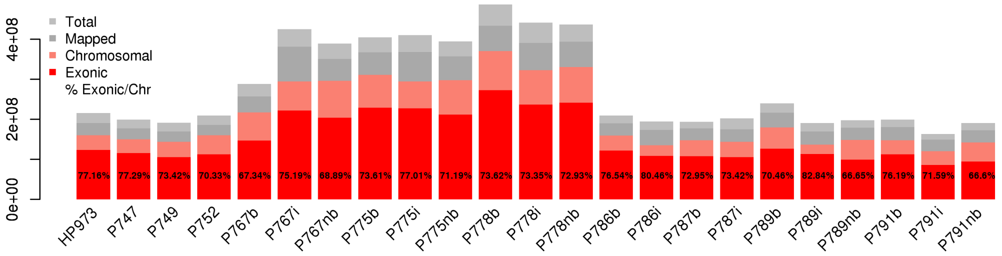
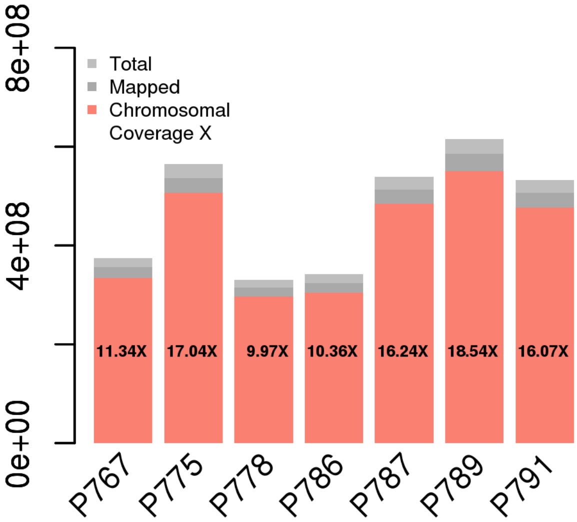
Supplementary Figure 1. Summary of RNA-seq (a) and DNA-seq (b) runs per sample. Barplots show total number of reads, total reads mapped to the genome, chromosomal reads (pairs of reads in right strand orientation and passing a mapping quality filter of 10) and exonic reads (subset of chromosomal reads where both mates of each read pair overlap exons of the same gene).

