumour mass.

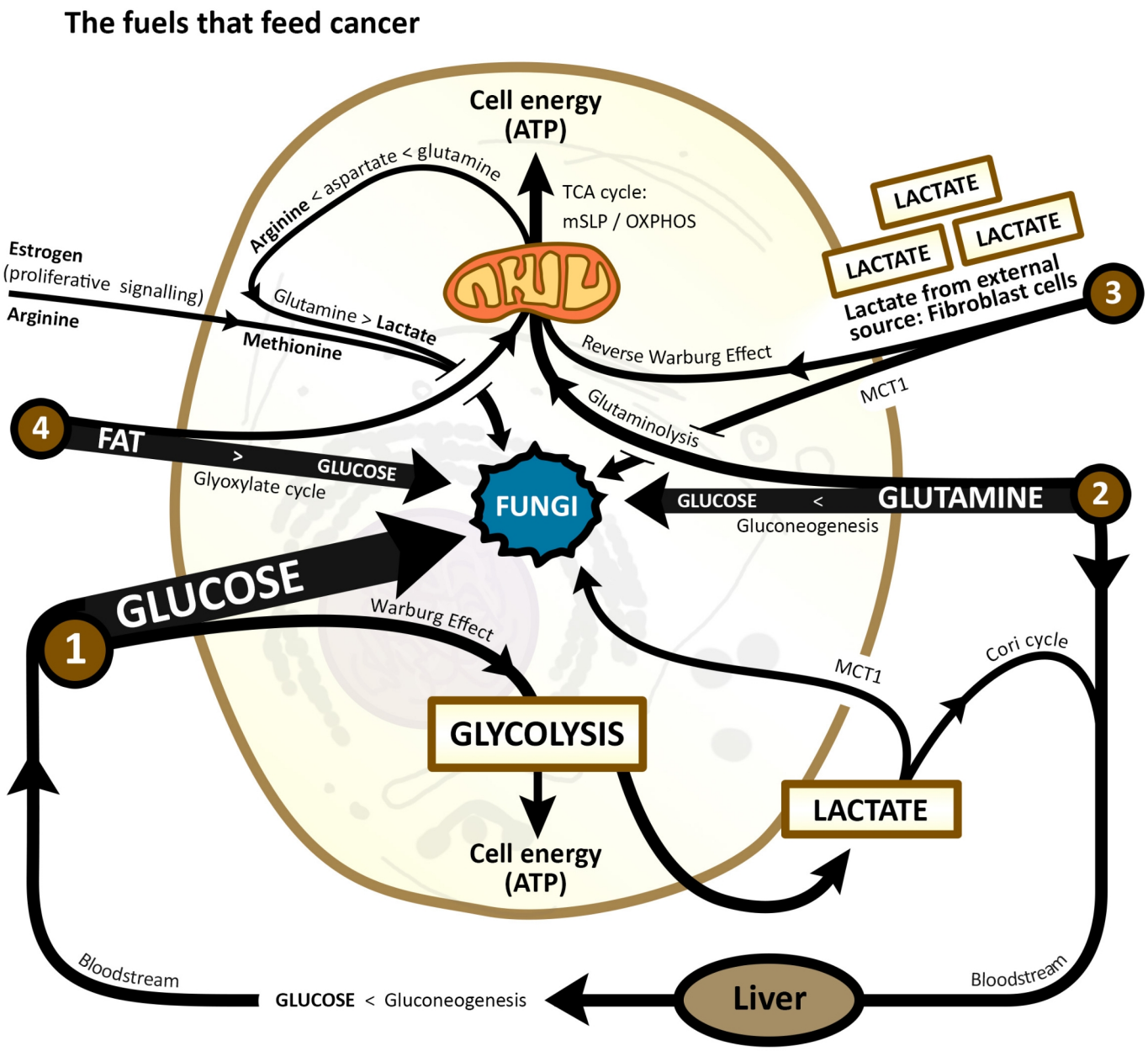
Blood vessel growth:
Blood vessels expand towards cells over-producing lactic acid. This corrosive environment, plus over-production of MMP-9, results in cells migrating into the bloodstream.

