Diet and hyperglycaemia affect vaccine immunogenicity and efficacy in mice

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Background

- People with diabetes are more susceptible to TB
- The mechanisms are not well understood.
- The effect of diabetes on vaccine efficacy is unclear.
- This information is essential as vaccines will need to be administered to an increasing pre-diabetic and diabetic population.

Aims and objectives

- Establish two complementary models of hyperglycaemia
- Investigate how hyperglycaemia affects immune responses to BCG vaccination

Methods

Two complementary mouse models of hyperglycaemia were used :

1. C57BL/6 female and male mice were administered a Western Diet (WD - 42 % fat) or high fat diet (HFD – 60 % fat)
2. Inducible mouse model (bV59M) selectively expressing a mutation on K_{ATP} channel of pancreatic β-cells[1]. Hyperglycaemia is induced within 2 days of tamoxifen administration.

Animals were vaccinated with BCG and splenocytes were used to set up immunogenicity and mycobacterial growth inhibition assays (MGIA)

Results

Figure 1: Stronger BCG-specific responses with high-fat diet feeding

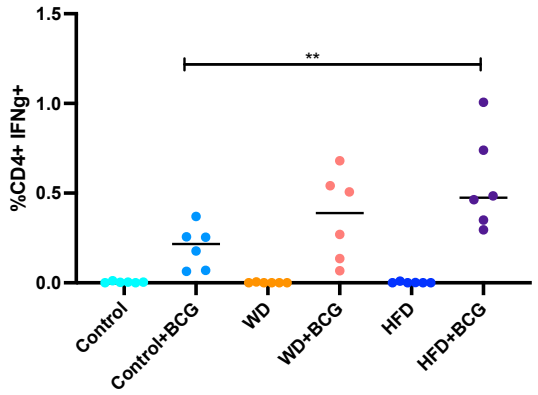


Figure 2: High-fat diet results in better mycobacterial control *in vitro*

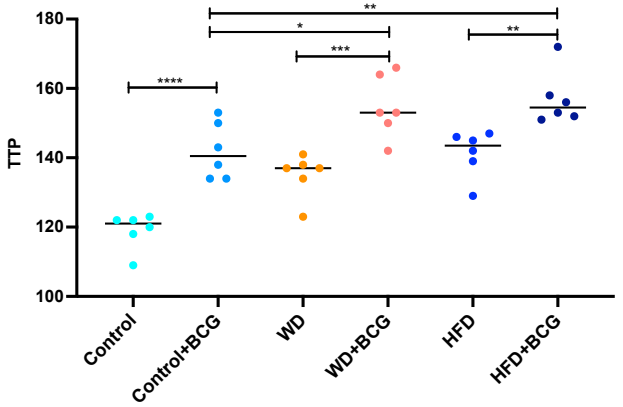


Figure 3: Better glucose control in BCG-vaccinated bV59M animals at moderate levels of hyperglycaemia

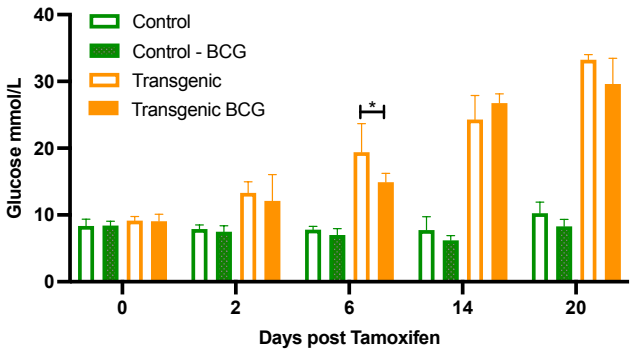
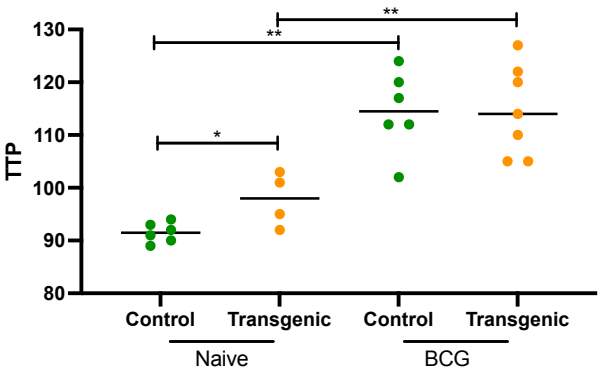


Figure 4: BCG protects mice despite high blood glucose levels



Conclusions

- Short-term high fat diet feeding resulted in higher weight gain and blood glucose levels compared to mice on control diet
- BCG vaccination induced stronger PPD-specific responses in mice fed high-fat diets
- Splenocytes from mice on high-fat diets performed better in an MGIA assay
- BCG-vaccinated bV59M mice had lower levels of blood glucose compared to littermate controls, at moderate, but not at high-levels of hyperglycaemia
- BCG efficacy was equivalent in bV59M and control mice despite the much higher levels of blood glucose

Future work

- *In vivo M.tb* challenge experiments will be conducted on both mouse models
- The two models will be used to assess the immunogenicity and efficacy of live-attenuated and subunit vaccines

References

1. Brereton *et al*. Nature Comms. 2014

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