**Functional diversity of CD301b+CD11b+ dermal DCs in**

**IL-17- and IL-4-mediated immune responses of the skin**

**Tae-Gyun Kim, MD, PhD**

Department of Dermatology, Severance Hospital, Cutaneous Biology Research Institute,

Yonsei University College of Medicine, Seoul, South Korea

Dendritic cells (DCs) are heterogeneous groups of specialized antigen-presenting innate immune cells located in almost every tissue of our body. Although the term ‘DCs’ generally represent highly mixed subsets with functional diversity, classical definition of DCs typically designates conventional DCs (cDCs) which arise from hematopoietic stem cell-derived DC-committed progenitors through FMS-like tyrosine kinase 3 ligand (FLT3L)-dependent developmental cascades. cDCs are mainly classified into type 1 (cDC1, CD103+ CD24+ XCR1+ IRF8+) and type 2 (cDC2, CD11b+ CD172α+ IRF4+) subsets according to marker expressions and transcription factor dependency. By applying DC subset-depleting mouse strains to inflammatory skin disease models, it has been demonstrated that different cutaneous DCs play either subset-specific or somewhat redundant roles in a model- and context-dependent manner. Among them, dermal cDC2 subset belongs to a heterogeneous CD11b+ myeloid population within the skin. We and other groups have shown that dermal cDC2 could be further divided into two subpopulations by C-type lectin CD301b (Macrophage galactose N-acetyl-galactosamine-specific lectin 2, Mgl2) expression. Interestingly, CD301b+ cDC2 specifically existed among migratory DCs of the skin, but not in resident DCs of the secondary lymphoid organs. Functional investigation for this distinct subset revealed that CD301b+ dermal cDC2 was essential to driving IL-17- and IL-4-mediated immune responses of the skin. Thus, targeting CD301b+ dermal DCs would be a potential future therapeutic and preventive approach against IL-17- and IL-4-mediated chronic inflammatory skin dermatoses, such as psoriasis and allergic eczema, respectively.