APPENDIX

PANCREATIC β-CELL ELECTRICAL ACTIVITY AND INSULIN SECRETION: OF MICE AND MEN

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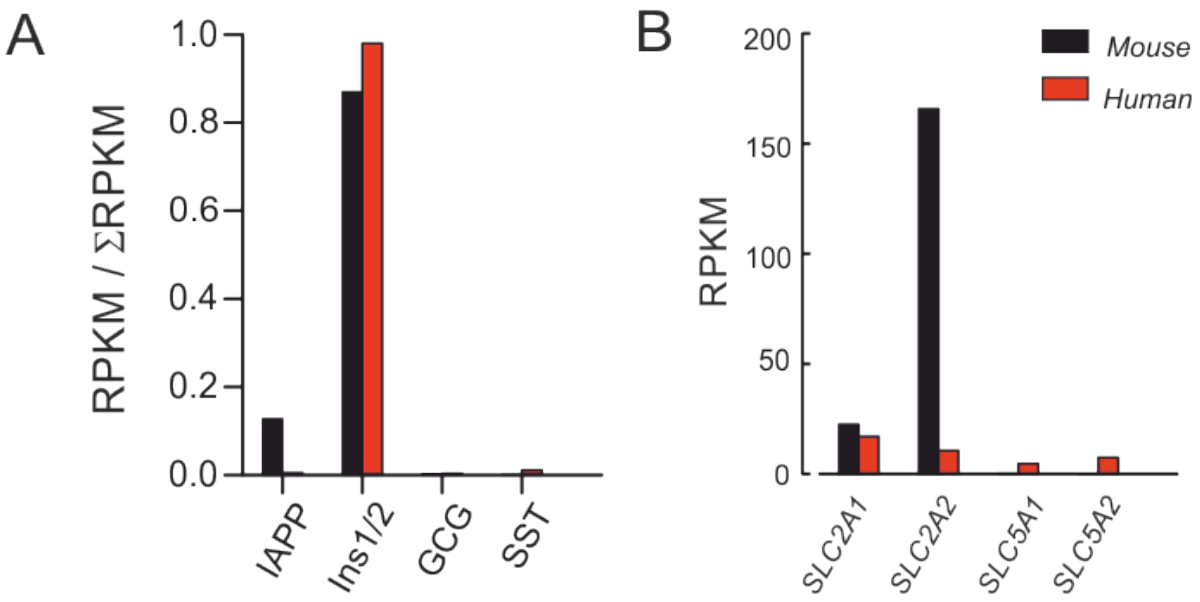

FIGURE 1. Expression analysis of hormones (A) and glucose transporters in mouse and human β-cells. Values here and in subsequent figures are means of published RNAseq data in mouse (3, 147) and human (69, 480) β-cells. RPKM indicates Reads Per Kilobase of transcript per Million mapped reads. Note that the β-cell fractions were obtained by fluorescence-activated cell sorting and were devoid of any mRNA for glucagon or somatostatin but contain low levels of *IAPP*. For clarity, only human gene names (i.e. in upper case italics) are given.

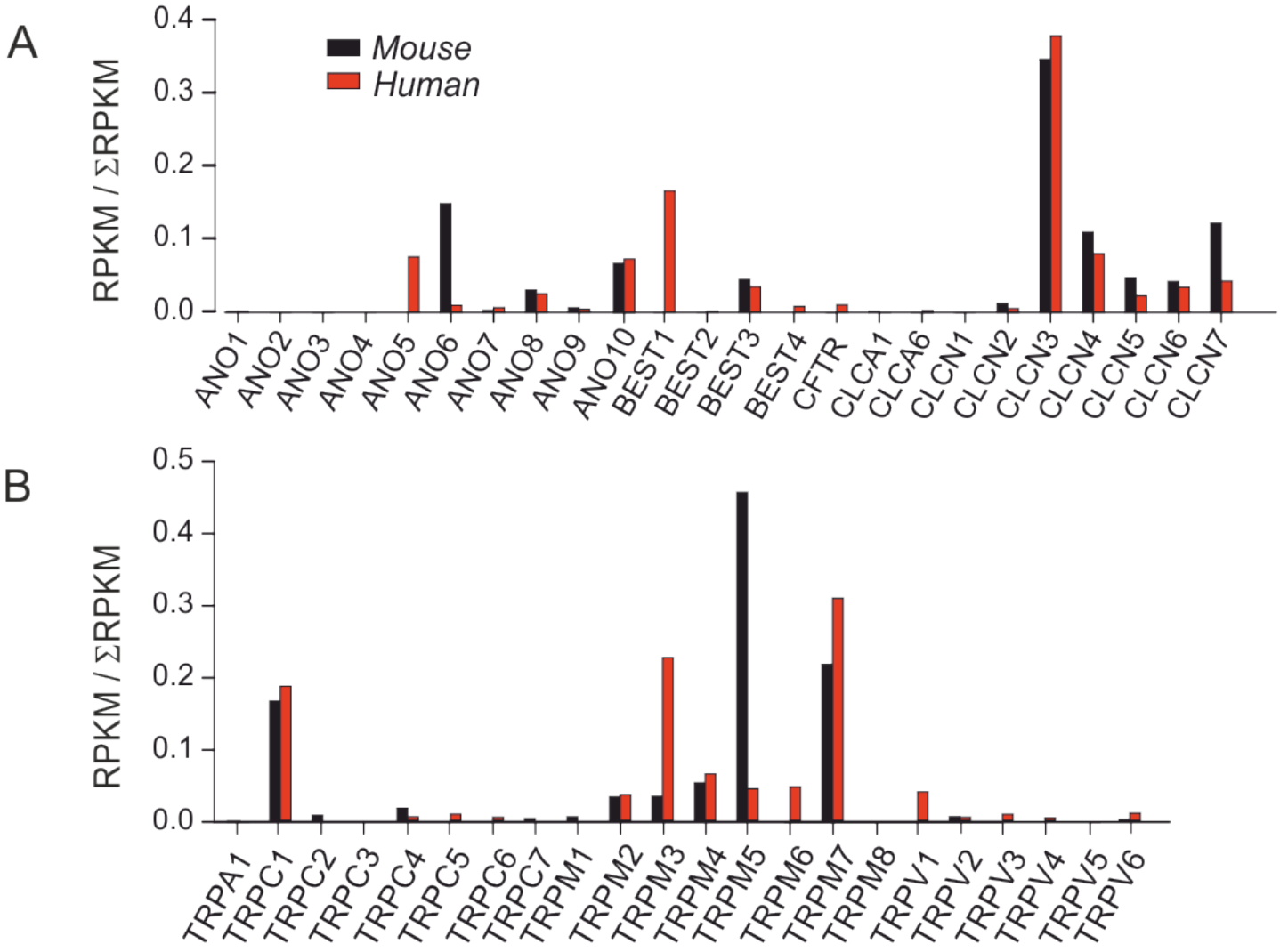

Figure 2. *A*: Relative expression of Cl^- channels in mouse and human β-cells. Data are expressed relative to the sum of all genes displayed (i.e. RPKM/ΣRPKM). *B*: As in A but showing data for Trp channels.

