The Impact of Human Microbiota in Ocular Inflammation

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Abstract

Microbiota corresponds to the microbial associates that exist in the human body, and the genes they encode, the microbiome. Recent advances in genetic techniques are contributing to a better microbiota characterization. Imbalance in the intestinal microbiota - dysbiosis - is associated with several pathologies and reveals its important role as immunomodulator. These developments are particularly significant in ocular immunology, revealing physiopathologic mechanisms and identifying potential therapeutic targets.

Introduction

An immeasurable amount of commensal microbes colonize the skin and mucosal surfaces. Together, the microbial associates that exist in the human body constitute the microbiota, and the genes they encode, the microbiome [1]. Referred to as our “forgotten organ”, the microbiota appears to play a major role in health and disease [2]. Recent advances in next generation sequencing (NGS) technology have enabled to characterize the human microbiota, with unprecedented resolution, and to identify possible related etiopathogenic mechanisms [3]. In this review, the authors give an overview of the current understanding of the microbiota and its potential impact on ocular health.

Table 1: Terms commonly used in the study of the microbiota [25].

| Term       | Meaning                                           |
|------------|--------------------------------------------------|
| Dysbiosis  | Microbial imbalance                              |
| Entero-type| Stratification based on the intestinal microbiota |
| Microbiome | Collection of the genomes of the microorganisms found on the host |
| Microbiota | Community of microorganisms found on the host    |
| Probiotic  | Dietary supplement containing live beneficial bacteria |

Factors Affecting Normal Microflora

Commensal microflora or microbiota consists of the microorganisms present on body surfaces covered by epithelial cells. These micro-organisms co-evolve with their hosts, however, under specific conditions they can overcome protective host responses and exert pathologic effects [4]. Several factors are known to favor the growth of relatively aggressive resident bacteria at the expense of beneficial commensals, leading to dysbiosis. Among them are aging, diet, antibiotic use patterns, exercise, smoking, public health measures and infections [5-7].

Intestinal Permeability and the Microbiota

Dysbiosis seems to modify intestinal mucosal permeability. The interaction between intestinal microbiota and the mucosal wall is mediated by the same receptors which can recruit effector Th cells and activate innate immunity ensuing inflammation [8]. Zonulin modulates the permeability of intestinal tight junctions and consequently is a marker for enhanced intestinal permeability. Lamprecht, et al. [9] showed that probiotic supplementation decreased Zonulin in feces adding more information on the dysbiosis role on increased intestinal permeability [9]. Accordingly, increased intestinal permeability is associated with autoimmune disease including ankylosing spondylitis, multiple sclerosis and autoimmune hepatitis [10-12].

Microbiota and Systemic Autoimmune Disease

It is theorized that dysbiosis may facilitate autoimmunity at both barrier sites and internal organs. Complex interactions
between genetics, environment, and the microbiota outline the inflammatory status and this encroaches autoinflammatory and autoimmune diseases [13]. Several animal models support a connection between intestinal bacteria and arthritis. On the one hand, germ-free rats developed severe joint inflammation in an adjuvant-induced arthritis model when compared to conventionally raised controls, suggesting that the gut microbiota may have important immunosuppressive effects [13]. On the other hand, it was reported the proarthritogenic role of Bacteroides species when introduced into germ-free arthritis-prone rats [14] (Figure 1).

In this study, the severity of the uveitis was modulated with oral antibiotics raising the idea of using a short course of antibiotics followed by repopulation of the intestine with beneficial species to mitigate disease severity.

**Ocular Surface Microbiota**

Most of the studies evaluating ocular surface microbiota have been performed with older technology that could not access for accurate biodiversity. However, more recent studies with NGS technology, found that healthy ocular surface microbiota is paucibacterial when compared to adjacent skin and different mucosa [22]. Greater bacterial counts are present in contact lens wear and dry eye disease [23-24].

**Conclusion**

There is increasing evidence that the microbiota has potent immunoregulatory functions, consequently, investigation with respect to ocular inflammatory diseases is wide open and auspicious.

