



CONVERGENCE

News, Links, and Insights
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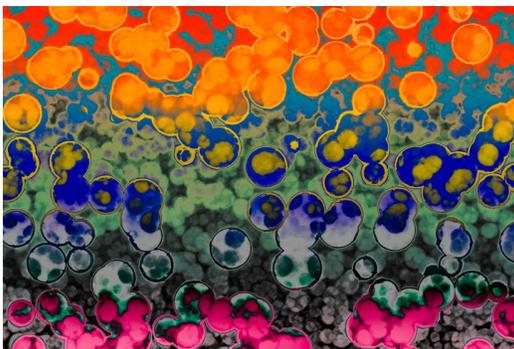


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Insulin, Prebiotics, and *Akkermansia* (Yours or Theirs)



Diet and environmental exposures grow the gut microbiome, which, in turn, interacts with these lifestyle inputs to cultivate function—or dysfunction. Increasing realization of how intestinal microbial communities reflect health (or lack of it) has medical and scientific communities interested in particular microbes that seem to signal a more adaptive approach to living. And while prebiotics exert a major influence on gut microbiome composition in most cases, habitual [physical activity](#) also

matters; in women, for example, the relative abundance of beneficial gut species including *Akkermansia muciniphila* and *Faecalibacterium prausnitzii* has been found to correlate with a [more active lifestyle](#).

Recent research on *Akkermansia muciniphila*, which has been associated with leanness and immunometabolic wellness, has focused on how to directly achieve its positive effects through supplementation in overweight populations at cardiovascular risk. In a small trial of insulin-resistant and overweight or obese study subjects, those receiving [heat-killed *A. muciniphila*](#) over a 3-month period showed significant improvements in insulin sensitivity and levels of insulin and total cholesterol as well as modest decreases in body weight and fat mass. *A. muciniphila* supplementation was also associated with improved levels of biomarkers for inflammation and liver function, yet was not found to significantly impact gut microbiome composition.

Prebiotics (including non-carbohydrate phytonutrients) are increasingly featured as metabolic benefactors that act, to an appreciable degree, through the gut microbiome.

One recent critical analysis has found that consumption of herbal products containing [prebiotic phytonutrients](#) may be a reasonably effective means of improving gut microbiome composition and, therefore, long-term immunometabolic function. It should be noted that while microbiome-directed treatments don't always result in quick weight loss, they may help set the stage for foundational metabolic adaptation that contributes not only to a better bodily energy economy but also to improved immune balance—admirable goals in pursuit of longer healthspans. Another comprehensive review of [plant-based prebiotics](#) confirms that targeted phytonutrition (e.g., dietary fiber, berberine, traditional medicinal herbs, quercetin, curcumin, phytonutrients from fruits, grains, herbs, seaweeds, and legumes, etc.) can increase the abundance of desirable gut residents such as *Akkermansia*, *Bifidobacteria*, and *Lactobacillus* genus members associated with better cardiometabolic, liver, and gut function and structural integrity.

In contrast, animal studies suggest that a [high-fat diet](#), [particular fat sources](#), and acute alcohol intake may interfere with proliferation of beneficial species like *Akkermansia*. In terms of dietary fats and oils, their constituent fatty acids may play unique roles in these differential effects, as levels of lauric, myristic, oleic, linoleic, and linolenic acids differ substantially between soy and coconut oils and individual fatty acids are known to have distinctive impacts upon microbial growth. While *Akkermansia* is not the 'be all and end all' of health, these and other studies seem to underscore how many lifestyle choices are manifested in wellness and function through this expressive intestinal 'spokes-microbe.'

GPCRs Help Broadcast the Message for Omega-3s and Other Fatty Acids

GPCRs (G protein-coupled receptors) are versatile intracellular communicators, accepting a wide variety of stimuli (ranging from ions and hormones to odorant molecules and photons of light) and capable of a broad range of qualitative and quantitative responses based upon the totality of input received. One of GPCRs' most important responsibilities is to transduce information from the types and amounts of dietary fats received into signaling that guides insulin function, the inflammatory response, and lipid metabolism. Some of these GPCRs are also known as [free fatty acid receptors \(FFARs\)](#), with FFAR1, FFAR2, FFAR3, and FFAR4 corresponding to GPR40, GPR43, GPR41, and GPR120, respectively. FFAR2 and FFAR3 are activated by short-chain fatty acids (SCFAs) produced by gut bacteria, while FFAR1 and FFAR4 respond to medium- and long-chain fats like lauric acid and alpha-linolenic acid. While these GPCRs can respond to individual stimuli, they exert greater control over target organs by acting with each other and networking with other modulators.

