Casual Friday Series

The Gut-based Genesis of Autoimmunity

A Biogenetix Clinical Presentation

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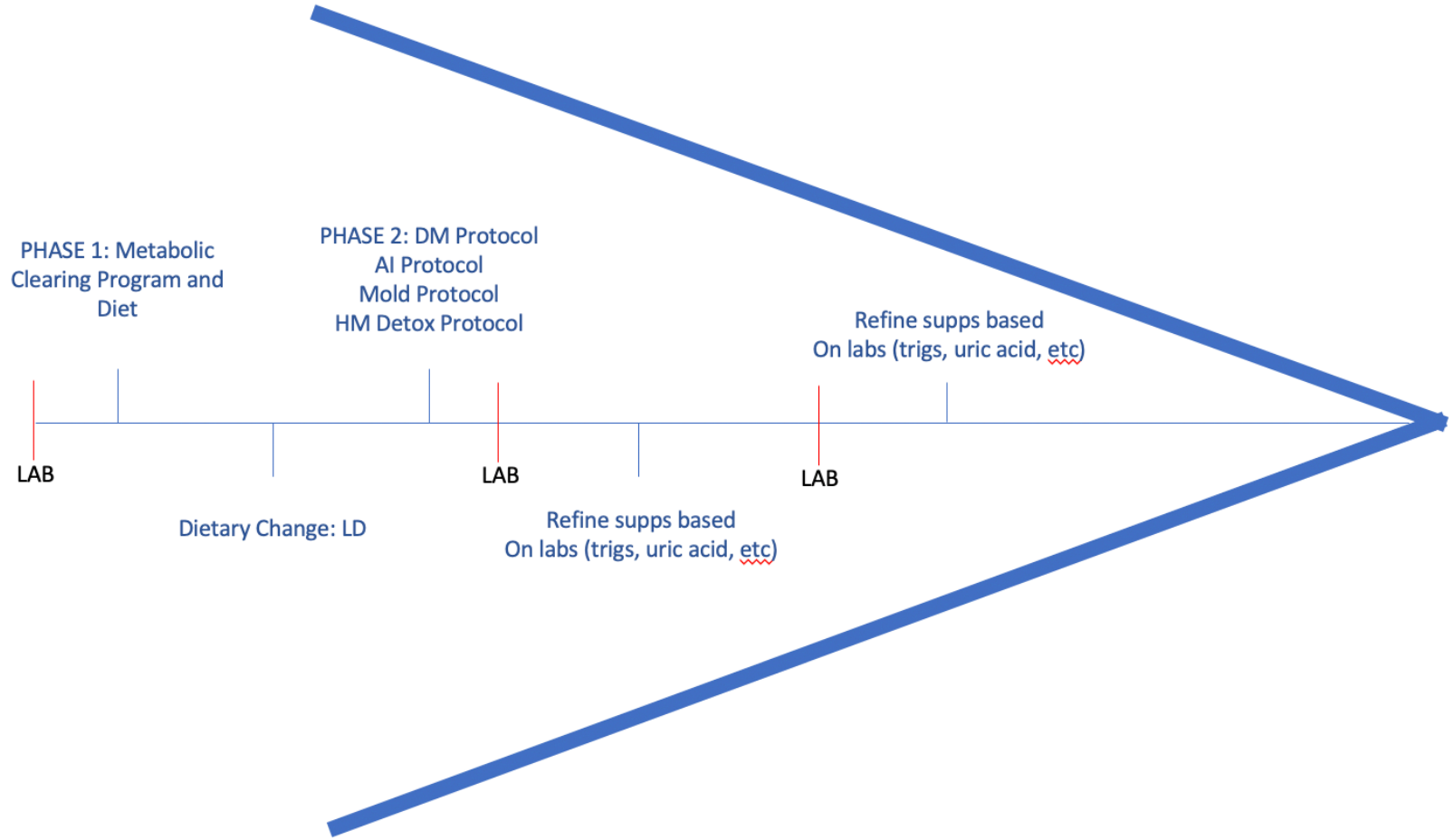
Disclaimer

- *Information in this presentation is not intended, in itself, to diagnose, treat, reverse, cure, or prevent any disease. While this presentation is based on medical literature, findings, and text, The following statements have not been evaluated by the FDA.*
- *The information provided in this presentation is for your consideration only as a practicing health care provider. Ultimately you are responsible for exercising professional judgment in the care of your own patients.*

