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How and Why Too Much Protein Triggers Aging and Cancer

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By Dr. Mercola

Anti-aging expert Ron Rosedale, M.D., was among the first to warn people about the dangers of eating too much protein — a stance that has received a fair share of criticism over the years, although mounting research now offers strong support for this notion.

He was the first to help me understand the importance of insulin in 1995 and more recently the importance of protein and mTOR as discussed in the above video. I consider him my most important nutritional mentor.

The featured lecture was given in February of this year at Vail. In it Dr. Rosedale details the ancestral connection between protein, mammalian target of rapamycin (mTOR), the aging process, and cancer formation.

He starts out by offering an absolutely simple yet profound piece of wisdom in that “your health and likely your lifespan will be determined by the proportion of fat versus sugar you burn over a lifetime.”

In essence, he proposes that any food that helps you burn fat is likely beneficial for health, and any that makes you burn sugar is likely not. This is largely because sugar is a “dirty” fuel and fats and ketones burn far cleaner causing far less oxidative damage.

Hormones and the communication between them play an important role here, and those hormones are determined by the foods you eat. According to Rosedale, “you should eat today to control the hormones that will tell you what you will need to eat tomorrow.”

In a nutshell, this hypothesis completely ignores the “calories in, calories out” dogma, and instead focuses on foods that support hormones and growth factors that make your body burn fat rather than sugar.

Story at-a-glance

mTOR is an ancient molecular signaling pathway that is responsible for either growth or repair, depending on whether it is stimulated or inhibited

To upregulate maintenance and repair, boost longevity, and reduce your risk for cancer, you need to suppress the mTOR pathway, and the most efficient way to do this is to limit your protein intake

For longevity, aim for a diet high in healthy fats, low in net carbs, with moderate amounts of high quality protein. Ideally no more than about 1 gram per kilo of lean body mass

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Protein Restriction — An Important Dietary Strategy for Optimal Health

The low-carb diet made its initial appearance some 40+ years ago. In particular, it was found that low carb diets facilitated weight loss.

At the time, most people recommended replacing carbs with high amounts of protein, and these low-carb, high-protein diets (such as Atkins') worked quite well for the purpose of shedding weight.

Dietary fat was almost universally avoided, as most experts embraced the "low fat myth" and fat was thought to promote obesity and heart disease. Rosedale, however, wanted to treat diabetics, and was one of the few who promoted a high-fat diet for that purpose.

One of the primary problems with excess protein or amino acids is that it stimulates mTOR, which stimulates growth rather than regeneration. Fat calories did not stimulate mTOR, leptin or insulin. They were essentially metabolically free calories.

Rosedale found a diet high in healthy fats worked quite well for diabetes and heart disease patients. Over time, he discovered that restricting protein was another important factor that could affect health, and even more specifically the aging process.

Why Paleo Diets Don't Promote Longevity

Dr. Rosedale is of the opinion that while the Paleo diet may help mimic a diet that will optimize reproductive success, it will not necessarily help you live longer, because life extension and reproductive capacity do not go hand in hand.

"We can't use nature, in general, to tell us how to live a long happy life," he says, "because nature doesn't care [about life extension]. Nature's purpose is to get genes passed along [to the next generation]."

From an evolutionary perspective, nutrients had to be allocated by an organism either for a) growth, replication, and reproduction, or b) maintenance and repair, which helps you stay alive longer.

As a rule, nature will keep an organism alive long enough to replicate and reproduce; it doesn't care much about staying alive post reproduction, and that's why we age and die. "What we want to do is apply that science post reproductively," Rosedale says.

Life Extension Depends on Upregulating Repair Mechanisms

At any given moment, there's competition in your body between cellular damage and repair. As the damage becomes greater than your body's ability to repair and regenerate, deterioration sets in. "If we could repair damage as fast as it occurs, we could live forever," he says.

The reason we cannot keep up with this maintenance is because our repair mechanisms become damaged over time as well. So your best chance of living longer is to upregulate your repair mechanisms, because you simply cannot stop damage from occurring. Simply breathing creates oxidation and damage.

