

ESM Table 1. HLA Class I Antibody details and conditions used in different assays.

Assay	Primary Antibody [Clone] RRiD	Manufacturer and Cat#	Conditions and Secondary Detection System
Western Blotting	HLA-ABCE-HRP [TP25.99SF] RRID:AB_2912972	Novus Biologicals C#NBP2- 68006H	1/1000 dilution overnight at 4°C + 1hr room temperature
	HLA-ABCE [HC10] RRID: AB_2728622	2B Scientific AM33035PU-N Mouse IgG2A	1/1000 overnight at 4°C
Flow Cytometry	HLA-ABCE-RPE [W6/32] RRID:AB_579554	Agilent C#R7000 Mouse mAb	1/10 dilution for 30 minutes at room temperature
ELISA	HLA-ABCE [W6/32] (Capture antibody for plate coating) RRID:AB_579554	Agilent/ Dako C#M073601-2 Mouse mAb	Agilent/ Dako polyclonal Rabbit anti-human β 2 microglobulin as detection antibody. 1/5000 dilution for 1hr at RT; Goat-anti rabbit IgG (whole molecule)- Alkaline Phosphatase as secondary antibody, 1/1000 dilution 1hr at RT.
Immunohistochemistry	HLA-ABCE [EMR8-5] RRID:AB_1269092	Abcam C#ab70328 Mouse mAb	Dako REAL Envision Detection System; antigen retrieval using 10mM citrate pH6.0, 1/1500 dilution 1h at RT

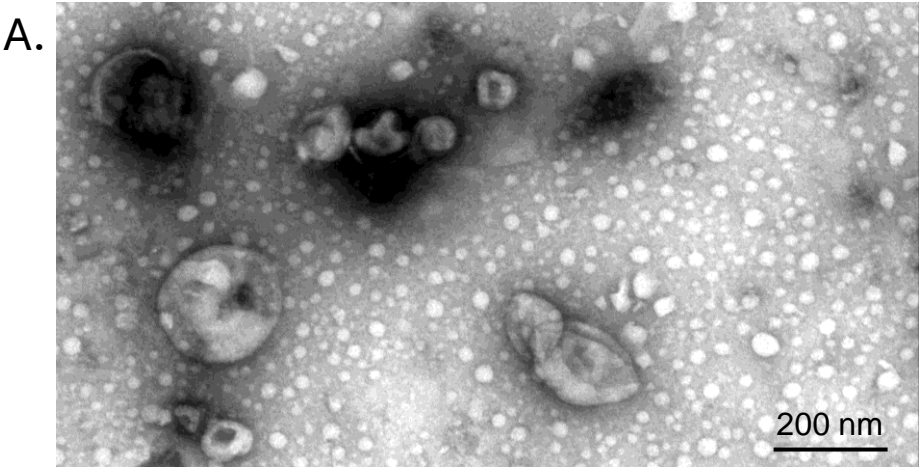
ESM Table 2: Human islet donors used for western blotting and sHLA-I ELISA.
NA – not available

Sample ID	Gender	Age (y)	BMI	HLA typing
1	Male	34	27	A1/A3/B7/B44/C5/C7
2	Male	44	26	A*02/A*32/B*08/B*51/C*07/C*14
3	Female	42	37	A*03:01/A*31:01/B*07:02/B*35:01/C*04:01/C*07:01
4	Female	46	35	NA

