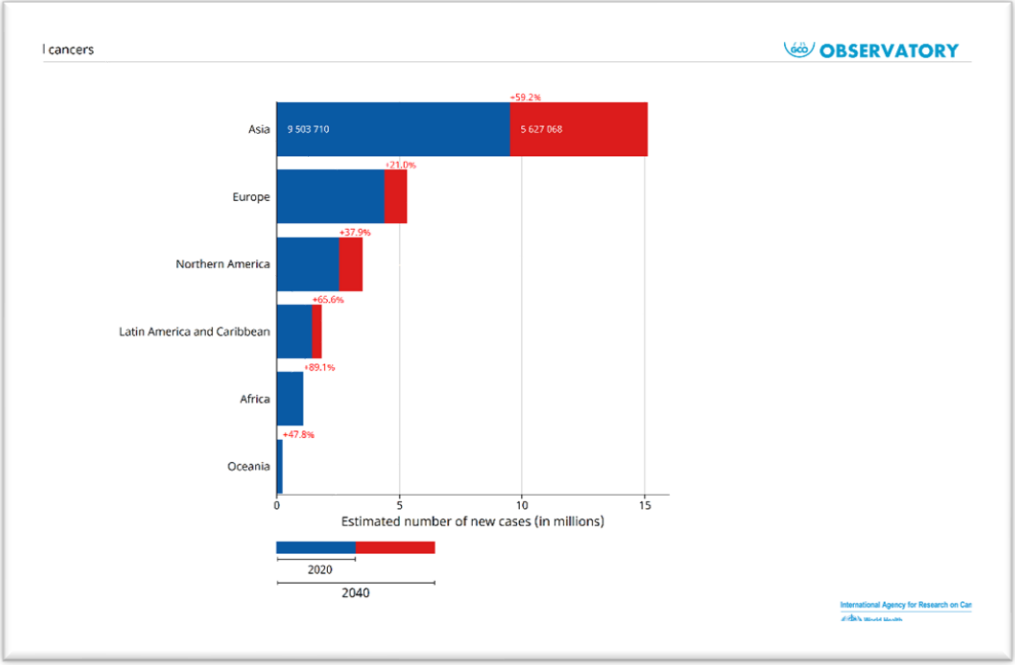
Cancer as a metabolic problem?

Where are we today?

Cancer is a disease that has existed as part of human history for thousand of years. In the past 100+ years, the number of people dying annually from cancer has almost tripled from 64.0 per 100,000 in 1900 to 185.9 per 100,000 in 2010.(1) Death from cancer was ranked as the 8th leading cause of death in 1900 while in 2010 it was ranked as second and still is currently. The International Agency for Research on Cancer estimates that between 2020 and 2040, the number of people newly diagnosed with cancer will increase by 9.5 million from 19.3 million in 2020 to an estimated 28.9 million worldwide.(https://gco.iarc.fr/tomorrow/en/dataviz/bars)



https://gco.iarc.fr/tomorrow/en/dataviz/bars (2)

The Science

Over time many different theories have been proposed to explain why cancer occurs. From a conventional oncology perspective, the Somatic Mutation Theory (SMT) is currently the dominant scientific explanation for the origin of cancer. It says that cancer arises from inherited or random mutations in a cell's genetic materials, the DNA (deoxyribonucleic acid), and alterations that occur in key areas or "driver gene mutations" are seen as responsible for the development of cancer. (3) The US National Cancer Institute also supports this view of cancer as a genetic disease. (https://www.cancer.gov/about-cancer/causes-prevention/genetics)

While the somatic mutation theory is the current dominant theory of cancer development, many other scientists have observed different behaviors in cancer cells.

In general, cells of the body create energy two ways: via fermentation using glucose (sugar) in a low oxygen environment or, when oxygen is available, through a process located in the mitochondria called oxidative phosphorylation.

