Supplementary Table 1: Dataset of dysregulated genes identified from the study. The table provides details of all those genes which were identified as dysregulated in one or more group comparisons. Columns display the Ensembl Gene ID (Rabbit; Oryctolagus cuniculus); the Gene Symbol (where available). Fold Change and False Discovery Rates (FDR_BH) are given for each group comparison; CDH vs Control; TO vs CDH; TO vs Control. Genes are sorted by the 3 gene clusters (Heatmap Cluster) identified from the hierarchical clustering heatmap shown in Figure 1 and described in the main text. Those genes contained within the significant STEM profiles (see main text) are also labelled with the STEM profile number.

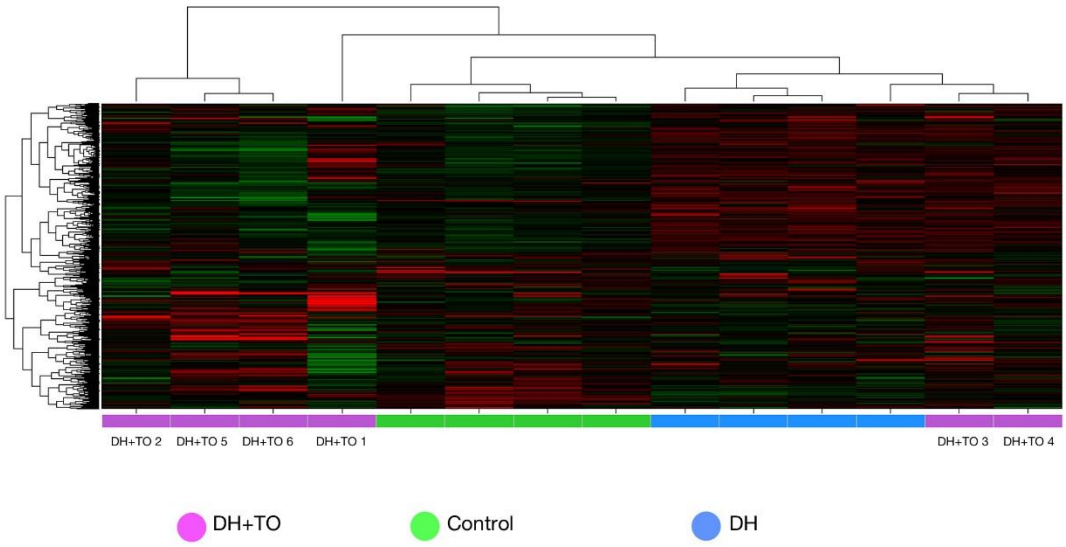
Click here to Download Table S1

Supplementary Table 2: Dataset of affected diseases and gene functions. The table gives an overview of the gene functions and categories that could be affected by the dysregulated genes of supplementary table 1.