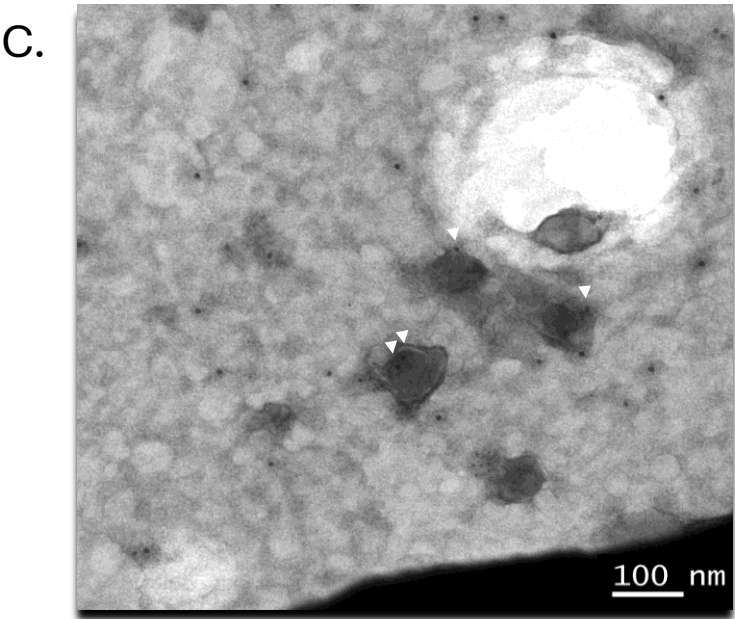
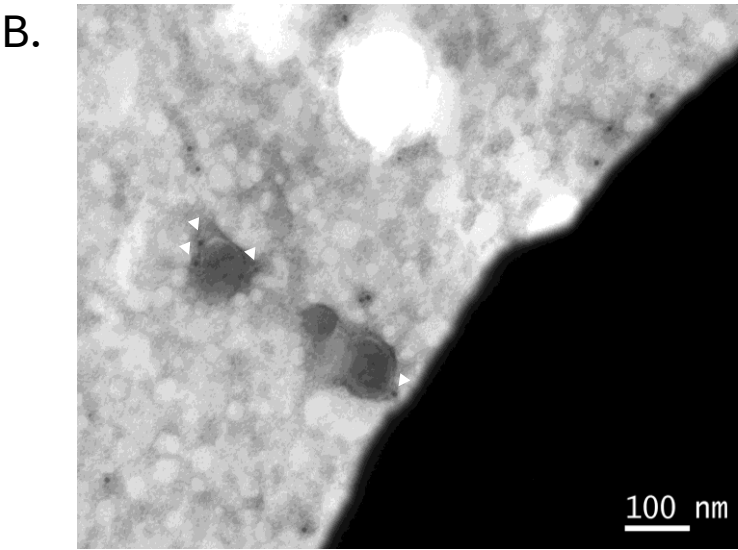
ESM Table 3: Primer sets for Spliced HLA variants.

Spliced Variant	Forward	Reverse
HLA-A	AGAGATACACCTGCCATG	CCTCCTTTTCTATCCCATCTCA
HLA-B	GGTCATCGGAGCTGTGGTCG	CTGTCGCTGCCCCATCTCAG
HLA-C	CCCTCGTGCTGAACATGGCA	CCATCTCAGGGTGAGGGGCT

