December 2019 - Mid-Month Bonus

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Happy Holidays from The Blands

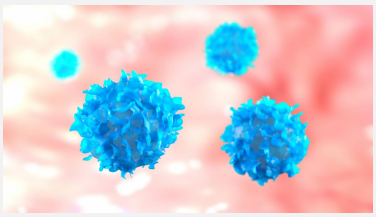
Warm wishes for a happy and healthy holiday season.
Jeff & Susan Bland

JJ Virgin's Reignite Wellness Podcast Presents Dr. Jeffrey Bland

Why Good Health is More Than the Absence of Disease

What's the difference between disease care and health care? This is one of Dr. Jeff Bland's favorite topics and he discussed it during a recent guest appearance on JJ Virgin's Reignite Wellness podcast. Listen to the interview now to hear more about healthy lifestyle choices, how to make health personal, and Dr. Bland's new project, Big Bold Health: subscribetojj.com

Note: The 30-Day Meal Plan mentioned in the podcast will be available soon. Would you like to be notified when it is ready to download? Go to www.bigboldhealth.com and click "Tell Us." Type #iwantthefoodplan and your email address, and we will make it happen! While you're there, let Dr. Bland know how YOU define health.



Th17 and Plasticity in the Modern Immune Response

Amidst the swell of inflammatory and autoimmune illness, it is not always easy to remember that the immune system is protective in essence, and that its actions are precisely tailored to answer to invasive challenges experienced as a result of both external and internal exposures. We've long understood how T-helper 1 (Th1) cells represent the cellular face of immunity, while Th2 cells stand for the tissue or humoral immune response, each the 'sheriff' directing a 'posse' of cytokines whose specialized biochemical arsenal effectively meets and neutralizes particular threats: toxins, allergens, wounds, pathogens, and other such challenges. In health, it then stands down to allow the immune 'clean-up crew' of resolution-attuned macrophages to bring tissue environments back to normal while immunoglobulin libraries record and catalogue their newly-acquired knowledge. We appreciate that functional equilibrium between the Th1 and Th2 systems has much to do with how well we overcome infections while remaining free from hypersensitivity reactions and chronic immune-related illness.

In 2005, however, we learned of another elemental facet of immunity, the independent Th17 immune cell lineage, which finds its strongest expression at outer epithelial borders where they can impact barrier integrity: skin, the lumen of the entire alimentary tract, and respiratory surfaces. Th17 immune cell expression can seem somewhat prone to dysregulation, as it is implicated in periodontal bone loss, fatty liver infiltration, cancer, allergy, inflammation, and in autoimmune conditions (like rheumatoid arthritis, inflammatory bowel disease, psoriasis, multiple sclerosis, and others) characterized by aberrant remodeling of tissues (hard and soft connective tissues, intestines, liver, etc.) during an ongoing, long-term immune response. It has also been seen in gestational diabetes, and one article proposes mechanisms through which it may be involved in endothelial dysfunction and high blood pressure. Th1/Th2/Th17 imbalance can also manifest in celiac disease and the response to gluten peptides, though one study employing a gluten-free diet over a 5-year period in affected individuals concluded that the diet did not alter the immune disequilibrium, possibly due to continuing alterations in the gut microbiome.

Th17 Plasticity

Th17-specific cytokines include interleukin-17 (IL-17; a family of related interleukins), IL-21 (which can influence Th1 and Th2 responses), and IL-22 (a relative of the immunomodulatory IL-10). IL-17 and IL-22 are both immunostimulatory during epithelial tissue infection, but IL-17 is regarded as more pro-inflammatory; both are also known to support barrier integrity, yet in dysfunction, they have been associated with chronic infection, impaired tissue healing, and tumor promotion. In addition, Th17 immune cells, upon specific provocation, are able to produce tumor necrosis factor-α, the Th1 cytokine interferon-γ, or IL-10, a more modulatory cytokine that is also formed by Th1, Th2, and T-regulatory immune cells, and activated Th17 cells can additionally stimulate the production of antimicrobial peptides or tissue enzymes. The ability of Th17 cells to simultaneously produce cytokines associated with Th1 and Th17 responses seems to confer pathogenicity (with perhaps some degree of ambiguity in targeting of the immune response) on Th17 cells, and this may in some cases be triggered by cytokines originating with inflammation or other immune responses. Th17 with this pathogenic plasticity are referred to as Th17.1 cells, and they have been found in patients with obesity and diabetes, gestational diabetes, multiple sclerosis, autoimmune arthritis, Crohn's disease, sarcoidosis, and other conditions.

