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Notch Protein as Leading Cause of World Cancer Epidemic

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ABSTRACT

Compared to patients who chose evidence-based cancer treatments, those who used unconventional methods tended to have high social and economic status (be from northwestern U.S. states), have advanced cancers and be in otherwise good health. The problem is, that people who decide to tackle their cancer using only unconventional methods are likely die sooner than patients who opt for conventional treatments, according to a new study. Mouse model shows that Notch activation can drive metastatic prostate, colon and other types of cancer. Notch protein complex signaling pathway is in our view one of the most important cause of the World Cancer Epidemic.

Keywords

Cancer epidemic, Patients, Vitamins, Risk.

Introduction

People with various kinds of cancer who turned down treatments like chemotherapy or radiation in favor of alternative medicine were two to six times more likely to die within six years, compared to people who accepted medically proven therapies. As it said lead author Dr. Skyler Johnson, of the Yale School of Medicine and the Yale Cancer Center in New Haven, in their clinical practice, they started seeing patients coming in with more advanced cancer, because they first tried alternative therapies that failed.

Many cancer patients add nonmedical therapies to the treatments prescribed by their oncologists. But little is known about patients who choose only unconventional methods to address their cancer, Johnson and colleagues write in the Journal of the National Cancer Institute (JNCI).

Cancer treatment is still risk for the patient's lives

To find out more about this group of patients, they used information collected on prostate, breast, lung, and colon cancers for the U.S. National Cancer Database between 2004 and 2013. The researchers had data on 280 people who tried only unproven methods administered by nonmedical personnel. They compared each of these patients to two people with similar cancer type, disease stage, age, race and other attributes, but who received conventional treatments. Half of the patients were followed for at least five and half a years.

Patients who chose unproven methods were more than twice as likely to die during the follow-up period, than those received treatments like chemotherapy, radiation and surgery. Compared to those receiving evidence-backed treatments, patients with breast cancer who opted for unproven methods were more than five times as likely to die, those with lung cancer were more than twice as likely to die and those with colon cancer were about five times as likely to die.

Their findings highlight the importance of timely proven care for cancer, Johnson told Reuters Health. If the patients were followed for a longer period of time, it's possible the differences could be greater, he said. Some prostate and breast cancers develop slowly even if untreated and may not be deadly within five to six years. Johnson also said, the researchers couldn't account for people who received science-based treatments when their unconventional methods failed. He told people should be cautious about what treatment advice they receive from the internet or through word of mouth. This is something they need to think a lot about, because choosing alternative medicine for their cancer treatment could risk their lives, Johnson said [1].

Vitamin B6 and B12 increase risk of the lung cancer for men

People looking for an energy boost may turn to vitamin B6 and

B12 supplements for help, but new research finds that men may be doubling their risk for lung cancer if they take it over an extended period of time – and tripling if they're smokers.

A long-term study followed 77,000 senior adults for over one decade and tracked their intake of vitamin supplements. Men who used high doses of the B6 and B12 supplements for 10 years doubled their risk of lung cancer, while men who were already smokers at the beginning of the study had a threefold to fourfold risk for developing cancer. The researchers found no such relationship among the women in the study.

While his study didn't examine the biological relationship between the vitamins and ling cancer, epidemiologist Theodore Brasky doesn't believe that the vitamin B supplements actually caused the cancer. Instead, he suspects that megadoses of the vitamins hasten the growth of lung cells that have already mutated, often due to smoking.

His first advice for men is: stop smoking. Smoking increases lung cancer risk fifteen-to-thirtyfold, and it also raises the risk of several other kinds of cancers. But if a man is unwilling or unable to quit, easing off the vitamin B supplements is the next step.

Regardless of how much a person smokes, if a man is taking a high dose of these vitamins, they're the ones who are at most risk, said T. Brasky, a researcher at the Ohio State University Comprehensive Cancer Center. If they're concerned, they should cut back to something like a multivitamin or simply just get their nutrient from diet like they're probably already doing.

Vitamin B12 can be found in meat, fish, eggs and dairy, B6 is found in fish, potatoes, non-citrus fruits and organ meats. The recommended daily intake of vitamin B6 for non-breastfeeding, non-pregnant adult is 1.3 milligrams (there are 1.1 milligrams of B6 in one cup of chickpeas), while that number is 2.4 micrograms for vitamin B12 (there are 5.4 micrograms of B12 in 3 ounces of trout).