FFAR1/GPR40, FFAR4/GPR120, and another GPCR, GPR119, [act singly or collectively to influence insulin](#) secretion and sensitivity as well as the release of incretins (like glucagon-like peptide 1, which helps control blood glucose levels and appetite), particularly in conjunction with GPCR-specific signal modifiers that can significantly amplify their intercellular messaging. Because diet-induced or genetic impairments in their function can result in dysglycemia and obesity, these GPCRs are popular targets for drug development. The omega-3 fatty acids [DHA and EPA strongly activate FFAR4/GPR120](#) and alpha-linolenic acid (ALA) is also reported to act upon this GPCR; effects of omega-3 binding at GPR120 include [improved insulin sensitivity and overall metabolic homeostasis](#) as well as inhibiting processes related to intestinal inflammation. FFAR1/GPR40 also responds strongly to ALA and its metabolites, elevating the immune-balancing activity of PPAR γ (peroxisome proliferator-activated receptor γ) and [encouraging M2 polarization of macrophages](#) to emphasize cellular "housekeeping" roles over the more pro-inflammatory actions of M1-polarized macrophages.

FFAR2/GPR43, FFAR3/GPR41, and FFAR4/GPR120 are also expressed in circulating and resident immune cells, allowing them also to influence Th1/Th2 balance and inflammatory processes. FFAR4/GPR120 is a particularly important avenue for the effects of omega-3 fatty acids and their cultivation of a less-inflammatory Th2-leaning immune response, while FFAR3/GPR41 appears crucial in alleviating airway inflammation and FFAR2/GPR43 signaling is most closely related to integrity and function of the digestive tract. Another

GPCR called GPR84 is under study as a [mediator of the actions of some medium-chain fatty acids](#) and/or their metabolites, and while its primary targets are immune, fat, microglial, and T cells, its actions appear to be more pro-inflammatory than those of other GPCRs.

Understanding the interactions among FFARs, their ligands, and their targets allows us to devise more personalized dietary and health strategies. Listen in as omega-3 researcher Bill Harris, PhD and Dr. Bland recount the challenges of [educating an initially skeptical medical public about the benefits of omega-3 fats](#), the development of the Omega-3 Index for clinically assessing individuals' omega-3 status, and their discussion of how these fats use GPCRs to modify the immune response.

The New Wave of Good Immunometabolic Vibes



In the not-so-distant past (around the 1950s), vibrating machines with belts for slinging around the waist and other areas in order to jiggle away the flab were the rage, and though many gave them a whirl, promised results went unproven and these devices eventually flopped. Whole-body vibration has since been investigated as a means of [maintaining mineral density](#) of weight-bearing bones and strength of postural muscles among those [confined to bed rest](#) or otherwise at risk for osteoporosis (though [results may depend](#) on how this therapy is applied) and it has been hypothesized that bouts of vibration provide a kind of anabolic stimulus to osteoblasts.

A 2007 clinical trial of type 2 diabetics found that performing [exercise on a vibrating platform](#) was as effective as strength training in reducing peak and area-under-curve glucose levels, and HBA1c levels tended to fall with vibration exercise while increasing in those performing strength or flexibility training. In 2015, a laboratory study found that regular application of whole-body vibration improved [glycemic control](#) (HBA1c levels) as well as measures of inflammation in diabetic animals, and also appeared to ameliorate diabetes-related polydipsia (heightened water intake). More recently, a 2019 animal study found that whole-body vibration of diabetic animals significantly increased interleukin-10 levels and counts of M2-polarized digestive tract macrophages (reflecting [less pro-inflammatory expression](#) and more equilibrated immune responsiveness), yet reduced overall fecal microbial diversity while increasing the abundance of *Alistipes* (a Bacteroidetes phylum member associated with greater plant food intake) and lactobacilli species.

Perhaps it is more reassuring than surprising that the gut environment and bone, endocrine, muscular, immune, and energy metabolism network with one another and that whole-body vibration can stand in as a partial mimetic of exercise. While exogenously-provided vibration is likely a limited proxy for the effects of walking, running, dancing, physical labor, and other forms of muscle-contracting and gravity-defying exertions, vibration platform machines may actually find a home in early stages of management of immunometabolic conditions—perhaps while more profound lifestyle changes are in the process of being implemented.

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Dr. Jeffrey Bland
and
Doug Greene
3-PART SERIES



THE BIG BOLD HEALTH PODCAST

Episode 9

Organic Reach:
How Natural Products Became
a Billion-Dollar Industry - Part 1

Big Bold Health is a new project that was announced earlier this year and the Big Bold Health Podcast is the first of many exciting activities. The podcast is published every other week on YouTube as well as on all major podcasting platforms.

What topics are covered?
ALL THINGS HEALTH!

If you're not already watching or listening, it may be time to tune in because quite a buzz is building after last week's launch of an ongoing 3-part series:

Organic Reach: How Natural Products Became a Billion-Dollar Industry

Intrigued? While co-host James Maskell was off on world travels, Dr. Jeff Bland sat down for a discussion with his longtime colleague and friend, Doug Greene, founder of New Hope Natural Media, organizer of the Natural Products Expo (now one of THE LARGEST trade shows in the world), and pioneer of a movement that has been supporting health creation for more than four decades. Take a walk through time with Jeff and Doug—along the way you'll catch their entrepreneurial spirit, absorb their business wisdom, and be inspired by their commitment to staying open to every opportunity that life has to offer.

Click [HERE](#) to watch Part 1 of the Jeff Bland/Doug Greene series.

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