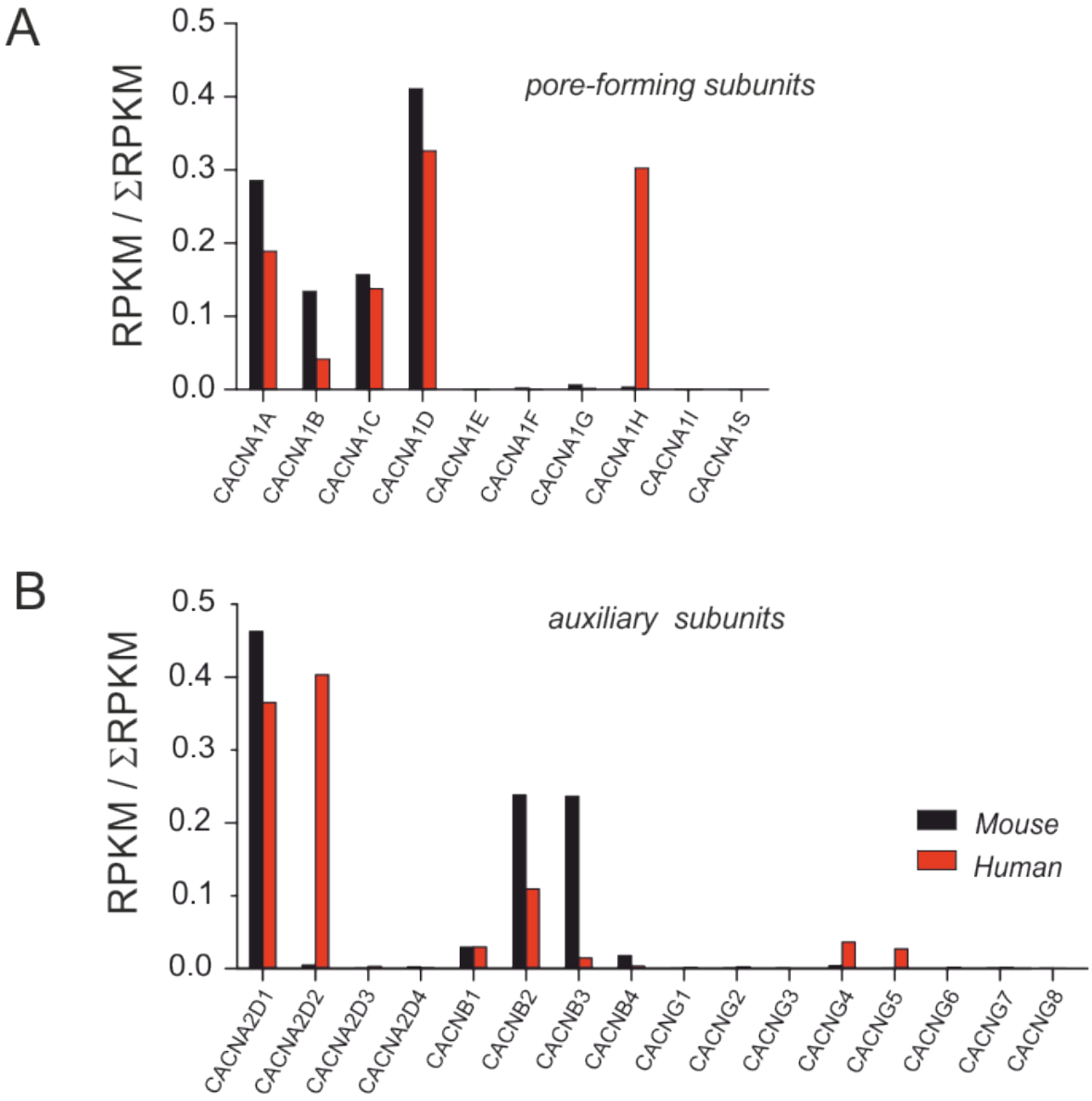

Figure 3. *A-B*: Relative expression of the pore-forming Ca^{2+} channel α-subunits (*CACNA1x*) (*A*) or auxiliary $\alpha_2\delta$ (*CACNA2D*), β- (*CACNBx*) and γ- (*CACNGx*) subunits (where x stands for a letter or number) (*B*).

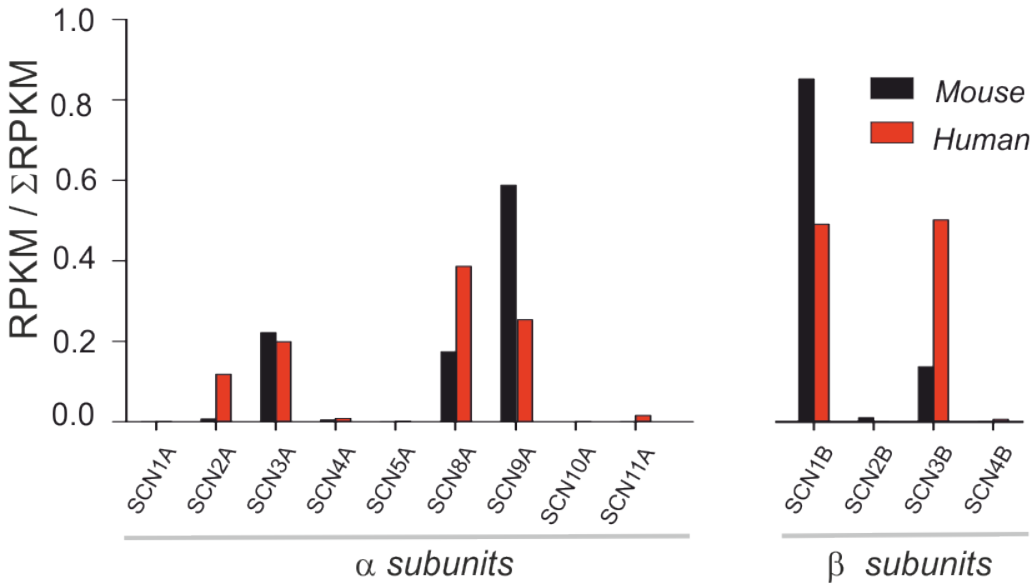

Figure 4. *A-B*: Relative expression of the pore-forming Na^+ channel α-subunits (*SCNxA*) (*A*) and auxiliary β-subunits (*SCNxB*) (*B*). Note that the numbering of the proteins (Nav1.1-Nav1.9) and genes (*SCN1A-11A*) do not correspond.