Energy boosters that contain these two vitamins often have megadoses of B6 and B12. If you look at these supplements bottles, they're being sold in pill form at up to 5,000 micrograms per dose, which is much, much higher than the daily recommended amount, said T. Brasky in a statement about his research.

While Brasky's research didn't explore why women didn't appear to be affected by the link between the supplements and lung cancer, he did point out that men tend to get tobacco-induced lung cancer more often than women because they smoke more. Perhaps high doses of vitamins B6 and B12 encourage more rapid cancer cell growth in the already-mutated cells of smoking men, he wrote in his study. Alternatively, the male hormone androgen interacts with important enzymes involved in the metabolization of vitamins B6 and B12, which could be an explanation for the more profound effect supplements had on men and their risk of lung cancer.

The only reason to take high doses of vitamin B is if you are diagnosed with a deficiency, T. Brasky said. People who are vegan or who have celiac disease or Crohn's disease may be advised by their doctor to take more than a regular multivitamin [2].

The vigilante killer destroys invaders and cancer cells

An unexpected role for a white blood cell called the Natural Killer (NK) cell – a critical cell for ridding the body of infection and cancer, has been discovered by researchers at New Zealand's University of Otago.

The NK cell is a "vigilante" killer" – a white blood cell that destroys invaders and cancer cells through a process of "identity card" checking. The researcher's new work shows that violent vigilante NK cells act as helper cells to start up the immune response.

Otago Associate Professor Alex McLellan says NK cells patrol the body and destroy abnormal cells, especially infected or cancer cells. NK cells closely examine the surface of all cells and look for molecules that are present on healthy cells. Certain molecules act like identity cards (ID), and NK cell are vigilantes, ready to respond if they don't see an ID card on cells. During infections or with cancer, the absence of these molecules triggers the NK cells to destroy the cells.

Dr. Sarah Saunderson and Associate Professor McLellan, who both work in Otago's Department of Microbiology and Immunology, have identified a new way that NK cells act during infections and cancer.

A few years' ago they showed that NK cells were required for the vaccination response against cancer. The group has now recognized that NK cells enhance the ability of the immune system to recognize fragments of tumor cells released into the blood. These fragments induce potent immune responses against cancer. Their new work shows that NK cells are absolutely critical for the immune activity of these cell fragments.

These latest findings also explain how such potent immune responses arise against cell fragments. Above work also reveals new ways that NK cells help the immune system, aside from in their rather violent vigilante role. The group is currently looking at ways to improve NK cell function through living vaccines and growth factors to enhance the immune response to cancer. Bacteria may assist the immune system response against cancer [3].

Bowel cancer patients have little or no confidence in treatment

New study is concluded, that more rigorous assessment of cancer patients' emotional needs is needed for successful treatment process. Bowel cancer patients who are single or live in deprived areas are twice as likely to struggle to cope with their disease compared to those in relationships or from wealthy areas, according to new research by the University of Southhampton and Macmillan Cancer Support. The study was published in the Journal of Cancer Survivorship.

Bowel cancer patients living in the most deprived areas are twice

as likely to have little or no confidence in managing their cancer (low self-efficacy) compared to those living in the most affluent areas (12 per cent vs 6 per cent).

Patients who are single are twice as likely to have little or no confidence compared to those who are married or living with a partner (13% vs 6%). Having little or no confidence in managing cancer could include feeling unable to stop pain or fatique associated with their cancer from interfering with their everyday lives.

Macmillan and the University of Southhampton are calling for better long-term support for cancer patients so they can manage their cancer and have a good quality of life. This should include more rigorous assessments of people's emotional needs at the point of diagnosis and after treatment, to enable doctors and nurses to identify those who lack confidence and ensure they get the support they need.

The Colorectal Wellbeing (CREW) study is following 1,000 people with bowel cancer for five years after surgery and is the largest study if its kind. It found that overall; around one in 10 people (9%) with bowel cancer had little or no confidence in managing their illness when they were diagnosed. This persisted for at least two years afterwards.

Previous research from the CREW study has shown that bowel cancer patients with low confidence before treatment are around 50% more likely to have poor health in the following two years, compared with those with high levels of confidence. This could include problems with pain, walking around and washing and dressing themselves.