**References**

1. Clemente JC, Ursell LK, Parfrey LW, Knight R (2012) The impact of the gut microbiota on human health: an integrative view. Cell 148(6): 1258-1270.
2. O’Hara, A M and F Shanahan (2006) The gut flora as a forgotten organ. EMBO Rep 7(7): 688-693.
3. Jovel J, Jordan Patterson, Wetwe Wang, Naomi Hotte, Sandra O’Keefe, et al. (2016) Characterization of the Gut Microbiome Using 16S or Shotgun Metagenomics. Front Microbiol 7: 459.
4. Tlaskalova-Hogenova H, Stepánková R, Hudcovic T, Tucková L, Cukrowska B, et al. (2004) Commensal bacteria (normal microflora), mucosal immunity and chronic inflammatory and autoimmune diseases. Immunol Lett 93(2-3): 97-108.
5. Sartor RB (2001) Intestinal microflora in human and experimental inflammatory bowel disease. Curr Opin Gastroenterol 17(4): 324-330.
6. Wu GD, Chen J, Hoffmann C, Bittinger K, Chen Y Y, et al. (2011) Linking long-term dietary patterns with gut microbial enterotypes. Science 334(6052): 105-108.
7. Luc Biedermann, Jonas Zeitz, Jessica Mwinyi,Eveline Sutter-Minder, Ateequr Rahman, et al. (2013) Smoking cessation induces profound changes in the composition of the intestinal microbiota in humans. PLoS One 8(3): e59260.
8. Marasco G, Di Biase AR, Schiumerini R, Eusebi LH, Iughetti L, et al. (2016) Gut Microbiota and Geliac Disease. Dig Dis Sci 61(6): 1461-1472.
9. Lamprecht M, Bogner S, Schippinger G, Steinbauer K, Fankhauser F, et al. (2012) Probiotic supplementation affects markers of intestinal barrier, oxidation, and inflammation in trained men; a randomized, double-blinded, placebo-controlled trial. J Int Soc Sports Nutr 9(3): 45.
10. Buscarini MC, Cerasoli B, Annibali V, Polciano C, Lionetto L, et al. (2017) Altered intestinal permeability in patients with relapsing-remitting multiple sclerosis: A pilot study. Mult Scler 23(3): 442-446.
11. Lin R, Zhou L, Zhang J, Wang B (2015) Abnormal intestinal permeability and microbiota in patients with autoimmune hepatitis. Int J Clin Exp Pathol 8(5): 5153-5160.
12. Martínez-Gonzalez O, Cantero-Hinojosa J, Paule-Sastre P, Gómez-Magán JC, Salvatierra-Ríos (1994) Intestinal permeability in patients with ankylosing spondylitis and their healthy relatives. Br J Rheumatol 33(7): 644-647.
13. Kohashi O, Kuwata J, Umehara K, Uemura F, Takahashi T, et al. (1979) Susceptibility to adjuvant-induced arthritis among germfree, specific-pathogen-free, and conventional rats. Infect Immun 26(3): 791-794.

14. Rath HC, Herfarth HH, Ikeda JS, Grentzer WB, Hamm TE, et al. (1996) Normal luminal bacteria, especially Bacteroides species, mediate chronic colitis, gastritis, and arthritis in HLA-B27/human beta2 microglobulin transgenic rats. J Clin Invest 98(4): 945-953.

15. Ruff WE, MA Kriegel (2015) Autoimmune host-microbiota interactions at barrier sites and beyond. Trends Mol Med 21(4): 233-244.

16. Wildner G, U Kaufmann (2013) What causes relapses of autoimmune diseases? The etiological role of autoreactive T cells. Autoimmun Rev 12(11): 1070-1075.

17. Cho I, MJ Blaser (2012) The human microbiome: at the interface of health and disease. Nat Rev Genet 13(4): 260-270.

18. Scher JJ, Ubeda C, Artacho A, Attur M, Isaac S, et al. (2015) Decreased bacterial diversity characterizes the altered gut microbiota in patients with psoriatic arthritis, resembling dysbiosis in inflammatory bowel disease. Arthritis Rheumatol 67(1): 128-139.

19. Consolandi C, Turroni S, Emmi G, Severgnini M, Fiori J, et al. (2015) Behcet's syndrome patients exhibit specific microbiome signature. Autoimmun Rev 14(4): 269-276.

20. Horai R Zárate-Bladés CR, Dillenburg-Pilla P, Chen J, Kieczewski JL, et al. (2015) Microbiota-Dependent Activation of an Autoreactive T Cell Receptor Provokes Autoimmunity in an Immunologically Privileged Site. Immunity 43(2): 343-353.

21. Nakamura YK, Christina Metea, Lisa Karstens, Mark Asquith, Henry Gruner, et al. (2016) Gut Microbial Alterations Associated With Protection From Autoimmune Uveitis. Invest Ophthalmol Vis Sci 57(8): 3747-3758.

22. Dooan T, Akileswaran L, Andersen D, Johnson B, Ko N et al. (2016) Paucibacterial Microbiome and Resident DNA Virome of the Healthy Conjunctiva. Invest Ophthalmol Vis Sci 57(13): 5116-5126.

23. de Paiva CS, Dan B Jones, Michael E Stern, Fang Bian, Quianta L Moore, et al. (2016) Altered mucosal Microbiome Diversity and Disease Severity in Sjogren Syndrome. Sci Rep 6: 23561.

24. Zhang H, Zhao F, Hutchinson DS, Sun W, Ajami NJ, et al. (2017) Conjunctival Microbiome Changes Associated With Soft Contact Lens and Orthokeratology Lens Wearing. Invest Ophthalmol Vis Sci 58(1): 128-136.

25. Rosser EC, C Mauri (2016) A clinical update on the significance of the gut microbiota in systemic autoimmunity. J Autoimmun 74: 85-93.