Healthy tissue

Immune cell

Warburg effect / anti-infection response > Tumour cell

Intracellular pathogens > Cancer cells



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PRESENTATION INFORMATION – 12th February event:

During the online event that was held on the 12th February, organised by the cancer care charity Yes to Life, I talked through three presentations. The first discussed the contention over the validity of two leading mainstream theories to explain the 10 Hanahan and Weinberg hallmarks of cancer. The Somatic Mutation Theory did not fare well, while the Metabolic Theory was shown to be far superior. These hallmarks also confirmed that there is a consistency to cancer that cannot be explained by the established multifactorial view of the disease. It became evident that there was contention over the underlying mechanism driving the Warburg effect in cancer, OXPHOS doesn't appear to be defective/inoperative. It was acknowledged that abnormal metabolism appears to be a pivotal mechanism associated with the disease, as many of the other hallmarks of cancer seem to be downstream events of Hallmark 7. With no mainstream theory able to explain Hallmark 7 (Warburg effect), and its pivotal role in cancer, I proposed that identifying the underlying cause of Hallmark 7 would bring us closer to identifying the driving mechanism of cancer.

The second presentation discussed the flaws associated with the mainstream paradigm of 'cell malfunction' – which most mainstream theories appear to have adopted. This is the notion that cancer arises from a malfunctioning cell, that is, any damage to the cell machinery may result in a loss of control and unbridled cell

proliferation; a fault within the cell itself, is to blame for cancer. I proposed an alternative paradigm of 'cell suppression', suggesting that the cell is not at fault or to blame for the disease. Rather, that an infectious, pathogenic, parasitic micro-organism has invaded the cell and is in control of it. To ensure its own survival the pathogen suppresses key cellular functions and pathways leading to the development of a tumour. I highlighted that the Warburg effect was an anti-infection response and that this energy state is sustained until the pathogen is eradicated. An inability to eradicate the intracellular pathogen results in sustained glycolysis, suppression of cell death, and stimulation of growth signals leading to tumour development. Ravid Struassman's recent work confirming that intracellular pathogens are present in all tumours was also presented to support this infection suppression model. Here I provided an explanation for the initiation phase of carcinogenesis.

In presentation 3 I provided evidence in support of identifying fungal pathogens as the most likely agent influencing the development of, and driving the disease. I provided an illustration of the tumour mass explaining how the infection was able to exist within the tumour and was protected by it. I discussed how communication between cells stimulates the Warburg effect within adjacent cells, which later become infected adding to the expansion of the tumour and infection. I touched on the varying fuels that can be utilised by the tumour to show that these fuels are used by the intracellular fungal pathogen, explaining the variability in fuel use by tumours. I also provided a complete explanation of carcinogenesis focusing on the promotion and progression phases. Here follows the references for the evidence provided within all three presentations.

PRESENTATION REFERENCES – 12th February event:

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SLIDE 03: Exploring the Origin of Cancer:

1. Thomas N. Seyfried. *'Cancer as a Metabolic Disease: On the Origin, Management, and Prevention of Cancer.'* 2012. ISBN: 978-0-470-58492-7

SLIDE 10: Exploring my Journey:

2. Thomas M. Ashton, W. Gillies McKenna, Leoni A. Kunz-Schughart and Geoff S. Higgins. '*Oxidative Phosphorylation as an Emerging Target in Cancer Therapy.*' Clin Cancer Res. June, 2018. (24) (11) 2482-2490. doi:10.1158/1078-0432.CCR-17-3070

SLIDE 19: Treatment success:

3. Professor Paul Davies. '*Cancer from a physicist's perspective: a new theory of cancer.'* New Scientist. National Cancer Institute. June 2013.

SLIDE 20: How effective are mainstream treatments?

4. Cliff Leaf, David Agus, MD, J. Craig Venter, Ph.D. *'How biology and big data converge in the medicine world.'* Fortune Magazine. 2015. https://www.youtube.com/watch?v=fDSQMeRgZHM
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SLIDE 21: Treatment success:

6. Dr. Andreas Eenfeldt, MD. '*Using a ketogenic diet to stop brain tumour growth.'* Diet Doctor. July 2016. https://www.dietdoctor.com/pablo-27-beats-cancer-using-ketogenic-diet – PlymouthHerald
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SLIDE 22: DNA Theory analysis – reproducibility crisis:

8. Professor Paul Davies. '*Cancer from a physicist's perspective: a new theory of cancer.'* New Scientist. National Cancer Institute. June 2013.
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SLIDE 27 & 30: Metabolic Theory analysis – Cancer Hallmarks:

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SLIDE 31: Metabolic Theory Re-evaluation – Cancer Hallmarks:

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SLIDE 32: Metabolic Theory Re-evaluation – Cancer Hallmarks:

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