Why does the immune response 'stretch' beyond what we might think is most adaptive for human health? It seems likely that modern immune systems face more frequent challenges on multiple simultaneous fronts: heightened exposure to environmental toxins, broader sharing of human pathogens, toxins created from metabolism of less-than-salutary forms of food nutrients, and accumulation of cellular damage with accelerated biological aging, to name just a few. While research into optimizing harmony among Th1, Th2, and Th17 responses is in its early developmental stages as yet, a few recent studies give insight into how overlap among these distinct axes of immunity may occur:

- Results from a preclinical study model of asthma suggests that exposure to lipopolysaccharides (LPS) may convert a Th2 response into one more Th17-like. Digestion of high-fat, high-sugar foods with subsequent release of LPS is one of the more common lifestyle-related means of exposure in humans.
- Air pollution in the form of particulate matter incites Th17 cells to develop the pathogenic, pro-inflammatory profile, especially in those with asthma, yet vitamin D sufficiency seems to encourage a more immune-tolerant expression in them.
- In a human study, a high-salt challenge was found to perturb gut microbiome lactobacilli populations and activate Th17 cell production.
- Viruses may potentially contribute to development of Th17 pathogenicity, as evidenced by oncogenic or immunosuppressive viruses, co-morbidity of chronic viral illness with other serious conditions (e.g., liver cancer or certain central nervous disorders associated with increased blood-brain barrier permeability), and the possibility that viruses may even be instrumental in the development of some chronic conditions (multiple sclerosis is one example).

Others provide clues on maintaining immune balance and neutralizing threats without 'burning down the house' with chronic inflammation:

- Obesity is often associated with chronic low-grade inflammation, but in obese women, vitamin A supplementation significantly improved the balance between T-reg- and Th17-associated cytokines—an overall improvement in immune expression in these women. Th17 gene transcription is regulated at a high level by a vitamin A-responsive nuclear receptor, which may at least partially explain this.
- A study into the early pathology of multiple sclerosis discusses evidence that high intakes of saturated fat, omega-6 fatty acids, or sodium may encourage Th17 pathogenicity, while higher intakes of omega-3 fats, flavonoids, and prebiotics that encourage short-chain fatty acid production in the gut may inhibit this transformation and instead cultivate a more moderate overall immune response.
- T-helper cells have both cellular and nuclear melatonin receptors (from the G protein-coupled receptor family) and also produce melatonin themselves. Melatonin appears to support a Th2 response while limiting Th1- and Th17-oriented polarization, and one review concluded that it limits excessive immune activation while stimulating immunity in conditions of immunosuppression. Early research suggests that adequate melatonin may inhibit development of the pro-inflammatory phenotype in Th17 cells, and may be instrumental in limiting the Th17 response during pregnancy; concurrent vitamin D adequacy could be another key aspect, along with regular good sleeping habits.
- Multi-omics analysis has found that vitamin D influences T-helper cell differentiation into Th1 and Th17 lines in multiple ways and at multiple timepoints in an immune response, and in a model of multiple sclerosis, vitamin D supplementation significantly altered gene expression related to T-helper cell maturation.
- A review of Oriental medicinal herbs, traditional combinations, and phytonutrients cites preclinical research finding many that beneficially modulate Th17 dynamics, some of the better known of which include berberine, Baikal scute (*Scutellaria baicalensis*), resveratrol, an extract of burdock (*Arctium lappa*), oleanolic acid, perilla leaf, the peony root phytonutrient paeoniflorin, puerarin, and possibly also curcumin.

At a fundamental level, the growing body of research on Th17 expression demonstrates that limiting the number of incoming immune challenges at a given time is a crucial means of optimizing the precision and efficacy of the immune response. In terms of lifestyle, this would seem to translate into remarkably simple behaviors that are nevertheless challenging to maintain in modern times: a nutrient- and phytonutrient-dense diet centered on unprocessed foods, keeping a healthy body composition, supporting cellular rejuvenation and metabolic detoxification processes, keeping one's

bedtime environment conducive to deep sleep (dark, quiet, and cool), and minimizing exposures to potential toxins, especially around pregnancy or when acutely or chronically unwell. The evolution of our understanding of how Th17 function is interwoven among the immune system's many other priorities will further clarify means of improving immunometabolic function.

Connect with Dr. Jeffrey Bland

Newsletter Team
Jeffrey Bland, PhD - Publisher
Cheryl Kos, ND - Content Developer and Writer
Kirsten Miller - Content Editor
Gillian Martin - Subscription Manager