(Lifestyle + Genetics) x Time = Chronic Health IMPROVEMENT

Supplement and Diet Protocols



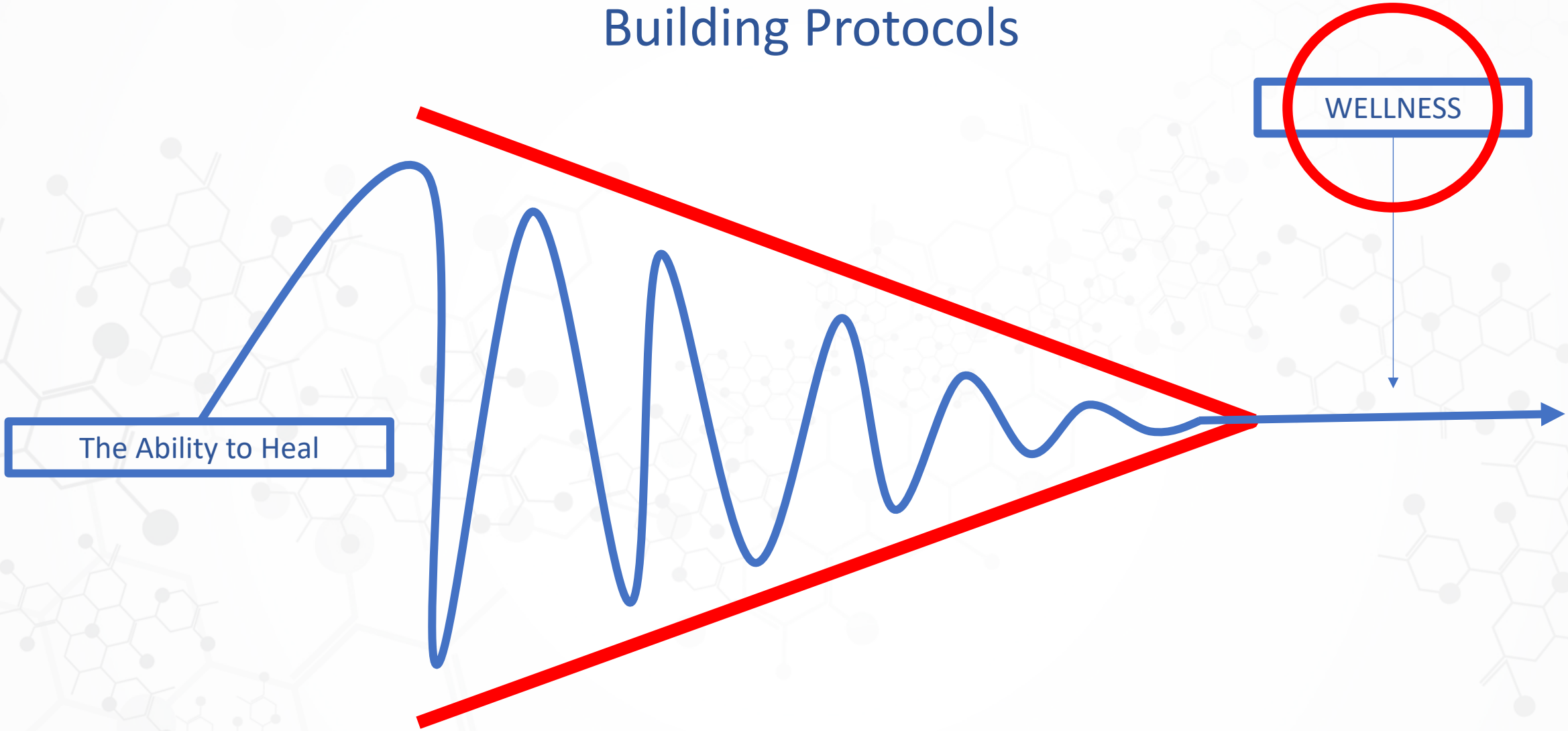
Retest a lab at least every 60 days.

85% of patients will improve with basic structures and healthy eating.

% of problem analysis: this is what the cleanse is for.

General → Fine Tune

Building Protocols



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PMID: 29920643

The microbiome in autoimmune diseases

F. De Luca[1,3] and Y. Shoenfeld[1,2]

The microbiome is represented by microorganisms which live in a symbiotic way with the mammalian. Microorganisms have the ability to influence different physiological aspects such as the immune system, metabolism and behaviour. In recent years, several studies have highlighted the role of the microbiome in the pathogenesis of autoimmune diseases. Notably, in systemic lupus erythematosus an alteration of the intestinal flora (lower *Firmicutes/Bacteroidetes* ratio) has been described. Conversely, changes to the gut commensal and periodontal disease have been proposed as important factors in the pathogenesis of rheumatoid arthritis. At the same time, other autoimmune diseases (i.e. systemic sclerosis, Sjögren's syndrome and anti-phospholipid syndrome) also share modifications of the microbiome in the intestinal tract and oral flora. Herein, we describe the role of the microbiome in the maintenance homeostasis of the immune system and then the alterations of the microorganisms that occur in systemic autoimmune diseases. Finally, we will consider the use of probiotics and faecal transplantation as novel therapeutic targets.

Alterations of the microbiome in pregnancy and childhood

During pregnancy, the microbiome undergoes profound changes, in particular in the vagina and gut. In a recent study, Koren *et al.* 2 found that there were differences between the microbiome in women in the first trimester of pregnancy with that of the third trimester: in the last months of pregnancy an abundance of *Proteobacteria* and *Actinobacteria* and a depletion of *Faecalibacterium* (bacterium butyrate-producer with anti-inflammatory effects) resulted. These alterations of microbiome, known as dysbiosis, can induce weight gain, insulin-resistant and metabolic inflammation if the microorganisms contained in the gut of the mice at the third trimester have been transferred into germ-free mice 2, 3. The fetal gastrointestinal tract is believed to be sterile, and microorganisms colonize the intestine of the fetus during delivery through the

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6300652/

birth canal (Fig. 1) 4, 5. During childhood, the gut microbiome can be influenced by several environmental factors, such as geographic area, breast feeding, solid food and ways of delivery. Vaginally delivered infants acquire bacterial communities resembling their own mother's vaginal microbiota (*Lactobacillus*, *Prevotella*, *Sneathia* spp.). Conversely, Caesarean-section infants harbour bacterial communities similar to those found on the skin surface (*Staphylococcus*, *Corynebacterium* and *Propionibacterium*) 4, 6. The ability of the gastrointestinal mucosa of the newborn to adapt to the colonization of microorganisms is not entirely understood. Realistically, the colostrum and breast milk are rich in immunoglobulin (Ig)A, which are important to neutralize pathogens and to avoid translocation through the intestinal epithelia, therefore ensuring the homeostasis between symbiotic gut bacteria and the mucosa epithelium. Maternal milk contains several metabolites, such as gangliosides, lactoferrin (Lf) and human milk oligosaccharides (HMOs) that provide protection against anti-infective agents 1, 7. Furthermore, HMOs exhibit some

