Having trouble viewing this email? Click here

To download or read a pdf version of this newsletter, click here. **July 2015**

BioMarketing Insight Newsletter

Creating Markets and Marketing Strategies

Dear Regina,

Welcome to BioMarketing Insight's monthly newsletter.

Last month I covered the highlights of the Medical Informatics World Conference held May 4-5, 2015 at the Renaissance Hotel in Boston. If you missed last month's article, click here to read it. This month's newsletter will cover part one of a two part series on Your Microbiome: What Is It and Why Is It Getting So Much Attention?

Read on to learn more about this topic and other current news. On the right are quick links to the topics covered in this month's newsletter. The next newsletter will be published on August 15th.

We encourage you to share this newsletter with your colleagues by using the social media icons at the top left, or by simply forwarding the newsletter via email.

Please email me, Regina Au, if you have any questions, comments, or suggestions.

Sincerely,
Regina Au
Principal, Strategic Marketing Consultant
BioMarketing Insight

In This Issue

Join Our Mailing List!

Join Our Mailing List - For Mobile

BioMarketing Insight Services

Product Development

Market Development

Marketing Strategies

Previous Newsletters

Developing a Product? Commercializing a Product?

If you are developing a product and have not conducted the business due diligence to determine commercial viability or success, contact me for an appointment. For successful commercial adoption of your product, contact me for an appointment.

Top

Guest Lecturer at MIT

Earlier this month, I was a guest lecturer at the Martin Trust Center for Entrepreneurship at MIT. I spoke on "How to Develop a Successful Product: Where Do You Start?" from a commercial perspective to 14 MIT entrepreneurial companies.

Top

From Genetic Engineering to Genome Engineering: What Impact Has it Made on Science and Society?

I am pleased to announce that my article "From Genetic Engineering to Genome Engineering: What Impact Has it Made on Science and Society?" was published in May 2015 in the Advanced Biology, Biotechnology and Genetics Journal. To read an electronic version, click here.

Top

Your Microbiome: What Is It and Why Is It Getting So Much Attention?

"Our Self-Portrait: the Human Microbiome"

Image courtesy of Broad Institute and Steven H. Lee (graphiko.com).

In 2001, Nobel Laureate, Joshua Lederberg, an American molecular biologist, coined the term microbiome as the ecological community of commensal, symbiotic, and pathogenic microorganisms that inhabit and share the space in our body. He argued that microorganisms inhabiting the human body should be included as part of the human genome, because of their influence on the human physiology of our well being and diseases.

The number of microbes in our body out number human cells by 10 to 1. Our body contains about 10 trillion human cells and we carry about 100 trillion bacterial cells. However, the entire microbiome only weighs about 200 grams (7.1 oz), with some estimates as high as 3 pounds (approximately 48 oz). The human microbiome (formerly known as human microbiota) resides on the surface and in deep layers of the skin, nasal and oral cavity, urogenital and gastrointestinal (GI) tract. The GI tract is the most densely colonized area with the colon alone harboring over 1010-1012 colony-forming units per gram of feces, or 70% of all microbes in the human body.

In 2007, the National Institute of Health funded the Human Microbiome Project (HMP) that engaged a consortium of researchers to map or sequence the normal microbial make up of health humans and in 2012 published their findings:

1) HMP researchers discovered more than 10,000 microbial species that occupy the human ecosystem accounting for approximately 81 to 99 percent of all microorganismal genera in healthy adults. Now that scientists know the normal microbial variation for a healthy Western population, they will begin studying how changes in the microbiome correlate with physiology and disease, said James M. Anderson, M.D., Ph.D., director of the NIH Division of Program Coordination, Planning and Strategic Initiatives.

2) HMP researchers found that more genes from our microbes are responsible for human survival than humans genes. The human genome carries about 22,000 protein-coding genes, while the human microbiome contributes about 8 million unique protein-coding genes, or 360 times more bacterial genes than human genes.

3) HMP researchers also found that genes from bacteria in the GI tract allow humans to digest foods and absorb nutrients, since humans don't have all the enzymes necessary to digest our foods, thus making these bacteria critical for human survival. "Microbes in the gut break down many of the proteins, lipids and carbohydrates in our diet into nutrients that we can then absorb. Moreover, the microbes produce beneficial compounds, like vitamins and anti-inflammatories that our genome cannot produce," said Lita Proctor, Ph.D., NHGRI's HMP program manager.

