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Review article

Understanding nutrition and immunity in disease management

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ABSTRACT

As we search for answers to modern medicine's most prevalent and challenging problems, the relationship between nutrition, immunity, and biological function of various natural compounds are preimminent. Nutritional research involving genomics provides rational capabilities for preventing disease. Scientific advances in genomic sequencing reveal opportunities for exploring diet-health relationships and potential for individual, genotype based dietary recommendations. Utilizing molecular and genetic technology to analyze impact of nutrition on genomics and metabolism reveals that nutrients may influence certain innate and/or acquired immune functions. By analyzing immune mechanisms including their cells and complex molecules, animal models have offered relevant insight that clarifies interrelations between immunity and nutrition. Plant products also provide numerous resources through bioengineering for designing novel pharmaceuticals. Having long been employed successfully in traditional and folk medicines, plant compounds exhibit anti-inflammatory, antimicrobial, and angiogenic activity. As a result, we now have a promising arsenal for successful application of bioactive compounds.

1. Nutrition and clinical practice

The impact of diet on human health has long been a topic of research, from its effects on human evolution during the Paleolithic times to its role in causing illness such as diabetes and heart disease, fueled by recent scientific advances in genomic sequencing, exploring diet-health relationships have expanded, revealing potential for genotype based dietary recommendations. Although double edged nutritional research and genomics reveal clues for preventing disease and promoting optimal health, these opportunities have not been enthusiastically utilized nor given necessary importance during discussions of national health care.[1] New technology presents novel approaches for advancing nutritional genomics and tools for analyzing biochemical mechanisms involved in disease. As nutrition is an important environmental factor that could affect disease, genome based diets potentially improve overall public health. Through nutritional guidelines based on individual genetics, we are then equipped to prevent and treat disease based on variations in the human genome.[2]

With recent progress in nutritional genomics and promotion of customized, genome based diets, individual guidelines for optimal health are more prevalent in Western medicine. Yet this approach also corresponds with patient centered philosophy of Eastern medicine focusing on the whole individual. Many nutritional concepts of Eastern medicine have not been adopted by systems of Western nutrition. However, while both Eastern and Western medicine possess varying strengths and weaknesses with respect to techniques, as well as interpretation of an integrated approach to nutrition could be achieved by selecting advantages of both systems based on knowledge and practice. Combining both systems may therefore create an inclusive, all-encompassing concept of medicine, providing holistic methods and improved care from each individual system.[3]

While western medicine tends to be reductionist, eastern complementary and alternative medicine (CAM) is inclusive. Understanding CAM and how it meshes with western practices and biological processes will help construct a workable framework for application of CAM in public health and clinical practice.[4] As nutrition has a profound effect on multiple body systems, clearly analysis of nutrition should seek to obtain a broad understanding of food. Food and its beneficial properties possesses the capability to provide answers and the potential to be utilized in preventing,

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treating, and even developing pharmaceuticals for the most perplexing and problematic diseases known to medicine.

2. Evolution of immunity and digestion

Investigating relationships between nutrition and immunity from an evolutionary perspective has revealed ancient connections in development and function. Historically, the digestive and immune systems have been viewed and analyzed as separate entities. However newly interpreted evidence demonstrates that both systems share essential similarities and common functions, both in nutrient acquisition and host defense with origins common to both systems. This provides a new and perhaps novel way to envision the emergence and evolution of host defense mechanisms.[5] Unicellular invertebrates phagocytose for food and defense, and phagocytosis represents the most ancient and ubiquitous form of food acquisition and defense against foreign insult. Multicellular invertebrates and vertebrates possess phagocytic cells for defense and have evolved more complex functions attributed to immunodefense cells that became specialized for effecting cellular and humoral immune responses. From the oral cavity through terminus of the intestine, our tubular digestive system is amply equipped with cells, tissues, and organs that coevolved and remain forever together. Digestive and immune systems are inextricable.[6]

