Tacedinaline-Induced Expression of LL37: A Novel Approach to Treating Tuberculosis Infection

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Tuberculosis (TB) is a contagious, airborne bacterial infection that has become the leading cause of death in the world. Approximately one third of the world population is infected with TB, and a colossal 1.7 million deaths occur each year. The lungs are the organs most commonly associated with TB infection. When bacteria enter the lungs, they encounter millions of cells called macrophages that are ready to defend the host. Unfortunately, over the years, mycobacterium tuberculosis (Mtb) has developed an extremely effective strategy to avoid and even take advantage of the host immune response. Therefore, new ideas are being discussed on how to address TB, and one of these ways includes targeting the host immune response to Mtb through host-directed therapeutics. Recent studies in Uganda indicated that there was wide variation in the mRNA expression of the HDAC1 gene. HDACs (histone deacetylases) are a class of enzymes that wind DNA tightly around histones thus, preventing transcription factors from binding to DNA binding sites. This, in effect, hinders the immune response to Mtb. Studies also hinted that tacedinaline, an HDAC1 inhibitor, directs the killing of Mtb in human macrophages. The purpose of this study was to determine the molecular mechanisms by which tacedinaline kills Mtb. It was hypothesized that tacedinaline induces the macrophage expression of anti-microbial peptide LL37 (which is directly toxic to Mtb). This hypothesis was accepted and suggests that LL37 may play a role in the targeting and destruction of Mtb. Tacedinaline shows much promise in the treatment arena and should be further investigated for its effects on the host immune response to tuberculosis.

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