

Where Autoimmunity, Cancer and Disease Collide

READERS SUMMARY:

1. What ties Levee 5, 6, and 16 all together in the QUILT?
2. Why is Vitamin D and Selenium the key to the gut?
3. How does Vitamin K play a role?
4. Why is autoimmune disease, cancer and neolithic disease more common today than ever before?
5. Is there another environmental toxin that we can not perceive that is behind this?

I believe heart disease and inflammatory bowel diseases are pre-cancerous states. I also believe autoimmunity is a precancerous state. I believe autoimmunity and cancer are just steps apart. [I also believe we will soon find that these diseases are linked to an altered environment and circadian signaling.](#) Epidemiological studies link all these disease to inflammation generation. The pathway in humans tied to inflammation is the NRF2 pathway. This pathway underpins the Hormone 101 and 102 blog posts. Most people and doctors already know there are links to inflammation but they are not sure how they link to circadian mismatches. But what is less talked about is how this all fits biologically. Today we are going to begin to tackle this. I think two critical co-variables need to be looked at in detail and are found in our immune system physiology. Those two critical factors are Vitamin D status and Selenium status. I have already shared with you how a leaky gut is tied to autoimmunity in some detail in my recent blog. Today we are going to begin to tie three levees together, oncogenesis, immunity, and the brain gut axis.

In the June 2010, American Journal of Pathology published a

study that caught my eye. It reviewed at the Vitamin D Receptor (VDR) and the generation of inflammation in the large intestine in a mice model. The paper looked at gut inflammation in the presence of a Salmonella infection. Salmonella is a bacterial infection. Mice which lacked VDR's, seemed to have higher states of gut inflammation and worse outcomes than control groups. The key difference however was the high levels of IL-6, an inflammatory cytokine. IL-6 is tied directly to the Nrf2 pathway. IL-6 is a bad actor in cellular homeostasis and in circadian signaling. It is seen in most cancers and all inflammatory conditions in humans to some degree. Most gut absorption is done via the transcellular pathway. (90% through gut cells) The remainder of gut transport occurs via intracellular methods (tight gut junctions) that are controlled by vitamin D status. The less Vitamin D you have the more leaky your tight junctions will be and this exposes your immune system to direct assault. This assault is then aimed directly at our liver for detoxification. And our liver has to defend the rest of our body from inflammatory cytokines, as I laid out in the VAP blog.

The key finding in the article was that animals with an intact VDR, [faced less gut inflammation](#) and had lower rates of Salmonella infection. The VDR mechanism of action is to block the signal transduction of [NF-Kb](#) (911 signal of the cell also from the nrf2 pathway) from the cell membrane to the nucleus of the cell. Once it gets into the nucleus it binds to our DNA to promote many inflammatory pathways that lead to more cytokine production. One pathway leads to IL-1b production seen in all autoimmune conditions. The other pathway leads to IL-6 and TNF alpha generation that alter the promoter region of p53 gene (protector gene of our entire genome) by hypomethylation and allows for cellular oncogenesis if the "switch" stays on long enough. VDR up regulates a protein called Ikb which won't allow the NF-k beta to enter the nucleus of the cell to set the plan of oncogenesis to commence

in action. It also appears that the VDR does not even require active vitamin D3 to be present for this to occur.

In 2002, in a study by Al-Tate et al., we learned about how Selenium (Se) affects gut inflammation and generation of autoimmunity and oncogenesis. 50% of plasma Selenium is contained in human glycoprotein selenoprotein P (SeP) and is highly expressed in the human gut, specifically in the liver (gut protector). In times of high inflammation from the gut, its expression is **DOWN** regulated by various inflammatory cytokines. Selenium is found in seafood in high quantities.

IL-1b is the most potent to do this followed by TNF- beta and interferon gamma. It appears that development of autoimmune diseases is the cellular choice if IL-1 is predominantly generated, and cancer of various gut organs are favored if other inflammatory cytokines are generated chronically. For autoimmune conditions, this cytokine pathway is altered in the microglia cells of the brain. This affects how the MHC 1 gene is expressed epigenetically.

