Clinical Summary

Big Bold Health® Professional

Netea MG, Joosten LAB, Latz E, et al. Trained Immunity: A program of innate immune memory in health and disease. Science 2016;352(6284):aaf1098.

Innate Immunity May Also Have Immune Memory

In the past, only the adaptive immune system was considered to create new immune memory (via antigen-antibody interactions) and update its function after novel experiences. Recent studies, however, suggest that innate immunity can also be 'trained' by immune events and exposures. This review details evidence showing that viruses and even dietary components can trigger epigenetic alterations in innate immune cells that adjust their later response to infection, inflammation, cell damage, and other immune scenarios.

The classical view of the immune response is that, in addressing a potential pathogen, the innate system is tasked with immediate yet nonspecific host defense, while the adaptive system studies the unique antigenic markers of the 'invader.' This approach provides host protection while allowing the time needed to creating antigen-specific antibodies: a better-targeted but time-consuming defense. These antigenic molecular patterns are cataloged into permanent immune memory, enabling more rapid identification and a more effective response to subsequent exposures.

According to this international team of researchers:

"Trained [innate] immunity most likely evolved as a primitive form of immune memory." "It is also likely that trained immunity plays an important role in ontogeny, enabling the maturation of the innate immune system of the newborn, a process in which microbiota plays an important role."

"It is also possible that Western-type diets, which are known to trigger systemic inflammatory responses, can precipitate maladaptive trained immune responses." "This type of maladaptation of innate immune cells could be a culprit for other common inflammatory diseases prevalent in Western societies, such as type 2 diabetes or Alzheimer's disease."

Review Summary

Research highlights from this review include the following:

- The traditional view of immune memory has been that it relies solely on genetic recombination of receptor elements in cells of the adaptive immune system, with creation and amplification of a customized molecular response: antibodies. The innate immune system was not previously considered to have memory function.
- However, cells of the innate immune system (such as macrophages and natural killer cells) have demonstrated the ability to improve their response—qualitatively and quantitatively—to potential pathogens and to stress-related cell signaling. This occurs via epigenetic reprogramming (altered regulation of genetic activity) of innate immune cell function. This 'training' can temporarily adjust the balance among various innate immune cell types, each having unique roles in cytokine production, amplifying or resolving an inflammatory response, communicating with the adaptive immune system, or pathogen clearance. Altering this balance may significantly alter overall immune function.
- Adaptive immune memory often confers years of protection, while innate immune memory generally persists for only weeks or months. Innate immune training is ongoing, and can upregulate the protective response or encourage immune tolerance. Previous training may be either reinforced or dampened by subsequent immune experiences.
- Dietary and environmental exposures can trigger innate "immune training" by providing innate immune cells the opportunity to 'practice' responding to non-pathogenic microbes, antigens, polysaccharides, and microbial cell components. Research on food-based beta-glycans (found in mushrooms, yeast, algae, and some grains) has demonstrated considerable therapeutic potential for beneficial innate immune training and "acquired resistance."
- Innate immune cells have recently been recognized as having "pattern recognition receptors" that can identify molecular signatures of infection and cell stress or damage. These signatures are referred to as PAMPs and DAMPs: pathogen-associated molecular patterns and damage-associated molecular patterns.
- Innate immune training is likely to contribute to the cross-protection conferred by some vaccines and viral infections, independent from the adaptive immune response. In these instances, partial immunity to a pathogen (or even certain types of cancer) occurs after infection or vaccination with a different organism, due to certain similarities between their molecular patterns.
- The gut microbiome is foundational in both innate and adaptive immunity, and its composition and extensive interactions with intestinal immune tissues is critical to continuous innate immune training. Nutrition and eating habits may therefore profoundly affect the quality of innate immune training.

NUTRITION CONCLUSION

Scientific advances are redefining or understanding of how immunity evolves and self-adjusts over time. New findings demonstrate that the distinction between innate and adaptive immunity is not as rigid as previously thought.

There is growing evidence that dietary composition in terms of macronutrients, phytonutrients, micronutrients, and microbiota-available nutrients influences the effectiveness of the immune response and the development of appropriate immune tolerance. Dietary beta-glucans, fats, and prebiotics may hold particular therapeutic promise for beneficial immune training. The future scope of innate immune training will emphasize the importance of lifestyle opportunities, such as a nutrient-dense diet, regular physical activity, and spending time in nature.