Abstract

J Immunol. 2018 Apr 15;200(8):2563-2570.

Biotin Deficiency Induces Th1- and Th17-Mediated Proinflammatory Responses in Human CD4$^+$ T Lymphocytes via Activation of the mTOR Signaling Pathway.

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BACKGROUND: Biotin (vitamin B7) is essential for human health because of its involvement, as a cofactor, in a variety of critical cellular metabolic reactions. Previous studies have shown that biotin deficiency enhances inflammation, and certain chronic inflammatory diseases are associated with biotin deficiency; however, the mechanisms that mediate the association between biotin status and inflammation are not well understood.

OBJECTIVE AND METHODS: In this study, we examined the effect of biotin deficiency on human CD4$^+$ T cell responses to determine their role in biotin deficiency-associated inflammation.

RESULTS: Our investigations revealed that anti-CD3/CD28-stimulated CD4$^+$ T cells cultured in biotin-deficient medium secreted significantly enhanced levels of the proinflammatory cytokines IFN-γ, TNF, and IL-17. Expression of the transcription factors T-bet and RORγt was increased, whereas Foxp3 expression was decreased, in biotin-deficient CD4$^+$ T cells. The percentage of T regulatory cells was also decreased under biotin-deficient condition. A similar increase in T-bet, RORγt, and proinflammatory cytokine levels, as well as a decrease in Foxp3, was observed in inguinal lymph nodes of mice fed a biotin-deficient diet relative to pair-fed controls. Furthermore, differentiation of CD4$^+$ T cells toward Th1 and Th17 cells was also enhanced. In vitro and in vivo investigations indicated that the increased inflammatory response was due to enhanced activation of the mammalian target of rapamycin signaling pathway in biotin-deficient CD4$^+$ T cells.

CONCLUSION: In summary, these results demonstrate that biotin deficiency enhances the inflammatory responses in CD4$^+$ T cells, which may contribute to inflammation associated with biotin deficiency.

PMID: 29531163

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