Fortunately, all organisms, including humans, are equipped with a mechanism by which cells can outlast nutrient deprivation (famine), and that's part of the answer.

Remember, the foods you eat will influence either a) repair, which will help you live longer, or b) reproduction, and your body is ingeniously equipped with "nutrient sensors" that help determine how the nutrition will be used.

Insulin, leptin, and insulin-like growth factor (IGF) are examples of nutrient sensing hormones that in turn regulate metabolism, growth, cell differentiation, and cellular survival. Organizing all of these nutrient sensors is the mammalian target

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of rapamycin (mTOR).

According to Rosedale, mTOR is the most important signaling pathway in your body. It's an ancient pathway found in virtually all organisms, including bacteria.

Why mTOR Is So Important for Longevity

Your mTOR pathway orchestrates all the available nutrient sensors in your body, and decides whether cells should replicate now or stay alive to replicate at a more opportune time in the future when nutrients are more plentiful.

The latter is part of the mechanism that allows for life extension, and this is why calorie restriction appears to be so effective at making organisms live longer. In one experiment, the lifespan of a mouse was extended from two to four years by inhibiting IGF receptors through a calorie restrictive diet.

Other research cited in Rosedale's lecture has demonstrated that by using a drug compound that inhibits growth hormone, they were able to reverse signs of aging, noting this may seem counterintuitive as some older people take growth hormone for revitalizing purposes.

As noted by Rosedale, "there's a dichotomy, apparently, between growth, reproduction, and longevity." He also points out that there's a cross-reaction between insulin and IGF. High insulin is detrimental to health *in part* by stimulating IGF receptors, which is a growth hormone.

High insulin also causes insulin resistance of course, which has an adverse effect on your metabolism. But by promoting growth hormone, high insulin effectively decreases longevity, as growth and longevity cannot be promoted simultaneously. You're choosing one or the other.

Calorie Restriction, Longevity and Thyroid Function

On a side note, since we're talking about hormones, a 2005 study noted that "some of the common and consistent effects of calorie restriction... include lower fat mass, particularly visceral fat, lower circulating insulin and IGF-1 concentrations, increased insulin sensitivity, lower body temperature, lower fat-free mass, decreased levels of thyroid hormones and decreased oxidative stress."

According to Rosedale, this is an important piece of information, because if you embark on a ketogenic, high-fat, low net carb diet you may notice your thyroid hormone levels going down, which may raise concerns about thyroid disease. Such concerns are unwarranted (as long as your TSH level is normal). In fact, this is a much healthier state, Rosedale says.

"You're running cooler, allocating more resources toward maintenance, repair, and longevity," he says. "It's not thyroid disease ... because TSH did not go up, which is how you define hypothyroidism."

Protein Intake Determines Your IGF Concentration

So IGF is a key player when it comes to longevity. It appears that by inhibiting IGF you can boost lifespan and reduce your risk of cancer (remember, cancer is an out of control proliferation of malignant cells. By redirecting energy from proliferation to repair and maintenance, cancer growth is impeded). And what nutrient determines your level of IGF? Protein. Higher protein intake elevates IGF, and lower intake decreases it.

As noted by Rosedale, there's a major difference between a low-carb/high protein diet and a low-carb/high-fat diet. The former raises IGF, and the latter does not. In the early days of the low-carb revolution, no distinction was made between high protein or high fat, and since fat was so vilified, most people replaced the carbs with protein. It worked well for weight loss, but drawbacks also became apparent.

Since then, researchers have discovered that low-protein diets extend lifespan in flies, and the underlying reason for that is improved mitochondrial function and mTOR inhibition. According to the authors, "the molecular mechanisms responsible for

the lifespan extension in the flies have important implications for human aging and diseases such as obesity, diabetes and cancer.”

Rapamycin, mTOR and Cancer Risk

Rapamycin, which is an mTOR inhibitor, is an antifungal agent that also inhibits cancer. Interestingly, it's also an immune suppressant, and in medicine it's used to suppress immune function during organ transplantation to avoid organ rejection.