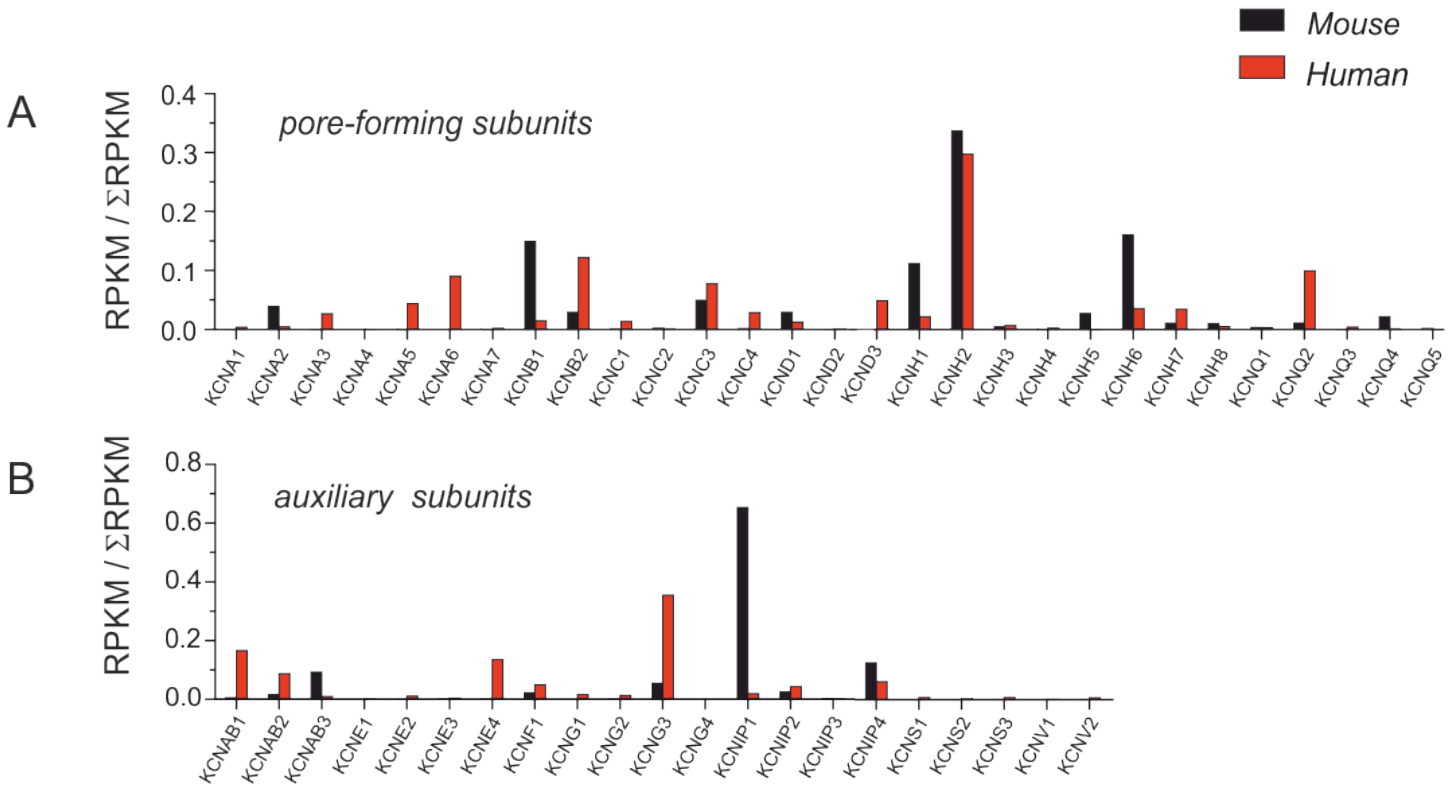

Figure 5. *A-B*: Relative expression of the pore-forming (*A*) or auxiliary subunits (*B*) of voltage-gated K^+ channels in mouse and human β-cells.

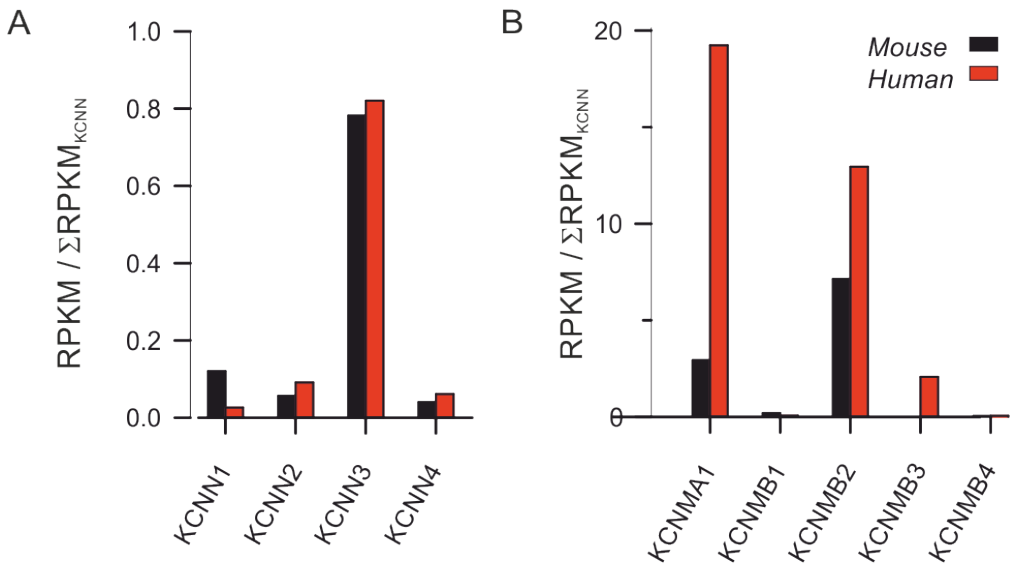

Figure 6. Relative expression of small- (*A*) and large-conductance (*B*) Ca^{2+}-activated K^+ channels (*KCNNx* and *KCNM*x). Expression has been normalized to the aggregate expression of all *KCNN*s ($\Sigma RPKM_{KCNN}$).

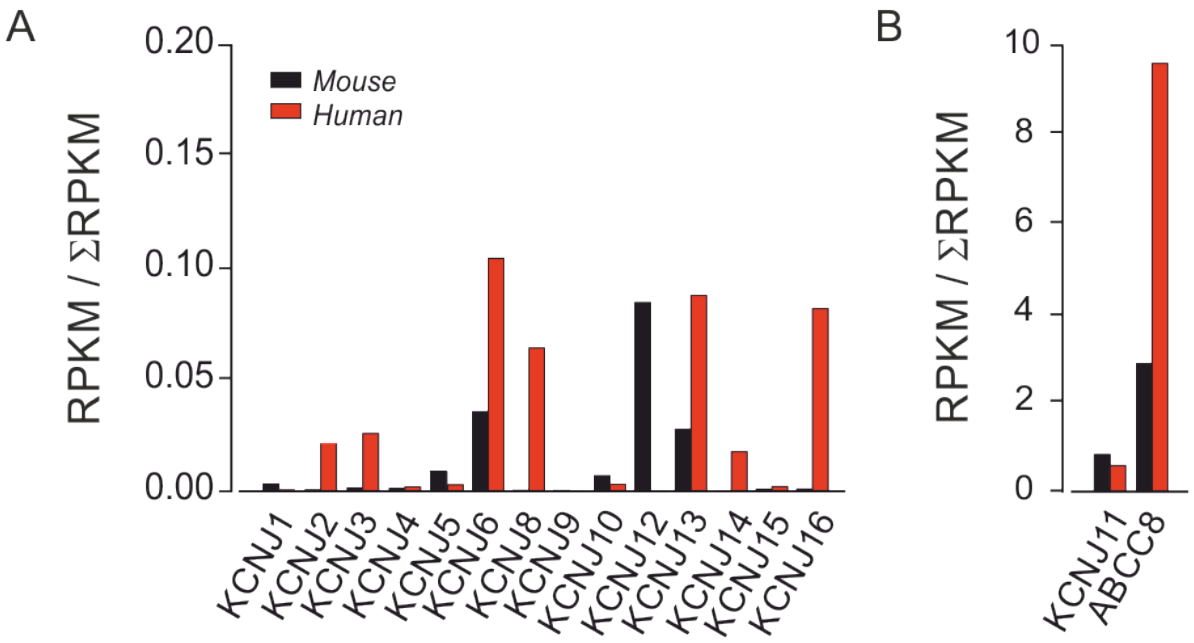

Figure 7. *A*: Relative expression of inwardly rectifying K^+ channels (*KCNJx*). Expression has been normalized to the aggregate expression of all *KCNJ*s ($\Sigma RPKM_{KCNJ}$). *B*: Expression of SUR1 (*ABCC8*, likewise normalized to $\Sigma RPKM_{KNCJ}$). Note that the expression of *KCNJ11* and *ABCC8* is displayed using a different ordinate scale than the other *KCNJ*s.