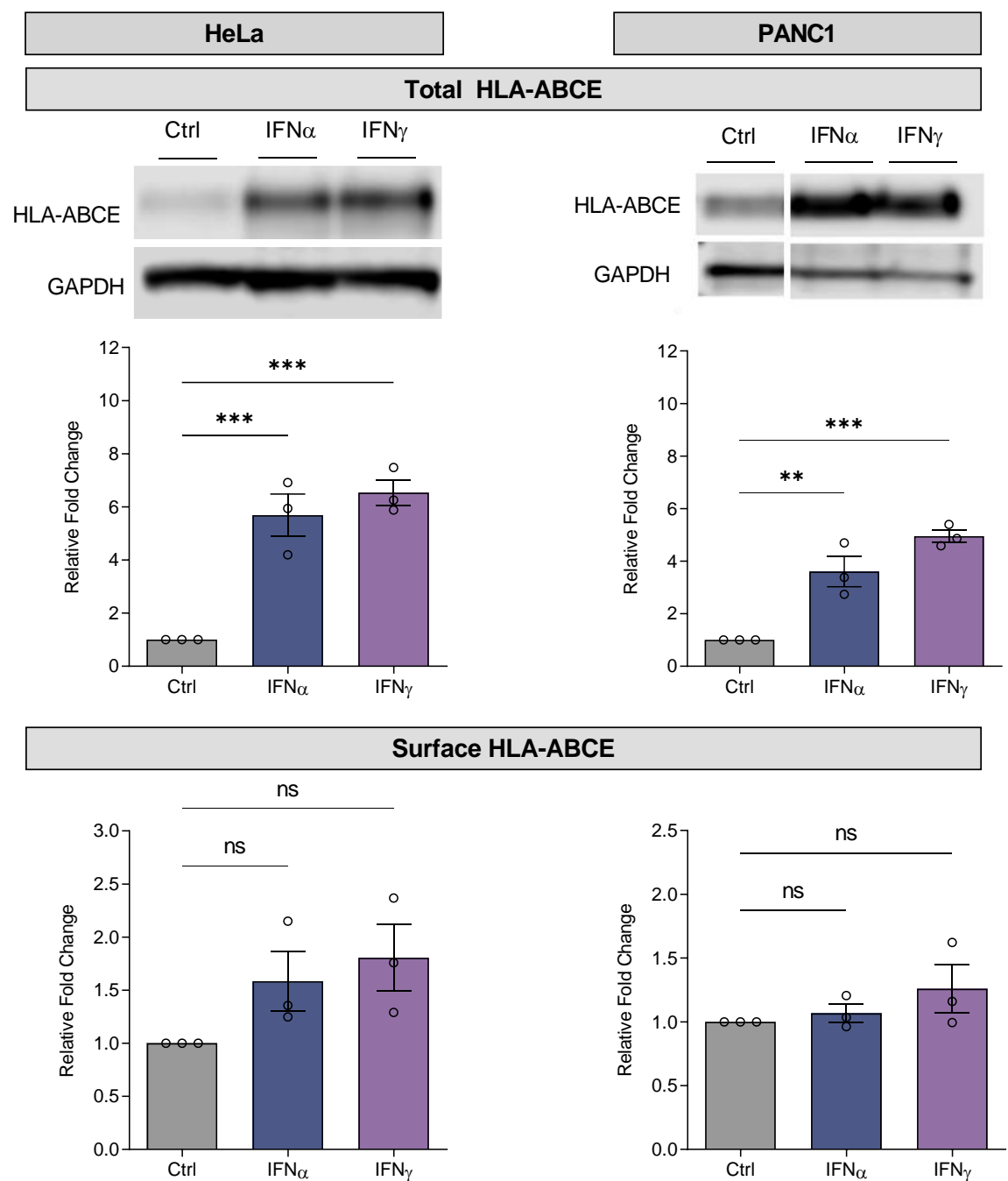
ESM Fig 1A Human β cells release EV under inflammatory conditions. Pellets were obtained from ultracentrifugation at 100,000 x g of supernatants of β cells



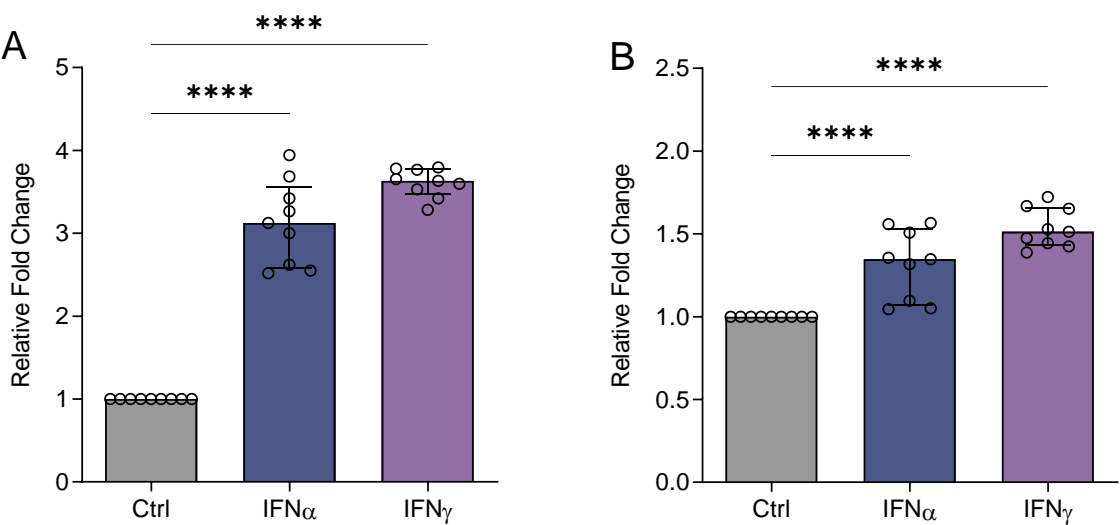
ESM Fig.1B/C: CD81 immunogold stained exosomes from IFN treated β -cells cultured for B. 24 h or C. 48h, respectively. Triangles indicate CD81 EV/exosomal specific labelling in the membranes (10 nm gold particles).