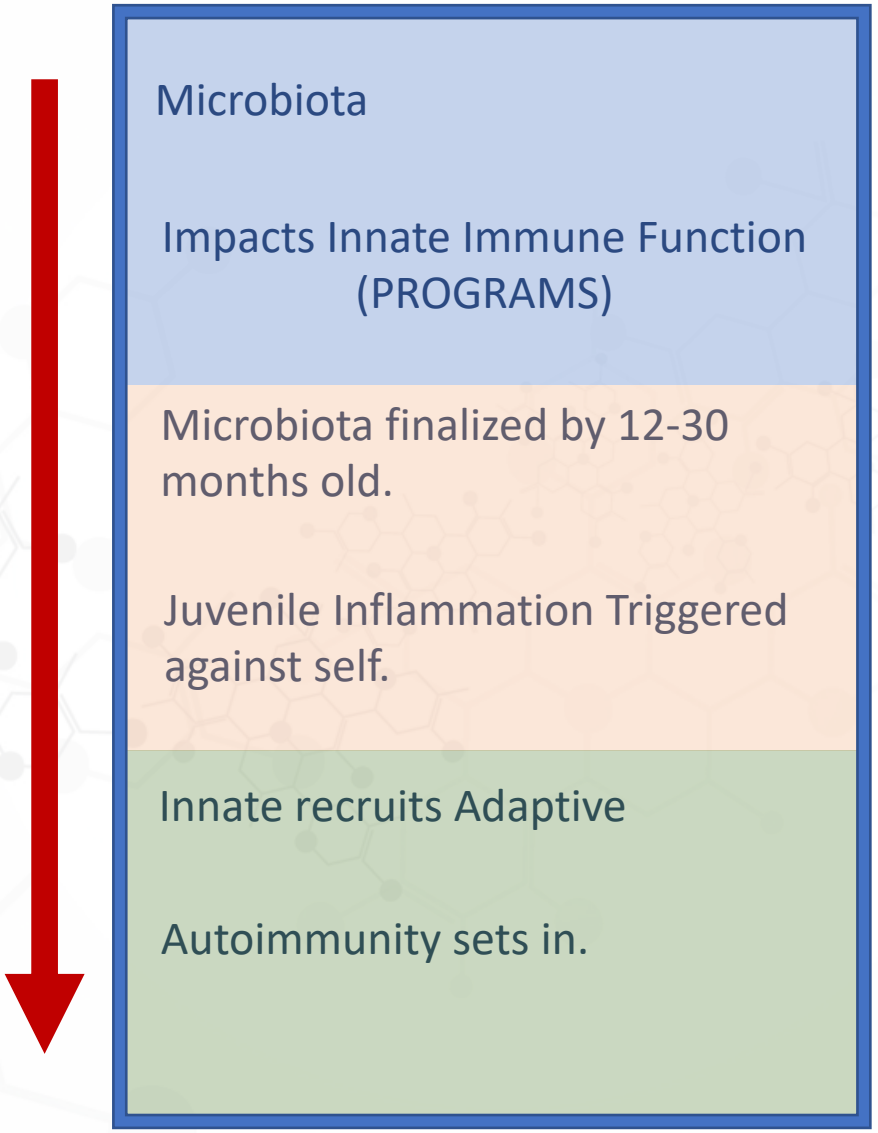
contribute to neonatal immunological imprinting by influencing the nature of the immune response to the commensal antigens 8, 9, 10, 11. The immaturity of the immune system of the newborn and tolerogenic environment factors could explain how the microbiome has been accepted by the neonate gut. Therefore, the dialogue between commensals and host plays a crucial role in the development and homeostasis of the

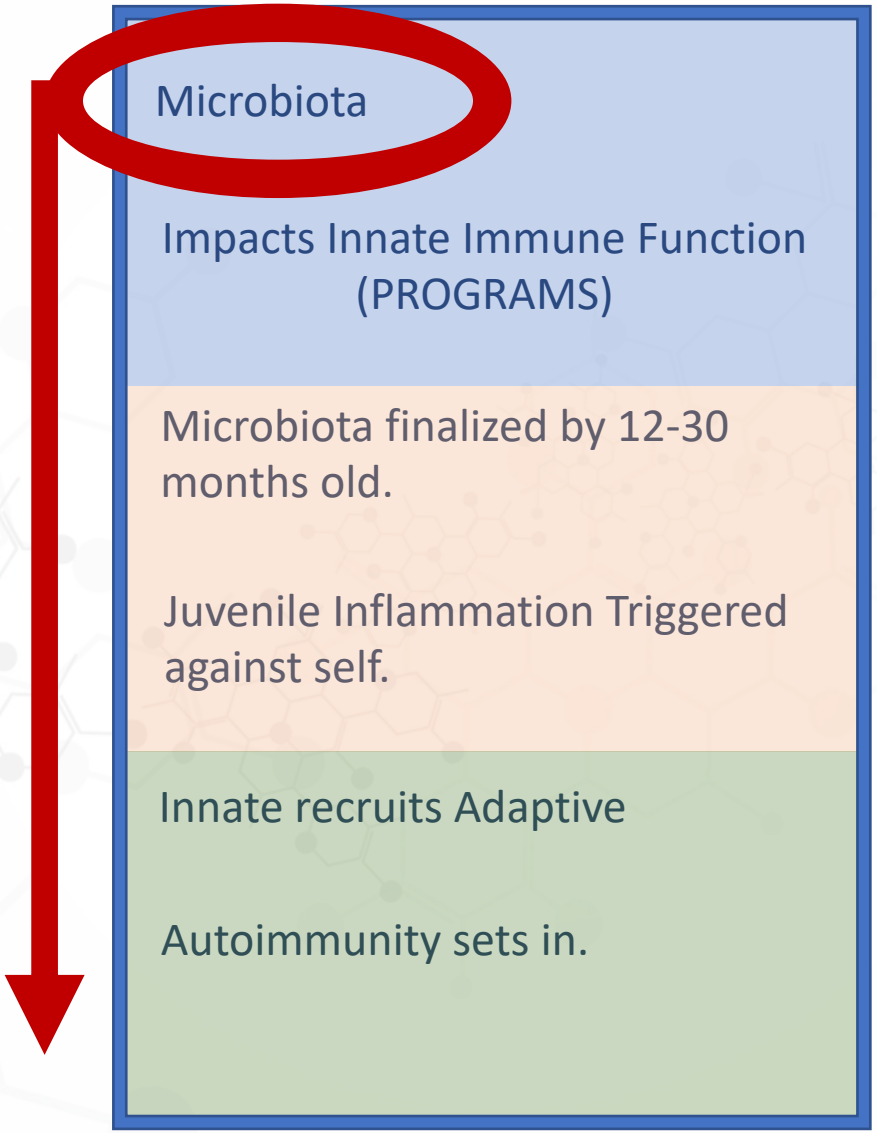
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6300652/

