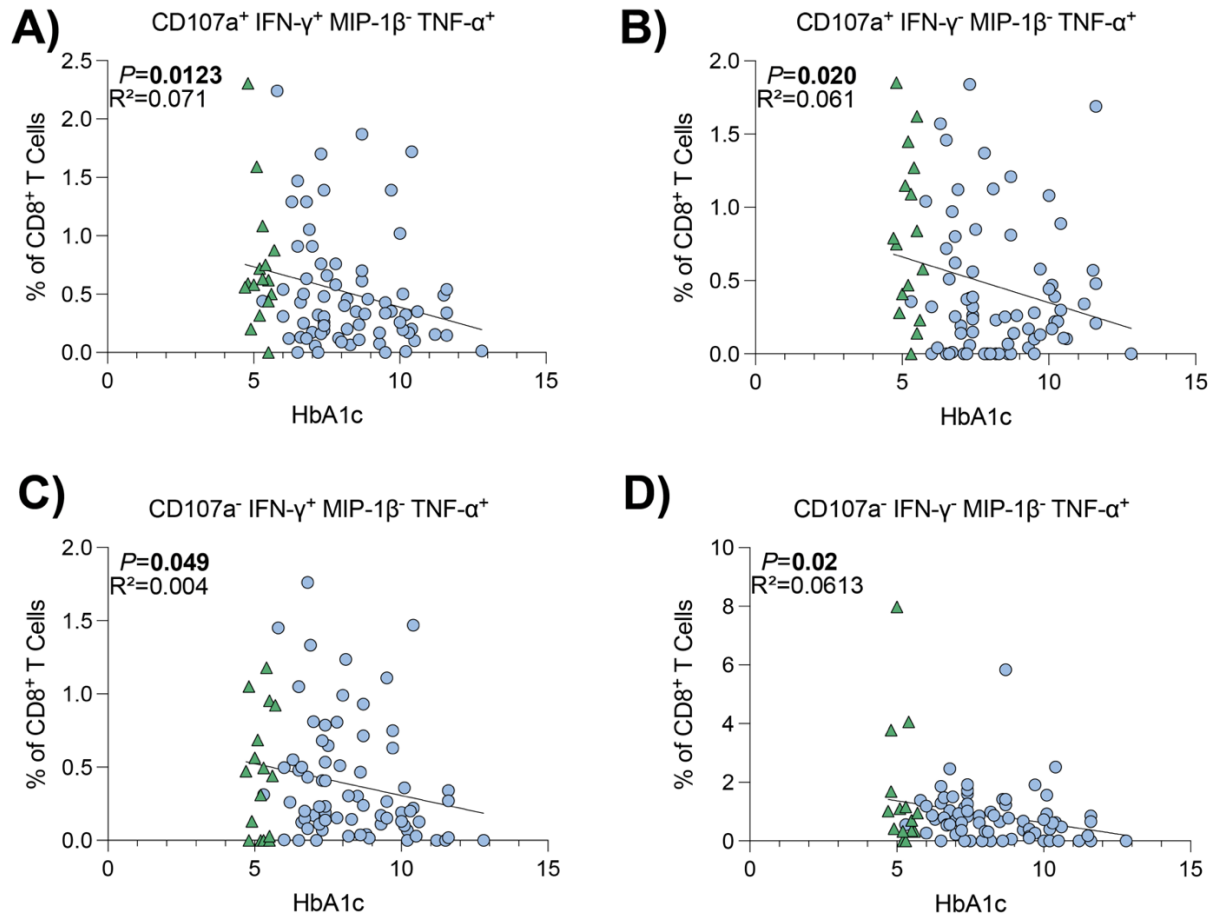


Increasing HbA1c is associated with reduced CD8⁺ T cell functionality in response to influenza virus in a TCR-dependent manner in individuals with diabetes mellitus