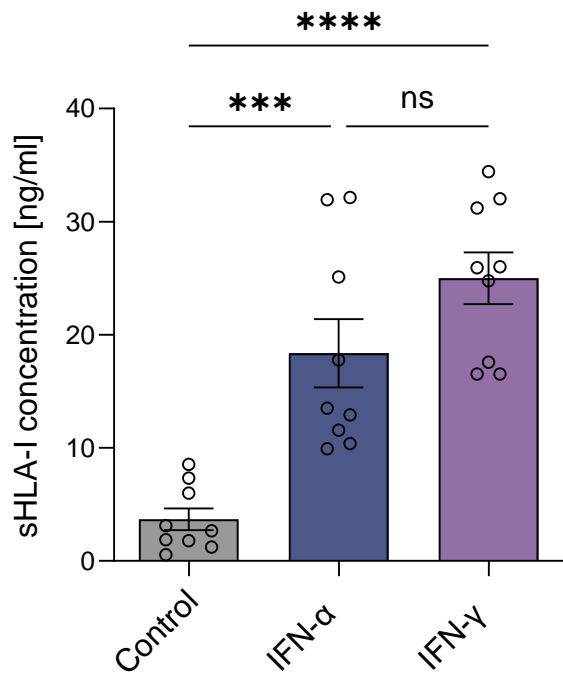
ESM Fig 2. Total and surface HLA-ABCE expression in IFN-treated HeLa and PANC-1 cell lines. Cell cultures were treated with IFN α or IFN γ for 24 h prior to preparing whole cell lysates for western blotting. HLA-ABCE protein expression was significantly upregulated in whole cell lysates of IFN α - and IFN γ -treated HeLa and PANC-1 cell lines. Cell surface expression of HLA-I was measured using flow cytometry. Surface HLA-I expression remains unchanged in both IFN α - and IFN γ -treated HeLa and PANC-1 cell lines. Statistical analysis was performed using one way ANOVA on data from three independent experiments. Error bars represent mean \pm SEM. $p < 0.05$: *; $p < 0.01$: **.



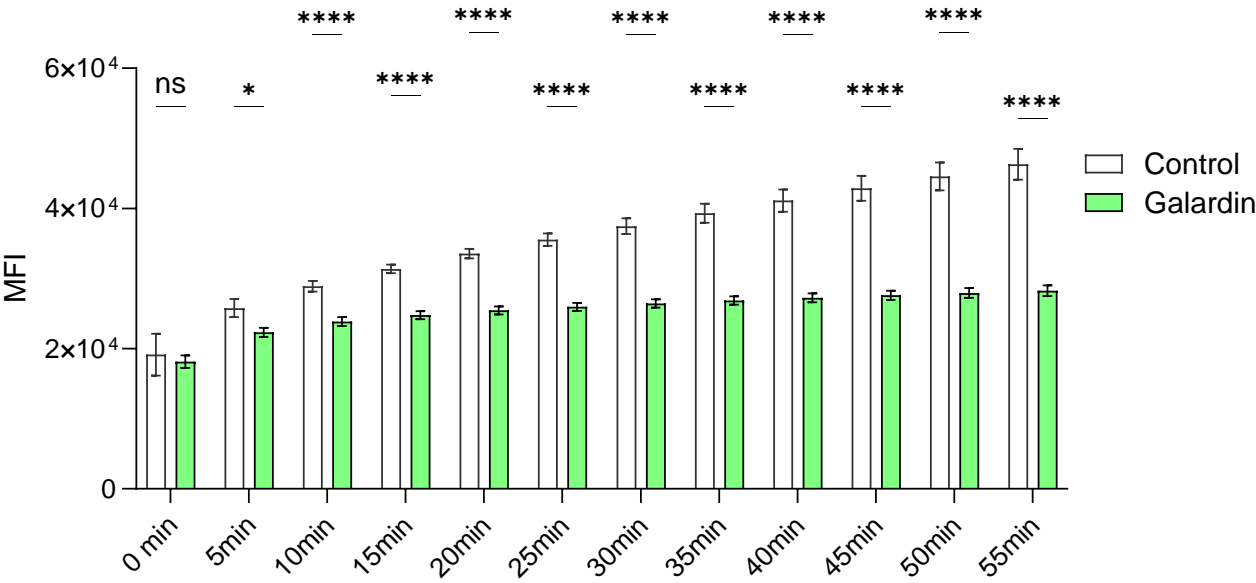
ESM Fig 3. sHLA-I expression in culture media of IFN-treated HeLa and PANC-1 cell lines. Cell cultures were treated with IFN α or IFN γ for 24 h prior to collecting cell culture media for ELISA. Levels of sHLA-I were significantly upregulated in culture media of IFN α - and IFN γ -treated HeLa (A) and PANC-1 cell lines (B). Statistical analysis was performed using one way ANOVA on data from three independent experiments. Error bars represent mean \pm SEM. $p < 0.01$: **; $p < 0.0001$: ****.



