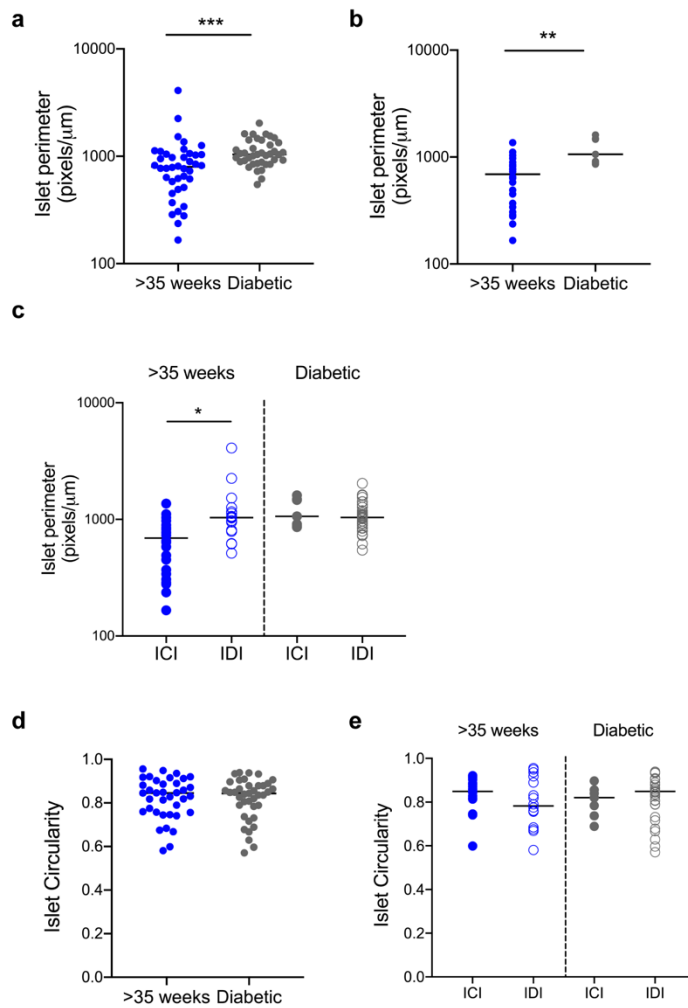


# Supplementary Figure 1

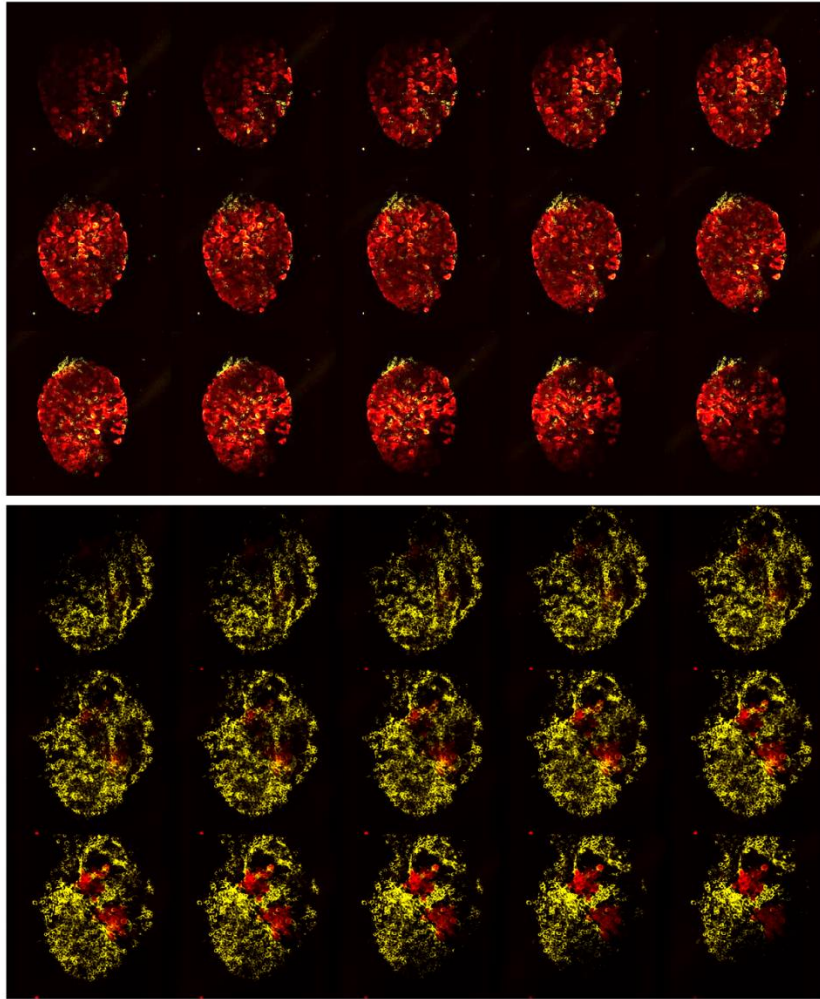


## Supplementary Figure 1. Islet circularity is not altered in protected NOD mice.

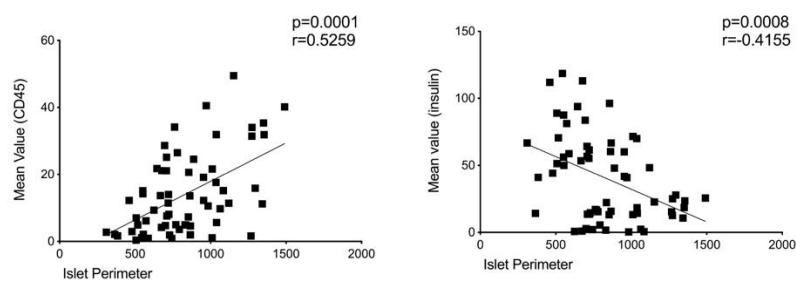
Pancreatic islet wholemounts and sections from naturally protected NOD mice (>35 weeks old; blue) and NOD mice that had developed diabetes (grey) were analysed by immunofluorescence staining. Summary graphs to show (a) islet perimeter (b) islet area for insulin containing islets (ICI) (c) islet perimeter for insulin containing islets (ICI) and insulin deficient islets (IDI) (d) for islet circularity (e) islet circularity (as measured by Image J;  $4\pi \times \text{area} / \text{perimeter}^2$  where a value of 1 is a perfect circle) for insulin containing islets (ICI) and insulin deficient islets (IDI). Data are from at least 2 independent experiments (protected  $n=3$ ; diabetic  $n=4$ ). \* $<0.05$ ; \*\* $<0.01$ ; \*\*\* $<0.001$ ; Kolmogorov-Smirnov test.

