



Letter to Editor

BCG, Autoimmune Diabetes and *M. paratuberculosis*

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The recent NPJ Vaccine journal included an article by Kuhlreier, et al. [1], wherein the authors reported that attenuated *Mycobacterium bovis* Bacillus Calmette-Guerin (BCG) given to individuals with autoimmune diabetes (T1DM) resulted in improved control of blood sugars. In a randomized 8-year study diabetics with long-term disease were given two doses of the BCG vaccine; at year three, the intervention group had lowered hemoglobin A1c to near normal levels and this was maintained for the next five years.

BCG, one of the oldest vaccines, was developed for Tuberculosis (TB) protection. Beyond infectious disease, BCG has immuno-stimulating properties that have made it standard therapy for bladder cancer [2].

There is a body of work that links *Mycobacterium Avium* ss. *Paratuberculosis* (MAP) to T1DM along with a number of other inflammatory/autoimmune diseases [3-8]. It purports that shared genetic risk for both mycobacterial infection and T1DM offers a permissive environ for latent MAP infection; and that MAP's immunodominant Heat Shock Protein 65 (HSP65) cross reacts with pancreatic Glutamic Acid Decarboxylase (GAD) through molecular mimicry [8] resulting in anti-GAD antibodies causing an immune mediated destruction of insulin producing islet cells of the pancreas. Humans are mostly exposed to MAP via food from infected animals [9].

The genus *Mycobacterium* includes important pathologic infectious agents causing human and animal diseases. The *M. tuberculosis* complex causes TB in humans and cattle. *M. leprae* causes human leprosy. MAP causes paratuberculosis in ruminant animals and is the

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putative cause of Crohn's disease in humans; it is also associated with T1DM, sarcoidosis, Blau syndrome, multiple sclerosis and autoimmune (Hashimoto's) thyroiditis [6]. Other *Mycobacterium* species are deemed "environmental" [10]. Interestingly, BCG has also been used to vaccinate against *M. leprae* infection-leprosy [11].

This correspondence suggests an alternative explanation: The favorable outcome of the Kuhlreier study was due to BCG curtailing MAP allowing recovery of pancreatic function. Further information on this topic is available on this podcast: <https://www.youtube.com/watch?v=1Mf7KtDquyM>.

Conflict of Interest

I declare potential competing interests in the material discussed in the correspondence as I have an investment interest in Paralab, LLC and MAP/PATH, LLC. Both companies were formed to advance treatments for MAP infections.

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