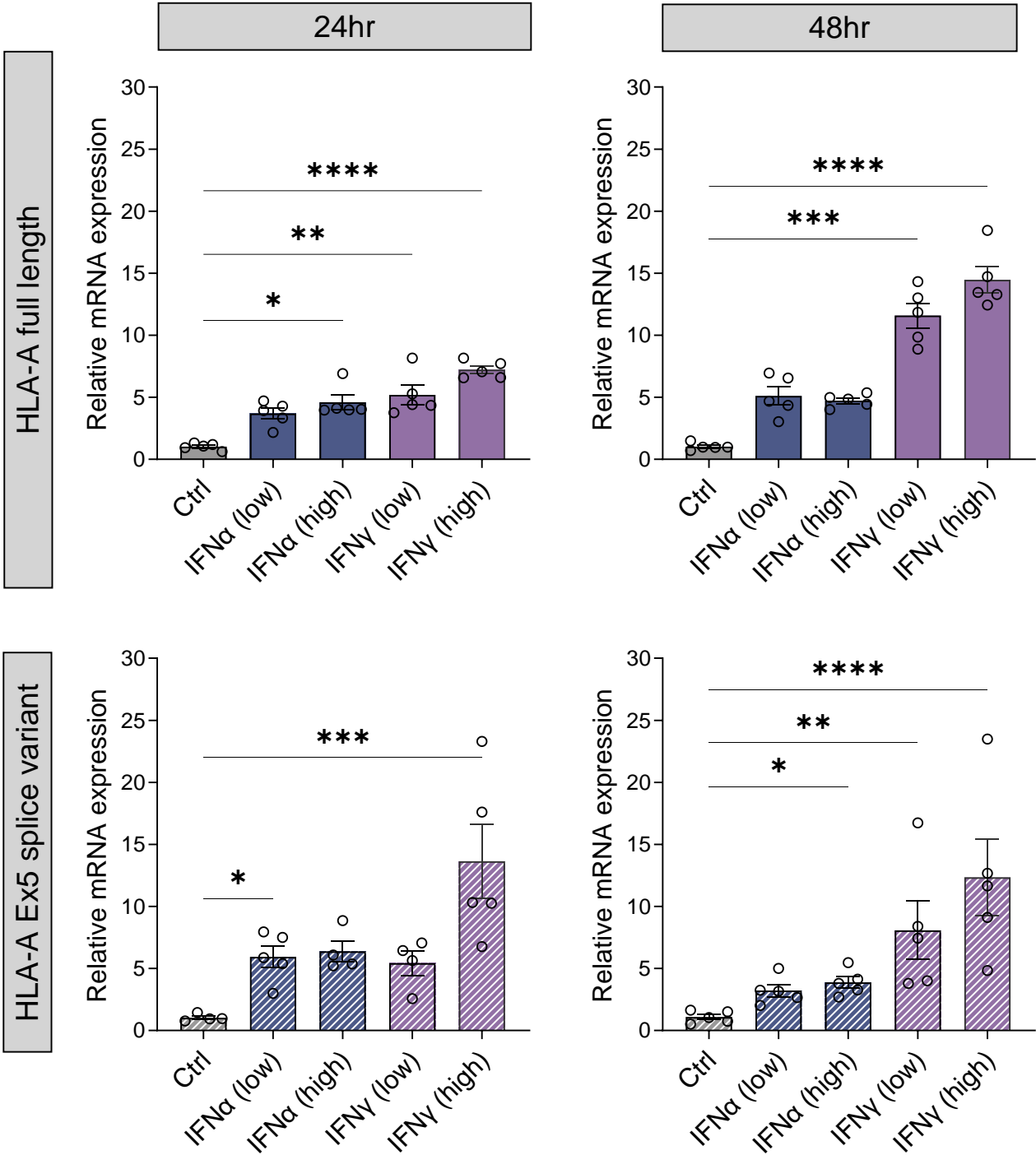
ESM Fig 4: Concentration of sHLA-I in the supernatant of IFN-treated EndoCβH1 cells.
The concentration of sHLA-I in the culture media was determined in untreated (control), IFNα (1000U/ml) or IFNγ (400U/ml)-treated EndoC-βH1 at 24 h. Each point represents the mean±SEM of three technical replicates, n=9 biological replicates. Statistical analysis was performed using one-way ANOVA. The HLA-I monomer standard curve was calculated on a separate plate. Normalisation of blank wells on each plate was performed to calculate the sHLA-I concentration.