4) HMP Researchers discovered that the microbial metabolic activities matters more than the microbial species that perform these activities. In a healthy gut, a population of bacteria is needed to help digest fats, but the bacterial species performing this job may not always be the same. The distribution of microbial species may change over time, as humans go from a healthy state to a disease state and then back to a healthy state--- but the function of the microbes will always remain the same.

Other have found that no two individuals share the same makeup of microbes and their genes, not even identical twins, an acknowledgement of the complexity and interconnectedness of this inner ecosystem of microbiome discussed by Joshua Lederberg.

The vast majority of the human microbiome is comprised of human-associated bacterial species in terms of microbial DNA content and cell count. Early on in life the human microbiome is established and influenced by things such as our mother's weight and diet, the way we are delivered (vaginal vs. C-section), and the foods we eat that determines the composition of bacterial diversity which in turn affects our immune system, metabolism, etc. There is a symbiotic relationship that develops between the colonizing bacteria and our immune (innate and adaptive immune responses) defenses which collectively comprise the intestinal mucosal barrier to pathogens and noxious antigens.

Dr. Deanna Gibson from British Columbia, Canada and her colleagues discussed the importance of the microbiota and its role in human physiology. She also discussed how diets indigenous to

geographical location or cultural influences can alter the intestinal microbiota both ecologically and functionally resulting in physiological consequences to the host.

The microbiota lies at the interface between the internal (intestinal epithelial cells - IECs) and the external (dietary antigens) environment in the gut forming a tripartite relationship. The microbiota plays several important biological roles including the following:

1) aiding in digestion and the absorption of nutrients from partially digested food
2) producing short-chain fatty acids (SCFA) - a primary energy source for IECs and regulating homeostasis in the gut
3) stimulating immune responses by releasing ligands
4) protecting against enteropathogens by producing antimicrobial peptides (AMPs)
5) regulating goblet cells to secreting mucus droplets that replenish the mucus layer covering the epithelium
6) acting (commensal bacteria) as a protective barrier against pathobionts (any disease-causing microorganism) by competing for food and space

The intestinal mucosa lining is a highly selective permeable monolayer consisting of IECs and adjacent tight junctions and acts as the only barrier separating the microbe-rich lumen side from the sterile submucosal area. Any damage to this layer or loss of integrity to the tight junctions when a disease state occurs, allows for increased passage of microorganisms and their immune-stimulating molecules to the submucosa, where they ultimately may enter circulation, induce pro-inflammatory signaling and recruit leukocytes.

The intestinal microbiota plays a crucial role in the GI tract development, systemic immunity and colonic homeostasis by interacting with the intestinal epithelial cells via the innate immune receptors. The gut associated lymphoid tissue (GALT) relays signals from the mucosal surface to the rest of the body through various immune cells and immune receptors, including innate toll-like receptors (TLRs) and NOD-like receptors (NLRs). The gut microbiota can modulate the intestinal immune cells, such as the T regulatory cells' function and responsiveness to bacterial products. This regulatory mechanism is required to keep the mucosal and systemic immunity in check, allowing the mucosal surfaces to tolerate harmless bacteria, yet respond to invading pathogens. The gut microbes play an important role in regulating gut homeostasis, with colonic microbes producing SCFA such as butyrate, the main energy source for colonocytes that also inhibits intestinal cell proliferation which can reduce colitis symptoms.

Dietary antigens can interact with both the microbiota and the intestinal mucosae, initiating biological reactions in the host. Dietary antigens are absorbed through the intestine as metabolites into the circulating fluids like blood and lymph and the chemical composition of the diet can define the gut microbial ecology. While dietary factors can directly affect the functionality of intestinal epithelial cells and the underlying immune cells, dietary antigens can also alter the intestinal ecosystem by enabling certain microbial populations to proliferate and dampening the dominance of others.

Studies have found that our diet can alter our intestinal ecology, particularly in infants, and these changes are associated with clinical consequences. For example, humans who consume a lot of red meat tend to have a predominantly Bacteroides -rich gut ecosystem, while vegetarians tend to have predominantly Prevotella species. European children tend to have predominately Enterobacteriaceae species and deficient in Bacteroides, compared to rural African children whose diet is rich in fiber. High fat diets promote dysbiosis, an unfavorable alteration of the microbiota resulting in an imbalance between protective and harmful bacteria. However, studies have found that it's the type of fat consumed that is important rather than the total calories from fat. For example, omega-6 polyunsaturated fatty acids (PUFAs) causes more pathobionts, but isocaloric diets supplemented with omega-3 PUFA can reverse such microbial alterations in mice.