Dr. Lynn Calman, Senior Research Fellow in the Macmillan Survivorship Research Group at the University of Southhampton, which manages the CREW study, said that their study has shown confidence to manage illness is an important factor in the recovery process and it should not be ignored. Exploring areas where people feel less confident to manage is key, if we are to help people through their cancer treatment and beyond.

By considering factors such as a where people live or their marital status, we will be able to ensure patients who could be vulnerable through their treatment and recovery are given the support and guidance they need. More needs to be done to identify and help people who are struggling in the months and years following cancer treatment.

Dany Bell, Specialist Adviser in Treatment and Recovery for Macmillan Cancer Support, think that your chance of coping with cancer should not be dictated by where you live or your relationship status. It is deeply worrying that so many people with bowel cancer are lacking the confidence to cope with pain or fatigue. It's even more concerning that this affects so many of those who are single or from a poor area as we know they are already more likely to lack the support they need. Bowel cancer patients without emotional support three times more likely to experience clinical depression.

Doctors, nurses, and Government must ensure cancer patients get help after treatment. Doctors and nurses can do this by working with the patient on a recovery package – a plan of care which identifies what kind of help they might need after treatment. This could include arranging access to support such as counseling or physiotherapy. Researchers urge healthcare professionals or patients needing more information to get in touch with relevant institutions [4].

Virus Zika can be used to fight brain cancer

Zika is known for causing birth defects like microcephaly and brain damage, it turns out the virus might also serve a very useful purpose - fighting brain cancer. In a study published on September 6, 2017 in The Journal of Experimental Medicine, researchers show that Zika can actually take on a very hard to treat type of brain cancer.

Glioblastoma is the most common type of a brain cancer in the US, for example Senator John McCain was just recently diagnosed with it. Treatment usually incorporates surgery, chemotherapy and radiation. Glioblastoma tumors often recur within months. Standard forms of therapy can do well against the majority of the tumor cells, but leave behind the stem cells that generate the tumors, allowing them to keep creating more tumors once the originals are removed. But Zika actually does the opposite – it can target the stem cells and skip over the other tumor cells. In theory these different treatments would work quite well when used together.

This feature of Zika is what makes it so problematic for fetuses. The virus gets into the developing central nervous system and kills neuroprogenitor cells – the cells that become various types of brain cells later on. The researchers noticed that the glioblastoma stem cells behaved a lot like neuroprogenitor cells, which turned them towards Zika as a potential therapeutic.

In experiments, Zika virus was able to kill stem cells removed from patients with glioblastomas and when it was injected into tumors in mouse brains, it caused the tumors shrink. The researchers also demonstrated that the virus didn't tend to infect non-cancerous brain cells and mutated versions of Zika that made the virus weaker against the body's immune system were also able to kill glioblastoma cells, though not quaite as well as the original strains.

The researchers aren't proposing it for human studies just yet, (but others are) and the virus works differently in mice than it does in humans. But because Zika isn't a major risk to adults, these findings show that it could be a promising brain cancer treatment in the future [5,6].

Whole grains decrease colorectal cancer risk

Eating whole grains daily, such as brown rice or whole-wheat bread, reduces colorectal cancer risk, with more you eat the lower risk, and finds a new report by American Institute for Cancer

Research (AICR) and the World Cancer Research Fund (WCRF). This is the first time AICR/WCRF research links whole grains independently to lower cancer risk.

Diet, Nutrition, Physical Activity and Colorectal cancer also found that hot dogs, bacon and other processed meats consumed regularly increase the risk of this cancer. There was strong evidence that physical activity prptects against colon cancer.

Colorectal cancer is one of the most common cancers, yet this report demonstrates there is a lot people can do to dramatically lower their risk, said Edward L. Giovannucci, MD, ScD, lead author of the report and professor of nutrition and epidemiology at the Harvard TH Chan School of Public Health. The findings from this comprehensive report are robust and clear: Diet and lifestyle have a major role in colorectal cancer.

The new report evaluated the scientific research worldwide on how diet, weight and physical activity affect colorectal cancer risk. The report analyzed 99 studies, including data on 29 million people, of whom over a quarter of a million were diagnosed with colorectal cancer.

Other factors found to increase colorectal cancer risk include:
Eating high amounts of red meat (above 500 grams cooked weight a week), such as beef or pork,
Being overweight or obese,
Consuming two or more daily alcoholic drinks (30 grams of alcohol), such as wine or beer.