As early as 1927, Otto Warburg, a German scientist, observed that cancer cells generate energy via fermentation even when oxygen is available. Generating energy in this manner bypasses the mitochondria and produces large amounts of lactic acid. It was originally thought that cells would only use the fermentation (anaerobic glycolysis) pathway to produce energy when oxygen was very low. Yet, in these cancer cells, oxygen was available for energy production. Warburg also noted that cancer cells had very high demand for glucose, consuming up to 200 times more glucose than normal cells. (4) This behavior in cancer cells has been coined the "Warburg effect" which Warburg hypothesized was because there was some damage to the mitochondria of cancer cells that made it necessary to use an alternate process of energy generation.(5) The Warberg effect, an effect which is very metabolic in nature, is seen in almost all cancers and provides a higher metabolic rate to sustain rapid growth.(6) (7) This altered metabolism of cancer cells, which is different from that of normal cells, has attracted a lot of interest. (8)

For a long time, Warburg's observations were swept aside in favor of the somatic mutation theory i.e., cancer as a genetic disease. More recently, the concept of cancer as a mitochondrial metabolic disease has been gaining traction with researchers, building on the earlier work of Warburg. In the 2011, Hanahan and Weinberg published their updated Hallmarks of Cancer article which lists the characteristics that define cancer and cancer cells. One of those characteristics is that cancer cells alter their cellular metabolism to support rapid growth which is known as the Warburg effect.(9)

Seyfried, in his 2015 paper on "Cancer as a mitochondrial Metabolic disease" reviews the various nuclear-cytoplasmic transfer experiments that had been performed over the years.(10) These were performed to determine whether DNA mutations in the nucleus could be responsible for directing cancer tumor formation. A tumor nucleus containing mutated DNA, when transplanted into a normal cell's cytoplasm, where the mitochondria are, did not result in the formation of a tumor cell *(please see Figure 1.)* However, when a normal cell's nucleus, which contains the cell's DNA, was transferred into the cytoplasm of tumor cells, this resulted in the either dead or cancerous cells. These experiments provided evidence that altered nuclear DNA was not responsible for the formation of a tumor, weakening the support for the Somatic Mutation Theory of cancer. The determining factor for tumor formation had to do with the where the cytoplasm came from, tumor cells or normal cells.

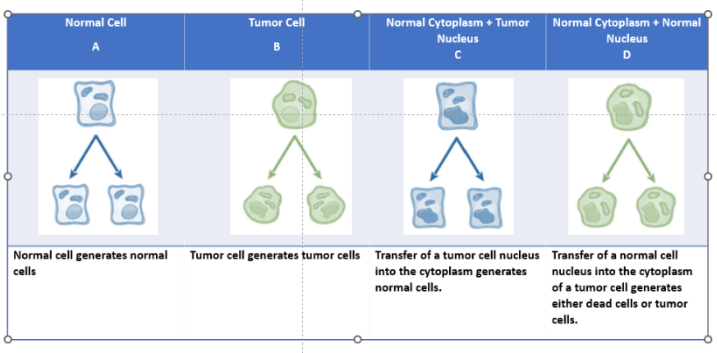


Figure 1: This is the diagram was adapted from Seyfried TN. Cancer as a mitochondrial metabolic disease. Front Cell Dev Biol. 2015 Jul 7;3:43.

These experiments, along with the work of other researchers, strongly suggest that cancer happens because the mitochondria in cytoplasm are damaged rather than the DNA in the nucleus and that these metabolic changes in the cell happen before DNA damage, further providing support for cancer as a metabolic disease. (11–13)

What might damage the mitochondria?