What shows up first…MATTERS

The first microbial introductions are often accepted as BASE/normal under the conditions of a function called tolerogenic activity. This dissipates as the “program” is set.

Tolerogenic therapy aims to induce immune tolerance where there is pathological or undesirable activation of the normal immune response. This can occur, for example, when an allogeneic transplantation patient develops an immune reaction to donor antigens, or when the body responds inappropriately to self antigens implicated in autoimmune diseases.. It must provide absence of specific antibodies for exactly that antigenes.


Microbiota
Impacts Innate Immune Function (PROGRAMS)
Microbiota finalized by 12-30 months old.
Juvenile Inflammation Triggered against self.
Innate recruits Adaptive
Autoimmunity sets in.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proposed 25, 26. The human microbiome might be a major player in autoimmunity, as the loss of immune tolerance can be caused by microbial composition changes 1, 5. Microorganisms can elicit the immune response against the host if the mechanisms of tolerance fail for several reasons (Fig. 2) 27, 28, 29, 30, 31. Recently, Rinaldi *et al*. 32 found that autoantibodies directed against the cell wall mannan of the yeast *Saccharomyce cerevisiae* (phosphopeptidomannan), a ubiquitous commensal microorganism, were detected in several autoimmune diseases with different sensibilities (i.e. rheumatoid arthritis, systemic lupus erythematosus, anti-phospholipid syndrome). More specifically, anti-*S. cerevisiae* antibodies (ASCAs) are a specific serological marker of Crohn's disease (CD) by appearing before CD onset in 32% of cases. In addition, *S. cerevisiae* is used as an adjuvant in vaccines, and this has led scientists to think of a hypothetical risk of developing abnormal immune activation that may be associated with an autoimmune/inflammatory syndrome induced by adjuvants (ASIA) 32, 33. Inflammatory bowel diseases (IBD) such as CD and ulcerative colitis (UC) represent an example of how the alteration of gut microbiome could induce disease. Notably, numerous studies have shown that both CD and UC are associated with a reduced complexity of the commensal microbiota and consistent shifts to a dysbiotic state. In a similar manner to that observed during acute mucosal infections, both CD and UC are

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6300652/

Review > Nat Rev Immunol. 2018 Feb;18(2):105-120. doi: 10.1038/nri.2017.111.
Epub 2017 Oct 16.

The hygiene hypothesis in autoimmunity: the role of pathogens and commensals

The incidence of autoimmune diseases has been steadily rising. Concomitantly, the incidence of most infectious diseases has declined. This observation gave rise to the hygiene hypothesis, which postulates that a reduction in the frequency of infections contributes directly to the increase in the frequency of autoimmune and allergic diseases. This hypothesis is supported by robust epidemiological data, but the underlying mechanisms are unclear. Pathogens are known to be important, as autoimmune disease is prevented in various experimental models by infection with different bacteria, viruses and parasites. Gut commensal bacteria also play an important role: dysbiosis of the gut flora is observed in patients with autoimmune diseases, although the causal relationship with the occurrence of autoimmune diseases has not been established. Both pathogens and commensals act by stimulating immunoregulatory pathways. Here, I discuss the importance of innate immune receptors, in particular Toll-like receptors, in mediating the protective effect of pathogens and commensals on autoimmunity.