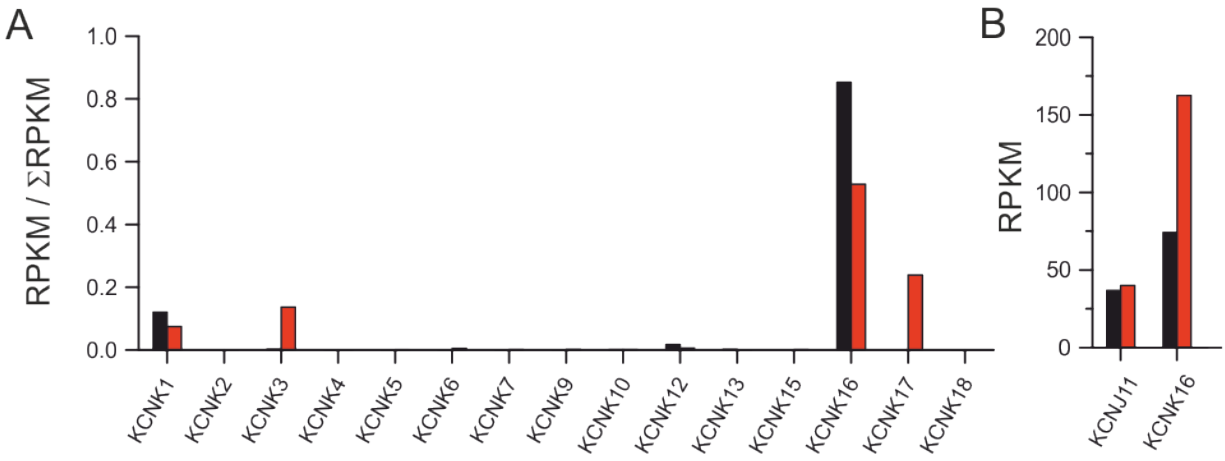

Figure 8. *A*: Relative expression of two-pore K^+ channels (*KCNKx*). Expression has been normalized to the aggregate expression of all *KCNK*s (ΣRPKM). *B*: Comparison of *KCNK16* expression with *KCNJ11* (values in RPKM).

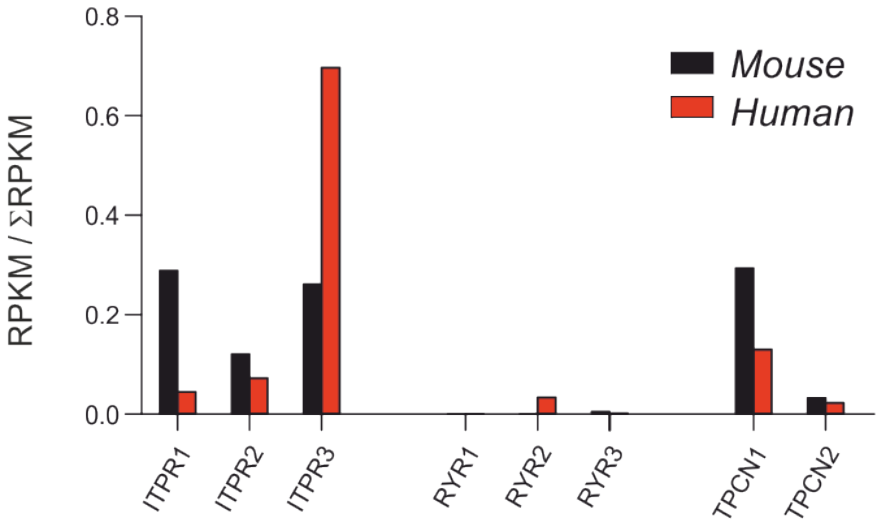

Figure 9. Relative expression of the intracellular ion channels: ryanodine receptors ((*RYRx*), $InsP_3$ receptors (*ITPRx*) and two-pore channels (*TPCNx*).

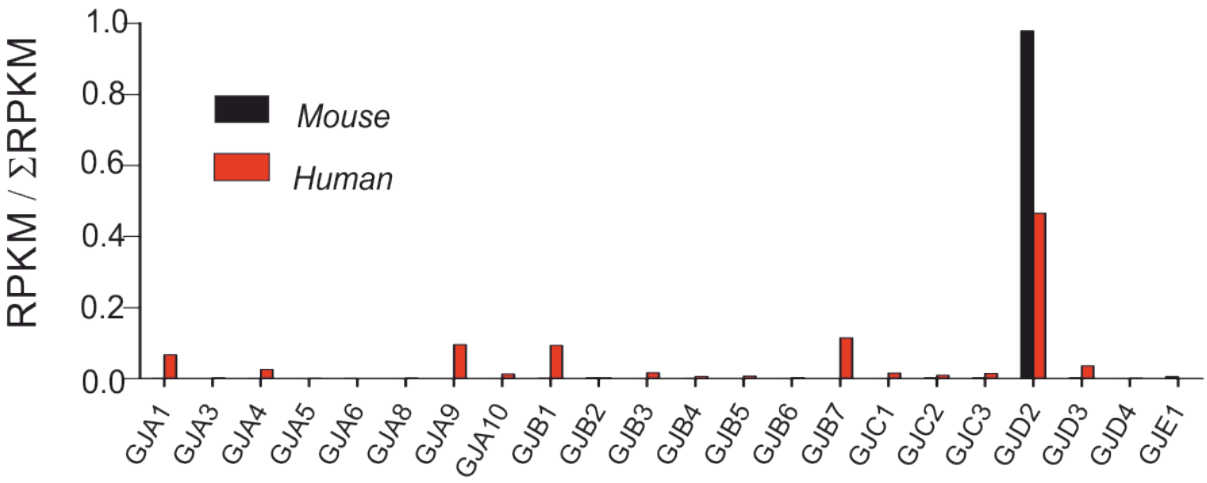

Figure 10. Relative expression of *GJAx*s, *GJBx*s, *GJCx*s and *GJDx*s.