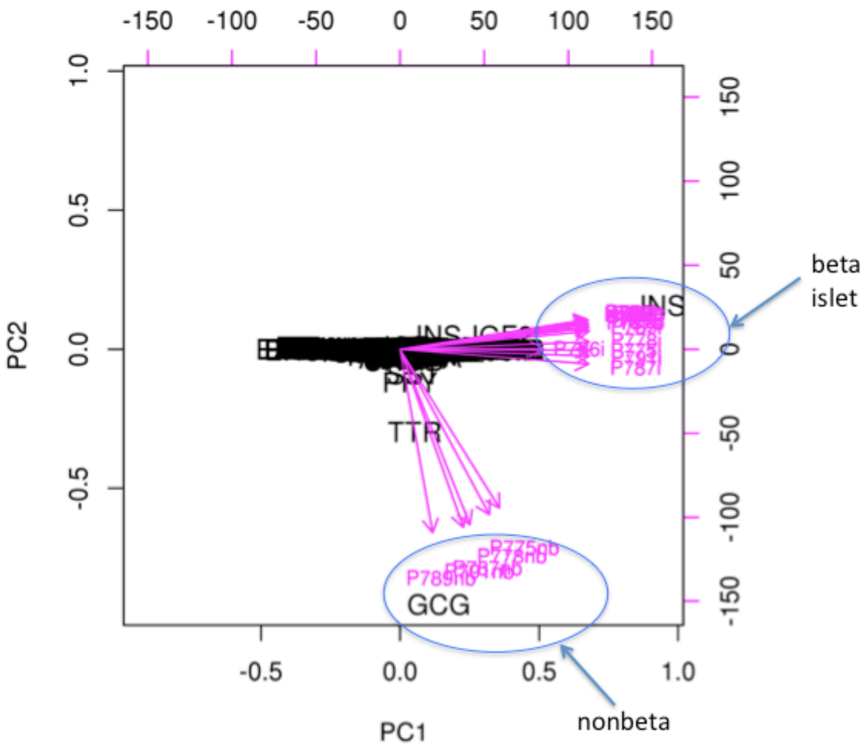
a



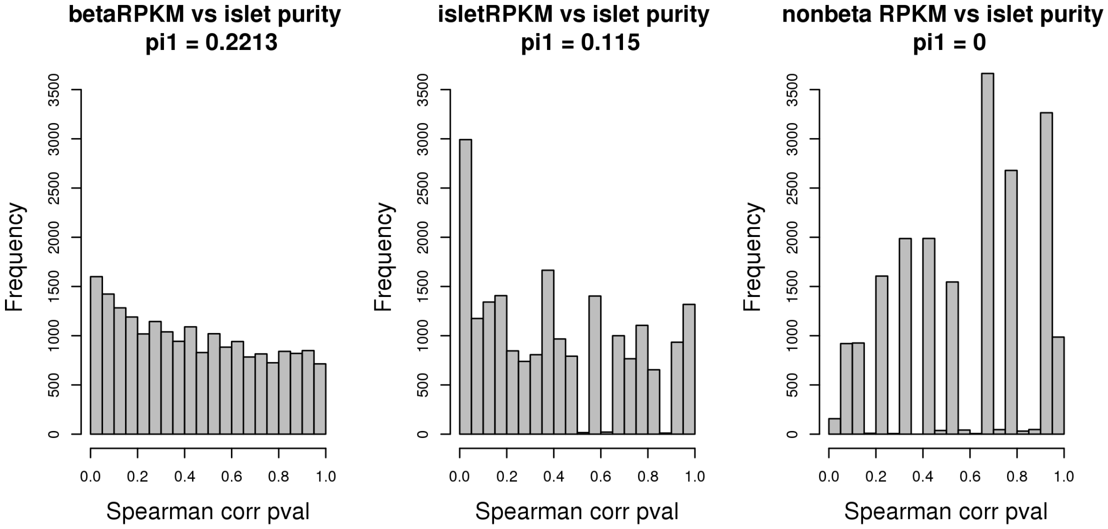
b



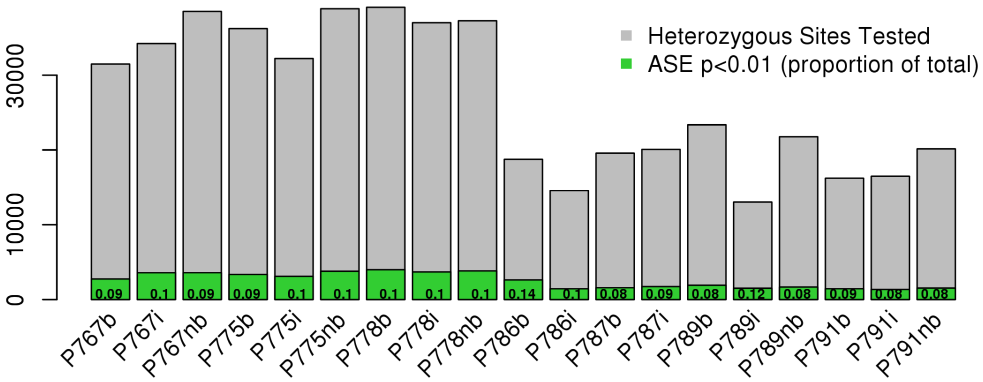
Supplementary Figure 2. Biplot of PCA results on RPKMs from beta, islet and nonbeta samples. Genes with highest loadings (contributing most to the sample separation) are plotted along with the samples.



