

METABOLIC REPROGRAMMING

We all have that friend or family member that can eat virtually anything and not gain weight. We also know people who can get away with a lot more deviations from a healthy eating plan and stay lean or at least not put on unwanted weight as quickly as most other people do. We typically credit those features to the person having a "high metabolism". This implies that they simply burn more calories just walking around, sitting, sleeping and doing daily activities. This is actually not true and recent scientific discoveries on the microbiome have shed some light on this topic.

As it turns out, our gut bacteria and the type of species we have in our digestive tract, play a critical role in determining if we are going to be lean or obese. They play a paramount role in our risk for developing Type 2 diabetes and they seem to determining how many unhealthy snacks or meals we can get away with before we start seeing the pounds come on.

The latest research has shown that the type of bacteria you have in your gut controls the amount of calories you extract from the food you eat, the types of food you crave and also what that food is converted to in the digestion process. Foods consumed, especially carbohydrates, can be converted to compounds that lead to insulin resistance, fat storage, gas production and metabolites that cause inflammation. The flip side to that coin is that the right bacteria can convert the very same foods to very important compounds that increase insulin sensitivity, increase fat burn, prevent fat storage, reduce inflammation, reduce gas production and actually improve satiety. These effects are realized by turning on crucial genes in the digestive tract that control our metabolic fate. We are either programmed to gain weight easily and retain weight all too well or to be lean; the good news is that this programming can be changed by using the right probiotic bacteria and feeding those good bacteria with the right types of nutrients.

How Do We Reprogram our Metabolism?

From the microbial side, there are 2 important things to pay attention to. The first one is the ratio of *bacteroidetes* to *firmicutes* in your gut. Lean people all over the world and among many different cultures studied tend to have a slightly higher ratio of bacteroidetes vs. firmicutes. Having higher firmicutes is directly associated with obesity, metabolic syndrome, diabetes and inflammation. There are a few simple things one can do to help alter the ratio of these 2 phylum of bacteria and reach the desired balance that will help keep you lean and healthy.

- 1) *Bacteroidetes* love fiber. So consuming foods and snacks that are high in fiber and low or absent in sugar will support the growth of the good bacteroidetes bacteria.
- 2) Firmicutes loves sugar and simple carbohydrates. In fact, if you have an overgrowth of firmicutes you likely get sugar and carbohydrate cravings. These bacteria are so powerful that they can send neurotransmitters to your brain to make you crave sugar. They do this to get the host (you) to feed them the nutrients they want. Processed simple carbohydrates and sugars feed *firmicutes* and thus lead to weight gain and metabolic syndrome. You can have chocolate without causing an unfavorable shift in your gut bacteria, as long as that chocolate doesn't have sugar, processed carbohydrates (like starches) and artificial sweeteners.
- 3) Try to consume all your calories for the day in an 8-10 hour window. Our microbes in the gut go through a cycle like our circadian rhythm does and we remain in a fed state for much of the day, we prevent this beneficial microbial recycling from happening. Having a 12+ hour period of fasting in our day allows for beneficial bacterial growth and seems to support the growth of bacteroidetes.

The second important microbial technique is to get the right probiotics into your system, with your meals, to ensure that the healthy fibers and protein you are consuming are being converted to fat busting



compounds instead of gas. It's not enough to just eat a high fiber diet as many of the "bad" or unfavorable bacteria can also consume the fiber and turn that fiber into gas. Many have experienced this. You eat a bunch of "healthy" high fiber foods and all you get is gas and bloat. This is because unfavorable bacteria in the gut convert the fiber into hydrogen and methane gas instead of the critical fat busting compounds known as short-chain fatty acids (SCFAs). If you consume sugar free, high fiber foods and snacks with the right probiotic bacteria, the fiber will be converted to SCFAs instead of gas. This is a critical step in getting the metabolic benefits out of the healthy fiber. Without this crucial conversion, your body simply continues to absorb high amounts of calories, suppresses fat burning, increases fat storage, produces gas and increases insulin resistance.

MegaSporeBiotic is formulated with a unique combination of probiotic bacteria that have been shown to convert fibers in the diet to the much desired SCFAs. This formulation is built with unique endospore forming gut bacteria called *bacillus* species. In studies completed at Ghent University's ProDigest research firm, it was demonstrated that the addition of the strains in MegaSporeBiotic with fiber increased the production of SCFAs by 40% and decreased the production of gas by 50%. This is exactly the type of modulation you want to see when consuming fiber rich foods with a probiotic and no other probiotic strains have shown this type of metabolic response to fiber thus far.

Short-Chain Fatty Acids and Metabolic Reprogramming

Dozens of clinical trials and published studies have shown that SCFAs control the entire metabolic process. SCFAs regulate the balance between fatty acid synthesis (making of fat), fatty acid oxidation (burning of fat), and lipolysis (breaking down and absorption of fat from diet) in the body. Burning of fat is activated by SCFAs, while production of stored fat and lipolysis are inhibited. The net result is a reduction of the concentrations of free fatty acids in plasma and a decrease in body weight. The studies published on SCFAs show a direct effect in the increased SCFA formation in the gut by good bacteria and their stimulation of fat burning, increased fat loss and reduction in fat accumulation. This is the most direct evidence there is for changing someone's metabolism. These changes are conducted at the genome level where SCFAs can actually turn on fat burning genes and turn off fat storage genes. That is the true goal for permanent weight loss, the reprograming of gene expression controls how one's body responds to food. With this approach, we are changing the epigenetics (modification of gene expression) of metabolism. We are affecting gene expression to favor a lean body. This approach is a much more powerful and permanent approach than the standard weight loss formulation of calculating calories in vs. calories out.

