This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author(s) and source are credited.

ISSN: 1745-7580

Immunome Research

The International Open Access Immunome Research

Editor-in-Chief

Yongqun “Oliver” He
University of Michigan Medical School, USA

András Falus
Semmelweis University, Hungary

Executive Editors

Alessandro Sette
La Jolla Institute for Allergy and Immunology, USA

Marie-Paule Lefranc
University of Montpellier, France

Darren Flower
Aston University, UK

Available online at: OMICS Publishing Group (www.omicsonline.org)

This article was originally published in a journal by OMICS Publishing Group, and the attached copy is provided by OMICS Publishing Group for the author's benefit and for the benefit of the author's institution, for commercial/research/educational use including without limitation use in instruction at your institution, sending it to specific colleagues that you know, and providing a copy to your institution's administrator.

All other uses, reproduction and distribution, including without limitation commercial reprints, selling or licensing copies or access, or posting on open internet sites, your personal or institution's website or repository, are requested to cite properly.

Digital Object Identifier: http://dx.doi.org/10.4172/1745-7580.1000e002
Potlatch in the Gut - Immunomodulatory Molecules of Potential Therapeutic Benefit from the Commensal Microbiota

Suryasarathi Dasgupta*

Division of Immunology, Department of Microbiology and Immunobiology, Harvard Medical School, Boston, MA, USA

Mutualism between members of the gut microbiota and their mammalian host offers several advantages to both. As revealed by recent research, the co-evolution of specific microbial species with their particular mammalian host directs the maturation of the host’s immune system in a way that enables it to respond to infectious or inflammatory challenges appropriately. In addition, changes in microbial species with the host’s age, sex, diet, and other variable conditions allow beneficial adjustments. The effect of the gut microbiota on the immune system is not limited to gut tissue but also extends to peripheral sites. Thus the gut microenvironment can be viewed as a specialized immunologic sensor responsible for maintaining the general health of the host.

Very little is known, however, about the ability of specific molecules from the commensal microbiota to effect changes in the host’s immune system. Molecules from the human gut commensal Bacteroides fragilis have been studied more extensively than molecules from other commensal microorganisms and can be described as “torch bearers” in the field. Two broad types of B. fragilis molecules have been determined to be immunomodulatory: polysaccharides and sphingolipids. Polysaccharide A (PSA), a zwitterionic capsular polysaccharide, is the best studied with regard to its presentation by the major histocompatibility class II (MHCII) pathway, its stimulation via the Toll-like receptor 2 (TLR2) pathway, its role in the maturation of the host’s immune system, and its immunoprotective role in murine models of colitis, multiple sclerosis, and surgical fibrosis. Our recent research, the co-evolution of specific microbial species with their mammalian host offers several advantages to both. As revealed by recent research, the co-evolution of specific microbial species with their particular mammalian host directs the maturation of the host’s immune system in a way that enables it to respond to infectious or inflammatory challenges appropriately. In addition, changes in microbial species with the host’s age, sex, diet, and other variable conditions allow beneficial adjustments. The effect of the gut microbiota on the immune system is not limited to gut tissue but also extends to peripheral sites. Thus the gut microenvironment can be viewed as a specialized immunologic sensor responsible for maintaining the general health of the host.

Very little is known, however, about the ability of specific molecules from the commensal microbiota to effect changes in the host’s immune system. Molecules from the human gut commensal Bacteroides fragilis have been studied more extensively than molecules from other commensal microorganisms and can be described as “torch bearers” in the field. Two broad types of B. fragilis molecules have been determined to be immunomodulatory: polysaccharides and sphingolipids. Polysaccharide A (PSA), a zwitterionic capsular polysaccharide, is the best studied with regard to its presentation by the major histocompatibility class II (MHCII) pathway, its stimulation via the Toll-like receptor 2 (TLR2) pathway, its role in the maturation of the host’s immune system, and its immunoprotective role in murine models of colitis, multiple sclerosis, and surgical fibrosis. Our recent research, the co-evolution of specific microbial species with their mammalian host offers several advantages to both. As revealed by recent research, the co-evolution of specific microbial species with their particular mammalian host directs the maturation of the host’s immune system in a way that enables it to respond to infectious or inflammatory challenges appropriately. In addition, changes in microbial species with the host’s age, sex, diet, and other variable conditions allow beneficial adjustments. The effect of the gut microbiota on the immune system is not limited to gut tissue but also extends to peripheral sites. Thus the gut microenvironment can be viewed as a specialized immunologic sensor responsible for maintaining the general health of the host.