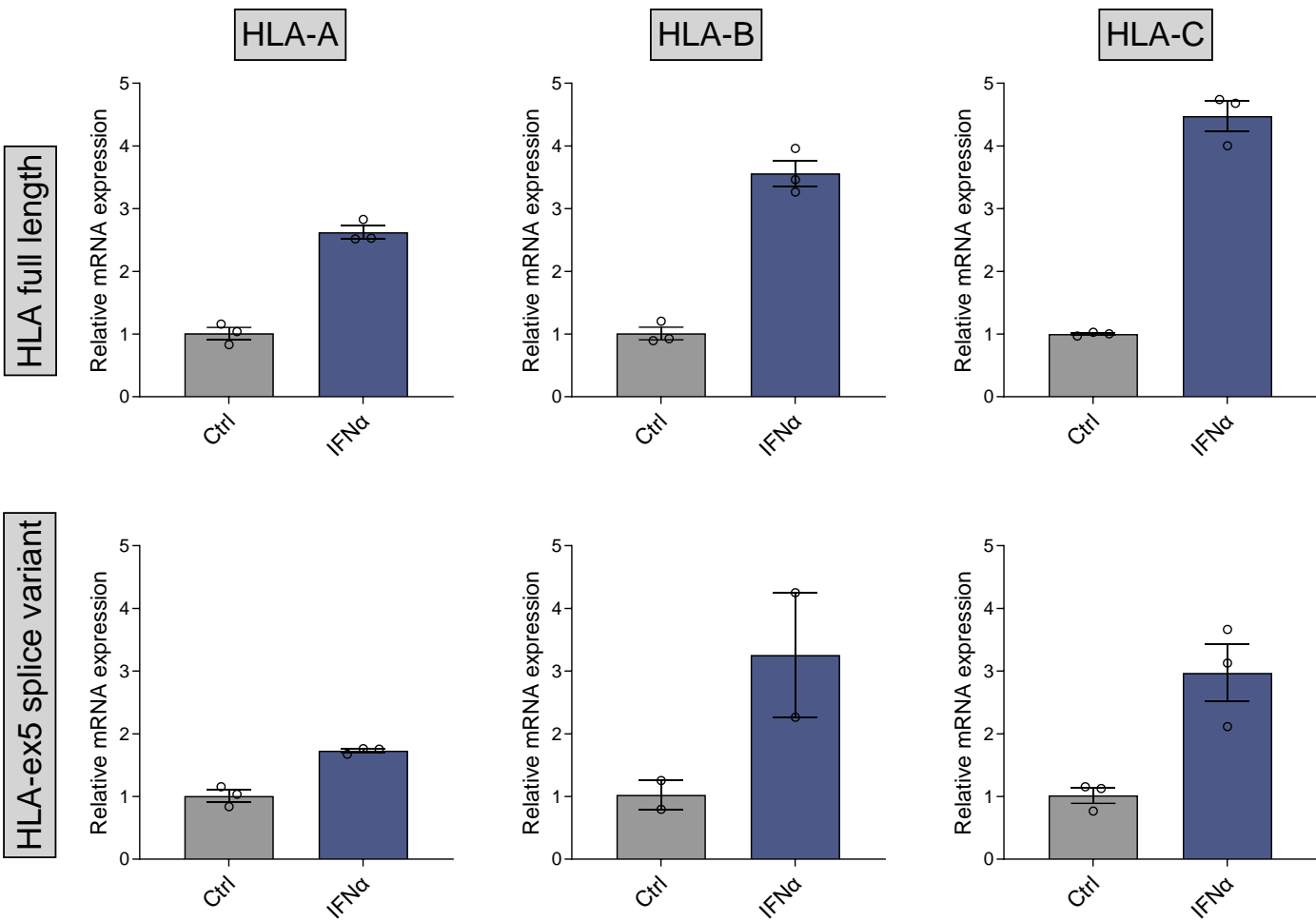
ESM Fig 5. MMP activity assay confirms the MMPase activity of galardin. To test whether galardin inhibits the activity of MMPases we used the fluorometric MMP Activity Assay Kit (Abcam). Briefly, EndoC-βH1 were lysed with RIPA buffer. Cell lysates were then mixed at 1:1 ratio with either Assay Buffer from the kit or with 10μM final concentration of galardin and incubated at 37°C for 30 minutes. These mixtures were then mixed at 1:1 ratio with MMP Green reagent and fluorescent intensity was measured immediately after mixing (time 0) and then every 5 minutes for a total of 55 minutes using a PHERAstar plate reader (BMG Labtech, UK).). Statistical analysis was performed using two way ANOVA on data from three independent experiments. Error bars represent mean +/- SEM. p < 0.01: **; p < 0.0001: ****.



