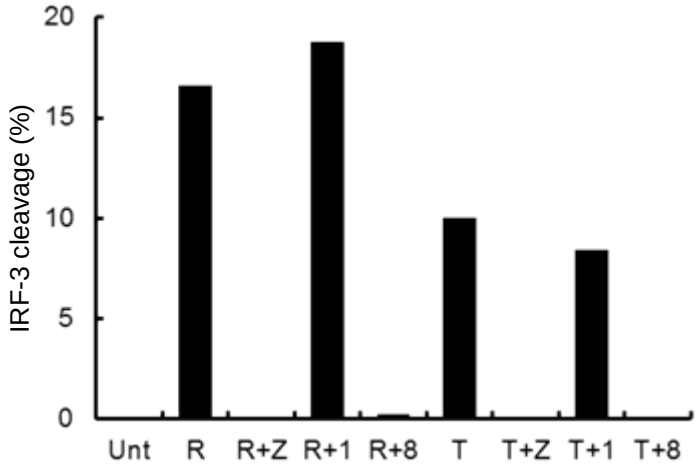

Figure S1: Caspase-8 activity is required for the cleavage of IRF-3. P2.1 cells expressing IRF-3, were either treated (T) or transfected (R) with poly(I:C) in the absence or the presence of inhibitors of multiple caspases (Z), caspase-1 (1), or caspase-8 (8) for 8 h (as described in Fig 3A), and cell lysates were analyzed by Western Blot for IRF-3 (shown in Fig 3A) and cleavage of IRF-3 (presented here.)

Figure S1

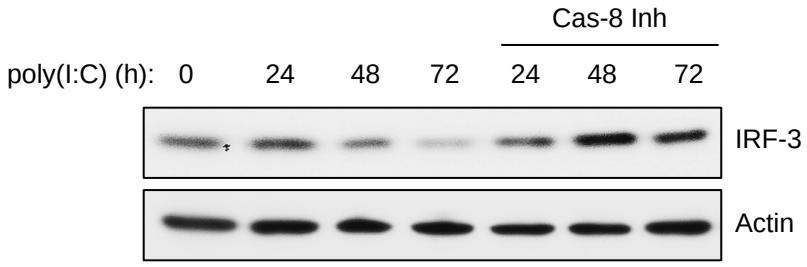

Figure S2: Caspase-8 inhibitor blocks TLR3 signaling induced degradation of IRF-3. HT1080 cells were treated with poly(I:C) (TLR3 activation) in the absence or presence of an inhibitor of caspase-8 (z-IETD) for the indicated times, and cell lysates were analyzed for IRF-3 by Western Blot.

Figure S2

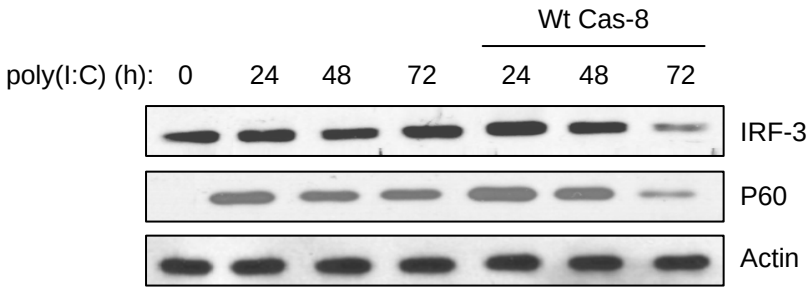

Figure S3: Ectopic expression of caspase-8 causes degradation of IRF-3 upon TLR3 signaling. ARPE19 cells, expressing Wt caspase-8, were treated with poly(I:C) (TLR3 activation) for the indicated times, and cell lysates were analyzed for IRF-3 and induction of P60 by Western Blot.