Host responses against invading pathogens are basic physiological reactions of all living organisms. Since appearance of first eukaryotic cells, a series of defense mechanisms have evolved to secure cellular integrity, homeostasis, and host survival. Invertebrates, ranging from protozoans to metazoans, possess cellular receptors, which bind to foreign antigens and therefore differentiate self from non-self. This rudimentary ability in multicellular animals is associated with phagocytes, bearing different names (e.g. amebocytes, hemocytes, coelomocytes) in various groups species such as sponges, round worms, cnidarians, mollusks, crustaceans, chelicerates, insects, annelid worms and echinoderms. The cells, macrophage-like in appearance, function, and associated repair are prominent even at the earliest evolutionary stage, and possess well conserved molecular structures such as pathogen recognizing receptors (PRRs) and pathogen-associated molecular patterns (PAMPs). Scavenger receptors, Toll-like receptors, and Nod-like receptors (NLRs) are also prominent members within this group of host receptors. Following receptor-ligand binding, signal transduction initiates a complex cellular reaction cascade, which leads to production of diverse effector molecules. As examples, cytokines participate in this response evoking orchestration even in “lower” invertebrates, which eventually may result in intruder elimination or inactivation. Important innate effector molecules are antimicrobial peptides, lectins, fibrinogen-related peptides, leucine rich repeats (LRRs), pentraxins, and complement-related proteins.[7]

3. Nutrition and immunity in relation to an animal model: the earthworm

Analysis of nutrition and immunity in animals other than humans, especially invertebrates, has introduced newer discoveries and insights. As a rich source of macromolecules and nutrients, earthworms have long been used as food among various indigenous cultures.[8] The nutritional and medicinal value of earthworms has been utilized for centuries among traditional and complementary practices such as Ayurveda, Traditional Chinese Medicine, Kampo, and Traditional Korean Medicine, the foundation from which current knowledge of the healing properties of earthworms stems. Earthworms and their nutritional products exhibit anti-inflammatory properties, and promise in treating human disorders of blood coagulation.[8,9] Their ability to regenerate lost appendages has prompted further research in mammalian applications, specifically by extending this ability in order to regenerate damaged nerves. Analyzing earthworms and invertebrates is advantageous since we can bypass ethical restrictions and financial constraints that normally more than ever impede research using vertebrates, especially mammals. Newer non-vertebrate models allow for generation of vast amounts of useful research surrounding biomedical capabilities and potential. Nutritional and therapeutic benefits of earthworms and their impact on chronic human conditions are closely tied to understanding evolution of innate immunity.[10]

Earthworm innate immunity has recently been analyzed through gene profiling of earthworm coelomic cells (leukocytes) which play an important role in immune function. Analysis of expressed sequence tags leads to identification of immune-related and cell defense genes, providing valuable knowledge for future research that focuses on earthworm immune systems.[11] Compounds derived from earthworms have the potential to provide groundbreaking treatments for conditions such as thrombosis. For example, analysis of the earthworm compound Lumbrokinase has revealed its efficacy as an extremely potent treatment of blood-clots, with the purification of a single Lumbrokinase increasing its antithrombotic activity and in turn improving the general use of Lumbrokinase.[12] Despite other available pharmaceuticals and drugs, thrombosis remains one of the main causes of death among Americans, making Lumbrokinase and its antithrombotic effects a valuable alternative treatment.[9] Development of molecular and genetic resources may help achieve a more complete understanding of earthworms as a genetic model that may facilitate research of the immune system.[13]

In general, animal products provide a wealth of resources for utilization in creating novel pharmaceuticals and in bioengineering. Historically, animal models have been successful subjects that offer insight into biological processes, and have long been used in various traditional and folk medicines. Animals are a valuable source of biological compounds, exhibiting extensive drug applications including anti-cancer, antimicrobial, and angiogenic activity. Recent discoveries and successful applications demonstrate great potential that will impact modern medicine, improving and revealing new treatments and methods of prevention.[14,15]

4. Nutritional models for disease treatment

Analysis utilizing molecular and genetic technology measuring impacts of foods on genomics and metabolism reveal how nutrients may influence certain immune functions.[16] Innate immunity and nutrient metabolism are complex biological systems that must work in concert to sustain and preserve life. Effector cells of the innate immune system rely on essential nutrients to generate energy, produce metabolic precursors for biosynthesis of macromolecules and tune their responses to infectious agents. Thus disruptions to nutritional status exert a substantial impact on immune competence and can result in increased susceptibility to infection during nutrient deficiency, or chronic inflammation associated with over-nutrition.[17]

Research concerning modulation of immune function by foods in persons varying from healthy to those with compromised immune systems have supported the general conclusion that foods are capable of influencing innate or even acquired immunity. Demonstrating capabilities for treating disease in compromised individuals, preventing disease in those who are healthy, and analyzing nutrition and its complex effects on immunity have contributed to an emerging discipline known as immunonutrition.[18] Immunonutrition is multidisciplinary, involving definition of relationships between nutrition, immunity, infection,