The very interesting fact is that with an adenoma (beginning of tumors in the colon that are initially benign) presence in the colon, there was a strong association with decreasing SeP. Patients with Se levels below 70 mcg/L are at the highest risk for oncogenesis.(Psathakis et al. 1998) People who eat a standard american diet as advocated by the USDA carry that risk. Selenium also allows us to generate a stable pipeline of **methyalted metabolites** that directly protects our DNA, and specifically the p53 gene. **It really up regulates the production of mono-methyalted species and has amazing chemotherapeutic potential.** These are rarely used in conventional chemotherapy. Remember that most methyl transfers occur in humans from mainly the B vitamins. B12 is most mentioned. It only comes from animal proteins and those of you who advocate the vegetarian method of eating all have to supplement B12 for this very reason. B12 is very abundant in seafood. In fact, B vitamins are very common in the marine

food chain. It is found nowhere else but in fish/animal protein and fat. So now you are starting to realize why being a vegetarian leads can lead to a higher oncogenic incidence, higher autoimmune disease risk, along with higher Crohn's disease, heart disease and diabetes risk!

To further illustrate how important methyl transfers are, I suggest a trip East. Just go to southern India to see what a life long vegetarian diet does to a human body. The epidemiology data out of India is just staggering with regards to these neolithic diseases. The southern region of India is filled with mostly vegetarian sects, while the Northern territories are more into animal protein diets. There is also more new modern technology industry found in southern India **which further alters the field that biology has to act in.**

It should be required of every person who thinks this is the "moral" way to eat. If it kills and hurts humans, how humane can it really be from the moral standpoint? I think it guarantees you a suboptimal life if you choose it. Enough of that PSA now. The amount of industrialization is massive over the last 40 years in this region of India. They have also ramped up their use of artificial light and modern technology. If you want to know why I mention it have a look at this: [Hyperlink](#)

Back to today's topic.

We also have seen in numerous papers that in both autoimmune and oncogenesis disease that vitamin D and Selenium decreases are seen much more commonly. Vitamin K production by the gut bacteria is also down regulated as well in inflammatory conditions like cancer, autoimmunity and inflammatory bowel diseases. It appears that chronic gut inflammation allows for the reduction of both selenium, vitamin D and vitamin K. Vitamin K reduction also shows a very strong correlation with many neolithic diseases as well.

Selenium deficiency is associated with many cancer lines as

well. Selenium deficiency has been shown to cause global hypomethylation in DNA. This is where the link of autoimmunity and oncogenesis seems to lie. Hypo-methylation is the “on and off switch” between these two disease processes. Hypo-methylation is more apparent when DNA is **not well hydrated** in vivo. The co factors important for switch activation are Selenium, Vitamin D, and bacterial Vitamin K production in the leaky gut. The differing concentrations of all three seem to predispose to what cellular fate or field will be faced in presence of a leaky gut. The less aggressive cellular terroir may predispose us to GI distress with bloating, malnutrition and bad bowel habits. It may progress to an elevated sdLDL cholesterol that causes chronic neolithic diseases like heart disease, Crohn’s disease or diabetes. More significant inflammation likely elevates IL-1b and favors autoimmune conditions to blossom. This is associated with NF kappa beta and IL-6 spikes in the brain. This is when the blood brain barrier becomes leaky. We can assess this with a GABA test clinically. Further inflammation changes the mix of the co factors and the cytokines to favor frank oncogenesis in many of our gut organs. We have no idea what is critical to each step but we do know the players today. So if you alter your diet to make sure each one is plentiful you can control the master switch in your own “leaky gut” to control your outcome.

When it comes to the leaky blood brain barrier, the key issue seems to be an environmental trigger that alters T helper cell maturation in the neuro-immune system.