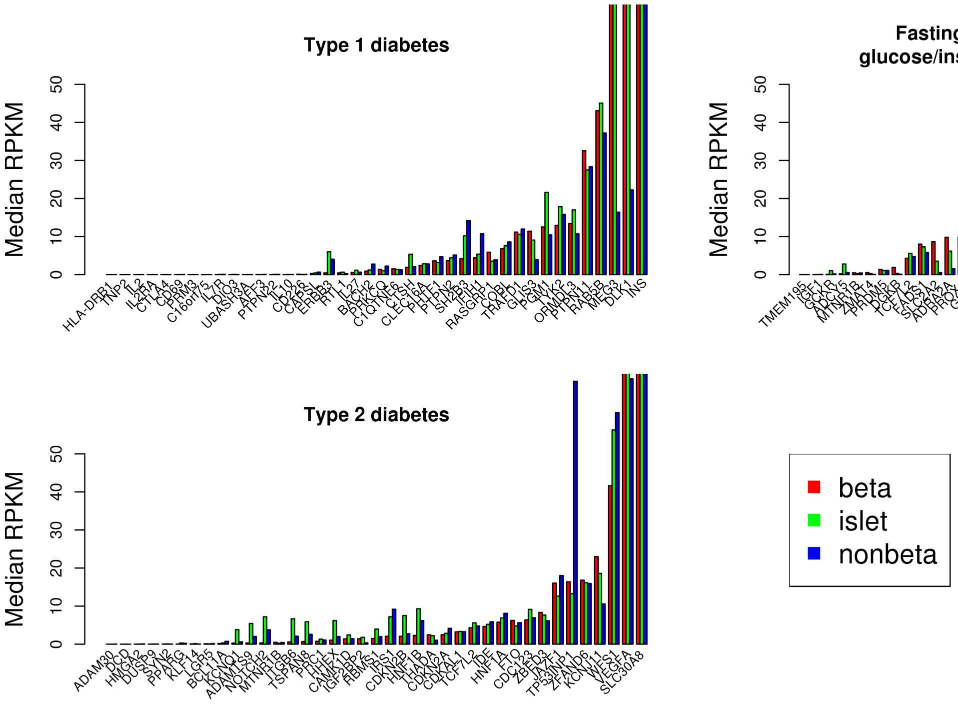
Supplementary Figure 3. Distribution of pvalues form Spearman Rank correlation between gene RPKMs and islet purity. 19,975 data points (corresponding to the number of genes tested) are plotted in each panel and the enrichment of low pvalues is estimated from the distributions using the pi1 statistic.



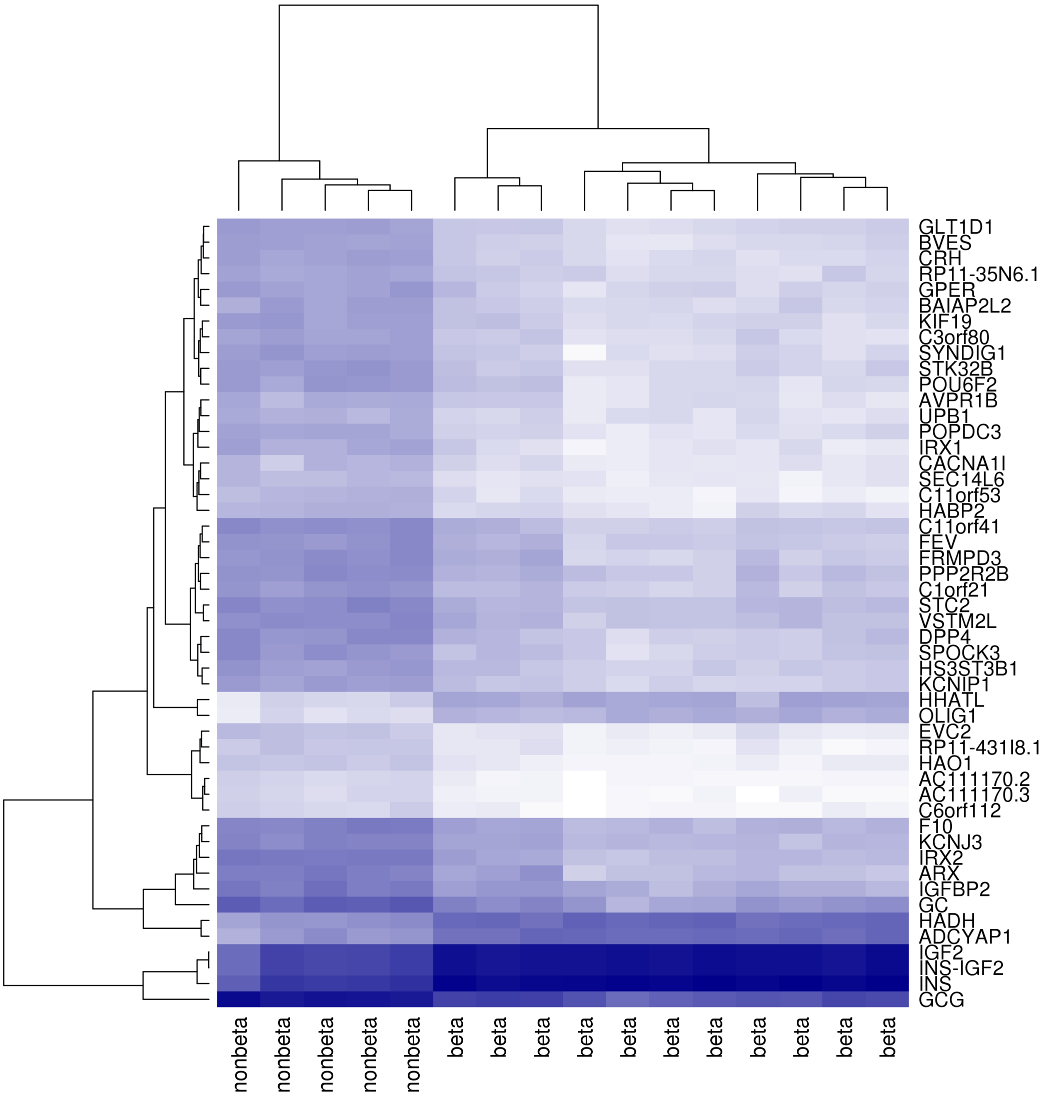
Supplementary Figure 4. Summary of ASE results per sample. Grey bars show the total number of heterozygous sites per individual and cell-type (beta –b, islet –i, nonbeta -nb) tested for ASE (require both alleles to be seen in the RNA-seq data with a minimum coverage of 16 reads per site). Green bars show the proportion of tested sites in significant ASE at 10% FDR.