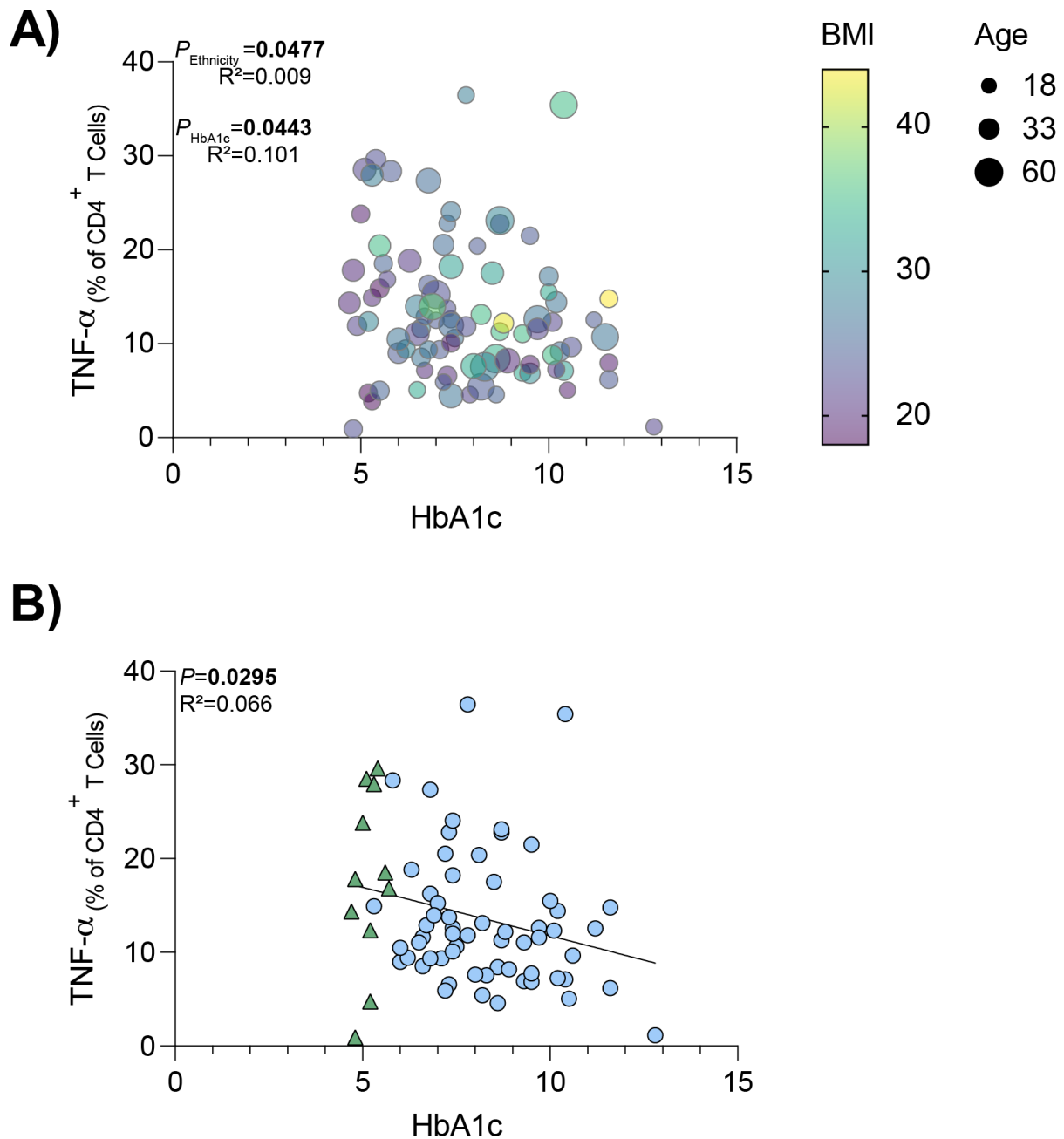
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Supplementary Material



Supplementary Figure 1: TNF- α expression was affected in multiple polyfunctional CD8⁺ T cell populations.

CD8⁺ T cells were stimulated for 18 hours using anti-CD3/anti-CD28 coated beads. Results are presented as the frequency of CD8⁺ T cells expressing the select markers, with background staining subtracted. Data points represent individual donors (n=88). Statistical significance was determined using simple linear regression, with significant P values displayed. **A-D)** Donors without diabetes are represented by green triangles. Donors with diabetes are represented by blue circles.



Supplementary Figure 2: Reduced TNF- α expression associated with increasing HbA1c was also observed in CD4⁺ T cells.

CD4⁺ T cells were stimulated for 18 hours using anti-CD3/anti-CD28 coated beads. Results are presented as the frequency of CD8⁺ T cells expressing TNF- α , with background staining subtracted. **A)** Data points represent individual donors (n=88). Statistical significance was determined using multiple variable regression analysis, where input variables were age, sex, BMI, HbA1c and ethnicity, with significant *P* values displayed. **B)** Relationship between HbA1c and TNF- α produced by CD4⁺ T cells in Caucasian donors. Each data point represents an individual donor (n=73). Statistical significance was determined using simple linear regression. Donors without diabetes are represented by green triangles. Donors with diabetes are represented by blue circles.