Selenium:

Selenium is needed for the proper functioning of the immune system cells. It is a co-factor in the activation of neutrophils, macrophages, and Natural killer cells and T lymphocytes and many other immunoregulatory functions as laid out in [Ferencik’s paper in 2003](#). Selenium seems to act by two modes to protect us from cancer. One is that it catalyzes many immune reactions to increase our immune function in the

GALT. Secondly, Se seems to hinder oncogenesis by protecting the p53 gene in the gut and does not allow oncogenesis to occur. In fact, it appears to favor low level inflammation, seen in autoimmune conditions vs. cancer, and thus, favors apoptosis of defective cells instead of oncogenesis. It appears that low plasma Selenium levels reduce the production of plasma glutathione peroxidase. **Patients with low selenium levels are known to have higher rates of polyps and autoimmunity.** ([Fernandez-Banares et al., 2002](#)) Naturally occurring Selenium is found in plants like garlic and broccoli as a compound called Se-methylselenocysteine (Se-MSC). Se-MSC produces 33% reduction in cancerous lesions (colon) than selenite (synthetic). It turns out cysteine is really important. [Read this hyperlink.](#) It also produces a 50% decrease in new tumor development locally in the gut. It also induces cells to undergo apoptosis and not oncogenesis. It has been shown to reduce angiogenesis to make the cellular terroir less hospitable to cancer. Se- MSC also directly down regulates vascular endothelial growth factor that is commonly found in most GI cancers. So the story seems to show that selenium is pretty critical to gut health and disease prevention.

Let's Talk Vitamin D:

We also know that Vitamin D activates T regulator cells ([specifically T Helper cells](#)) and helps maintain the intestinal brush border of the gut to make it less leaky to inflammation. It strengthens the tight junctions between gut cells. [Glutamine also helps with this too by providing the "building blocks" for zonulin production. Zonulin is the protein that makes a tight junction "tight".](#) This in turn, directly protects the liver from seeing high levels of inflammation in the portal circulation. Once the brush border becomes a sieve for any environmental reason, due to development of a "leaky gut", the liver is the last line of defense of the gut. The remainder of the body then faces an

inflammatory onslaught, and this is where all neolithic diseases begin. To understand how the liver reacts to this assault, I suggest you re read my blog on the VAP and Liver to tie these concepts together.

Vitamin D is also a renin inhibitor. Renin acts on the kidney to control blood pressure, so Vitamin D may help to lower blood pressure. Vitamin D suppresses activity of the inflammatory proteins NF-kB and TNF-alpha as well. It works as a natural antibiotic by increasing the protein cathelicidin found in WBCs such as neutrophils, macrophages and also epithelial cells. These cells then can kill bacteria more effectively. Moreover, higher Vitamin D levels are associated with increased adiponectin levels. Low levels of adiponectin are seen in obesity and leptin resistance. The more obese you are, the more likely you will face inflammation and the disease associated with it. This may be the mechanism of how Vitamin D may improve type two diabetes. The current levels recommended by the recent Institutes of Medicine report completely ignore most of these medical benefits. You can speak to your doctor about the levels they recommend, but I believe we need much higher protection because of the disease risk we are now seeing from neolithic disease. This is a controversial point today.

WRAPPING IT UP?

How is this related through an evolutionary lens you ask? It is clearly tied to environmental and dietary changes in the host. Humans likely began eating seafood and meat and being exposed to many bacteria like Salmonella as we evolved. Without the effects of the VDR, they would have had severe inflammatory bowel disease and possibly higher rates of colon cancers. Hey wait Dr. Kruse! Is not that we currently face today in our country? For those of you who don't know this, consider these facts of epidemiology in 2011.

Inflammatory bowel diseases and autoimmune disease are now **BOTH** at all time highs in prevalence and incidence world wide!

Today the incidence and prevalence of autoimmune disease out numbers all deaths from cancer and heart disease by a factor of ten. Have you ever stopped and asked **WHY?**

In the USA, in 1900, colon cancer was the 37th leading cause of death in the USA. Today after 110 years of increased fructose and hybridized grains and an ending source of electromagnetic force from modern technology has been introduced into the Standard American Lifestyle. Since 1900, we have caused the electrification of the surface of our planet, and simultaneously altered our diet, yet we wonder why colon cancer is now the third leading cause of cancer deaths in the USA?

So do you still think this leaky gut and leaky brain thing is BS? Well.....it now up to you to ponder.

CITES

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