Expanded View Figures

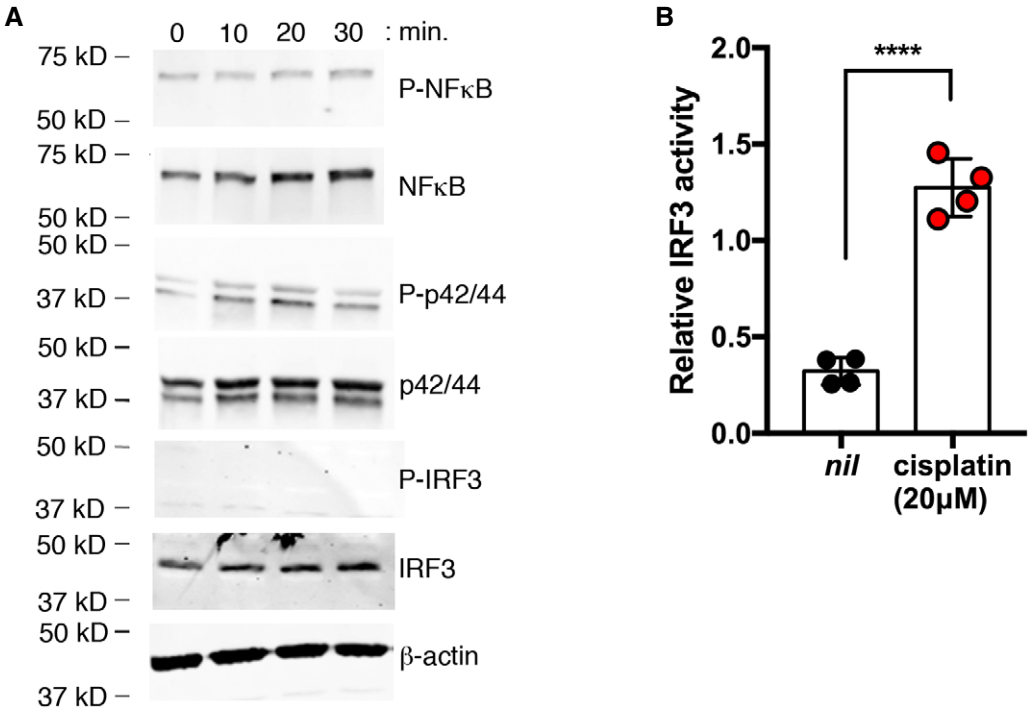

Figure EV1. Cisplatin induces rapid MyD88-dependent signaling and slower MyD88-independent signaling downstream of Tlr4.

A Phospho-signaling in HEI-OC1 cells following treatment with 20 μM cisplatin or 10 ng/ml LPS at the indicated time points (representative of 3 independent biological replicates).

B IRF3 reporter activity in HEI-OC1 cells treated with and without 20 μM cisplatin after 24 h ($n = 4$ independent biological replicates).

Data information: In (B), data are shown as mean and standard deviation. ****$P < 0.0001$ (unpaired Student's t-test).
Source data are available online for this figure.

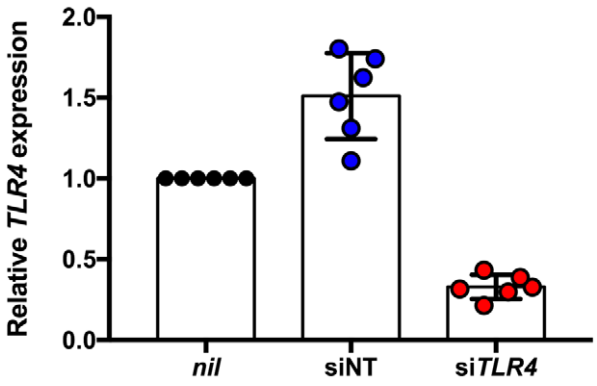

Figure EV2. *TLR4* expression in HeLa cells is significantly reduced by transient silencing.

TLR4 expression levels (relative to *nil* treatment) in HeLa cells transfected with non-targeting (siNT) or *TLR4*-targeting (si*TLR4*) siRNA molecules and treated with 30 μM cisplatin.

Data information: Actual individual data from 2 independent experiments are plotted with mean and standard deviation indicated.
Source data are available online for this figure.