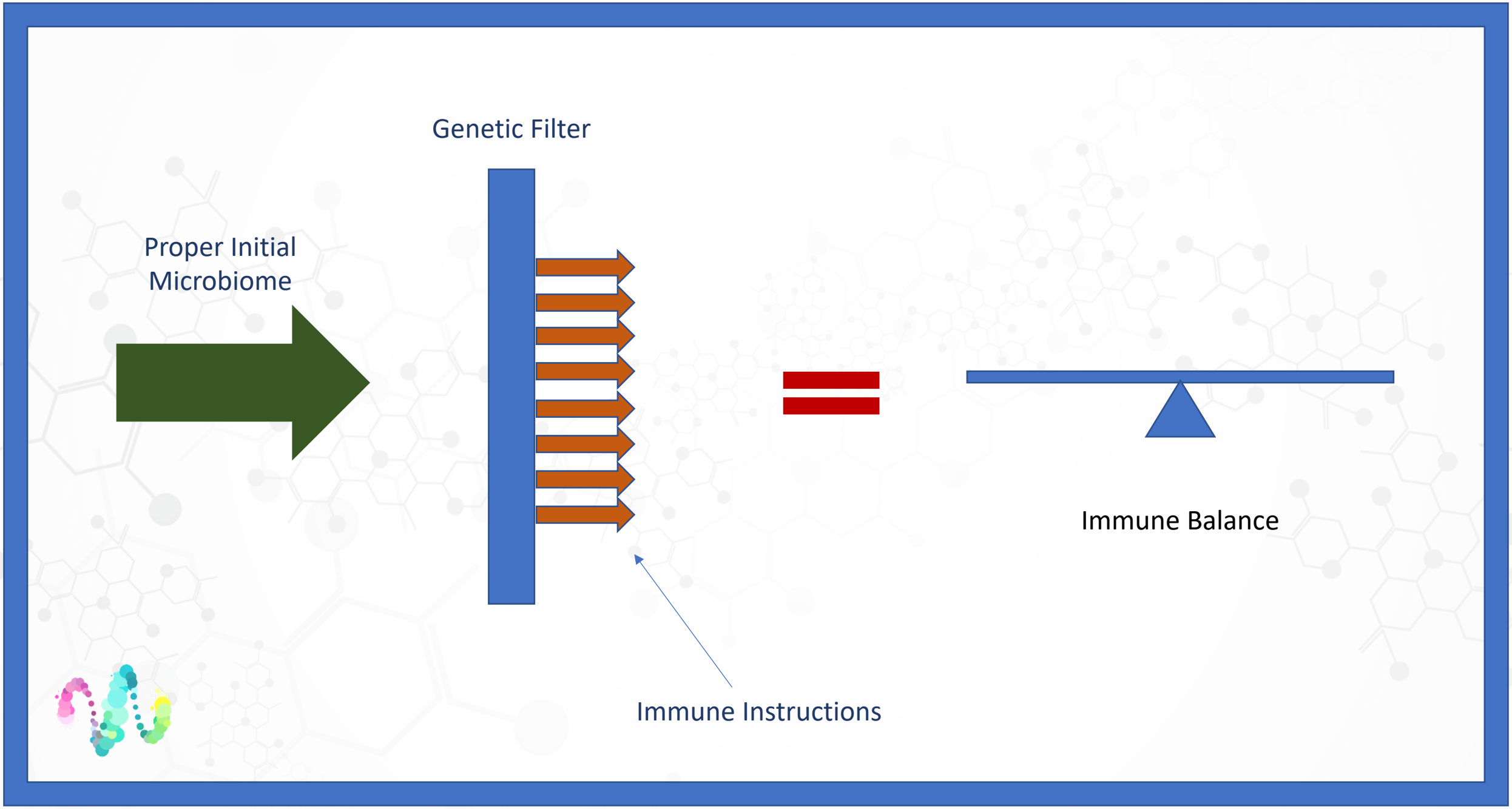
My Summary of the hygiene hypothesis: The immune system is made for war. If you don’t let it war, it will war against you.

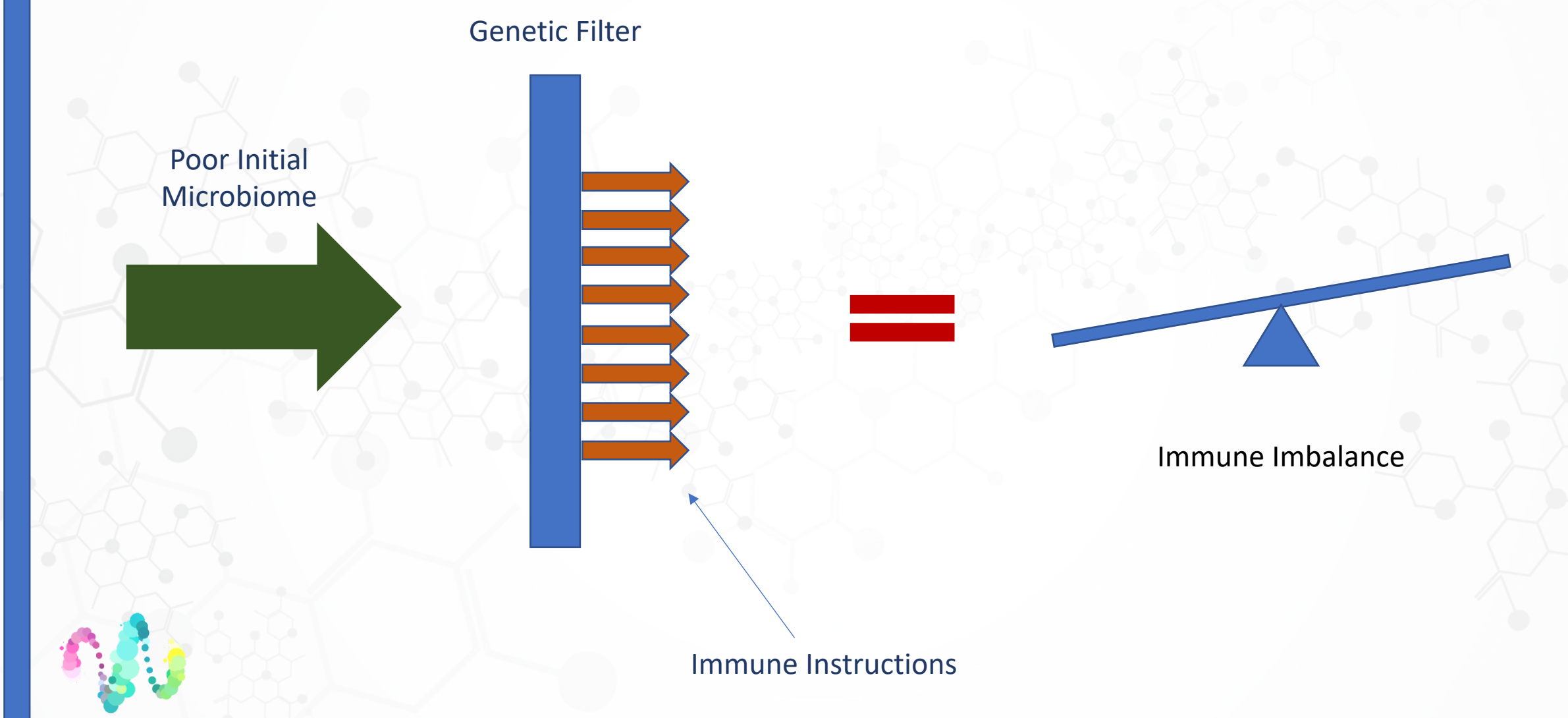
> J Pediatr Gastroenterol Nutr. 2019 Apr;68(4):533-540. doi: 10.1097/MPG.0000000000002226.