The report concluded that eating approximately three servings (90 grams) of whole grains daily reduces the risk of colorectal cancer by 17 percent. It adds to previous evidence showing that foods containing fiber decreases the risk of this cancer. For physical activity, people who are more physically active have a lower risk of colon cancer compared to those who do very little physical activity. Here, the decreased risk was apparent for and not rectal cancer.

IN the US, colorectal cancer is the third most common cancer among both men and women, with estimated 371 cases diagnosed each day. AICR estimates that 47 percent of US colorectal cancer cases could be prevented each year through healthy lifestyle changes. E. Giovannucci notes that many of the ways to help prevent colorectal cancer are important for overall health. Factors such as maintaining a lean body weight, proper exercise, limiting red and processed meat and eating more whole grains and fiber would lower risk substantially. Limiting alcohol to at most two drinks per day and avoidance or cessation of smoking also lower risk.

The report found other links between diet and colorectal cancer that were visible but not as clear. There was limited evidence that risk increases with low intake of both non-starchy vegetables and fruit. A higher risk was observed for intakes of less than 100 grams per day (about a cup) of each. Links to lowering risk of colorectal cancer was with fish and foods containing vitamin C. Oranges, strawberries and spinach are all foods high in vitamin C.

The research continues to emerge for these factors, but it all points to the power of a plant-based diet, says Alice Bender, MS RDN, AICR Director of Nutrition Programs. Replacing some of your refined grains with whole grains and eating mostly plant foods, such as fruits, vegetables and beans, will give you a diet packed with cancer-protective compounds and help you manage your weight, which is so important to lower risk.

When it comes to cancer there are no guarantees, but it's clear now there are choices you can make and steps you can take to lower risk of colorectal cancer and other cancers, said A. Bender [7,8].

The report is part of the Continuous Update Project (CUP), which monitors and analyzes research on cancer prevention from around the World and draws conclusions on how weight, diet and physical activity can reduce the risk of developing cancer.
(Reports are located here: www.aicr.org/continuous-update-project)

Good and bad news on aspirin and colon cancer

Daily aspirin use – known to reduce the risk of colon cancer – could also make the disease harder to treat if it does occur, researchers reported in the Journal of the Royal Society Interface in September 6, 2017 issue.

The new findings based on mathematical modeling. If confirmed statistically and in the lab, would mean that aspirin's ability towards off colon cancer may come at an unacceptable high cost. Taking aspirin regularly has been shown to reduce the incidence of a variety of cancers, including of the colon. But at the same time, the drug may render the cancer more difficult to manage therapeutically. This indicates a potential trade-off.

A growing body of research has known that daily micro-doses of aspirin taken for at least five years can slash the risk of cancer later in life. Rates of prostate, throat and non-small-cell lung cancer all drop off significantly, with the incidence of colon cancer by up to half.

Other studies, meanwhile, have tested the impact of aspirin directly on cancer cells in the laboratory, showing that the common painkiller can slow the rate of cell division and boost cell death. But scientists do not yet understand the mechanism at work, or know whether aspirin might have as-yet-undiscovered effects on cancer spread. To find out more, researchers led by Dominik Wodarz of the University of California at Irvine, who conducted these earlier experiments, investigated whether the drug may cause dangerous cancer mutations.

Indeed, aspirin did boost the cancer's ability to produce aggressive, mutant cells that are drug-resistant. The results could challenge the protocol for aspirin use in cancer prevention. It is now critical to ensure that aspirin delays the onset of colorectal cancer by a sufficient

amount of time to avoid the negative effects of this trade-off.

People, who take the drug, especially in middle age, should be regularly screened for cancer, the study authors said.
Roughly half of adults in the United States take small doses – 80 to 325 miligrames of aspirin towards off cardiovascular disease. In Britain the figure is about 40 percent. The general public has not yet recognized the potential benefits for cancer prevention, notes Peter Rothwell, a professor at the Centre for Prevention of Stroke and Dementia at the University of Oxford.

It takes a while, and more replication studies, to convince that the benefits are real. P. Rothwell published a study earlier this year showing an increased risk of internal bleeding in people over 75 who take aspirin regularly.

You might want to take aspirin in your 50s and 60s, but then stop! The benefits you get from cancer prevention carry in for another 10 years or so [9].

New cancer therapy inhibiting the Notch signaling pathway

EPFL spin-off Cellestia Biotech has just been given the regulatory go-ahead to start clinical testing a molecule it has developed to treat cancers involving mutations of the Notch gene. The molecule is a ray of hope for the 250,000 patients diagnosed every year with this mutation, which sharply reduces their chances of recovery.