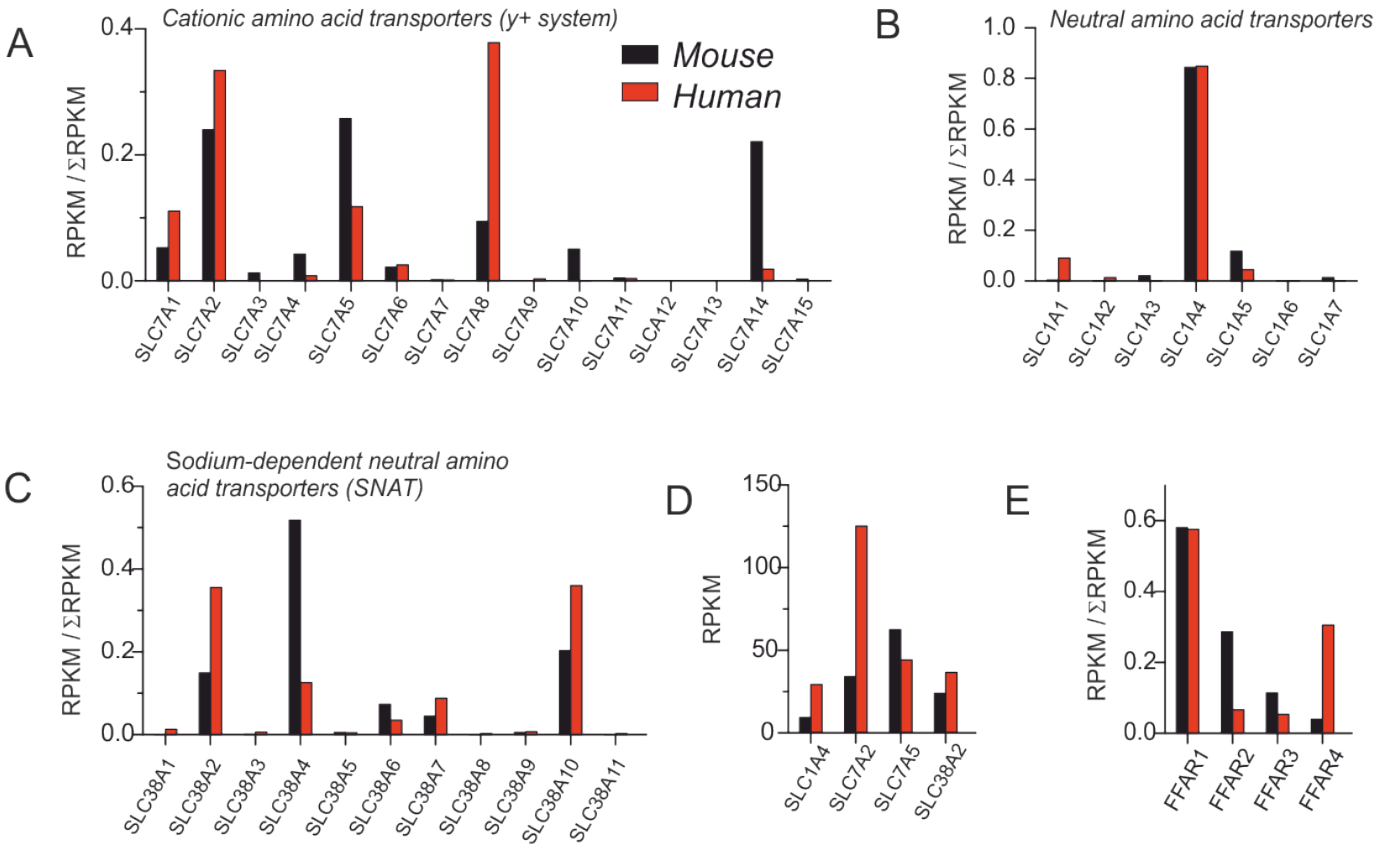

Figure 11. *A*: Relative expression of cationic amino acid transporters (y+ system) in mouse and human β-cells. *SLC7A14* mediates uptake of cationic amino acids into lysosomes and may not be important for generation of electrical activity. Human and mouse β-cells express high levels of *SLC7A5* and *SLC7A8*, which is believed to transport neutral amino acids when associated with *SLC3A2*. *B*: As in *A*, but showing expression of neutral amino acid transporters. *C*: As in *A*, but displaying expression of Na^+-dependent neutral amino acid transporters (SNATs). In addition to the high expression of *SLC38A2* and *A4*, both mouse and human β-cells also express the putative neutral amino acid transporter *SLC38A10*. *D*: Absolute expression (in RPKM) of *SLC1A4*, *SLC7A2*, *SLC7A5* and *Slc38A2* in mouse and human β-cells analyzed as described in legend to Figure 2D. *E*: Relative expression of free fatty acid receptors (*FFAR*s) in mouse and human β-cells.

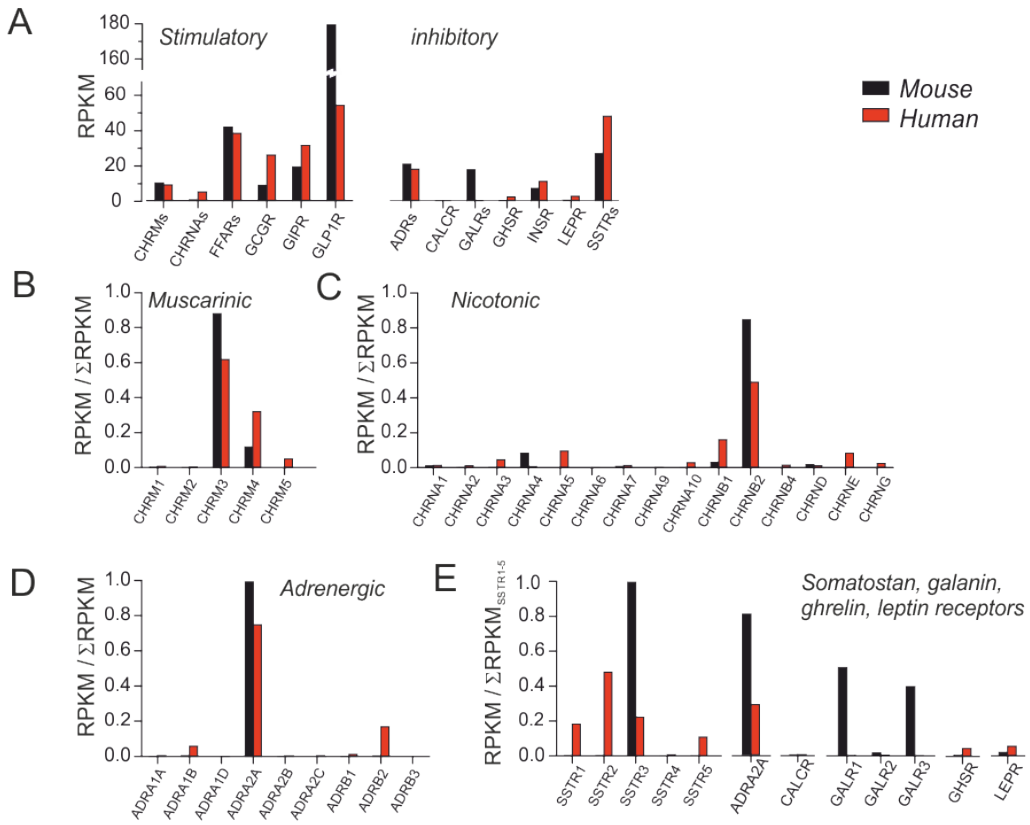

Figure 12. *A*: Expression (in RPKM) of receptors for stimulatory and inhibitory agonists. Abbreviations: *CHRM*s, cholinergic receptors muscarinic; *CHRNA*s, cholinergic receptor nicotinic α-subunit; *FFAR*s, free fatty acid receptors; *ADR*s, adrenergic receptors; *GALR*s, galanin receptors; *INSR*, insulin receptor: *SSTR*s, somatostatin receptors. *B*: Relative expression of muscarinic receptors (*CHRMx*). *C*: As in *B* but showing relative expression of nicotinic receptor α- (*CHRNAx*), β- (*CHRNBx*), δ- (*CHRND*), ε- (*CHRNE*) and γ- (*CHRNGx*) subunits. Note that expression of *Chrna*s is very low in mouse β-cells so the functional significance of *Chrna4* is uncertain. *D*: As in *B* but showing relative expression of adrenergic α_1- (*ADRA1x*), α_2- (*ADRA2x*) and β-receptors (*ADRBx*). *E*: Relative expression of somatostatin (*SSTRx*), α_2 (*ADRA2A*), galanin (*GALx*), ghrelin (*GHSR*) and leptin (*LEPR*) receptors normalized to the aggregate expression of the SSTRs ($\Sigma RPKM_{SSTR1-5}$).