Supplementary Figure 5. Expression of diabetes GWAS genes. In each cell type, we plot the expression estimates (median RPKM) of genes associated to type 1 diabetes, type 2 diabetes and fasting glucose or insulin levels respectively (Y limit set to median RPKM=50).



Supplementary Figure 6. Heatmap clustering of top 50 most differentially expressed genes between beta and nonbeta cell preparations.



Supplementary Table 1. Summary of donor information, sample purity and sequencing experiments performed per individual.

Sample	**Age (yrs)**	**Sex**	**BMI (kg/m^2)**	**Cause of death**	**Cold ischemia time (hours)**	**Islet purity (%)**	**Beta cell purity (%)**	**Beta RNA-seq**	**Islet RNA-seq**	**Nonbeta RNA-seq**	**DNA-seq**
HP973	32	F	26.9	Trauma	8h	80	93	✓	-	-	-
P747	56	F	23	Subarachnoid hemorrhage	7h	74	89.5	✓	-	-	-
P749	61	M	27.8	Cerebral edema	3h24	68	88	✓	-	-	-
P752	52	F	58	Cerebral hemorrhage	7.5h	89	91	✓	-	-	-
P767	52	M	23.1	Cardio circulatory death	6h	96	91	✓	✓	✓	✓
P775	62	F	29	Rupture aneurysm	4h50	81	73	✓	✓	✓	✓
P778	66	F	23.5	Cerebral hemorrhage	7h	88	86	✓	✓	✓	✓
P786	56	M	29.1	Cerebral hemorrhage	7h20	70	85	✓	✓	-	✓
P787	58	F	26.7	Cerebrovascular accident	6h	99	86	✓	✓	-	✓
P789	53	F	29.8	Cerebral hemorrhage	8h52	78	95	✓	✓	✓	✓
P791	54	M	24.8	Cerebral hemorrhage	9h22	80	76	✓	✓	✓	✓

Supplementary Table 2. Functional annotation of beta cell specific genes (N=471) in the context of 18 different tissues. Most significant top 50 DAVID annotation terms.