Research shows that kidney transplant patients actually have a lower incidence of cancer — despite having lowered immune function — and this effect is thought to be due to the protective effects of rapamycin. It seems counterintuitive, since strong immune function is typically considered to be foundational for cancer suppression, so these findings suggest something else, and something quite powerful, is at play.

That “something,” is mTOR. By inhibiting mTOR, rapamycin powerfully inhibits cancer, despite lowered immune function. So what else affects mTOR? Amino acids and glucose both affect TOR directly, which is why carbs and protein have such a detrimental effect on health and aging. Insulin and other growth factors all upregulate TOR, which is why it's so important to keep your insulin and IGF low.

Remember, TOR regulates growth and repair. Either growth is promoted or maintenance and repair, depending on whether TOR is up- or downregulated. When TOR is *suppressed*, maintenance and repair is upregulated and that results in increased longevity, which is what you want.

Exercise and Fasting Upregulates Genetic Expression of Maintenance and Repair

Again, mTOR senses nutrient availability, and directs energy accordingly. Hence your diet can have a tremendous influence on your lifespan. Glucose and amino acids are the nutrients and fuel necessary for replication and reproduction. If you keep glucose, amino acids, insulin, and growth factors like IGF low, you will suppress mTOR, thereby allowing the upregulation of the genetic expression of maintenance and repair.

TOR also plays an important role in autophagy, the process by which your body cleans out debris, including toxins, and recycles damaged cell components. A similar process is known as mitophagy, where damaged mitochondria are cleaned out and replaced with new, healthy ones, and this process is also largely regulated by mTOR.

By boosting your body's autophagy processes, you dampen inflammation, slow down the aging process, and optimize biological function. Autophagy occurs in response to stress. Exercise is one way by which you boost autophagy. Fasting is another. As noted in a 2011 study published in *Molecular Cell Biology*:¹

“In all eukaryotes [incl. humans], the TOR signaling pathway couples energy and nutrient abundance to the execution of cell growth and division, owing to the ability of TOR protein kinase to simultaneously sense energy, nutrients and stress and, in metazoans [incl. humans], growth factors. In the past few years, a significant advance in our understanding of the regulation and functions of mTOR has revealed the crucial involvement of this signaling pathway in the onset and progression of diabetes, cancer and aging.”

Excessive Protein Shuts Down Autophagy and Increases Cancer Risk by Stimulating mTOR

Of all the components that stimulate mTOR, amino acids are the most potent stimulators. Hence, eating large amounts of protein is also one of the quickest ways to shut down autophagy, which prevents your body from effectively cleaning out debris and damaged cells. According to Rosedale, even if you do everything else right to keep glucose and insulin low, your mTOR would still be elevated if you eat too much protein.

He also notes that virtually all cancers are associated with mTOR activation, so activating mTOR is something you'll definite-

ly want to avoid. This is why I recommend limiting protein to about 40 to 70 grams per day, depending on your lean body mass.

The specific formula is one gram of protein for every kilogram of lean body mass, or one-half gram of protein per pound of lean body mass. To determine your lean body mass, subtract your percent body fat from 100. For example, if you have 30 percent body fat, then you have 70 percent lean body mass. Then multiply that percentage (in this case, 0.7) by your current weight to get your lean body mass in pounds or kilos.

In the past, Rosedale used to recommend cutting that down to 0.75 grams per kilo of lean body mass if you were diabetic. Today, he believes this may actually be a more ideal amount for everyone, and you could even go below that because your body will conserve protein when you suppress mTOR and increase maintenance and repair. That said, protein is important for muscle maintenance and growth, so there's definitely a fine balance that needs to be struck.

Protein Sources

Substantial amounts of protein can be found in meat, fish, eggs, dairy products, legumes, nuts, and seeds. Some vegetables also contain generous amounts of protein — for example, broccoli. Forty grams of protein is not a large amount of food — it's the equivalent of one 6-ounce chicken breast.