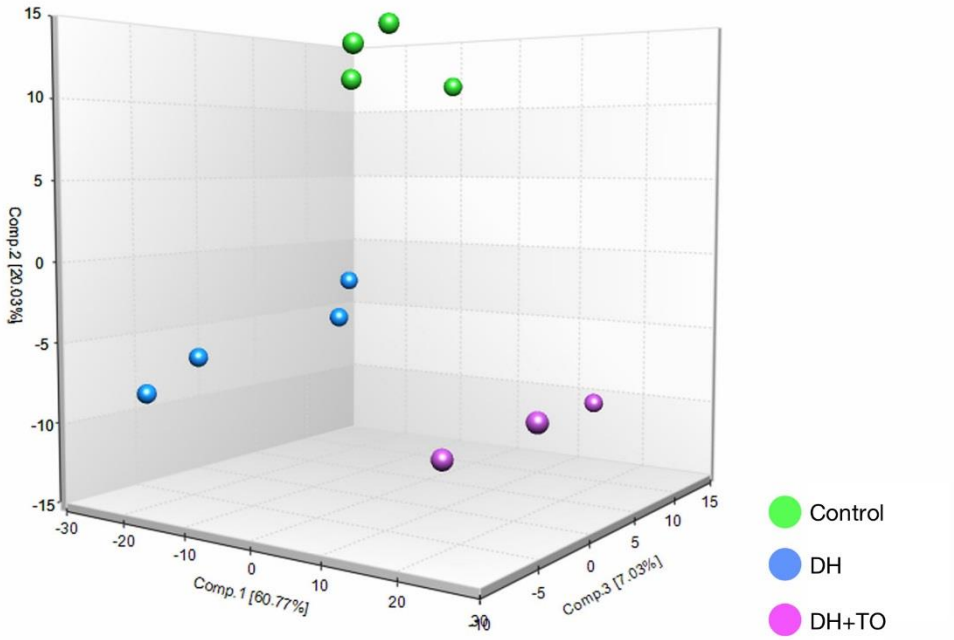
Click here to Download Table S2

Supplementary Table 3: List of genes investigated by qPCR, sequences of the forward and reverse primers and the corresponding PCR efficiencies.