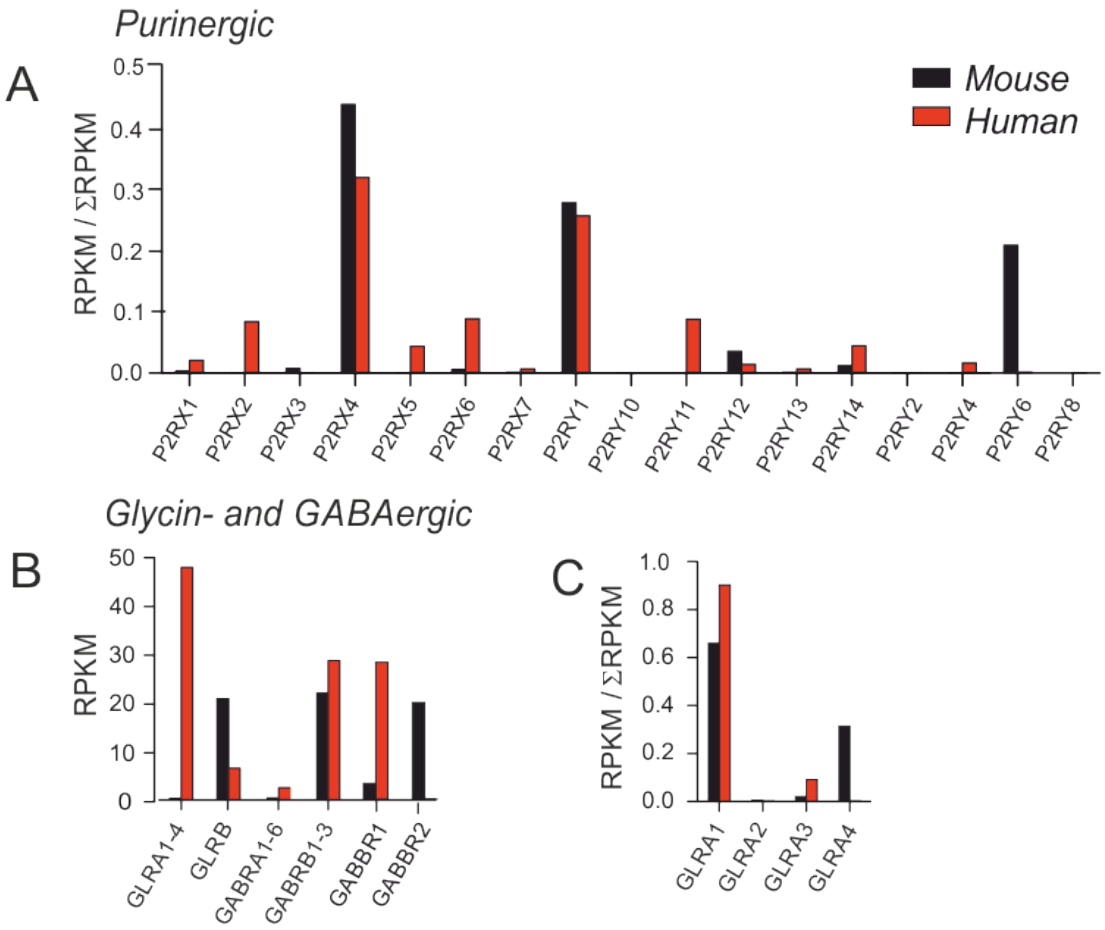

Figure 13. *A*: Relative expression of ionotropic (*P2RXx*) and metabotropic (*P2RYx*) purinergic receptors in mouse and human β-cells. *B*: Comparison of expression (in RPKM) of glycine receptor α- (*GLRAx*) and β-subunits (*GLRB*), ionotropic $GABA_A$ α- (*GABRA1-6*) and β-subunits (*GABRB1-3*) and metabotropic $GABA_B$ (*GABRBx)* receptors. Note that mouse β-cells are almost devoid of $GABA_A$ receptors. *C*: As in *A*, but showing relative expression of glycine receptor α-subunits (*GLRAx*) normalized to the aggregate expression of *GLRA*s.