The molecule developed by Cellestia Biotech, an EPFL spin-off, is a targeted therapy designed to treat cancers resulting from mutation of the Notch gene. Clinical trials are scheduled to start soon in Spain. This oral treatment is the first to work by stopping the problem at its roots, i.e., in the cell's nucleus. It inhibits the protein complex allowing cancerous cells to multiply – that they cannot generate signals.

One of the alternatives to chemotherapy currently being investigated by experts is the array of signals generated by proteins in a cell nucleus. A normal Notch protein plays an indispensable role in embryonic development and in the formation and maintenance of stem cells. Genetic lesions can result in an abnormal signaling pathway that facilitates the development of cancerous cells and causes resistance to conventional therapies. This vicious signaling pathway has been the subject of several recent studies that have confirmed its link to breast cancer, leukemia and several types of lymphoma. Around 250,000 patients worldwide are diagnosed each year with cancer related to this type of genetic lesion.

The safest way to block the signaling pathway is to cut it off at the source, preventing the protein from activating signals in the nucleus. Molecule CB-103, discovered by Rajwinder Lehal during his doctoral studies in Freddy Radtke's laboratory at EPFL, binds with the protein complex and inhibits its activity inside the nucleus. This cuts off all Notch signals regardless of how they are activated, thereby killing off the cancerous cells.

Other therapies that target the Notch signaling pathway have also been investigated by research groups – some block a part of the pathway, while others inhibit different mechanisms involved in other cellular processes [10].

Patents have been filed for the molecule and for the development and marketing of several similar molecules. Both in-vitro and in-vivo tests carried out on the molecule showed excellent efficacy and tolerance. It also demonstrated rapid reuptake and distribution in tissues.

The clinical trial will be partly funded by the CHF 8 million in seed financing raised by the startup early this year. The researchers will investigate several factors such as tolerability and dosages for adult patients with advanced or metastatic solid tumors and hematologic malignancies. Biomarkers have also been developed to ensure that patients taking part in the trial have the right type of cancer for the molecule.

The Notch pathway has become a key target for cancer therapies because of the critical role it plays in tumorigenesis. That's why it's being researched by so many pharmaceutical companies, says Rajwinder Lehal, Chief Science Officer at Celestia Biotech. Oving to its potential application for numerous indications, the market for these inhibitors is estimated to be around CHF 10 milion, and sales of CB-103 are expected to amount to CHF 1 billion if several treatments can be developed. The startup has also discovered other molecules that can act in a similar way, and it plans to test them as a therapy for other types of cancer [11].

Notch protein as leading cause of World Cancer Epidemic

The activation of Notch signaling is implicated in tumorigenesis in the colon due to the induction of pro-survival signaling in colonic epithelial cells. Chemoresistance is a major obstacle for treatment and for the complete eradication of colorectal cancer (CRC). The inhibition of Notch is an attractive target for CRC and several groups are working on this topic. Dietary agents have gained momentum for targeting several pro-survival signaling cascades, and recent studies demonstrated that inhibit Notch signaling result in growth inhibition in preclinical models of CRC [10].

Cancer is a hyper-proliferative disease in which cells grow in an uncontrolled manner and acquire an invasive phenotype, leading to metastatic disease. Worldwide, colorectal cancer is the third most common malignancy in males and the second most common malignancy in females. In the United States, CRC is the third leading cause of cancer-related deaths in men and women. It accounts for 136,830 new cases and 50,310 deaths annually.

As per the National Institute of Health, total cost for the treatment of CRC for the year 2010 was 14 billion dollars in USA. Despite the early detection of CRD, the mortality rate remains high due to chemoresistance and systemic toxicity to normal cells and organs.

CRC is a multistep process that involves the disruption of molecular mechanisms for intestinal homeostasis by maintaining intestinal proliferation, differentiation and programmed cell death.

The repercussion of this deregulation of cellular signal promotes oncogenic phenotypes, in which cells exhibit uncontrolled proliferation, the loss of apoptosis, a highly invasive phenotype that advances to metastasis, the induction of angiogenesis and chemoresistance to drugs. We can use in fight against CRC also the potential of the natural compound Withaferin A (WA) and its ability to target Notch signaling and so impede CRC development and progression. Withaferin A [(4,5,6,22R)-4,27-dihydroxy-5,6;22,26-diepoxyergosta-2,24-diene-1,26-dione)] is a bioactive compound derived from the medicinal plant Withania somnifera Dunal [12,13].