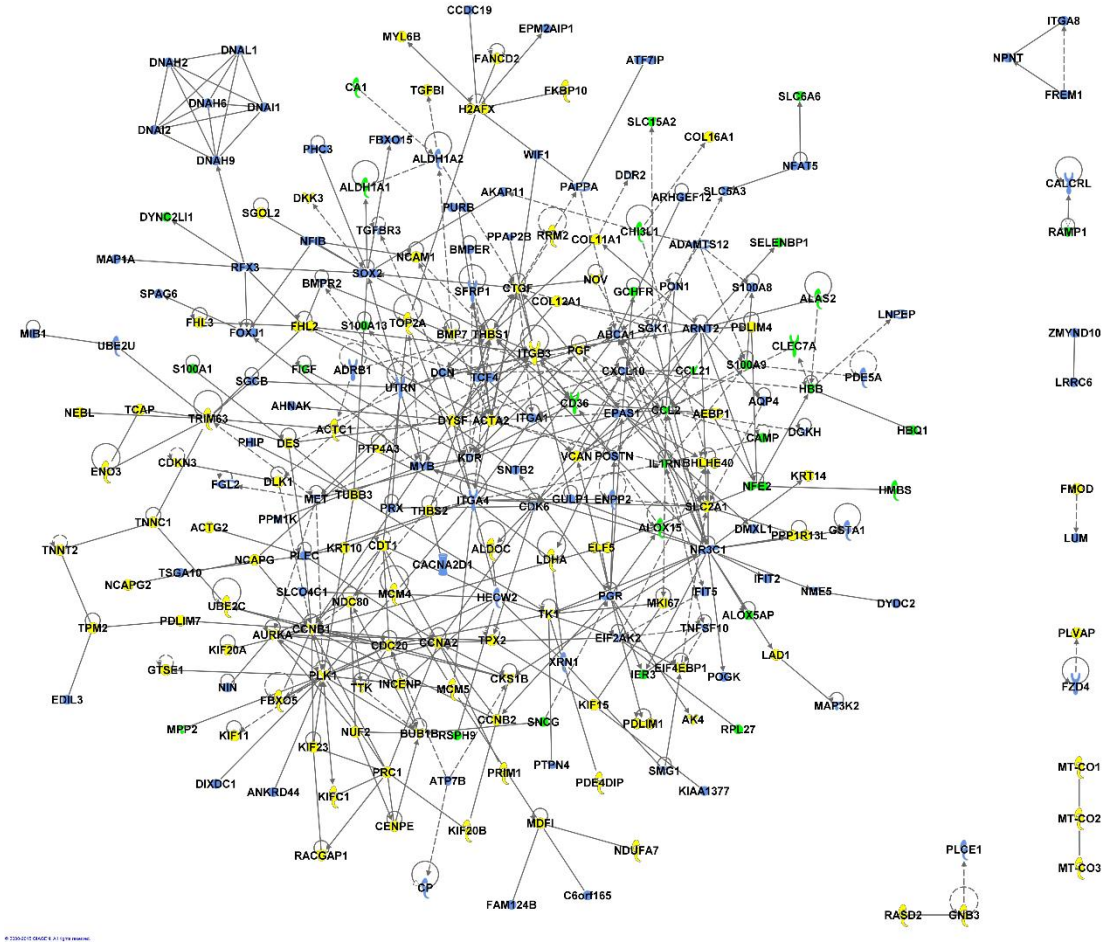
Gene name	Accession number	Forward Primer	Reverse primer	E	R^2
SDHA	ENSOCUG00000023573	CAGAACTGAAGACGGGAGGA	TCGCAGAGACCTTCCATACA	1.96	1
TOP1	ENSOCUG00000008221	TTCTCCAGTCCACCACGAAT	ATCCTCATCCCGAGGTCTCT	2.04	0.999
GAPDH	ENSOCUG00000022054	GAGCTGAACGGGAAACTCAC	AGGTCAGGTCCACGACAGAC	1.95	0.998
RFX3	ENSOCUG00000014086	GCTCAGGTGCAGTATGTGGA	GGCTGTACATCTGGGTTTCTG	1.99	0.994
FOXJ1	ENSOCUG00000011472	GCCACCAAGATCACCCTGT	GTTGTGGCGGATCGAGTT	2.01	0.999
PDE5A	ENSOCUG00000009417	CTTGGGCTACACCAACAACC	CCTCGGTTCAATGCAGAAGT	2.01	0.999
VEGFR2/KDR	ENSOCUG00000005062	GCAAGAAGGGTTTCAGCATC	GCTCACCAGCACGTCATAAA	2	0.999
ACTA2	ENSOCUG00000008193	CATCCAACCCTGTTGACTGA	GAGGCATAGAGGGACAGCAC	1.99	0.989
MKI67	ENSOCUG00000005133	AGGCAGGTGAACAAAAGACC	ATGAGCCCTCCCTATGACAA	1.97	0.996
WIF1	ENSOCUG00000014907	GTATGAACGGCGGACTTTGT	GTCCTGGTGGGCAAATACAT	2.02	0.997
BMPR2	ENSOCUG00000001971	TGTGAACCTGAGGGACTGTG	CAGATTCACCTGGGAAGAGG	1.96	0.999
LRRIQ1	ENSOCUG00000017527	AAGCCCATTGTTCCAGTCC	CTGTCTGCACCTTTCTTCCA	2.08	0.999
SPAG17	ENSOCUG00000007586	CAGCTCCCAAGGTTGCTAAA	CATCATCTGGCTCATCGTCA	2.04	0.999
CCDC39	ENSOCUG00000000812	ACCCGTTCCTCTCTGAAACA	CCCTTTAGCCGTGACATTCT	2.06	0.981
VEGFR1/FLT1	ENSOCUG00000008523	GGCGATTACACCATCTTGCT	AGAGTCGGGTCTGGAAATGA	2.01	0.999