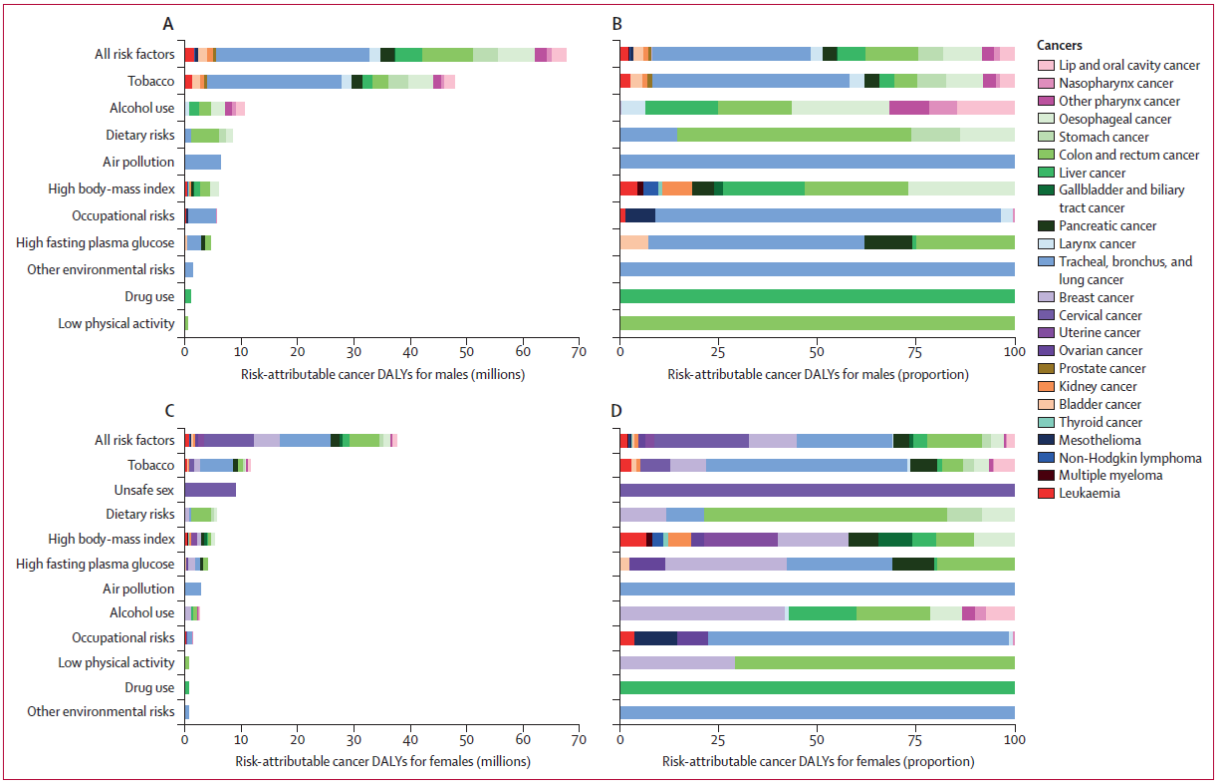
In the past two hundred years, we've made major changes to our planet, our air, water, and soil. These changes have created a lack of adaptability within ourselves, within our genetics, and in our lives, and a loss of flexibility to adapt to the pressures of modern living. This lack of adaptability and flexibility damages our metabolic systems and the health of our mitochondria; putting our bodies into a state of disease and the cancer process.

From a conventional treatment perspective, the cancerous tumor is the focus and the treatments used generally include some combination of chemotherapy, radiation; possibly medication, depending upon the type of tumor. These treatments are, in and of themselves, carcinogenic, i.e., cancer causing. Not only do these treatments attack the cancerous cells but also attack healthy cells and further deplete the body's immune system, damage DNA, eliminate important microbes in the gut, contribute to inflammation and oxidative damage; all which are also cancer promoting. Also, these treatments do not address damaged mitochondria.

As early as 2008, researchers from the Anderson Cancer Center identified that 90–95 percent of cancer cases are caused by poor diet and unhealthy lifestyles that damage mitochondrial function.(14)

More recently, the Global Burden of disease study in 2019, examined the modifiable risk factors that are attributable to the adjusted life years lost in cancer for both sexes.(15) These modifiable risks factors can be classified as environmental and occupational, behavioral, and metabolic. For males, all modifiable risk factors contributed to 67.5 million DALYs (Disability adjusted life years) and 50.6% of all deaths and for females, the modifiable risk factors contributed 37.6 million DALYs and 36.3% of deaths.

The global burden of cancer attributable to risk factors, 2010–19: a systematic analysis for the Global Burden of Disease Study 2019 (15)



From the work done by these research groups (14, 15), highlighting that a considerable portion of cancer's risk factors are modifiable, it is clear that the focus of treatment needs to go beyond solely the tumor. To eliminate the cancerous cells, we must optimize the mitochondria and the body's healing mechanisms. This is done by identifying what is causing the body to go into the cancering process, then treating the terrain, not just the tumor, with the right therapies for biological and mitochondrial needs.

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