

Prebiotin Structure/Function Claim: Supports Health & Immunity

Doc No.: VR002

Revision: 1

AUTHOR: Dr. Frank Jackson, MD

1. PURPOSE/SCOPE

The purpose of this document is to explain how Prebiotin supports immunity and the clinical literature published in support of this structure/function claim.

This includes studies performed and an evaluation of the relevant scientific literature related to how prebiotin acts to support a healthy gut microbiota and therefore supports health and immunity.

2. GENERAL DETAILS

2.1 Dietary Supplement Name

Proprietary Product Name:
Prebiotin

2.2 Manufacturer

Jackson GI Medical
1714 N. 2nd Street
Harrisburg, PA 17102
USA

2.3 Dietary Supplement Description

Oligofructose Enriched Inulin

3. BACKGROUND

Prebiotin, a Prebiotic Fiber Supplement offers a full-spectrum prebiotic (Oligofructose-Enriched-Inulin, or OEI). OEI is obtained by combining chicory long-chain inulin and oligofructose. Inulin and oligofructose belong to a class of carbohydrates known as fructans. Because of the beta-configuration of the anomeric C2 in their fructose monomers, inulin -type fructans resist hydrolysis by intestinal digestive enzymes, they classify as 'non-digestible' carbohydrates, and they are dietary fibers.

The main sources of inulin and oligofructose that are used in the food industry are chicory and Jerusalem artichoke. Inulin and oligofructose are considered as functional food ingredients since they affect the physiological and biochemical processes in rats and human beings, resulting in better health.

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Unlike ordinary prebiotics such as Inulin or FOS, OEI ensures that Prebiotin nourishes beneficial bacteria throughout the colon. OEI is also the most-researched prebiotic, used in many university and clinical studies.

A prebiotic has been defined as *'a non-digestible food ingredient that beneficially affects the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon, and thus improves host health*. Inulin and oligofructose are the best-studied prebiotics so far. They are selectively fermented by the microflora in the human colon leading to a bacterial composition that is dominated by bifidobacteria, a perceived health-promoting genus.

The National Cancer Institute defines OEI as:

A substance that is used to improve the health of the digestive system and bones and is being studied in the prevention of colon cancer. Oligofructose-enriched inulin is made by combining two substances that occur naturally in many plants, including chicory root, wheat, bananas, onion, and garlic. Oligofructose-enriched inulin helps healthy bacteria grow in the intestines and helps the body absorb calcium and magnesium. OEI is also called Raftilose Synergy.

Source: (<http://www.cancer.gov/dictionary>)

4. PUBLISHED LITERATURE

4.1 Literature Search

A literature search was conducted using PubMed and Medline to identify articles that contained studies on prebiotin (oligofructose enriched inulin) related to the importance of maintaining healthy or good colon bacteria in support of immunity.

The following articles support the claim that a healthy microbiota is needed to develop and maintain a strong immune system within the human and animal colon. Conversely when dysbiosis of the gut occurs as frequently happens with the Western lifestyle and diet and the overuse of antibiotics, then dysbiosis of the gut frequently occurs and with it certain disorders of the body. Prebiotin has been shown to nourish beneficial bacteria throughout the colon. Prebiotics have already been defined medically as 'The selective stimulation of growth and/or activity(ies) of one or a limited number of microbial genus(era)/species in the gut microbiota that confer(s) health benefits to the host.

The articles and/or studies listed in Table 1 are summarized individually.

