

S024 New Treatment Strategies: Should we Target the Innate or the Adaptive Immune System? Targeting the innate immune system

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IBD is a highly complex condition in which environmental, genetic, microbial and immune factors interact in an intricate but still poorly understood way to cause chronic gut inflammation. The immune factors represent the effector arm of gut inflammation, and there is clear evidence that both innate and adaptive immune responses are involved in IBD pathogenesis. Both responses are believed to be directed primarily against the luminal commensal flora, but each has distinct components and mechanisms that represent potential targets for therapeutic intervention.

Intestinal innate immunity encompasses microbial molecular patterns expressed by Gram-positive and -negative bacteria and their respective receptors, which are primarily Toll-like receptors (TLRs) and NOD-like receptors (NLRs) expressed by monocytes, macrophages and dendritic cells. RIG-I-like receptors (RLRs) recognizing viruses, and other receptors recognizing self-danger signals derived from damaged tissue, DNA and RNA also exist. Bacterial products recognized by TLRs and NLRs trigger multiple pro-inflammatory networks, including the so-called "inflammasomes", ultimately resulting in the production of a variety of cytokines, chemokines and other soluble factors that mediate inflammation. The innate immune response actually does not act alone, and will eventually impact on the adaptive immune response, and both will modulate each other in a reciprocal fashion.

Taking a simplistic view, targeting of the innate immune system for treatment of IBD should include gut microbes on one side, and TLRs, NLRs and the cells bearing these receptors on the other side. Modulation of the gut flora with antibiotics, probiotics and dietary manipulations has been in use for a long time with mixed results, but it still is a valid evidence-based approach. On the other hand, therapeutic targeting of innate immunity with TLR and NLR agonists and antagonists is in its infancy, and its potential efficacy is unknown. Direct targeting of monocytes, macrophages and dendritic cells is not a viable alternative considering the detrimental consequences of blocking immunologically essential cells. Finally, anti-cytokine strategies, as those currently based on various biologicals, is still another legitimate option, but one that in reality concomitantly affects both the innate and adaptive immune systems.

Session : Clinical Session 4 – Therapeutic Strategies for Pediatric IBD : Evidence-Based Controversies (part II)