

Harmless $\gamma\delta$ T cells associated with *Corynebacterium* sp. can be harmful during immune dysregulation



Culture of *Corynebacterium* from the skin (culture de *Corynebacterium* sur GTS). Source Manurx27 (own work), Wikimedia Commons

The skin, one of the first lines of immunological defence, is colonised by diverse microbes which play a crucial role in the control of skin immunity. However, only a handful of these microbes have been directly linked to defined immunological processes, particularly under inflammatory conditions.

Research led by Yasmine Belkaid aimed to identify dominant microbe-derived metabolites that have immune modulatory capacity.

Corynebacterium sp. is one of the three most abundant bacterial genera on human skin, and is also abundantly found on mice. However, very little is known about their immunomodulatory effects. Researchers showed a direct relationship between *Corynebacterium sp.* and T cell function. Where increased proportions of IL-17+ $\gamma\delta$ T cells that express low levels of T cell receptor (TCR) (IL-17+ $\gamma\delta$ TCR^{low}) were preferentially observed in the presence of *Corynebacterium accolens* compared with microbial sp.: *E.coli*, *C.albicans*, *S.epidemicidis*.

Riduara et al., showed that IL-17+ $\gamma\delta$ TCR^{low} T cells detected in the presence of *C.accolens* were predominantly V γ 4+, CCR6+ expressing high transcript levels of CCR4 and T cell activation markers (OX40, PD-1 and STAT5). To determine if high levels of IL-17+ $\gamma\delta$ TCR^{low} is generally associated with *Corynebacterium sp.* Riduara et al., inoculated 9 different *Corynebacterium sp.* onto the skin of wild type mice. Surprisingly, they observed high proportions of IL-17+ $\gamma\delta$ TCR^{low} with all screened *Corynebacterium sp.* except *C. amycolatum*, a rare *Corynebacterium* species that does not have mycolic acids. This suggested that mycolic acid from *Corynebacterium sp.* is responsible for induction of IL-17+ $\gamma\delta$ TCR^{low} T cells. To confirm this, they showed that no V γ 4+IL-17+ $\gamma\delta$ TCR^{low} T cells were induced in the presence of mycolic acid-deficient *C.accolens* (Δ 503). Additionally, V γ 4+IL-17+ $\gamma\delta$ TCR^{low} T cells were not responsive to heat killed *C.accolens* nor dendritic cells loaded with lipoarabinomannans, molecules also present on the outer surface of *Corynebacteria*. This confirmed that the presence of the metabolite, mycolic acid, is required for induction of V γ 4+IL-17+ $\gamma\delta$ TCR^{low}.

Finally, researchers also showed that though *Corynebacterium* sp. in healthy mice is not associated with inflammation. V γ 4+IL-17+ γ δ TCR^{low} T cells primed by *Corynebacterium* sp. contribute to increased skin inflammatory pathology in mouse models of experimental psoriasis and obesity.

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