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Table 1 Clinical Literature

	Author	Source/Published	Title of Publication	Year of Publication
1	Petersen C, Round JL.	Cell Microbiology 2014 May 5. doi: 10.1111/cmi.12308.	Defining dysbiosis and its influence on host immunity and disease.	2014
2	Nikoopour E, Singh B	Inflamm Allergy Drug Targets. 2014 Mar 30.	Reciprocity in Microbiome and Immune System interactions and its implications in Disease and Health.	2014
3	Neish AS.	Ann Am Thorac Soc. 2014 Jan;11 Suppl 1:S28-32. doi: 10.1513/AnnalsATS.2013 06-161MG.	Mucosal immunity and the microbiome.	2014
4	Roberfroid M ¹ , Gibson GR, Hoyles L, McCartney AL, Rastall R, Rowland I, Wolvers D, Watzl B, Szajewska H, Stahl B, Guarner F, Respondek F, Whelan K, Coxam V, Davicco MJ, Léotoing L, Wittrant Y, Delzenne NM, Cani PD, Neyrinck AM, Meheust A.	British Journal of Nutrition 2010 Aug;104 Suppl 2:S1-63. doi: 10.1017/S000711451000 3363.	Prebiotic effects: metabolic and health benefits.	2010
5	Gibson GR, Roberfroid MB.	Journal of Nutrition 1995 Jun;125(6):1401-12.	Dietary modulation of the human colonic microbiota: introducing the concept of prebiotics.	2005

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Article #1

Defining dysbiosis and its influence on host immunity and disease.

Petersen C, Round JL.

Author information

Department of Pathology, Division of Microbiology and Immunology, University of Utah School of Medicine, Salt Lake City, UT 84112.

ABSTRACT

Mammalian immune system development depends on instruction from resident commensal micro-organisms. Diseases associated with abnormal immune responses toward environmental and self antigens have been rapidly increasing over the last fifty years. These diseases include inflammatory bowel disease (IBD), multiple sclerosis (MS), type I diabetes (T1D), allergies and asthma. The observation that people with immune mediated diseases house a different microbial community when compared to healthy individuals suggests that pathogenesis arises from improper training of the immune system by the microbiota. However, with hundreds of different microorganisms on our bodies it is hard to know which of these contribute to health and more importantly how? Microbiologists studying pathogenic organisms have long adhered to Koch's postulates to directly relate a certain disease to a specific microbe, raising the question of whether this might be true of commensal-host relationships as well. Emerging evidence supports that rather than one or two dominant organisms inducing host health, that the composition of the entire community of microbial residents influences a balanced immune response. Thus, perturbations to the structure of complex commensal communities (referred to as dysbiosis) can lead to deficient education of the host immune system and subsequent development of immune mediated diseases. Here we will overview the literature that describes the causes of dysbiosis and the mechanisms evolved by the host to prevent these changes to community structure. Building off these studies, we will categorize the different types of dysbiosis and define how collections of microorganisms can influence the host response. This research has broad implications for future therapies that go beyond the introduction of a single organism to induce health. We propose that identifying mechanisms to re-establish a healthy complex microbiota after dysbiosis has occurred, a process we will refer to as rebiosis, will be fundamental to treating complex immune diseases.

<http://www.ncbi.nlm.nih.gov/pubmed/24798552>

Article #2

Reciprocity in Microbiome and Immune System interactions and its implications in Disease and Health.

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Nikoopour E, Singh B

Author information

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ABSTRACT

Adaptation of the whole microbial normal flora residing in a host to its natural habitat over an evolutionary period has resulted in peaceful coexistence with mutual benefits for both microbiota and host in steady state. This symbiotic relationship between host and microbiota has a significant impact on shaping the immune response in the host to achieve an immune tolerance to microbiota but retaining the ability to respond to invading pathogens. Perturbation of this balance by manipulation of microbial communities in the host can lead to immune dysregulation and susceptibility to diseases. By studying the host in the absence of microbiota or with alteration of microbiota the complexity of microbial impact on the immune system can be resolved. Conversely, the study of microbiota in the absence of immune system factors can show how the immune system contributes to preservation of the host-microbiota balance. The absence of molecules involved in innate or adaptive immunity in knockout models can perturb the balance between host and microbiota further adding to more immune dysregulation. A better understanding of microbiome-immune system interaction provides a new opportunity to identify biomarkers and drug targets. This will allow the development of new therapeutic agents for modulating the immune system to improve health with little or no toxicity. The study of interplay between host and microbiota has a promising role in the design of therapeutic interventions for immunopathological diseases arising from imbalanced host and microbiota interactions.

<http://www.ncbi.nlm.nih.gov/pubmed/24678760>

Article #3

Mucosal immunity and the microbiome.