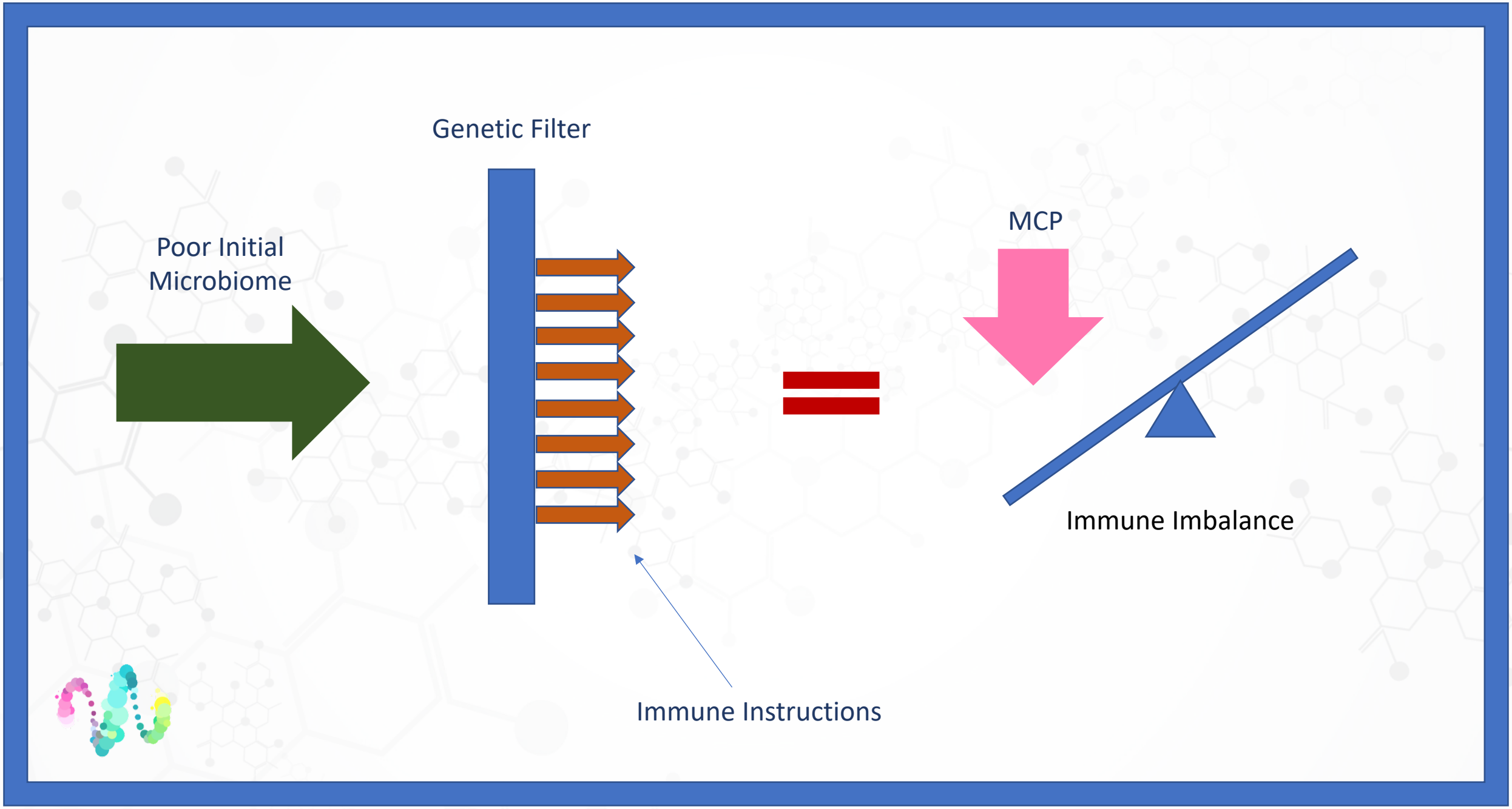
Social Stress Affects Colonic Inflammation, the Gut Microbiome, and Short-chain Fatty Acid Levels and Receptors

Results: Stress exposure reduced colonic SCFA levels. Stress exposure and C rodentium, however, significantly increased SCFA levels and changed the expression of SCFA receptors. The levels of SCFAs did not correlate with the severity of colonic inflammation, but the colonic expression of the SCFA receptor GPR41 was positively associated with inflammatory cytokines and colonic histopathology scores. The relative abundances of several taxa of colonic bacteria were significantly changed by stress exposure, including SCFA producers.