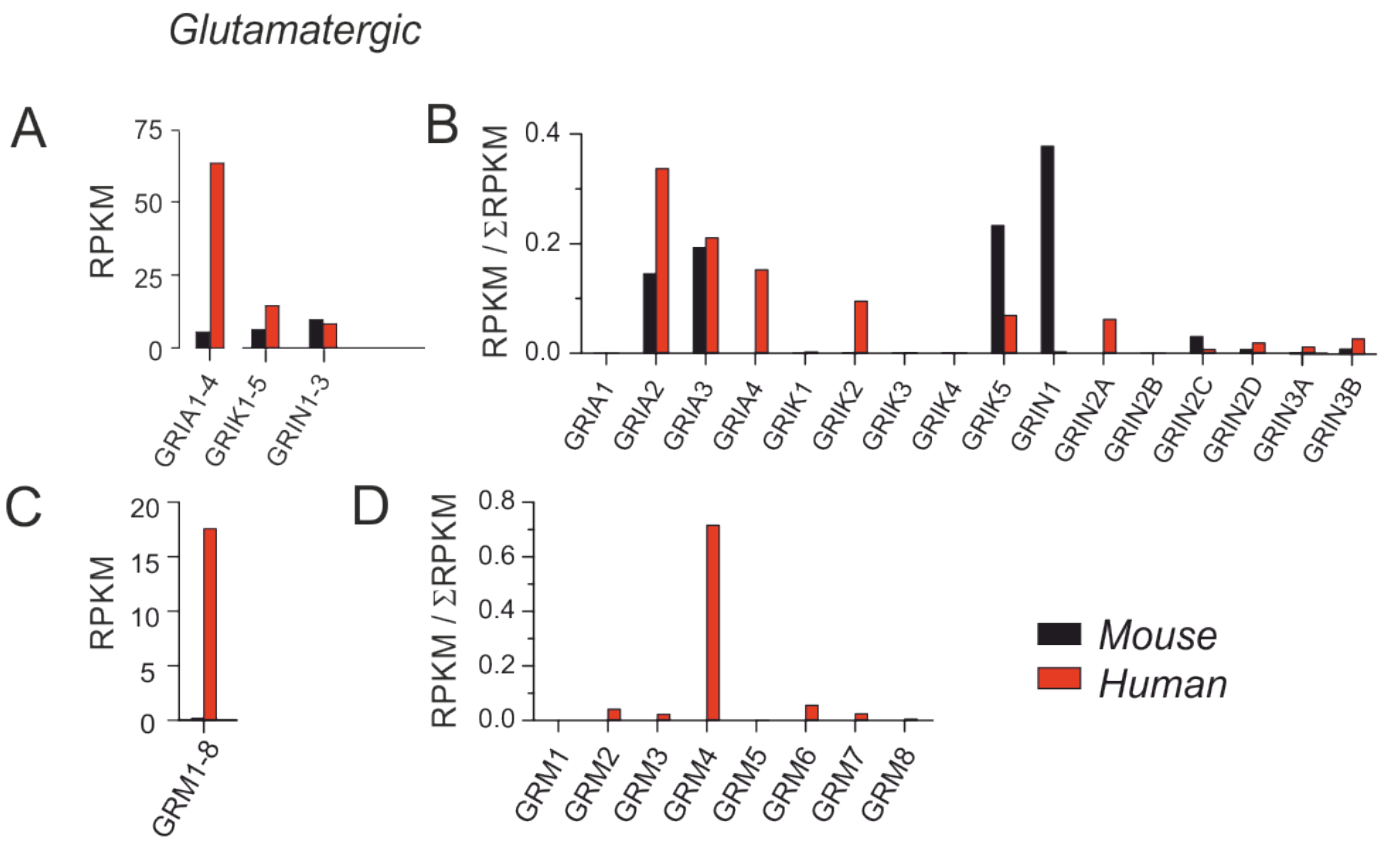

Figure 14. *A*: Comparison of expression (in RPKM) of AMPA (*GRIA1-4*), kainate (*GRIKx*) and NMDA (*GRINx*)-subunits. *B*: Relative expression of *GRIAx*, *GRIKx* and *GRINx* normalized to aggregate expression of all ionotropic glutamate receptors. *C*: As in *B* but comparing expression of metabotropic glutamate receptors (*GRMx*) in mouse and human β-cells. Note very low expression of *GRIM*s in mouse β-cells. *D*: As in *B* but showing relative expression of *GRMx* in human β-cells (relative expression in mouse β-cells not shown because of low expression).

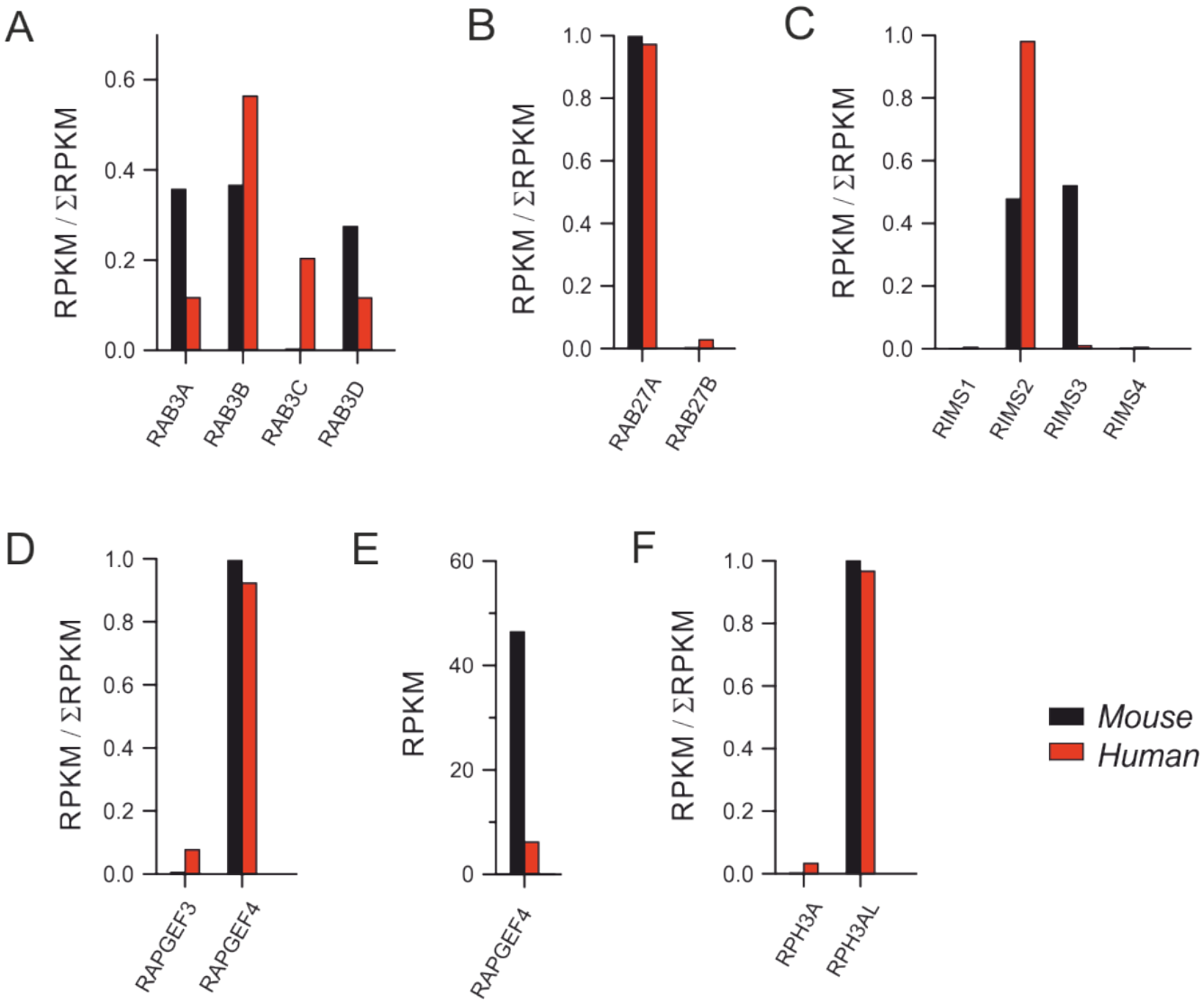

Figure 15. *A*: Relative expression of Rab3 (*RAB3x*) in mouse and human β-cells. *B*: As in *A* but showing Rab27 (*RAB27x*). *C*: As in *A* but showing RIM (*RIMx*). *D*: As in A but showing RAPGEFs (*RAPGEFx*). *E*: Comparison of expression (in RPKM) of *RABGEF4* in mouse and human β-cells. Note that expression in mouse β-cells is much higher than in human β-cells. *F*: As in *A* but showing relative expression or *RPH3A* and *RPH3AL*.

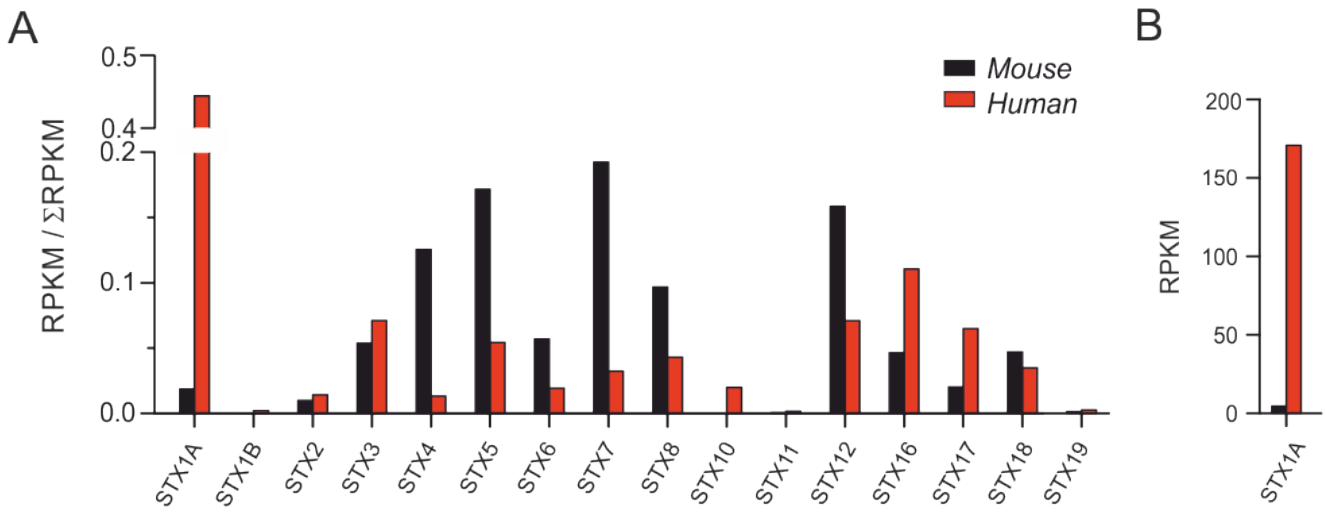

Figure 16. *A*: Relative expression of syntaxins (STXs) in mouse and human β-cells. *B*: Expression (in RPKM) of *STX1A* in mouse and human β-cells. Note the much higher expression in human than in mouse β-cells.