Neish AS.

Author information

Department of Pathology, Emory University School of Medicine, Atlanta, Georgia.

ABSTRACT

By definition, the mucosal immune system is responsible for interfacing with the outside world, specifically responding to external threats, of which pathogenic microbes represent a primary challenge. However, it has become apparent that the human host possesses a numerically vast and taxonomically diverse resident microbiota, predominantly in the gut, and also in the airway, genitourinary tract, and skin. The microbiota is generally considered symbiotic, and has been implicated in the regulation

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of cellular growth, restitution after injury, maintenance of barrier function, and importantly, in the induction, development, and modulation of immune responses. The mucosal immune system uses diverse mechanisms that protect the host from overt pathogens, but necessarily has coevolved to monitor, nurture, and exploit the normal microbiota. As a whole, mucosal immunity encompasses adaptive immune regulation that can involve systemic processes, local tissue-based innate and inflammatory events, intrinsic defenses, and highly conserved cell autonomous cytoprotective responses. Interestingly, specific taxa within the normal microbiota have been implicated in roles shaping specific adaptive, innate, and cell autonomous responses. Taken together, the normal microbiota exerts profound effects on the mucosal immune system, and likely plays key roles in human physiology and disease.

<http://www.ncbi.nlm.nih.gov/pubmed/24437401>

Article #4

Prebiotic effects: metabolic and health benefits.

Roberfroid M¹, Gibson GR, Hoyles L, McCartney AL, Rastall R, Rowland I, Wolvers D, Watzl B, Szajewska H, Stahl B, Guarner F, Respondek F, Whelan K, Coxam V, Davicco MJ, Léotoing L, Wittrant Y, Delzenne NM, Cani PD, Neyrinck AM, Meheust A.

Author information

Université Catholique de Louvain, Brussels, Belgium.

ABSTRACT

The different compartments of the gastrointestinal tract are inhabited by populations of micro-organisms. By far the most important predominant populations are in the colon where a true symbiosis with the host exists that is a key for well-being and health. For such a microbiota, 'normobiosis' characterises a composition of the gut 'ecosystem' in which micro-organisms with potential health benefits predominate in number over potentially harmful ones, in contrast to 'dysbiosis', in which one or a few potentially harmful micro-organisms are dominant, thus creating a disease-prone situation. The present document has been written by a group of both academic and industry experts (in the ILSI Europe Prebiotic Expert Group and Prebiotic Task Force, respectively). It does not aim to propose a new definition of a prebiotic nor to identify which food products are classified as prebiotic but rather to validate and expand the original idea of the prebiotic concept (that can be translated in 'prebiotic effects'), defined as: 'The selective stimulation of growth and/or activity(ies) of one or a limited number of microbial genus(era)/species in the gut microbiota that confer(s) health benefits to the host.' Thanks to the methodological and fundamental research of microbiologists, immense progress has very recently been made in our understanding of the gut microbiota. A large number of human intervention studies have been performed that have demonstrated that dietary consumption of certain food products can result in statistically significant changes in the composition of the gut microbiota in line with the prebiotic concept. Thus the prebiotic effect is now a well-established scientific fact. The more data