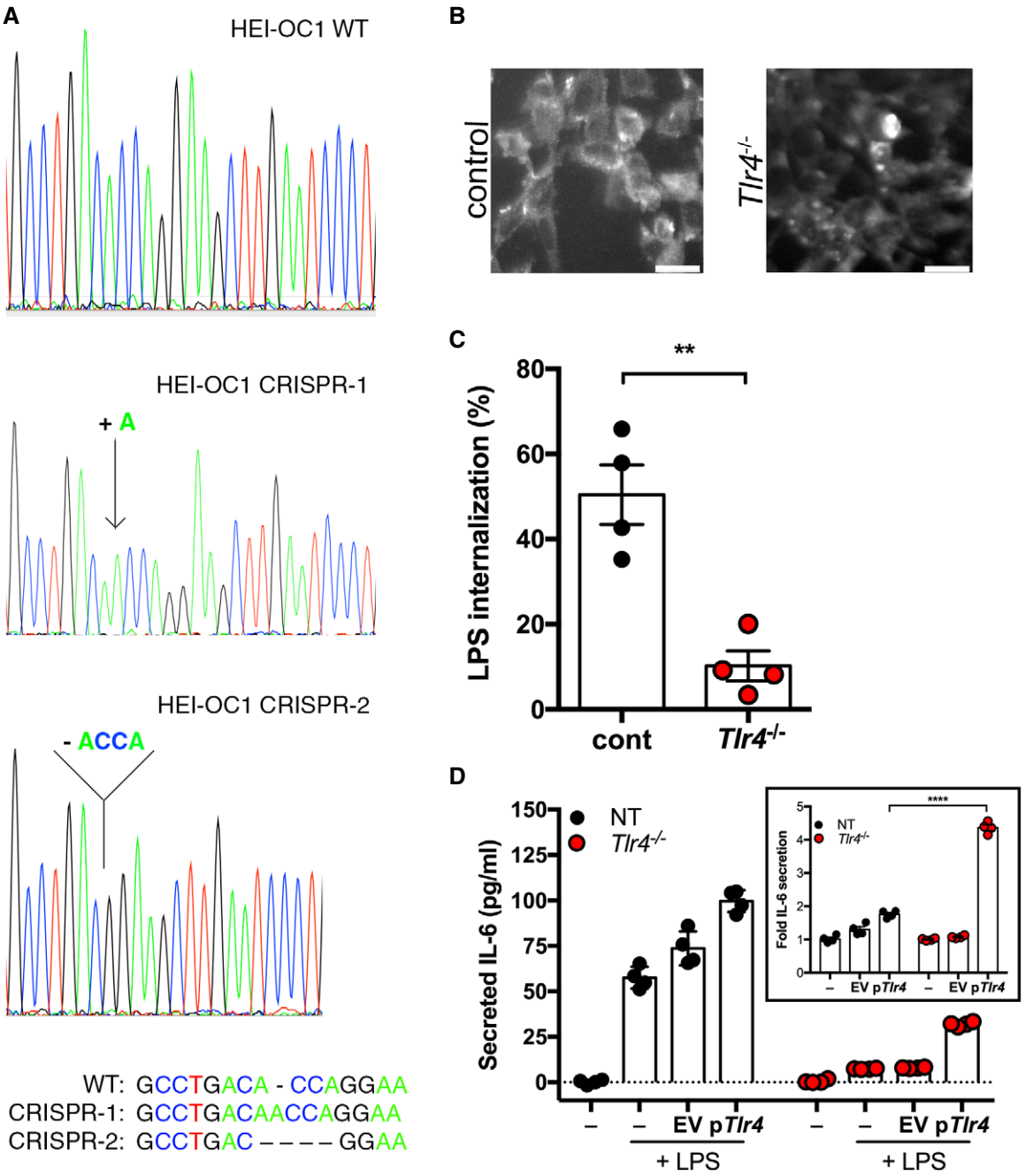

Figure EV3. *Tlr4*$^{-/-}$ HEI-OC1 cells show diminished LPS-responsiveness unless complemented with *Tlr4*.

A Comparison of genomic DNA at the *Tlr4* locus from *Tlr4*$^{-/-}$ HEI-OC1 and wild-type cells. Sequences from the *Tlr4*$^{-/-}$ cell line contained a single nucleotide insertion or four nucleotide deletion and summarized below.

B Anti-TLR4 staining in *Tlr4*$^{-/-}$ and control HEI-OC1 cells. Bars (lower right) are 50 μm.

C Flow cytometric analysis of conjugated LPS internalization in *Tlr4*$^{-/-}$ and control HEI-OC1 cells ($n = 4$ independent biological replicates).

D IL-6 secretion in *Tlr4*$^{-/-}$ and control HEI-OC1 cells transfected with empty vector (EV), *Tlr4* (p*Tlr4*), or left untransfected (–) and subsequently treated with 100 ng/ml LPS ($n = 4$ independent biological replicates). *Inset*, fold induction of IL-6 secretion was determined relative to the untransfected cells treated with LPS.

Data information: In (C and D), data are presented as mean and standard deviation. Statistical comparisons were assessed by 2-way ANOVA (D). $^{**}P < 0.01$; $^{****}P < 0.0001$ (unpaired Student's *t*-test, C; Bonferroni test, D).
Source data are available online for this figure.

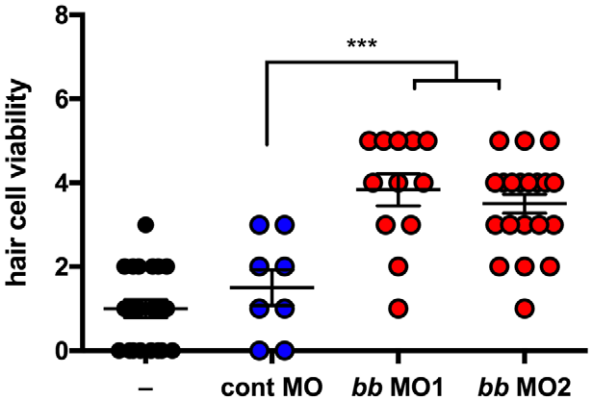

Figure EV4. Cisplatin-induced neuromast toxicity is reduced in independent *tlr4bb* knockdowns.

Hair cell viability in larval zebrafish pre-treated with control-, splice-targeting *tlr4bb* (MO1) or translation-targeting *tlr4bb* (MO2) morpholinos prior to treatment with 15 μM cisplatin.

Data information: Each data point represents a score of hair cell integrity in an individual animal (taken from multiple samples per animal) with lines representing mean and standard deviation. Statistical comparisons to control morpholino were assessed by one-way ANOVA. ***$P < 0.001$ (Tukey test). Source data are available online for this figure.