Very little is known, however, about the ability of specific molecules from the commensal microbiota to effect changes in the host’s immune system. Molecules from the human gut commensal Bacteroides fragilis have been studied more extensively than molecules from other commensal microorganisms and can be described as “torch bearers” in the field. Two broad types of B. fragilis molecules have been determined to be immunomodulatory: polysaccharides and sphingolipids. Polysaccharide A (PSA), a zwitterionic capsular polysaccharide, is the best studied with regard to its presentation by the major histocompatibility class II (MHCII) pathway, its stimulation via the Toll-like receptor 2 (TLR2) pathway, its role in the maturation of the host’s immune system, and its immunoprotective role in murine models of colitis, multiple sclerosis, and surgical fibrosis. Our recent research, the co-evolution of specific microbial species with their mammalian host offers several advantages to both. As revealed by recent research, the co-evolution of specific microbial species with their particular mammalian host directs the maturation of the host’s immune system in a way that enables it to respond to infectious or inflammatory challenges appropriately. In addition, changes in microbial species with the host’s age, sex, diet, and other variable conditions allow beneficial adjustments. The effect of the gut microbiota on the immune system is not limited to gut tissue but also extends to peripheral sites. Thus the gut microenvironment can be viewed as a specialized immunologic sensor responsible for maintaining the general health of the host.

Very little is known, however, about the ability of specific molecules from the commensal microbiota to effect changes in the host’s immune system. Molecules from the human gut commensal Bacteroides fragilis have been studied more extensively than molecules from other commensal microorganisms and can be described as “torch bearers” in the field. Two broad types of B. fragilis molecules have been determined to be immunomodulatory: polysaccharides and sphingolipids. Polysaccharide A (PSA), a zwitterionic capsular polysaccharide, is the best studied with regard to its presentation by the major histocompatibility class II (MHCII) pathway, its stimulation via the Toll-like receptor 2 (TLR2) pathway, its role in the maturation of the host’s immune system, and its immunoprotective role in murine models of colitis, multiple sclerosis, and surgical fibrosis. Our recent research, the co-evolution of specific microbial species with their mammalian host offers several advantages to both. As revealed by recent research, the co-evolution of specific microbial species with their particular mammalian host directs the maturation of the host’s immune system in a way that enables it to respond to infectious or inflammatory challenges appropriately. In addition, changes in microbial species with the host’s age, sex, diet, and other variable conditions allow beneficial adjustments. The effect of the gut microbiota on the immune system is not limited to gut tissue but also extends to peripheral sites. Thus the gut microenvironment can be viewed as a specialized immunologic sensor responsible for maintaining the general health of the host.

Very little is known, however, about the ability of specific molecules from the commensal microbiota to effect changes in the host’s immune system. Molecules from the human gut commensal Bacteroides fragilis have been studied more extensively than molecules from other commensal microorganisms and can be described as “torch bearers” in the field. Two broad types of B. fragilis molecules have been determined to be immunomodulatory: polysaccharides and sphingolipids. Polysaccharide A (PSA), a zwitterionic capsular polysaccharide, is the best studied with regard to its presentation by the major histocompatibility class II (MHCII) pathway, its stimulation via the Toll-like receptor 2 (TLR2) pathway, its role in the maturation of the host’s immune system, and its immunoprotective role in murine models of colitis, multiple sclerosis, and surgical fibrosis. Our recent research, the co-evolution of specific microbial species with their mammalian host offers several advantages to both. As revealed by recent research, the co-evolution of specific microbial species with their particular mammalian host directs the maturation of the host’s immune system in a way that enables it to respond to infectious or inflammatory challenges appropriately. In addition, changes in microbial species with the host’s age, sex, diet, and other variable conditions allow beneficial adjustments. The effect of the gut microbiota on the immune system is not limited to gut tissue but also extends to peripheral sites. Thus the gut microenvironment can be viewed as a specialized immunologic sensor responsible for maintaining the general health of the host.

Sphingolipid molecule(s) from B. fragilis have an immunomodulatory mechanism distinct from that of PSA. They are essentially inhibitory molecules, suppressing the expansion of pathogenic invariant natural killer T (iNKT) cells in the colon at the neonatal stage of development. B. fragilis sphingolipids significantly protect mice challenged with oxazolone, which otherwise induces colitis (mimicking ulcerative colitis in humans) through the action of iNKT cells and antigen presentation by the CD1d mode. Thus B. fragilis employs a two-pronged strategy to maintain homeostasis in the intestine with two distinct types of molecules.

In general, other major classes of molecules, such as nucleic acids and proteins, are better recognized as immunomodulators. Whether commensal molecules use these well-known immunomodulators will be determined definitively in the future. Research on the microbiome provides a holistic approach to elucidation of the gut ecosystem. However, the clues obtained from microbiome research must be verified experimentally in the design of novel therapeutics. Also needed is an understanding of the metabolites (e.g., butyrate) that are produced by interaction of commensal microbes with the mammalian host and that then modulate the host’s immune system. An enormous repertoire of immunomodulatory molecules provided generously by our guests, the commensal microbes, awaits therapeutic exploitation.