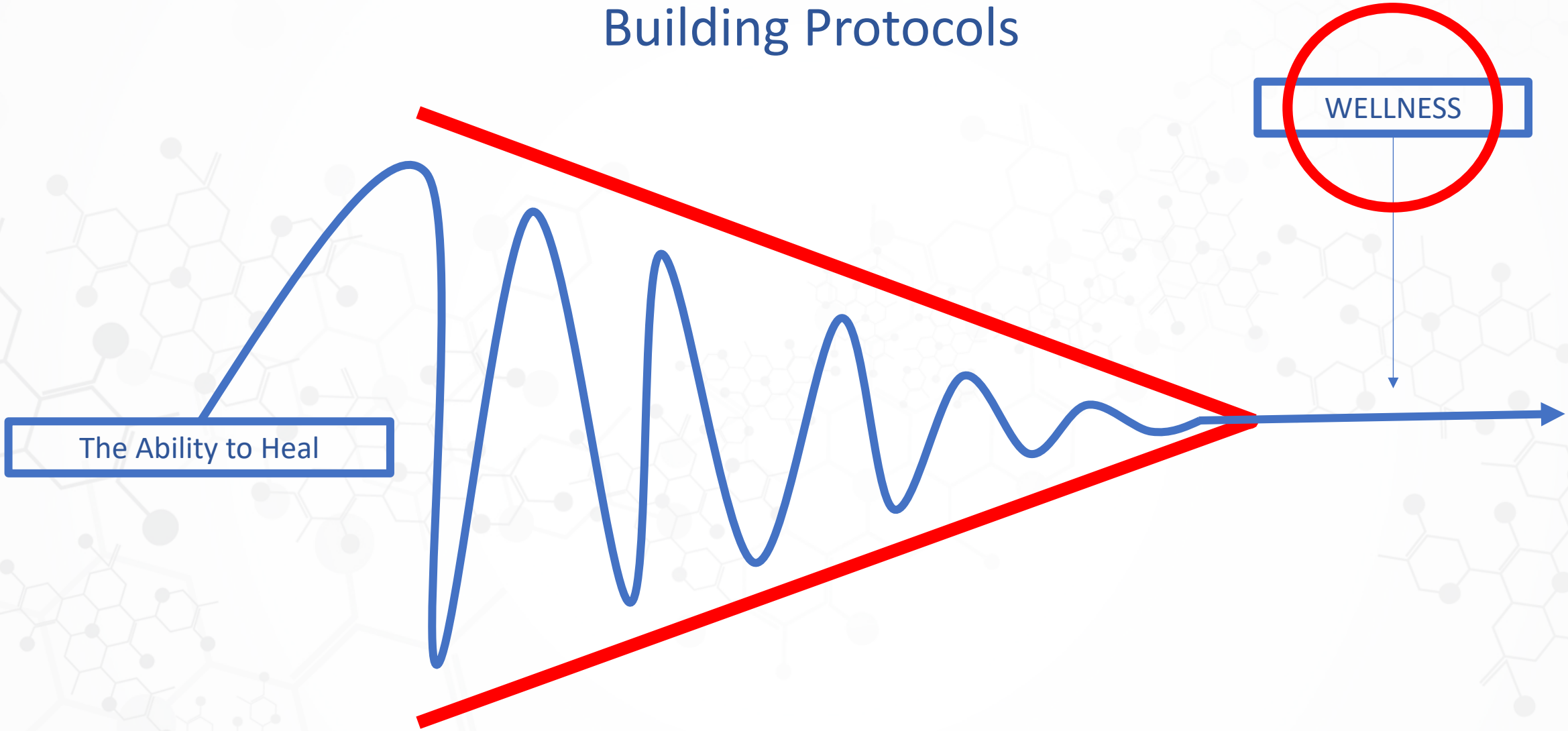
Conclusions: Social stress can have a significant effect on infection-induced colonic inflammation, and stress-induced changes in microbial-produced metabolites and their receptors may be involved.