Notch signaling is critical for maintaining the balance between cell proliferation, differentiation, and apoptosis and is also involved in angiogenesis and the migration of cancer cells. Deregulation of these processes that are regulated by Notch signaling may lead to the initiation and progression of CRC [14].

Notch receptors and their ligands are aberrantly activated in many human cancers, such asnT-ALL, pancreatic cancer, breast cancer, prostate cancer, liver cancer, cervical cancer, Kaposi's sarcoma, lung cancer, ovarian cancer, lymphoma, renal cancer and CRC. Overexpression of Notch elements, such as receptors, ligands and downstream target genes, is correlated with increased progression, metastatic potential, and recurrence and poor prognosis and clinical outcome in various cancers. For example, overexpression of Notch 1 is associated with decreased time to recurrence in breast cancer. High expression of Jagged-1 is correlated with the recurrence of prostate cancer, etc. Moreover, inhibiting Notch signaling with -secretase (GSI) in rodents caused an overproduction of goblet and enteroendocrine cells [15].

Notch is activated in primary CRC rather than metastatic colon cancer, implying that the activation of Notch may be an early step of CRC development. In contrast, high expression of Notch-1 and its target gene Hes-1 during both, colon cancer progression and metastasis. Mutations in the Notch receptor may play a significant role. In addition, the activity of Notch 1 is also increased as a result of -catenin-mediated upregulation of Notch ligand Jagged-1.

Notch ligand Jagged 1 is highly confined to enteroendocrine cells and undetectable in the mucosa of the small or large intestine, however, higher expression of this ligand is observed in human colon tumors. Recent studies showed that downregulation of Jagged 1 decreases cell viability and causes cell cycle arrest by downregulating the expression of Cyclin D1, Cyclin E and c-Myc in CRC. These in vitro studies also demonstrated a reduction of the migratory and invasive behavior of CRC cells. Further, knocking down Jagged-1 inhibited the growth of xenograft tumors compared to controls, supporting the therapeutic role of Notch in CRC models. Activation of Notch signaling has been reported to be indispensable for the development of adenomas in mice and for the self-renewal of tumor-initiating cells [13].

Discussion

Nutritionists warn that the trans fats can be harmful, but that the bigger issue is that people are consuming far too many calories. Frying food with sunflower or corn oil could be more damaging than using butter or lard, scientists are warning. When vegetable oils are heated, researchers have shown that they release toxic chemicals which have been linked to cancer.

They are now recommending that cooks use olive oil, coconut oil. For years, health advice has suggested using oils high in polyunsaturated fats are better for health than saturated animal fats. But experts say that heating the vegetable oils release aldehydes, which have been linked to illnesses like heart disease, dementia and cancer. Heating vegetable oils produces toxic chemicals [16].

The research team at De Montfort University in Leicester says fish and chips fried in vegetable oil could contain 100 to 200 times more aldehydes than the daily safe limit recommended by the World Health Organisation (WHO). Measured in millimoles, the research showed that when heated to high temperatures over a period of 30 minutes coconut oil released half a milimole of toxins, butter had over one millimole, whilst sunflower oil had over five millimoles.

Dr. Monsah Mansoori told Sky News that things like vegetable oil, when we do heat them to very high temperatures, produce toxic chemicals called aldehydes, which are thought to be linked to heart disease and cancer. Some forms of neuro diseases like Alzheimer's have been linked to this and unfortunately the longer you fry the oils for, the worse they get for you.

Things cooked with butter or lard can taste better, but you don't to overuse them as ingredients. But we perhaps should not start stocking up on butter and lard just yet, as they still contain lots of calories.

Dr. Alison Tedstone, chief nutritionist at Public Health England, said that trans fats are harmful to health. The majority of trans fats in our diets comes from natural sources in meat and milk.

The bigger issue is that we are all consuming too many calories and too much saturated fats and sugar leading to weight gain and obesity which increases your risk of heart disease, type 2 diabetes and cancer (Maude, 2015).

There is a growing amount of evidence that Notch activation can drive metastatic prostate, colon and other types of cancer. Notch protein complex signaling pathway, is in our view, one of the most important cause of the World Cancer Epidemic.

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