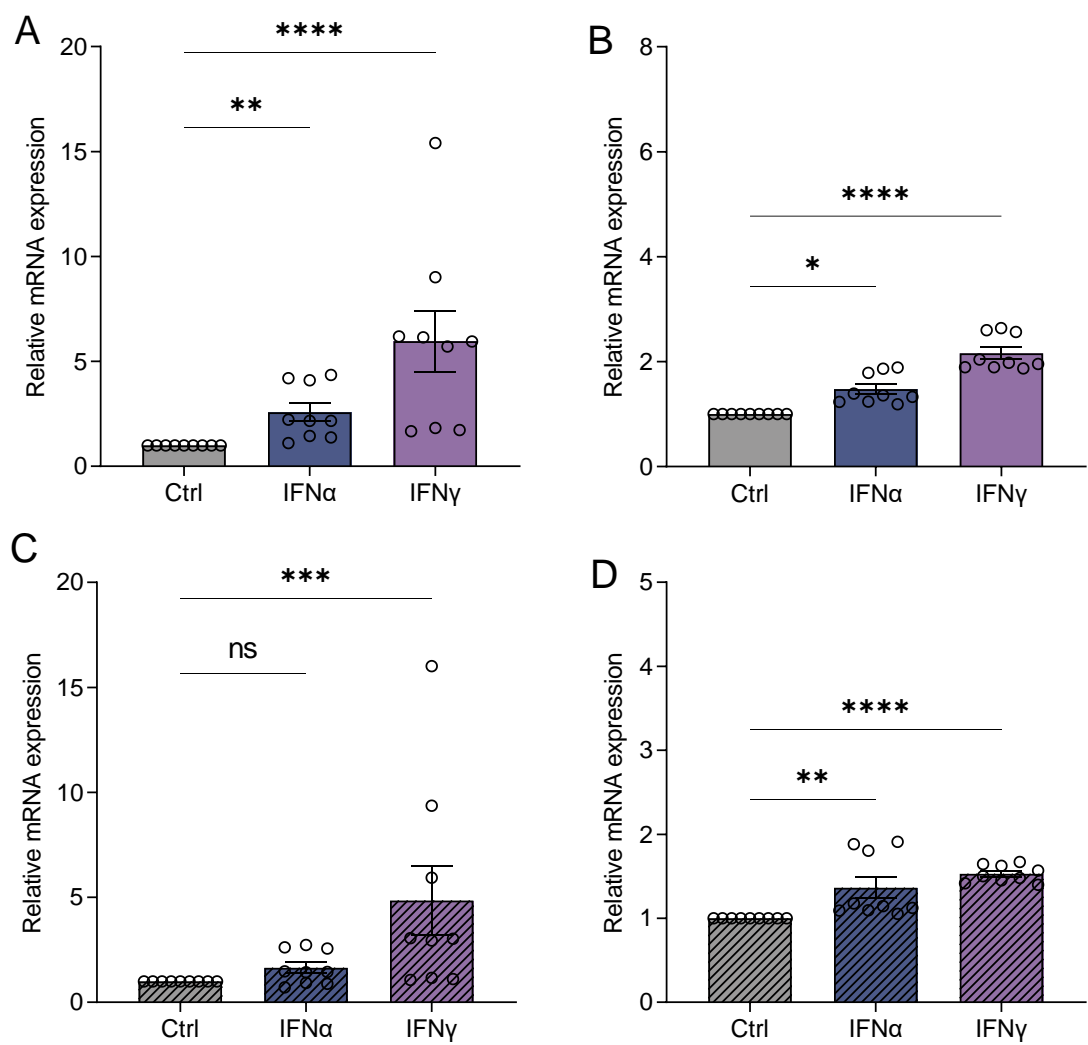
ESM Fig 6. mRNA expression of HLA-A and HLA-A exon 5 splice variant measured by qRT-PCR in IFN-treated ECN90 cell lines. Cell cultures were treated with IFN α or IFN γ for 24 or 48 h prior to extracting total RNA for cDNA synthesis. Expression of HLA-A mRNA (open bars) and HLA-A exon 5 splice variant mRNA (hashed bars) were upregulated in IFN-treated ECN90s. qRT-PCR was run for each cDNA and the data represent five independent experiments. Each data point represents 2^{- $\Delta\Delta$ CT} values of a treated sample normalised to the untreated (Ctrl) sample. Statistical analysis was performed using Kruskal-Wallis test. Error bars represent mean \pm SEM. p < 0.05: *; p < 0.01: **; p < 0.001: ***; p < 0.0001: ****.