Category	Term	Benjamini
SP_PIR_KEYWORDS	pancreas	1.27E-13
KEGG_PATHWAY	hsa04950:Maturity onset diabetes of the young	2.47E-12
GOTERM_BP_FAT	GO:0032940~secretion by cell	6.33E-10
GOTERM_BP_FAT	GO:0046903~secretion	4.48E-10
GOTERM_BP_FAT	GO:0010817~regulation of hormone levels	2.53E-08
GOTERM_BP_FAT	GO:0007267~cell-cell signaling	2.11E-08
GOTERM_BP_FAT	GO:0003001~generation of a signal involved in cell-cell signaling	2.80E-08
SP_PIR_KEYWORDS	signal	2.75E-07
UP_SEQ_FEATURE	signal peptide	2.55E-06
SP_PIR_KEYWORDS	diabetes mellitus	3.16E-07
GOTERM_BP_FAT	GO:0046883~regulation of hormone secretion	2.20E-06
GOTERM_BP_FAT	GO:0050796~regulation of insulin secretion	2.73E-06
GOTERM_BP_FAT	GO:0035270~endocrine system development	2.68E-06
UP_SEQ_FEATURE	topological domain:Cytoplasmic	8.82E-06
UP_SEQ_FEATURE	propeptide:Activation peptide	8.41E-06
GOTERM_BP_FAT	GO:0007586~digestion	4.76E-06
GOTERM_BP_FAT	GO:0051046~regulation of secretion	5.60E-06
GOTERM_BP_FAT	GO:0046879~hormone secretion	5.25E-06
GOTERM_BP_FAT	GO:0002791~regulation of peptide secretion	5.90E-06
SP_PIR_KEYWORDS	ionic channel	4.31E-06
GOTERM_BP_FAT	GO:0031016~pancreas development	8.46E-06
GOTERM_BP_FAT	GO:0009914~hormone transport	9.03E-06
UP_SEQ_FEATURE	transmembrane region	2.69E-05
GOTERM_BP_FAT	GO:0060341~regulation of cellular localization	1.42E-05
SP_PIR_KEYWORDS	transmembrane	9.30E-06
GOTERM_BP_FAT	GO:0030072~peptide hormone secretion	1.70E-05
SP_PIR_KEYWORDS	serine proteinase	9.22E-06
GOTERM_BP_FAT	GO:0031018~endocrine pancreas development	1.67E-05
GOTERM_BP_FAT	GO:0030073~insulin secretion	1.60E-05
GOTERM_BP_FAT	GO:0002790~peptide secretion	2.16E-05
PIR_SUPERFAMILY	PIRSF001135:trypsin	4.43E-05
KEGG_PATHWAY	hsa04080:Neuroactive ligand-receptor interaction	1.35E-05
SP_PIR_KEYWORDS	cleavage on pair of basic residues	2.04E-05
SP_PIR_KEYWORDS	membrane	1.96E-05
GOTERM_BP_FAT	GO:0019226~transmission of nerve impulse	9.93E-05
SP_PIR_KEYWORDS	zymogen	4.59E-05
GOTERM_MF_FAT	GO:0015267~channel activity	7.55E-04
GOTERM_MF_FAT	GO:0022803~passive transmembrane transporter activity	3.93E-04
GOTERM_MF_FAT	GO:0005179~hormone activity	2.71E-04
GOTERM_BP_FAT	GO:0007268~synaptic transmission	1.49E-04
GOTERM_MF_FAT	GO:0005216~ion channel activity	2.43E-04
GOTERM_BP_FAT	GO:0015833~peptide transport	1.69E-04
SP_PIR_KEYWORDS	ion transport	8.48E-05
GOTERM_MF_FAT	GO:0022838~substrate specific channel activity	3.15E-04
UP_SEQ_FEATURE	active site:Charge relay system	8.24E-04
GOTERM_MF_FAT	GO:0022836~gated channel activity	3.58E-04
SP_PIR_KEYWORDS	glycoprotein	1.52E-04
SP_PIR_KEYWORDS	voltage-gated channel	1.49E-04
KEGG_PATHWAY	hsa04930:Type II diabetes mellitus	2.13E-04
GOTERM_BP_FAT	GO:0009749~response to glucose stimulus	4.97E-04

Supplementary Table 3. Comparison of read number statistics between genome mapping and exon junction mapping.

Sample	Total #Reads	Total Genome Mapped (% total)	Total Exon Junction Mapped	Total Junction Mapped of the Genome Unmapped	Junction Mapped reads with >MAPQ and >algmLength than Genome Mapped
HP973	215,481,438	190,651,029 (88.48%)	37,317,339	3,189,822	7,734,263
P747	199,458,186	177,164,550 (88.82%)	33,632,128	2,872,239	7,058,808
P749	191,019,990	169,839,707 (88.91%)	33,333,152	2,869,816	7,541,596
P752	209,178,830	186,058,762 (88.95%)	34,531,472	3,121,555	7,742,289
P767b	288,251,610	256,736,887 (89.07%)	39,131,716	2,957,054	8,056,467
P775b	405,108,364	367,170,906 (90.64%)	63,995,726	5,234,012	14,047,896
P778b	486,887,690	433,443,548 (89.02%)	68,019,955	5,159,412	14,700,904
P786b	209,165,278	189,986,172 (90.83%)	34,409,245	2,939,738	7,415,269
P787b	193,842,028	176,930,316 (91.28%)	30,187,038	2,642,982	6,694,964
P789b	239,710,804	216,578,177 (90.34%)	37,326,273	3,122,508	8,287,222
P791b	198,932,724	180,648,752 (90.8%)	30,402,305	2,417,496	6,548,825