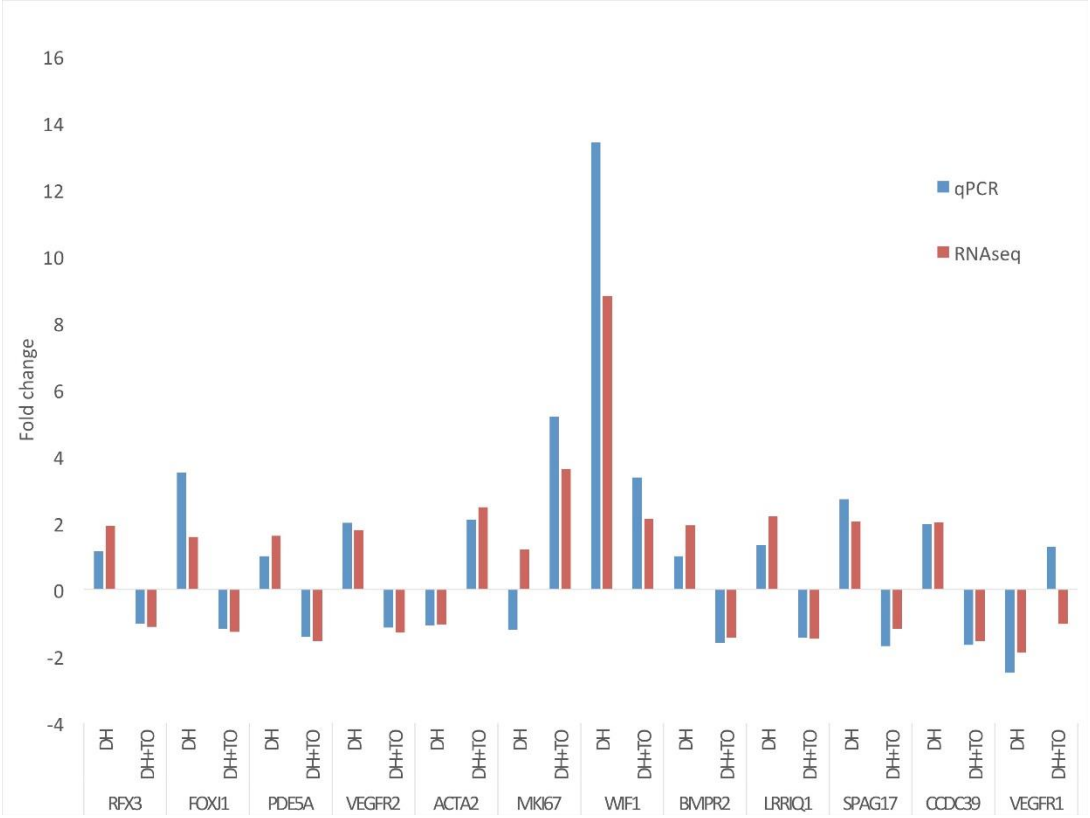
Supplementary Figure 1: Heatmap generated from unsupervised hierarchical clustering of all samples which underwent RNA-Seq. Samples are clustered horizontally, with TO in purple (n=6), Control in Green (n=4), and DH in Blue (n=4). Genes are clustered vertically, with red representing high expression and green representing low expression, with intensity corresponding to expression level. The Control and DH groups cluster together. Samples TO-3 and TO-4 cluster with the DH group and were removed from subsequent downstream analysis, as was sample TO-1 which was deemed a statistical outlier. The heatmap was generated using the Array Studio software, and was applied to Log2 transformed RPKM expression values per gene for each sample which underwent RNA-Seq, and to all those 11,267 genes with expression values >1 RPKM (as described in the Methods section on the text).



