### **Supplementary File 1:**

**Supplementary Figure 1**: Experimental protocol

**Supplementary Figure 2**: Heatmap showing the expression level of selected genes in the INS+/UCN3+ ( $\beta$ 1-cells), INS+/CD9+ ( $\beta$ 2-cells), INS+/ST8SIA1+ ( $\beta$ 3-cells), INS+/GRHL+, INS+/ARX/GCG+, INS+/PPY+, INS+/STT+ populations extracted from Loupe browser analysis.

**Supplementary Figure 3:** Heatmap showing the expression levels of top 10 highly expressed genes in the 10 clusters identified from the data driven analysis from Loupe browser analysis.

**Supplementary Figure 4:** Enriched KEGG pathways identified by the top 200 representative genes of the PPY+/IAPP+ subpopulation.

**Supplementary Figure 5:** Enriched KEGG pathways identified by the top 200 representative genes of the DPP4+/KDR+ subpopulation.

**Supplementary Figure 6:** Enriched KEGG pathways identified by the top 200 representative genes of the TTR+/GCG+/STT+ subpopulation.

**Supplementary Figure 7:** Enriched GO biological processes identified by the top 200 representative genes of the cycling cell subpopulation.

**Supplementary Figure 8:** (A) Enriched GO biological processes characterized by the top 200 representative genes in the CD9+/SPARC+/REST+ subpopulation. (B) Network of enriched biological processes in the CD9+/SPARC+/REST+ subpopulation.

**Supplementary Figure 9:** Enriched KEGG pathways by the top 200 genes of CD9+/SPARC+/REST+ cell subpopulation

**Supplementary Figure 10:** Enriched KEGG pathways by the top 200 genes of SOX2+/NEUROG3+ subpopulation

**Supplementary Figure 11:** Enriched KEGG pathways by the top 200 genes of HNF1A+/APOA2+ subpopulation

**Supplementary Figure 12:** Enriched KEGG pathways by the top 200 genes of KCNJ3+/TPH1+/MYH4+ subpopulation.

# **Supplementary File 2:**

Supplementary file 2: word file of additional information on bioinformatics analysis

# **Supplementary File 3:**

**Supplementary file 3:** Excel file with cell subpopulation clustering using knowledge-based markers

#### **Supplementary File 4:**

**Supplementary file 4:** Excel file with cell subpopulation clustering using data driven analysis by K-means

#### **Supplementary File 5:**

**Supplementary file 5:** Excel file with cell subpopulation re-clustering from K-means cluster CD9+/SPARC+/REST+ subpopulation