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are accumulating, the more it will be recognised that such changes in the microbiota's composition, especially increase in bifidobacteria, can be regarded as a marker of intestinal health. The review is divided in chapters that cover the major areas of nutrition research where a prebiotic effect has tentatively been investigated for potential health benefits. The prebiotic effect has been shown to associate with modulation of biomarkers and activity(ies) of the immune system. Confirming the studies in adults, it has been demonstrated that, in infant nutrition, the prebiotic effect includes a significant change of gut microbiota composition, especially an increase of faecal concentrations of bifidobacteria. This concomitantly improves stool quality (pH, SCFA, frequency and consistency), reduces the risk of gastroenteritis and infections, improves general well-being and reduces the incidence of allergic symptoms such as atopic eczema. Changes in the gut microbiota composition are classically considered as one of the many factors involved in the pathogenesis of either inflammatory bowel disease or irritable bowel syndrome. The use of particular food products with a prebiotic effect has thus been tested in clinical trials with the objective to improve the clinical activity and well-being of patients with such disorders. Promising beneficial effects have been demonstrated in some preliminary studies, including changes in gut microbiota composition (especially increase in bifidobacteria concentration). Often associated with toxic load and/or miscellaneous risk factors, colon cancer is another pathology for which a possible role of gut microbiota composition has been hypothesised. Numerous experimental studies have reported reduction in incidence of tumours and cancers after feeding specific food products with a prebiotic effect. Some of these studies (including one human trial) have also reported that, in such conditions, gut microbiota composition was modified (especially due to increased concentration of bifidobacteria). Dietary intake of particular food products with a prebiotic effect has been shown, especially in adolescents, but also tentatively in postmenopausal women, to increase Ca absorption as well as bone Ca accretion and bone mineral density. Recent data, both from experimental models and from human studies, support the beneficial effects of particular food products with prebiotic properties on energy homeostasis, satiety regulation and body weight gain. Together, with data in obese animals and patients, these studies support the hypothesis that gut microbiota composition (especially the number of bifidobacteria) may contribute to modulate metabolic processes associated with syndrome X, especially obesity and diabetes type 2. It is plausible, even though not exclusive, that these effects are linked to the microbiota-induced changes and it is feasible to conclude that their mechanisms fit into the prebiotic effect. However, the role of such changes in these health benefits remains to be definitively proven. As a result of the research activity that followed the publication of the prebiotic concept 15 years ago, it has become clear that products that cause a selective modification in the gut microbiota's composition and/or activity(ies) and thus strengthens normobiosis could either induce beneficial physiological effects in the colon and also in extra-intestinal compartments or contribute towards reducing the risk of dysbiosis and associated intestinal and systemic pathologies.

<http://www.ncbi.nlm.nih.gov/pubmed/20920376>

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Article #5

Dietary modulation of the human colonic microbiota: introducing the concept of prebiotics.

Gibson GR, Roberfroid MB.

Author information

MRC Dunn Clinical Nutrition Centre, Cambridge, United Kingdom.

ABSTRACT

Because the human gut microbiota can play a major role in host health, there is currently some interest in the manipulation of the composition of the gut flora towards a potentially more remedial community. Attempts have been made to increase bacterial groups such as Bifidobacterium and Lactobacillus that are perceived as exerting health-promoting properties. Probiotics, defined as microbial food supplements that beneficially affect the host by improving its intestinal microbial balance, have been used to change the composition of colonic microbiota. However, such changes may be transient, and the implantation of exogenous bacteria therefore becomes limited. In contrast, prebiotics are nondigestible food ingredients that beneficially affect the host by selectively stimulating the growth and/or activity of one or a limited number of bacterial species already resident in the colon, and thus attempt to improve host health. Intake of prebiotics can significantly modulate the colonic microbiota by increasing the number of specific bacteria and thus changing the composition of the microbiota. Nondigestible oligosaccharides in general, and fructooligosaccharides in particular, are prebiotics. They have been shown to stimulate the growth of endogenous bifidobacteria, which, after a short feeding period, become predominant in human feces. Moreover, these prebiotics modulate lipid metabolism, most likely via fermentation products. By combining the rationale of pro- and prebiotics, the concept of synbiotics is proposed to characterize some colonic foods with interesting nutritional properties that make these compounds candidates for classification as health-enhancing functional food ingredients.

<http://www.ncbi.nlm.nih.gov/pubmed/7782892>

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5. DATA SUMMARY – CLINICAL LITERATURE

Based on the clinical literature and research presented, prebiotin, oligofructose-enriched inulin has been proven to support health and immunity by maintaining healthy or good colon bacteria. Based on studies and literature, normal microbiota exert profound effects on the mucosal immune system and therefore maintaining healthy or good colon bacteria is key to supporting health and immunity.

6. ATTACHMENTS

6.1 Clinical Literature referenced is maintained in the Structure/Function Technical File for Health & Immunity Support.

APPROVALS:

CEO: _____ Date _____

COO: _____ Date _____

QUALITY/REGULATORY: _____ Date _____