

Extended Data Fig. 3 | Stage-6 SC- $\beta$ -cells express characteristic  $\beta$ -cell markers. a, b, t-SNE projection of stage-6 time-course data shaded by sampling time (a) and by representative marker genes (b). Expression is normalized relative to maximum value and smoothed over neighbouring cells. c, Expression profiles for key genes necessary for  $\beta$ -cell function. Shading displays mean expression (TPM, log-scaled) and diameter denotes fractional expression. d, e, Comparison of global expression between human islet  $\beta$ -cells and in vitro progenitors (d) and SC- $\beta$ -cells (e).

Note the shift in gene expression from progenitors to SC- $\beta$ -cells. All genes shown in all panels from  ${\bf c}$  are circled in red.  ${\bf f}$ , Results from GSEA show that gene sets from  ${\bf c}$  are significantly upregulated during differentiation. Value plotted is  $-\log_{10}$  of the GSEA-reported FDR q-value (capped at 10), with sign (positive or negative) showing the direction of the effect (that is, purple positive values are upregulated in SC- $\beta$ -cells compared to NKX6.1 progenitors).