The roadmap for extending longevity has been discovered: Are you following it?

This month, in a landmark article in the journal *Cell*, an international consortium of anti-aging researchers published a prescription for grabbing the reins of longevity.

They boldly assert that *"The main features of the 'westernized lifestyle, including hypercaloric nutrition and sedentariness, can accelerate aging as they have detrimental metabolic consequences . . . the introduction of strategies that promote metabolic fitness may extend healthspan in humans."*

To give you the flavor of the sophistication of this ambitious analysis, here's a sentence plucked at random from the acronym-rich 20-page scientific article:

"MOTS-c promotes the biosynthesis of an endogenous AMP analog, 5-aminoamidazole-4-carboxamide ribonucleotide (AICAR), which stimulates AMPK and hence counteracts diabetes, obesity and aging."

Good luck if you don't possess an advanced degree in molecular biology! You can try skimming the article, but don't get lost in the weeds.

Instead, I'll help you decipher this research paper and boil it down into some practical recommendations that you can begin to implement right away on your own.

The authors of the study have parsed the aging process into 9 components (Trigger Warning—Medspeak ahead!):

- GENOMIC INSTABILITY
- TELOMERE ATTRITION
- EPIGENETIC ALTERATIONS
- LOSS OF PROTEOSTASIS
- DEREGULATED NUTRIENT SENSING
- MITOCHONDRIAL DYSFUNCTION
- CELLULAR SENESCENCE
- STEM CELL EXHAUSTION
- ALTERED INTERCELLULAR COMMUNICATION

Some of these terms may be familiar to you, others not. That's of no importance for this discussion, which is about proposed *solutions*.

The authors write: "Several metabolic interventions can increase longevity, including global CR [caloric restriction], the selective limitation of specific

nutrients like methionine, and the administration of agents—which we refer to as 'CR mimetics' (CRM)—that mimic the biochemical effects of CR but do not provoke a sizeable weight loss." Additionally, the use of certain drugs, like metformin and rapamycin, is discussed.

Let's consider these interventions one by one:

Caloric Restriction (CR): Many animal studies confirm that dramatically curtailing food intake, say, to 40% of usual calories, can significantly extend lifespan. But, as some wags have suggested, "You may or may not live longer, but it will certainly *seem* like longer!"

While people should avoid over-eating, I'm no fan of caloric restriction. It's simply not practical. But research demonstrates that many of the benefits of CR can be achieved through intermittent fasting or a fasting-mimicking diet (FMD). Restricting access to food for a few hours per day is sufficient to improve health and longevity in mice. Alternatively, attempts are underway to design satisfying but low-calorie dietary regimens that can be consumed periodically. When such a diet is administered to middle-aged mice (4 days twice a month), it resulted in lowered levels of inflammation, less incidence of cancer, rejuvenated immune function, improved skin aging and muscle deterioration, reduced bone mineral density loss, as well as prolongation of lifespan. I sometimes have patients do this with short bouts (3 to 10 days) of a detox program, Core Restore.

Additionally, it's thought that certain dietary amino acids may be targets for restriction, methionine and tryptophan among them. The paradox is that, while low-protein diets may be beneficial in some ways, new studies suggest that the elderly actually need more protein than was previously thought to fend off sarcopenia (progressive age-related muscle loss). A compromise solution might be to selectively administer branched chain amino acids to seniors.

Calorie Restriction Mimetics (CRM): There are several ways that calorie restriction slows aging and prolongs lifespan. Might there be a way to gain the benefits of caloric restriction without the pain of deprivation? That's where CRMs come in.

One of the ways that CR extends longevity is via the sirtuin pathway. Resveratrol is a classic activator of SIRT1. So is nicotinamide riboside (Tru Niagen). I consider nicotinamide riboside and resveratrol to be premier anti-aging supplements. A new supplement, Resveracel, combines the two.

But there are some surprises here. The authors of the *Cell* paper include D-glucosamine among potential anti-aging agents; it's readily available in the form of glucosamine sulfate and glucosamine hydrochloride used for prevention and treatment of joint problems.

Making the list as well is hydroxycitric acid. It's the main ingredient in Garcinia cambodgia, touted as a weight loss agent. Studies are mixed on whether Garcinia delivers on its anti-obesity claims, but it promotes the process of autophagy, a lifespan extending mechanism. Curcumin and EGCG from green tea share this property.

Spermadine makes the list, too. It's described as a "novel autophagy inducer and longevity elixir." Spermadine is not available as a supplement. It's plentiful in foods like soy and wheat germ; studies show it can be manufactured in the intestine when l-arginine is given with probiotics.

Medications: Metformin (Glucophage), a diabetes medication, shows promise as a life-prolonging agent. Interestingly, while its mode of action remains unclear,

speculation has arisen that its age-defying effects might derive from its impact on the microbiome, the bacterial population of the GI tract. The first-ever clinical trial to investigate metformin's effect on longevity—TAME (Targeting Aging with Metformin)—is currently being planned. Non-diabetics can safely take metformin.

A second potential anti-aging drug that's attracting a lot of attention is rapamycin (sirolimus, brand name Rapamune), a medication used to prevent organ transplant rejection and to coat heart stents. Rapamycin has been found to improve cognition, prevent neurodegeneration, reduce inflammation, and support heart function in aging mice. It's not known whether rapamycin confers these benefits in humans; because of safety concerns due to its immunosuppressant effects, clinical trials have not been vigorously pursued, and its off-label use for anti-aging has been discouraged. But its potential advantages may eventually pave the way for development of safer rapamycin analogs (rapalogs).

Exercise: Less glamorous, but potentially as efficacious, regular exercise has been shown in numerous studies to reduce illness burden, i.e. it extends "healthspan," if not lifespan. In fact, exercise is one sure way to impact all of the above nine components of aging. The metabolic effects of exercise resemble those of caloric restriction.

Avoidance of a Western Diet: The industrialized world's eating patterns promote aging in a multitude of ways. Dietary Advanced Glycation End-Products (AGEs) damage critical proteins; caloric excess promotes obesity and insulin resistance; non-stop eating and snacking preclude food-free intervals that allow metabolism to "reboot"; poor quality oils and refined carbohydrates drive inflammation ("inflamm-aging"); processed foods bereft of vital micronutrients impair cellular repair and regeneration; environmental toxins undermine mitochondrial function; low-fiber sugary foods, synthetic chemicals, artificial sweeteners and emulsifiers devastate the composition of the microbiome, with pervasive metabolic consequences.

Obesity itself has been found to shorten telomeres, the "caps" that prevent chromosomes from unraveling, resulting in premature organ senescence and death.

The authors of the *Cell* paper issue a final call-to-action:

"The current tendency to adopt a westernized lifestyle all over the world is creating new hazards that must be counteracted by public health campaigns . . . there is no doubt that a combination of regular exercise and appropriate diet can delay the onset and progression of the hallmarks of aging . . . personalized advice from a nutritionist may be recommendable in some situations."

A hearty "Amen!" from me.