Figure S3

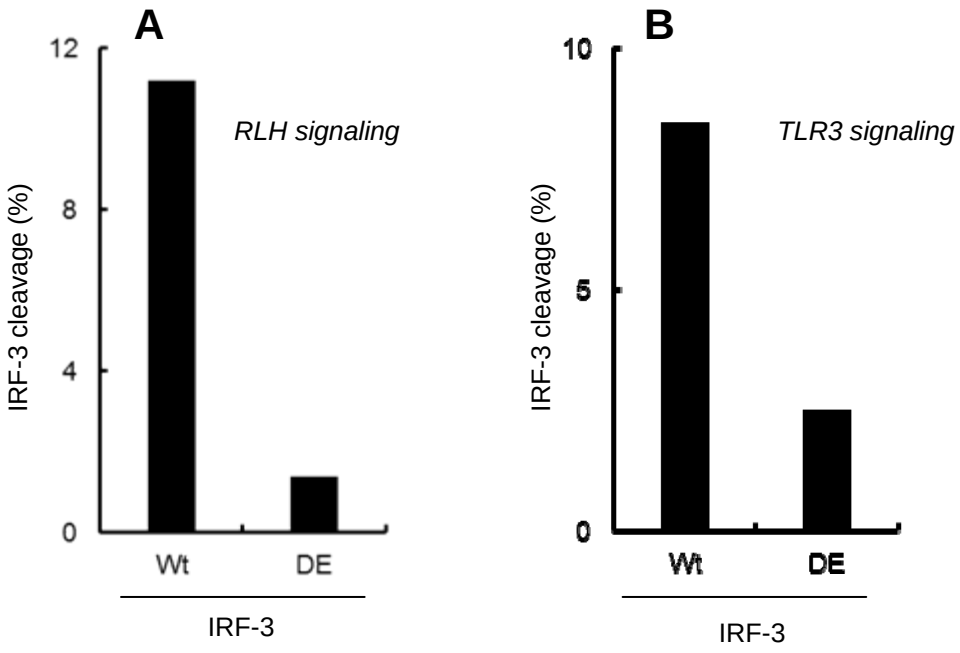

Figure S4: Mutation of caspase-8 recognition motif leads to impaired cleavage of IRF-3. P2.1 cells expressing Wt or the D121E (DE) mutant of IRF-3,were either transfected (A) or treated (B) with poly(I:C), and cell lysates were analyzed by Western Blot for IRF-3 (shown in Fig 6A and 6B) and cleavage of IRF-3 (presented here).

Figure S4

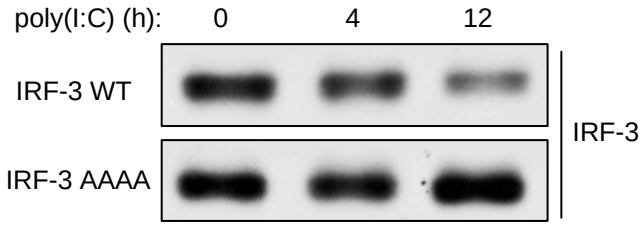

Figure S5: Cleavage deficiency leads to impaired degradation of IRF-3. P2.1 cells expressing Wt or IRF-3 AAAA mutant (^{118}SQPD^{121} to AAAA), were transfected with poly(I:C) for the indicated times, and cell lysates were analyzed for IRF-3 by Western Blot.