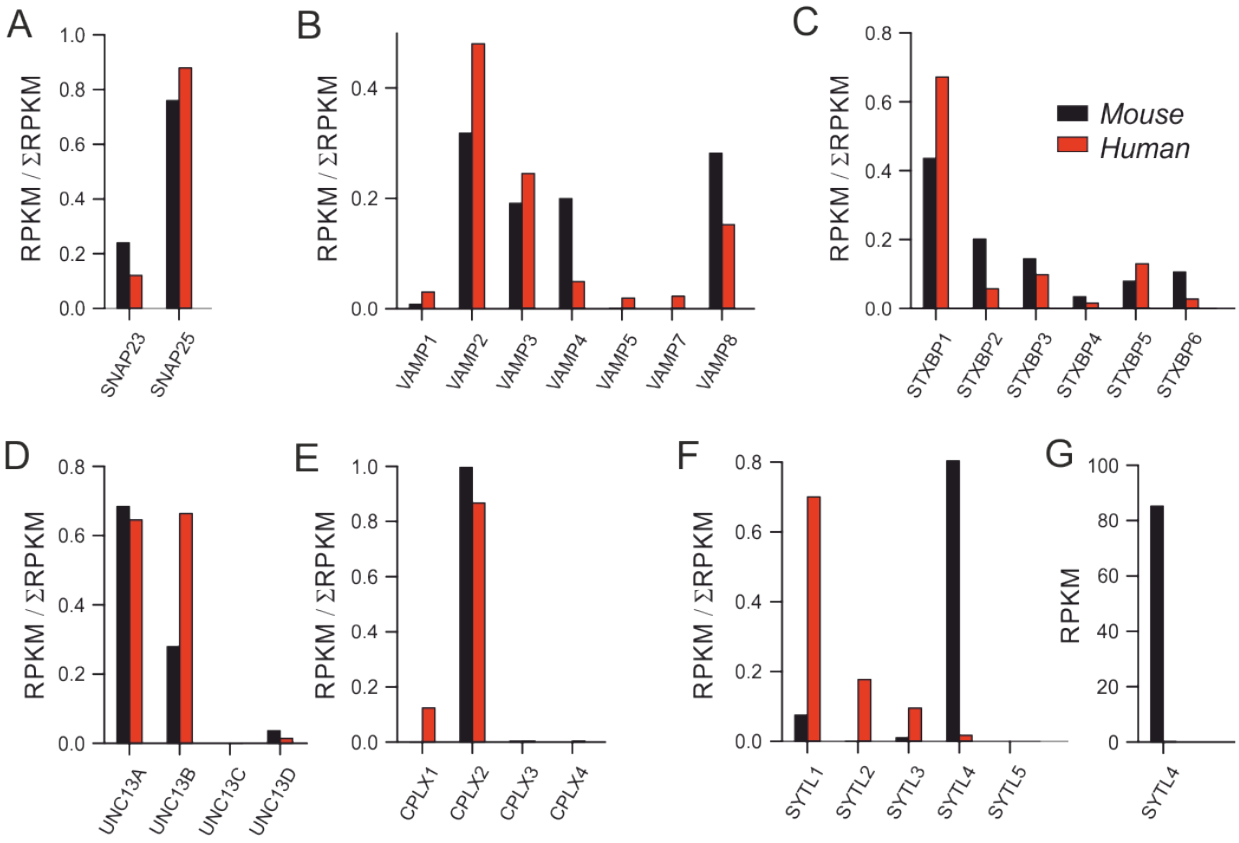

Figure 17. *A*: Relative expression of SNAP23 and 25 (*SNAPx*) in mouse and human β-cells. *B*: As in *A* but showing VAMPs (*VAMPx*). *C*: As in *A* but showing syntaxin-binding proteins (*STXBPx*). *D*: As in *A* but showing Munc13 (*UNC13x*). *E*: As in *A* but showing complexins (*CPLXx*). *F*: As in *A* but showing synaptotagmin-like proteins (*SYTLx*). *G*: Comparison of expression (in RPKM) of *SYT4L* in mouse (black) and human β-cells (red). Note absence of *SYTL4* in human β-cells.

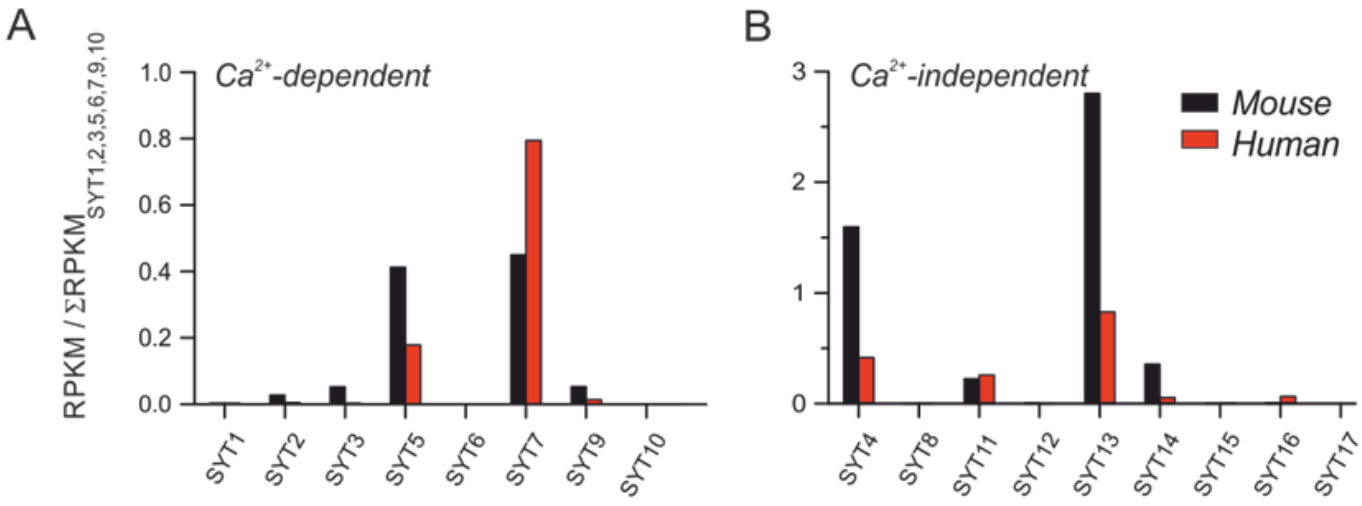

Figure 18. Relative expression of Ca^{2+}-dependent (*A*) and –independent (*B*) synaptotagmins in mouse and human β-cells. Expression has been normalized to the summed expression of the Ca^{2+}-dependent synaptotagmins (*SYT1, SYT2, SYT3, SYT5, SYT6, SYT7, SYT9, SYT10*). For display, the expression of the Ca^{2+}-dependent and -independent SYTs (*right*) has been separated. Note the high expression of Ca^{2+}-*in*dependent SYTs.