Skin Commensals Regulate Skin Immunity

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A wide array of commensal microbes harbors the mammalian body that helps in digestion, immunity and tissue development. Such relationships between the microbiota and the host are believed to have formed ever since the evolution of eukaryotes. The symbiont hypothesis suggesting the descent of organelles like mitochondria and chloroplast from prokaryotes is yet another example of such interactions. Studies have shown that as the eukaryotes became complex, these microbes too clustered into diverse communities, inhabited different niches and benefited the host in various life processes such as digestion (breakdown of complex carbohydrates and proteins), immunity and tissue development [1]. Further evidence came up when germ free (GF) animals became available which showed abnormalities in the development of tissues like GALT (gut associated lymphoid tissue), Peyer's patches and even affected the integrity of the intestinal epithelial cells in absence of microbiota. Recent research has revealed the role of microbiota in shaping the evolution of adaptive immune system [1] by sending signals and modulating the immune response; and letting the cells to distinguish pathogenic microbes from the symbiotic dwellers. Adding to this is the observation that dysbiosis of skin microbiota is linked with the development of skin disorders such as psoriasis, atopic dermatitis and rosacea [2].

Not only has recent studies given better understanding of these commensals but has also shed light on their diversity and distribution within the body of the host. Earlier culture techniques allowed study of only those microorganisms that could be grown under laboratory conditions, but now, with

the use of 16S ribosomal RNA gene phylotyping, identification of many other micro-organisms that dwell within diverse communities has become possible [3]. This community diversity varies and also depends on its location like the skin which is characterized into three micro-environments: (i) Sebaceous-glabella, alar crease, external auditory canal, occiput, upper chest and back; (ii) Moist-nare, axillary vaults, antecubital fossa, interdigital web space, inguinal crease, gluteal crease, popliteal fossa, plantar heel and umbilicus; (iii) Dry-volar forearm, hypothenar palm and buttock [3]. The common bacteria that constitute the microbiota belong to the following phyla: Actinobacteria (36.6 %), Firmicutes (34.3 %), Proteobacteria (11.9 %), Bacteroidetes (9.5 %) [4]. Microbiota that dwells deep in the dermis layers and hair follicles help in recolonization of the epidermis, upper portion of hair follicles and sebaceous glands and produce by-products that coat the hair follicles and skin of the host, these microbial products exert immunoregulatory effects [5].

Recently Dr. Yasmine Belkaid's team at US National Institute of Allergy and Infectious Diseases in Bethesda has described the effect of resident commensals on skin immunity [6]. They conducted tests on two mice—one GF that was raised under aseptic conditions and simultaneously on the other which was specific pathogen free (SPF) with a normal skin microbiota. Their findings indicated that immunoregulatory molecules like various cytokines were more abundant in SPF mice than in GF mice, the release of which affected and modulated the function of various T cell subpopulations and other immune cells to mount an immune response [6]. Additionally, screening was done to detect the contribution of gut flora in eliciting immune response [6]. For this, segmented filamentous bacteria was used to infect GF mice which restored cytokine level in the gut to that of SPF mice but no such restoration was seen in the skin of GF mice. Also oral antibiotic treatment and skin

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commensal *Staphylococcus epidermidis* was used on the mice subjects which concluded that the gut and skin microbiota did not play role in immune response of each other; i.e. gut flora did not affect the cutaneous immune response and vice versa [6]. The GF mice were also infected with *Leishmania major* and they found that immune response mounted was severely impaired as compared to the response mounted by SPF mice. The reason for this was attributed to reduction in the production of cytokines interferon- γ and tumor necrosis factor- α by the cutaneous T cells. Thus, cutaneous commensals produce cytokines that are necessary for generation of normal skin immune response [6]. Also, by the use of mice deficient in interleukin-1 receptor (IL-1R) and its downstream signaling complex MyD88 they were able to determine the role of IL-1R as signaling molecule that was being contributed by the skin commensals for the generation of other cytokines taking the immune response further. Thus, these commensals are able to establish and maintain a state of T cells for proper immune functioning by providing essential cytokine environment [6].

Such studies have not only enabled us to understand the important role played by skin commensals but further investigations will add to our knowledge of many other skin disorders. This in turn would help in improving human health by contributing towards development of better tissue

specific adjuvants and vaccine approaches [6]. Moreover, characterization of the microbiota will also help us in understanding the delicate balance between healthy skin and diseased conditions.

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