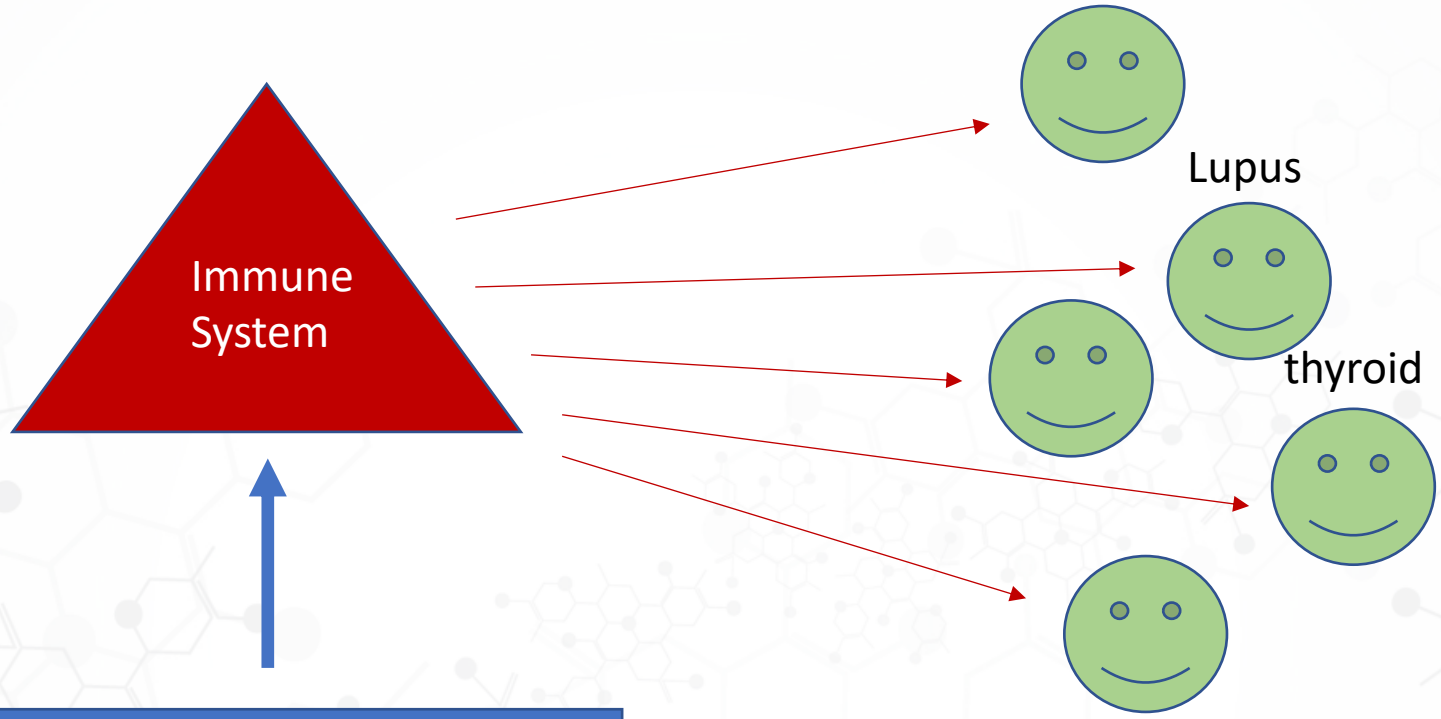

Genetic Filter
Proper Initial Microbiome
Immune Balance
Immune Instructions


Genetic Filter
Poor Initial Microbiome
Immune Imbalance
Immune Instructions

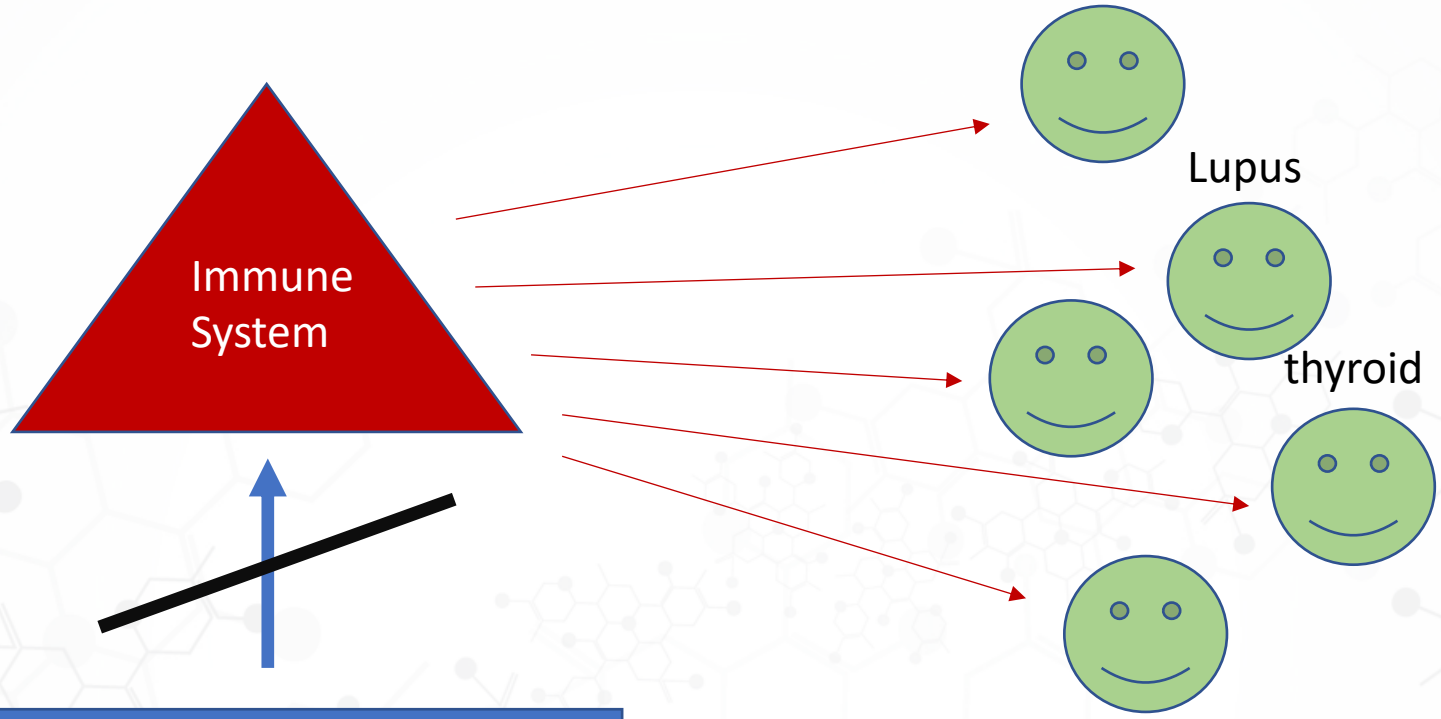

Genetic Filter
Poor Initial Microbiome
MCP
Immune Imbalance
Immune Instructions

Building Protocols





Lifestyle:
Microbiome
Hormone Surges
Glucose Balance
Infection
Food
Organic Dysfunction
Emotional balance, etc….



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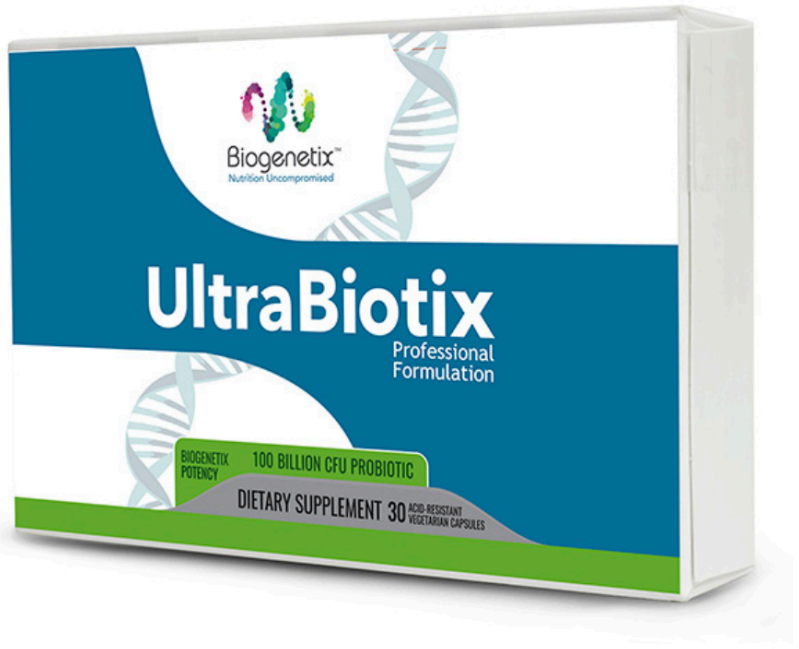
Phase 2 Intervention



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