ESM Fig 7: IFN-treatment of human islets induces an increase in mRNA for the exon 5 splice variant forms of HLA-A, B and C. Isolated human islets (n=1) were treated with or without IFN-α for 24 h prior to extracting total RNA for cDNA synthesis. Expression of HLA-A, B, C mRNA and HLA-A, B, C exon 5 splice variant mRNA were upregulated following IFN-α treatment. qRT-PCR was run for two-three individual aliquots of the cDNA samples (technical replicates). Each data point represents 2^{-ΔΔ CT} values of a treated sample normalised to the untreated control (Ctrl).



ESM Fig 8. mRNA expression of HLA-A and HLA-A exon 5 splice variant measured by qRT-PCR in IFN-treated HeLa and PANC-1 cell lines. Cell cultures were treated with IFN α or IFN γ for 24 h prior to extracting total RNA for cDNA synthesis. Expression of HLA-A mRNA (open bars) and HLA-A exon 5 splice variant mRNA (hashed bars) were upregulated in IFN-treated HeLa (A and C), and PANC-1 (B and D). qRT-PCR was run for three technical cDNA replicates in three independent experiments. Each data point represents $2^{-\Delta\Delta CT}$ values of a treated sample normalised to the untreated (Ctrl) sample. Statistical analysis was performed using Kruskal-Wallis test. Error bars represent mean \pm SEM. $p < 0.05$: *; $p < 0.01$: **; $p < 0.001$: ***; $p < 0.0001$: ****.



ESM Fig 9. Comparison of untreated cells revealed that EndoC-βH1 express significantly lower levels of surface HLA-I compared to PANC-1 and HeLa cells. Statistical analysis was performed using one way ANOVA on data from three independent experiments. Error bars represent mean +/- SEM. p < 0.05: *; p < 0.01: **; p < 0.001: ***.

