

# Mathematical Model for the BCG-based Treatment of Type 1 Diabetes

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We introduce a model of immunotherapy treatment, namely the Bacillus Calmette-Guerin (BCG) vaccine, of type 1 diabetes (T1D). The model takes into consideration a clinical interaction network between multiple immune cells and compartments. A set of ordinary differential equations (ODEs) is introduced to capture the connectivity between these variables and clinical presentation of the disease, taking into consideration BCG cells, resting macrophages, activated macrophages, dendritic cells, glucose, autolytic T-cells, and  $\beta$ -cells. Four subsets of the T1D patients and healthy controls that exhibit normal and high-level glucose consumption are evaluated. The results that obtained for mice, suggest that BCG treatment of the T1D patients that follow healthy eating habits normalizes glucose to levels observed in non-diabetic controls. Furthermore, glucose consumption profoundly influences disease progression. The stable equilibrium state with constant glucose levels is not attainable without repeated BCG treatment. This outcome suggests that immunotherapy may modulate molecular and cellular manifestations of the disease but it does not eliminate T1D. Of note, our data indicate that the BCG immunotherapy treatment may benefit healthy controls on a high-glucose diet. One may speculate the preventive BCG treatment to provide long-term health benefits in this specific cohort.