To determine whether or not you're getting too much protein, simply calculate your body's requirement based on your lean body mass, and write down everything you eat for a few days. Then calculate the amount of daily protein you've consumed from all sources. If you're currently averaging a lot more than what is optimal, adjust downward accordingly. The following chart provides a quick overview of how much protein is in various foods.

<p>Red meat, pork, poultry, and seafood average 6 to 9 grams of protein per ounce.</p> <p>An ideal amount for most people would be a 3-ounce serving of meat or seafood (not 9- or 12-ounce steaks!), which will provide about 18 to 27 grams of protein</p>	<p>Eggs contain about 6 to 8 grams of protein per egg. So an omelet made from two eggs would give you about 12 to 16 grams of protein</p> <p>If you add cheese, you need to calculate that protein in as well (check the label of your cheese)</p>
<p>Seeds and nuts contain on average 4 to 8 grams of protein per quarter cup</p>	<p>Cooked beans average about 7 to 8 grams per half cup</p>
<p>Cooked grains average 5 to 7 grams per cup</p>	<p>Most vegetables contain about 1 to 2 grams of protein per ounce</p>

Is Protein Restriction Even More Important Than Net Carbohydrate Restriction?

Since mTOR can be elevated even if your glucose and insulin levels are low, and since mTOR regulates energy distribution, growth, and repair, Rosedale now believes protein restriction may be even more important than the restriction of net carbohydrates (total carbs minus fiber). This theory has in fact been tested, and found to hold true. As noted in a 2014 study in Cell Metabolism:²

“Longevity and health were optimized when protein was replaced with carbohydrate to limit compensatory feeding for protein and suppress protein intake ... The results suggest that longevity can be extended in ad libitum-fed animals by

manipulating the ratio of macronutrients to inhibit mTOR activation."

It's worth noting they didn't test a high-fat diet. They were only looking at carbs versus protein, and if those were your only choices, protein restriction may in fact be more important than carb restriction. However, there are many drawbacks with eating lots of non-fiber carbs too, so it's far from an ideal solution. Your best alternative is to replace net carbs with high quality healthy *fats*, and restrict protein to just what your body needs (as described above).

Beware: Ketogenic Diets Can Be High-Protein or High-Fat, But Only the Latter Is of True Benefit

Now, here's where things might get confusing, because research³ has also shown that ketone body utilization drives tumor growth and metastasis. (Ketones are acids made by your body when it burns fat rather than carbohydrates as its primary fuel.) This finding appears to be completely contradictory to so many other studies that show a ketogenic diet effectively "starves" cancer. But there is an answer to this apparent contradiction, which Rosedale explains in his lecture.

*"It isn't ketogenesis, really, that we're after," he says. "It's fat burning. They're not the same. You can have a ketogenic diet by eating protein. It isn't the ketones, necessarily, that give you the benefit, it's the fact that you're burning fat, and the ketones are a byproduct. So you have to specify if you're going to [promote a] ketogenic diet that it's a **high fat** ketogenic diet.*

It's really the burning of fat that's of benefit. As a result, you'll get ketones that your brain needs. They do good things too ... So a ketogenic diet is a good diet, but not because it's ketogenic. It's [good] because it's an indication that you're burning fat."

The Ideal Diet? Think Low-Carb, Moderate-Protein, High-Fat

I believe it's absolutely crucial, no matter what type of cancer you're trying to address, to incorporate a high-fat ketogenic diet, meaning a diet high in healthy fats like avocado, coconut oil, butter, olive oil and macadamia nuts, low in net carbs (total carbs minus fiber), and moderate amounts of high quality protein, ideally no more than about 1 gram per kilo of lean body mass.

Such a diet, along with Peak Fasting can be easily integrated into whatever cancer treatment plan you decide to follow. More importantly, this kind of diet may be key for *preventing* cancer and other chronic diseases in the first place. It also appears to be key for longevity, and will help optimize your weight as well, since eating this way will help you convert from burning sugar to burning fat as your primary fuel.

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