The consequences of dysbiosis, can be detrimental when pathobionts become prominent in the microbial communities and lead to an increased expression of immune-mediated and allergic disease states. Diet-induced dysbiosis is a contributing factor in the development of gastrointestinal diseases like inflammatory bowel disease, irritable bowel syndrome and colorectal cancer, as well as systemic diseases like obesity, diabetes, atherosclerosis and nonalcoholic fatty liver disease.

Dr. Erika Isolauri and colleagues at the University of Turku Nutrition, Allergy, Mucosal Immunology

and Intestinal Microbiota (NAMI) department in Finland looked at whether reshaping the microbiome at an early age could have a functional impact on the risk of obesity. Studies have found that a high-fat/energy (sugar) diet alters the gut microbiota composition, which promotes excessive energy harvesting and storage that relates to obesity. Microbial imbalance can also lead to increase gut permeability, metabolic endotoxemia, inflammation and insulin resistance.

The NIH funded a number of studies to look for correlations between the microbiome and diseases. There have been a number of studies that correlate the activity of the microbiome to various diseases. Some scientists and pharma/biotech companies are now taking a different approach to either restore or protect our microbiome. Next month, I will cover some of these findings. So stay tuned.

Top

Closing Thoughts

We've known that microbiota (formerly known as flora) normally resides on our skin, yet there is no problem until we get a cut or an open sore. When MRSA was a problem in the hospitals, healthcare workers were found to harbor MRSA in their noses and they weren't affected, yet hospitalized patients were affected. These scenarios reinforce the commensal, symbiotic and pathogenic microorganisms that share space in and on the bodies of healthy humans. Some say that our microbiome is a "newly discovered organ", since its existence was not acknowledged until now. The gut microbiome is considered the "second immune system", since our exposure to the environment is through our gut with the foods we eat, the drugs we take, the environment itself (where we live and experience exposure to toxins), and the amount of stress, sleep and exercise that we receive, all of which affect our immune system.

Scientists have discovered that our microbiome is vital for our survival with respect to our GI development, digestion of our foods and intake of nutrients, regulating our immune system (innate and adaptive responses), acting as a protective barrier against pathobioants and gut hemostatis. Gut microbes also produce beneficial compounds, such as vitamins and anti-inflammatories, properties that our genome cannot produce in affecting how well our immune system works. One of the factors that can alter our gut microbiota is our diet. Depending on the type of diet we consume, it can lead to either a favorable alteration or to dysbiosis. We've heard the old saying "you are what you eat" and it's been validated with scientific evidence.

Drs. Deanna Gibson and Erika Isolauri and colleagues both discussed how our initial dietary intake as infants helps determine our gut microbial ecology, but a person's long-term diet can also alter ones intestinal microbiota. Any imbalance or dysbiosis to ones microbial ecology due to diet could lead to a number of serious diseases, including gastrointestinal disease and systemic diseases.

Next month, I will cover what scientists have uncovered on the changes in microbiome and its correlation to various types of diseases.

Top

New Technology - "Intestinal Gel Improves Non-Motor Symptoms in Parkinson's Disease"

A preliminary open-label study showed that delivering a levodopa/carbidopa gel (Duopa) directly and continuously to the gut diminished non-motor symptoms in patients with advanced Parkinson's disease. In an interim analysis, patients had significant improvement, a 20-point reduction in the Non-Motor Symptom Scale (NMSS) from baseline. Although there was no control or placebo arm, previous studies showed that the placebo arms achieved at most a reduction of 10-points. The study also showed that patients improved on several of the NMSS domains, including sleep/fatigue, attention/memory, gastrointestinal tract, urinary, sexual function, and miscellaneous.

The drug-pump device, approved by the FDA in January 2015, delivers the gel directly to the jejunum, where it's absorbed. The drug is delivered as a gel since levodopa is unstable and unefficacious when constituted with water. This drug-pump device is considered minimally invasive and competes with deep brain stimulation, an invasive surgery compared to the pump. There are pros and cons to both.

To read the full article in *Medpage Today*, click here.

Top

About BioMarketing Insight

We help companies de-risk their product development process by conducting the business due diligence to ensure that it is the right product for the right market and the market opportunity for the product meets the business goals of the company. We can then develop marketing strategies to drive adoption for the product.

Top