Post-Graduate Course: Microbiome and omics in allergy

Skin Microbiota and Atopic Dermatitis

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Atopic Dermatitis(AD) is a chronic recurrent inflammatory skin disease affecting up to 10~30% of population, with more prevalence in children. Severely dry skin is a hallmark of AD. This results from compromise of the epidermal barrier, which leads to excess transepidermal water loss, allergen penetration, and microbial colonization.

The skin is a dynamic and complex ecosystem characterized by different environmental niches, which are inhabited by heterogeneous microbial communities. The healthy skin microbiome include hundreds of species, and its composition displays a inter- and intra-personal variability and site-specific variability. Also, the microbiome composition varies by layer of the skin and changes with skin barrier disruption. Recent advance in culture-independent methods to study microbial communities has increased our understanding of the microbiome and its impact in health and disease.

In normal skin, 19 different bacterial phyla most of which fall into the following phyla: Actinobacteria, Firmicutes, Proteobacteria and Bacteroidetes,were detected. Within these phyla, *Propionibacerium* and *Staphylococci* species are dominated in sebaceous area(ala crease, glabella, external auditory canal, occiput, manubrium and back) and *Corynebcteria* species predominated in moist sites(nare, axillary vault, antecubital fossa, interdigital web space, inguinal crease, gluteal crease popliteal fossa, planter heel, umbilicus). In dry site(volar forearm, hypothenar palm and buttock), a mixed population of micorbiome resided. Human skin microbiome develop and change over time. Skin microbiome colonization begins during the birthing process and regardeless of delivery method, the newborn skin microbiome is remarkably less diverse than the adult skin microbiome. As infants come into contact with various environmental microbiota and their skin develop distinct characteristics, distinct skin microbial composition arise and becoming diverse over time.

Dysbiosis in the skin microbiome often alters skin health and is linked to atopic dermatitis and other similar disorders of the skin such as psoriasis, eczema, acne. Conventional culture-based work has shown that skin dysbiosis is a another hallmark of AD, 70-90% of lesional and 30-90% non-lesional skin sites are

colonized by *Sta. aureus*, which adversely affects disease severity. Therefore, treatment with clinical improvement is associated with a reduction in the colonization of *Sta. aureus*. Other microbes such as *Propionibacterium*, *Streptococcus*, *Acinetobacter* and *Malassezia* have been bound to be implicated in AD dysbiosis. A birth cohort study showed that absence of early colonization with commensal Staphylococci might precede AD presentation and another animal study indicated that skin dysbiosis was a driving factor in pathogenesis of eczema. This alteration in surface microbial composition in AD is due to dysfunction of the skin barrier caused by the mutations in the gene that encodes for filaggrin, a protein involved in cornification . Increase in *S. aureus* colonization may induce the availability of *S. aureus* binding receptors, decreases in the expression of antimicrobial peptides (AMPs), and elevated levels of IL-4 expression. In this regard, the lack of an intact stratum corneum in AD skin could expose extracellular matrix proteins to the surface and promote *S. aureus* colonization. Greater susceptibility to AD may also be attributable to decreased expression of antimicrobial proteins in the skin. Increased levels of irritants and allergens trigger cytokine release, leading to dermal inflammation and expression of AD.

Therefore, applications which can increase microbiome diversity in atopic skin are desirable.