ESM Fig. 1. Enriched functions of DEG sets

Differentially expressed genes (DEGs) were identified between non-diabetic controls and diabetic samples using ChipInspector, and the numbers of the identified DEGs are given below. These DEG sets were subjected to functional enrichment analysis using Database for Annotation, Visualization and Integrated Discovery (DAVID). A heat map of overrepresented biological functions based on significant values (log₂-transformed BH-correct P-values) was generated using the top 10 most overrepresented biological functions within each DEG set. White to red color indexing reflects increasing significance to visually represent similarities and differences between DEG sets.



ESM Fig. 2. Comparisons of kidney and nerve DEGs.

Venn diagrams depicting shared and unique DEGs from glomerulus (Glom) and sciatic nerve (SCN) in type 1 diabetes (a) and type 2 diabetes (b). The pie charts reflect percentages of concordant (same direction; white) and discordant (opposite direction; black) shared DEGs.



ESM Fig. 3. Comparisons of type 1 and type 2 diabetes DEGs.

Venn diagrams depicting shared and unique DEGs from type 1 and type 2 diabetes in glomerulus (Glom) (a) and sciatic nerve (SCN) (b). The pie charts reflect percentages of concordant (same direction; white) and discordant (opposite direction; black) shared DEGs.



ESM Fig. 4. Type 1 diabetes DN vs. type 1 diabetes DPN.

A heat-map of over-represented biological functions among the DEG subsets from the comparison between STZ-Glom (type 1 diabetes DN) and STZ-SCN (type 1 diabetes DPN), based on significant values (log₂-transformed BH-correct P-values). This heat-map corresponds to Fig. 2a.



ESM Fig. 5. Type 2 diabetes DN vs type 2 diabetes DPN.

A heat-map of over-represented biological functions among the DEG subsets from the comparison between db/db-Glom (type 2 diabetes DN) and db/db-SCN (type 2 diabetes DPN), based on significant values (log₂-transformed BH-correct P-values). This heat-map corresponds to Fig. 2b.



ESM Fig. 6. Correlation in the gene expression levels (fold-changes) of the concordant genes between type 1 diabetes DN vs type 2 diabetes DN.

The fold-changes of the concordant genes between STZ-Glom (type 1 diabetes DN) and *db/db*-Glom (type 2 diabetes DN) were examined for their correlation. The Pearson correlation coefficient was r = 0.9552 (R² = 0.9125). T1DM, type 1 diabetes mellitus; T2DM, type 2 diabetes mellitus.



ESM Fig. 7. Type 1 diabetes DN vs type 2 diabetes DN.

A heat-map of over-represented biological functions among the DEG subsets from the comparison between STZ-Glom (type 1 diabetes DN) and db/db-Glom (type 2 diabetes DN), based on significant values (log₂-transformed BH-correct P-values). This heat-map corresponds to Fig. 3a.



ESM Fig. 8. Type 1 diabetes DPN vs type 2 diabetes DPN.

A heat-map of over-represented biological functions among the DEG subsets from the comparison between STZ-SCN (type 1 diabetes DPN) and *db/db*-SCN (type 2 diabetes DPN), based on significant values (log₂-transformed BH-correct P-values). This heat-map corresponds to Fig. 3b.



ESM Fig. 9. Shared transcriptional networks.

A representative transcriptional network shared between DEG sets was identified by Tool for Approximate Subgraph Matching of Large Queries Efficiently (TALE) graph matching program for the four pairs of comparison: STZ-Glom vs. STZ-SCN (*a*), *db/db*-Glom vs *db/db*-SCN (*b*), STZ-Glom vs. *db/db*-Glom (*c*), and STZ-SCN vs. *db/db*-SCN (*d*). The nodes represent the shared genes between two DEG sets and the blue lines (edges) are the connections between the genes. The highly connected genes are aggregated in the center, where the genes with fewer connections are distributed in the middle and outer layer.

(9-a) STZ-Glom vs. STZ-SCN

- Cytoscape network file
 - <u>http://jdrf.neurology.med.umich.edu/DPNDN/Cytoscape/T1DM_shared-sub-network.cys</u>
- Network image file
 - o http://jdrf.neurology.med.umich.edu/DPNDN/Images/STZ-Glom_vs_STZ-SCN.jpg



(9-b) db/db-Glom vs db/db-SCN

- Cytoscape network file
 - <u>http://jdrf.neurology.med.umich.edu/DPNDN/Cytoscape/T2DM_shared-sub-network.cys</u>
- Network image file
 - o <u>http://jdrf.neurology.med.umich.edu/DPNDN/Images/dbdb-Glom_vs_dbdb-SCN.jpg</u>



(9-c) STZ-Glom vs. db/db-Glom

- Cytoscape network file
 - <u>http://jdrf.neurology.med.umich.edu/DPNDN/Cytoscape/Glom_shared-sub-network.cys</u>
- Network image file
 - <u>http://jdrf.neurology.med.umich.edu/DPNDN/Images/STZ-Glom_vs_dbdg-Glom.jpg</u>

For readability the center graph is zoomed in and provided in the red box.





(9-d) STZ-SCN vs. db/db-SCN

- Cytoscape network file
 - <u>http://jdrf.neurology.med.umich.edu/DPNDN/Cytoscape/SCN_shared-sub-network.cys</u>
- Network image file
 - <u>http://jdrf.neurology.med.umich.edu/DPNDN/Images/STZ-SCN_vs_dbdb-SCN.jpg</u>



ESM Fig. 10. Enriched biological functions in the shared networks

A heat map of overrepresented biological functions among the shared transcriptional networks, based on significant values (log₂-transformed BH-correct P-values), was generated using the top 10 most over-represented biological functions. White to red color indexing reflects increasing significance to visually represent similarities and differences between shared transcriptional networks. Glom, glomerulus; SCN, sciatic nerve; T1DM, type 1 diabetes mellitus; T2DM, type 2 diabetes mellitus.



ESM Fig. 11. Distribution of the number of genes belonging to the JAK-STAT pathways from the 1,000 simulated gene datasets against the real data.

This Fig. illustrates the significant difference between the real data and the randomly simulated data in terms of the total number of JAK-STAT-related genes in the shared networks. The comparison between **STZ-Glom** and *db/db*-Glom sets is given in this figure. The shared network derived from the real data set has 38 genes in the JAK-STAT pathway, while the majority of the shared networks obtained from the 1,000 simulated datasets had an average of 10 genes in this pathway.



Histogram of gene count (random sets)