Let's take a deeper look at how SCFAs actually make genetic expression changes in the body to effect metabolic health. The 3 main SCFAs are butyrate, propionate and acetate. These are ONLY produced by good bacteria, such as those found in MegaSporeBiotic, and are not extracted from foods or produced by the human body itself. Butyrate has been shown in published trials to be able to prevent diet-induced insulin resistance. This is achieved by promoting the expression of genes that increase energy expenditure, thus burning off more blood sugar and fat, as well as increasing mitochondria function – the powerhouse of each cell. Acetate for example has been shown to decrease the expression of several genes in the liver that produce fatty acids for storage. This inhibition may inhibit fat storage and thus acetate has the potential to improve obesity and obesity-linked type 2 diabetes. Butyrate and propionate have been shown in published studies to induce gut hormones that cause improved satiety and reduce food intake. Overeating is a fundamental issue in dysfunctional metabolic health. The sensitivity to satiety hormones tend to decrease over time with continued overeating, improving satiety is a key component to reprogramming the metabolism. Acetic acid has been shown to increase the expression of genes that support fat burning in the liver and also that suppress body fat accumulation. This type of gene reprogramming is done by upregulating genes for PPAR-alpha and fat burning related proteins by alpha2



AMPK mediation. This is an example of the specific gene modifications these amazing nutrients make in our metabolic system, thus reprograming our bodies to become fat burning machines.

The Story Gets Deeper if You Want More Specific Technical Information

SCFAs have been shown to increase the AMPK activity in liver and muscle tissue. AMPK is AMPactivated protein kinase, which is a critical, keystone enzyme found in the liver and muscle tissues that plays a major role in the control of metabolism. Activation of AMPK triggers peroxisome proliferatoractivated receptor gamma coactivator (PGC)-1 α expression, which is known to control the transcriptional activity of several transcription factors such as peroxisome proliferator-activated receptor (PPAR) α , PPAR δ , PPAR γ , liver X receptor (LXR), and farnesoid X receptor (FXR), all important in regulation of cholesterol, lipid, and glucose metabolism. As a consequence, fatty acid oxidation (fat burning) is enhanced in both tissues (liver and muscles) and new fatty acid synthesis (production of new fat) in the liver is decreased. In addition, SCFAs have been shown to increase protein expression of PGC-1 α and uncoupling protein (UCP)-1 in brown adipose tissue, thereby increasing thermogenesis (calories burn) and fatty acid oxidation (fat burn).

With a diet rich in healthy fibers, low or absent in sugars and high in protein, taken with these key strains of *bacillus* endospores, the body becomes reprogrammed (through modification of key genetic activation) to favor fat burn, reduces fat accumulation, increase energy metabolism, increase caloric burn, increases thermogenesis, increase satiety and increase insulin sensitivity.

This is where permanent and powerful weight loss and metabolic health comes from. Weight can be lost with simply taking in less calories than you expend and there are dozens upon dozens of weight loss products out there that help with weight reduction in the short term but this Metabolic Reprogramming is the only way to change the body to become a fat burning machine.

References:

- Gao Z, Yin J, Zhang J, et al. Butyrate Improves Insulin Sensitivity and Increases Energy Expenditure in Mice. *Diabetes*. 2009;58(7):1509-1517. doi:10.2337/db08-1637.
- Yamashita H, Fujisawa K, Ito E, Idei S, Kawaguchi N, Kimoto M, Hiemori M, Tsuji H. Improvement of obesity and glucose tolerance by acetate in Type 2 diabetic Otsuka Long-Evans Tokushima Fatty (OLETF) rats. Biosci Biotechnol Biochem. 2007 May;71(5):1236-43. Epub 2007 May 7.
- Lin HV, Frassetto A, Kowalik Jr EJ, et al. Butyrate and Propionate Protect against Diet-Induced Obesity and Regulate Gut Hormones via Free Fatty Acid Receptor 3-Independent Mechanisms. Brennan L, ed. *PLoS ONE*. 2012;7(4):e35240. doi:10.1371/journal.pone.0035240.
- Tomoo Kondo, Mikiya Kishi, Takashi Fushimi, and Takayuki Kaga. Acetic Acid Upregulates the Expression of Genes for Fatty Acid Oxidation Enzymes in Liver To Suppress Body Fat Accumulation. Journal of Agricultural and Food Chemistry 2009 57 (13), 5982-5986.
- Kondo T, Kishi M, Fushimi T, Ugajin S, Kaga T. Vinegar intake reduces body weight, body fat mass, and serum triglyceride levels in obese Japanese subjects. Biosci Biotechnol Biochem. 2009 Aug;73(8):1837-43. Epub 2009 Aug 7.
- Lin J, Handschin C, Spiegelman BM. Metabolic control through the PGC-1 family of transcription coactivators. Cell Metab. 2005 Jun;1(6):361-70.
- Zhanguo Gao, Jun Yin, Jin Zhang, Robert E. Ward, Roy J. Martin, Michael Lefevre, William T. Cefalu, and Jianping Ye. Butyrate Improves Insulin Sensitivity and Increases Energy Expenditure in Mice. DIABETES, VOL. 58, JULY 2009.