## Supplementary Figure 2

a

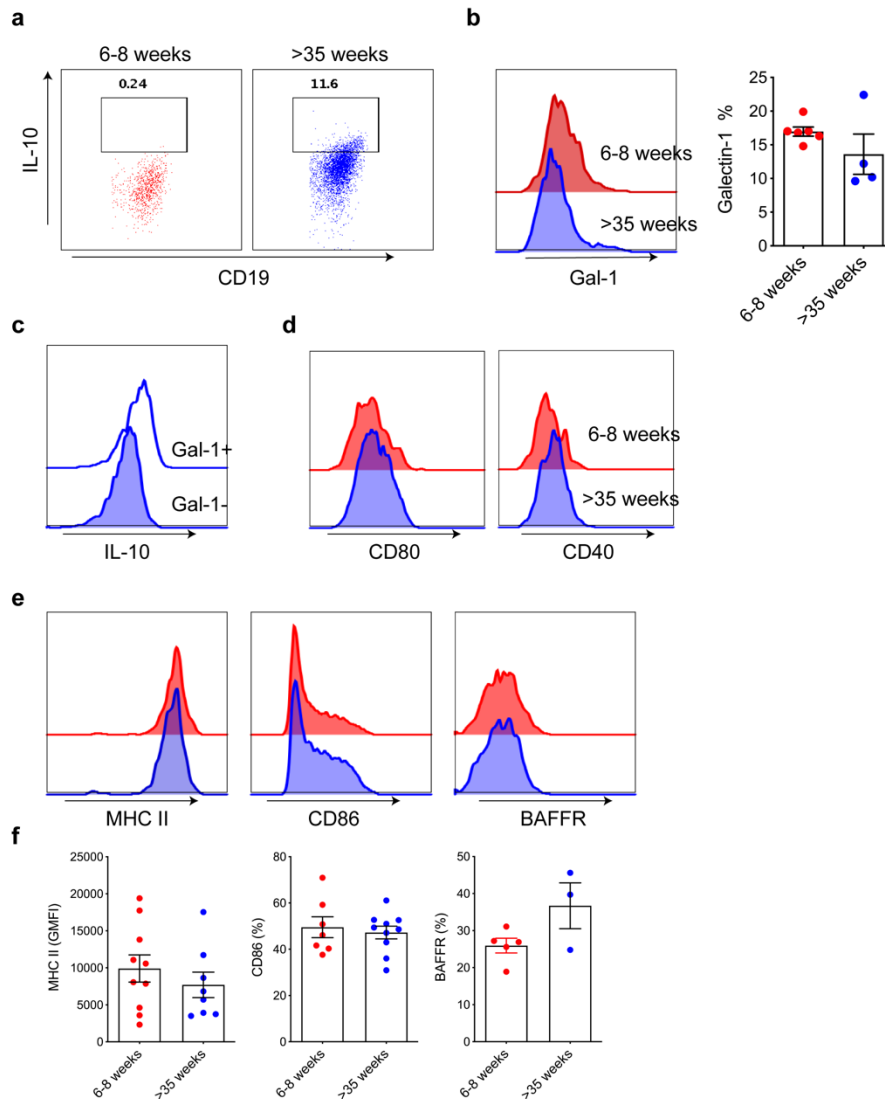


b



**Supplementary Figure 2.** Morphological characterisation of pre-diabetic NOD pancreatic islets. Pancreatic islet wholemounts from NOD mice aged 12-18 weeks were analysed by immunofluorescence staining for the immune marker CD45 (yellow) and beta cell marker insulin (red). (a) Representative montages of islet z-stacks from 2 (top panel, bottom panel) individual NOD mice. (b) Correlative graphs for both CD45 and insulin expression against islet perimeter. Data are from 4 independent experiments, n=8.

### Supplementary Figure 3



**Supplementary Figure 3.** Regulatory B-cells are increased in the islets of naturally-protected NOD mice. Pancreatic islets from groups (n=2-3) of NOD mice aged >35 weeks old (protected; grey) and 6-8 weeks old (younger prediabetic; black) were taken and pancreatic islets pooled together before flow cytometric analysis. (a) Representative flow cytometry plots for IL-10-expressing B cells (b) Histogram (left) and summary graph (right) of total Galectin-1<sup>+</sup> B cells in islets. (c) Histogram showing increased IL-10 expression in Galectin-1<sup>+</sup> B cells compared to Galectin-1<sup>-</sup> B cells. (d) Histograms showing expression of CD80 (left) and CD40 (right) on B cells (e, f) expression of MHC II (left), CD86 (middle), BAFFR (right) on B cells (e) histograms showing average expression (f) summary graphs. Cells were gated on singlets, live, CD3<sup>-</sup>CD11b<sup>-</sup>CD11c<sup>-</sup>CD19<sup>+</sup> populations. Data are from at least 4 independent experiments.