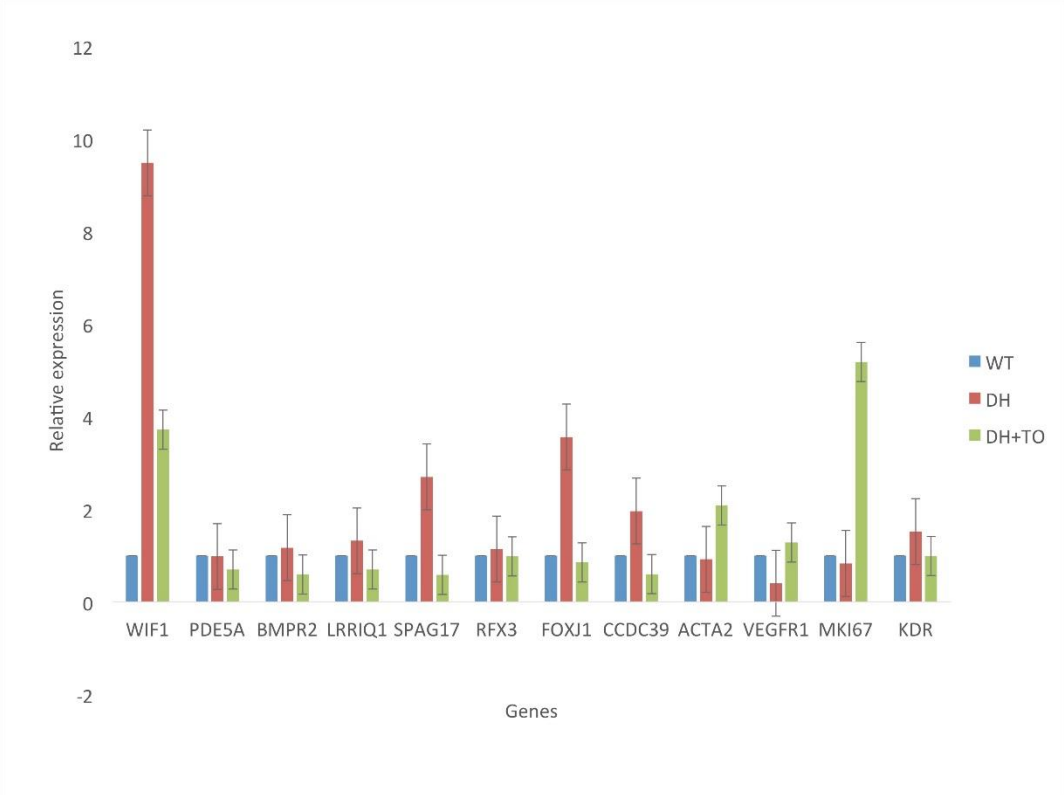
Supplementary Figure 2: Three dimensional PCA plot generated from those samples used for the downstream analysis. Samples are displayed according to component 1 (x-axis), component 2 (y-axis), component 3 (z-axis), with samples for TO in purple (n=3), Control in Green (n=4), and DH in Blue (n=4). The PCA plot was generated using the Array Studio software, and was applied to Log2 transformed RPKM expression values per gene, for all those 641 genes which were dysregulated (as described in the Methods section of the text).



Supplementary Figure 3: Protein-Protein Interaction (PPI) network generated using the IPA web application. Molecules are linked where a known interaction exists, supported by evidence from the literature (i.e. not a predicted interaction). Molecules are coloured to represent the gene cluster in which they are found (see main text for further description of the gene clusters defined from the heatmap in Figure 1, and for which the data is given in Supplementary Table 1). Molecules in gene cluster 1 are coloured in yellow (low expression in both DH and control, and high expression in DH+TO only). Those molecules in gene cluster 2 are coloured in blue (high expression in DH only and low expression in control and DH+TO). Those molecules in gene cluster 3 are coloured in green (high expression in controls, and low expression in both DH and DH+TO). The PPI network was generated from the total of 641 unique genes found to be dysregulated (FC +-2; FDR <0.1) in any group comparison (see main text). 560 of 641 genes mapped within IPA to known functional genes. Molecules with evidenced interactions were linked and any orphan molecules (i.e. those not known to interact with any other in the dataset) were removed, generating the final PPI network displayed in which genes were color coded according to gene cluster.



Supplementary Figure 4: Fold changes of gene expression level in DH and DH+TO group, identified by qPCR and RNA seq. The figure shows similar gene expression variation between the two techniques. Values are shown in relation to the WT expressions.



Supplementary Figure 5: Relative expression determined by qPCR. The increase of LRRIQ1 and RFX3 in DH was not significant and there was no differential expression of BMPR2 and PDE5A in DH group.