**S1 Fig : ER stress and apoptosis induction in response to different concentrations of Tunicamycin**. ***A and B.*** INS-1E cells were treated with indicated doses (mg/ml) of Tunicamycin for 8h and then the expression of ER stres markers BiP and XBP1s were analysed by Western blot (representative out of two experiments) (A) or cells were further infected with CVB5 at MOI 5 or mock infected (B). Cell viability was quantified using nuclear dyes 14h post-infection (n=2). Data are mean + SEM

**S2 Fig. CVB5 induces the expression of c-jun.** INS-1E cells were infected with CVB5 at MOI 5 and the expression of c-jun mRNA was measured by qRTPCR at different time points and normalized by the housekeeping gene GAPDH (n=4) (\*P<0.05 vs. time 0h (uninfected), ANOVA). Data are mean + SEM.

**S3 Fig. Both PKR and PERK activate eIF2α during CVB infection of beta cells**. INS-1E cells were transfected with siCTL or specific siRNAs against PERK (A, C) or PKR (B, C) and, after 48h of recovery, infected or not with CVB5 at MOI 1 for 24h. ***A and B.*** PERK and PKR knockdown was confirmed by Western blot; ***C.*** phosphorylation of eIF2α protein was evaluated by Western Blot (n = 3). \*P < 0.05, \*\*P < 0.01, \*\*\*P<0.001 vs. control condition or vs. the indicated conditions, ANOVA. Data are mean ± SEM.

**S4 Fig. CVB4 and CVB1 infection of the human pancreatic cell line EndoC-bH1 trigger the IRE1a pathway but do not induce CHOP expression**. ***A and B.*** EndoC-bH1 cells were infected with CVB4 at MOI 5 (A) and CVB1 at MO 0.1 (B) and the expression of the viral capsid protein (VP1), ER stress markers (p-eIF2a, XBP1s, CHOP) and JNK phosphorylation (p-JNK) was evaluated by Western Blot at different time points. One representative experiment out of 3 is shown.

**S5 Fig. JNK inhibition reduces CVB4-induced beta cell apoptosis and viral replication**. ***A to E***. INS-1E cells were infected with CVB4 at MOI 1 for 24h in the presence or absence of the chemical JNK inhibitors (SP600125 (10 μM) or JNK inhibitor V (5 μM)); A.Phosphorylation of JNK was determined by Western Blot and quantified by densitometry (n = 3 - 4); ***B and C.*** Apoptosis was evaluated using nuclear dyes and confirmed by the cleavage of caspase 3 as evaluated by Western Blot (n = 3 - 4); ***D.*** Viral replication was quantified by evaluation of viral titration as described in Material and Methods (n = 2 - 4); ***E .*** VP1 expression was determined by Western Blot and quantified by densitometry (n = 3). \*P < 0.05, \*\*P < 0.01 vs. the indicated conditions, ANOVA. Data are mean ± SEM.

**S6 Fig. The late, but not the early viral protein expression, is modified by chemical JNK inhibition.** INS-1E cells were infected or not with CVB5 at MOI 5 for the indicated time points. CVB5 infection was done in the presence of JNK inhibitor (SP600125 (10 μM)) or the vehicle DMSO and the viral capsid protein VP1 was evaluated by Western Blot and quantified by densitometry. (n = 3, \*P < 0.05, vs time 0h (uninfected), \*\*P < 0.01 vs. DMSO 8h, ANOVA). Data are mean ± SEM.

**S7 Fig. Prevention of JNK phosphorylation inhibits virus-induced cell death and viral protein expression in EndoC-βH1 cells. *A to F***. EndoC-βH1 cells were infected or not with CVB4 at MOI 5 alone or in combination with JNK chemical inhibitors (SP600125 (10 μM) or JNK inhibitor V (5 μM)) for 24h; ***A and D.*** JNK activation was determined by Western Blot (n = 3); ***B and E***. Cell viability was quantified using nuclear dyes (n = 4). ***C and F***. VP1 expression was evaluated by Western Blot (n = 3 - 4). \*P < 0.05, \*\*P < 0.01 vs. the indicated conditions, ANOVA. Data are mean ± SEM.

**S8 Fig. Prevention of JNK phosphorylation reduces CVB1 viral protein expression in EndoC-βH1 cells**. ***A to B.*** EndoC-βH1 cells were infected or not with CVB1 at MOI 0.1 alone or in combination with JNK chemical inhibitors (SP600125 (10 μM)(A) or JNK inhibitor V (5 μM)(B)) for 24h; VP1 expression was evaluated by Western Blot (one representative experiment).

**S9 Fig. JNK is required for CVB amplification at a post-entry step.** INS-1E cells were infected with CVB5 at MOI5 and treated or not (NT) with the JNK inhibitor SP600125 (10 μM). SP600125 was added at the time of infection (T0) or after 1h (T1), 2h (T2) or 3h (T3) post infection. The viral capsid protein VP1 and the housekeeping protein tubulin were evaluated by Western Blot 24h post infection. (The figure is representative of 2 independent experiments).