Figure S5

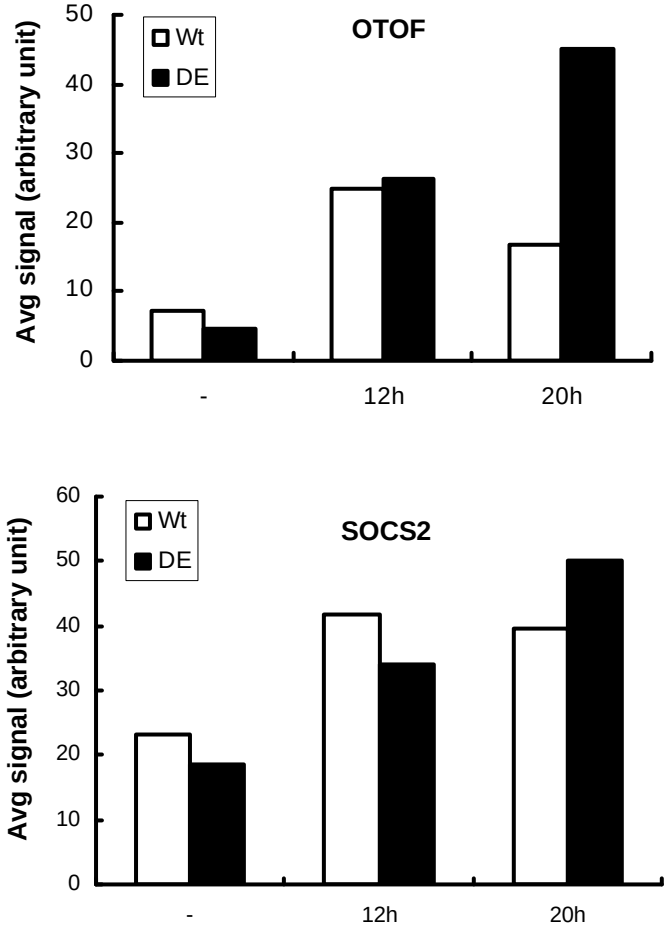

Figure S6: Sustained expression of genes by non-cleavable mutant of IRF-3. Two candidate genes (OTOF and SOCS2) which followed the sustained expression patterns at the later time (20h) by the mutant IRF-3 (DE); average signal from the microarray analysis is presented here for the two indicated genes.

Figure S6

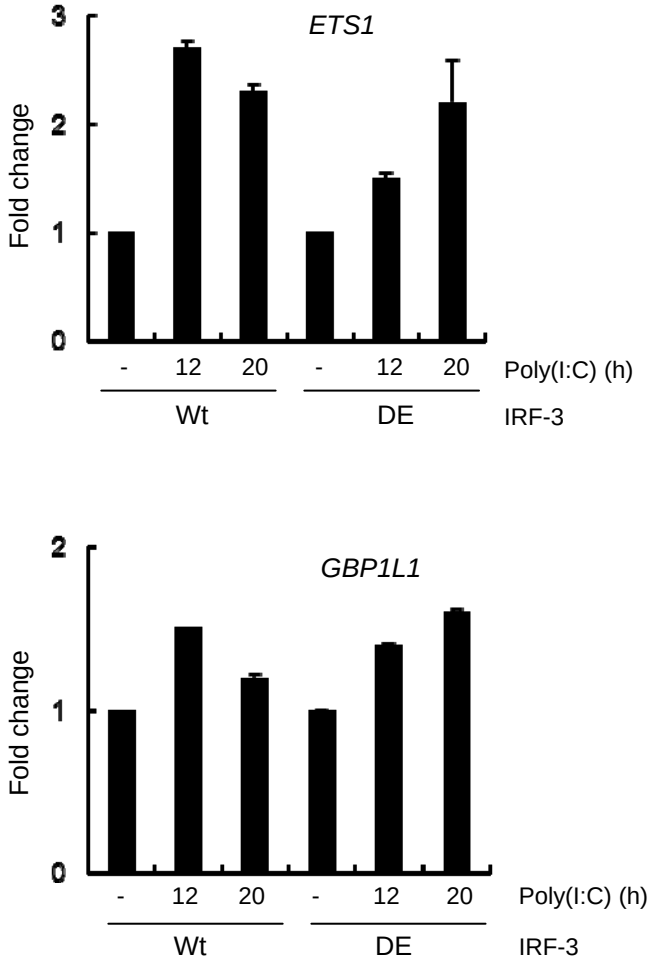

Fig S7. Altered expression of dsRNA-induced genes by impaired cleavage of IRF-3. Two genes were selected from the microarray analyses (Table 1) and tested for their average expression by quantitative real-time PCR from the same samples which were used for microarray, using the software LightCycler 480 SW 1.5. The data represent the average fold changes of triplicate samples for these mRNAs following poly(I:C) transfection, at the indicated times, of wild-type or mutant (D121E) IRF-3. Error bars represent the standard deviation of the fold changes between triplicate samples.

Figure S7