SUPPLEMENTARY FIGURE LEGENDS

Figure S1: Harringtonine treatment optimization. (A) Example of the bell shaped curve read distribution encountered at TIS locations (GAPDH transcript). (**B)** Metaplots of reads distribution around the annotated start and stop codons after 2' (upper) or 30' (lower) harringtonine treatment (**C)** Metaheatmaps of the density of extremities of sequenced footprint fragments around the annotated start after 2'(upper) or 30'(lower) harringtonine (**D),(E)** IGV browser screenshots of reads mapping on GAPDH and ACTB genes after 2'(upper) or 30'(lower) harringtonine. The small boxes depict the UTRs, the large boxes the CDS, and the dashed lines the intronic region.

Figure S2: Enrichment algorithm. (A) Schematic representation of enrichment algorithm applied on the Ribowaltz output. (**B)** Example for HLA-B transcripts showing potential TIS distribution before (upper) and after (lower) applying the enrichment algorithm. The orange bar colour indicate an increased enrichment upon cytokine stimulation.

Figure S3: Protein validation. CHGA, STAT1, STAT2, PSMB8, PSMB9 and PSMB10 expression level in EndoC-βH1 cells (A) and primary human islets (B) after exposure to cytokine (IFNɣ and IL1β). Protein quantification is performed using ImageJ and shown as relative expression using actin as reference. n.d. indicate no detected band. *indicate the immunoproteasome subunit position. The blots shown are representative of 2 independent experiments (2 islet preparations).

Figure S4: Examples of TIS mapping. (A),(B) TAP1 and PSMD8 TIS profiling. x axes represent transcript location. X=0 shows the annotated translation start. Arrows indicate the

detected main TIS, consistent with the TIDdb database. Orange bars show TIS significantly upregulated upon cytokine treatment. (**C),(D)** YBX1 and PGRMC1 TIS profiling. x axes represent transcript location. X=0 shows the annotated translation start. Arrows indicate TIS detected by mass spectrometry(53). The orange bars show TIS significantly upregulated upon cytokine treatment. Internal in frame TIS are not depicted in all graphs. (**E,F)** TIS mapping on CHGA and VEGF transcripts. The orange bars show TIS significantly upregulated upon cytokine treatment. The ORFs' amino-acid sequence based on the upregulated TIS are shown in the table below. The aa highlighted in red indicate potential HLA-A2 binder based on NetMHCI prediction. x axes represent transcript location. X=0 shows the annotated translation start.

Figure S5: Validation of the *de novo* transcriptome. A) Venn diagram showing the number of transcripts (table S4) supported by reads in splicing junction. B) Similar representation for T1D susceptible transcripts. From 6892 TALON transcripts, 3425 novel intronic junctions (and 212 novel intronic junctions in T1D susceptible genes specifically) were detected out of the 2305 intronic containing transcripts. By comparing datasets, 2550 intronic junctions (163 out of 212 novel introns detected in all T1D transcripts) were detected by Illumina bulk RNAseq. C) RT PCR performed on EndoC-βH1 RNA and primary islet isolated RNA using TALONT ALONT000709680 specific primers for detection of PSMB9 transcript variant. D) RT PCR performed on EndoC-βH1 RNA and primary islet isolated RNA using TALONT000700063 specific primers for detection of HLA-C transcript variants.

Figure S6: Inflammation disturbs the translational process and fidelity. Volcano plot representing the differential read expression at start site position in newly identified transcripts (**A**) and within non-coding RNA (**B**). T1D susceptible genes are depicted on the figures.

Figure S7: Pathway analysis of alternative start sites more upregulated than the corresponding canonical starts. Analysis performed by Stringdb at medium confidence and two k-mean clusters. The red nodes show proteins of the mRNA processing pathway, and the red-blue nodes show proteins specifically involved in mRNA splicing and located in stress granules. The combs colouring is based on the default String settings.

Figure S8: Characterization of the CHGA 5'-UTR region. A) Representation of the (Alt-CHGA)-GFP fusion construct. The 5'-UTR region of CHGA is represented as white box; the GFP ORF deleted from the AUG is shown as dark blue box; The CHGA canonical start site and its ORF are presented in blue. The Alt-CHGA-GFP ORF is represented in green and position of the in frame start sites -103; -40 and -22 are shown with black arrow. B) sequence of the (Alt-CHGA)-GFP construct. C) GFP FACS profile of HEK 293 cells transfected with the (Alt-CHGA)-GFP or GFP (with AUG) constructs. D) Western blot analysis showing expression of the GFP fusion proteins after transfection in HEK 293 cells and cytokine stimulation. 0.5ug protein loaded of CMV-GFP transfected cells; 50ug protein loaded on of (Alt-CHGA)-GFP transfected cells. NT: non transfected; MW: molecular weight showing the bands at 37kDa and 25kDa. Upper panel stained with anti-GFP antibody (* show unspecific band); Lower panel stained with anti-Actin antibody (uncut blots are presented as supplementary material)