Th17: A New Player to be Considered in Tuberculosis Studies

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Mycobacterium tuberculosis is the main causal agent of tuberculosis among people around the world. According to the World Health Organization (WHO) in its 2011 report, M. tuberculosis causes more than 1.4 million deaths around the world each year. Moreover, an increase of mortality has been observed among people co-infected with HIV. M. tuberculosis is transmitted after inhalation of contaminated droplets that are deposited in the distal alveoli, in this region, alveolar macrophages and dendritic cells ingest the bacteria [1]. One of the main functions of these cells is to destroy the pathogen by forming intracellular compartments such as the phagosome. However, M. tuberculosis has the ability to modulate phagosome maturation and in consequence is in some instances not eliminated.

For years, immunological studies have suggested that T-cell rather than B-cell mediated immunity is related with bacterial contention in animal models, and among infected people [1]. This bias can be justified by the fact that T cell mediated immunity is essential for containment of intracellular pathogens by several mechanisms. One of these mechanisms is related with CD4+ T helper cells. Studies in mice have suggested that an active CD4+ T helper cells 1 (Th1)-mediated response is essential for bacterial containment at the site of infection. This lineage of T cells is dependent of the presence of IL-12 (IL12p40/IL12p35, also named IL-12p70) that is mainly produced by antigen presenting cells such as Dendritic Cells (DCs), monocytes and macrophages; the last one, the principal host for M. tuberculosis. The secretion of IFN-γ characterizes Th1 population that in concert with other Th1 cytokines activates macrophages to destroy the bacteria.

In recent years, a new CD4+ T cells lineage emerged from investigations related with autoimmune diseases and inflammation, independent of IFN-γ, first reported in mouse models, called Th17. Interleukin 17 production (family composed of 6 members IL-17A-F) and lack of IFN-γ secretion characterizes this T cell population. The presence of IL-23 (IL-12p40/IL12p35) and small amounts of TGF-β and IL-6 are required for Th17 differentiation [2]. Evidence suggests that Th17 has a protective role when Th1-Th2 profiles are unable to act, for example against some extracellular pathogen and fungi.

Recent research has tried to determine the role of this new T CD4+ T cells lineage emerged from investigations related with autoimmune diseases and inflammation, independent of IFN-γ, first reported in mouse models, called Th17. Interleukin 17 production (family composed of 6 members IL-17A-F) and lack of IFN-γ secretion characterizes this T cell population. The presence of IL-23 (IL-12p40/IL12p35) and small amounts of TGF-β and IL-6 are required for Th17 differentiation [2]. Evidence suggests that Th17 has a protective role when Th1-Th2 profiles are unable to act, for example against some extracellular pathogen and fungi.

In conclusion, although more in deep research is required for a real understanding of pathology related to Th17 immune response during tuberculosis, this knowledge must be taken into account for rational vaccine design.

References

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