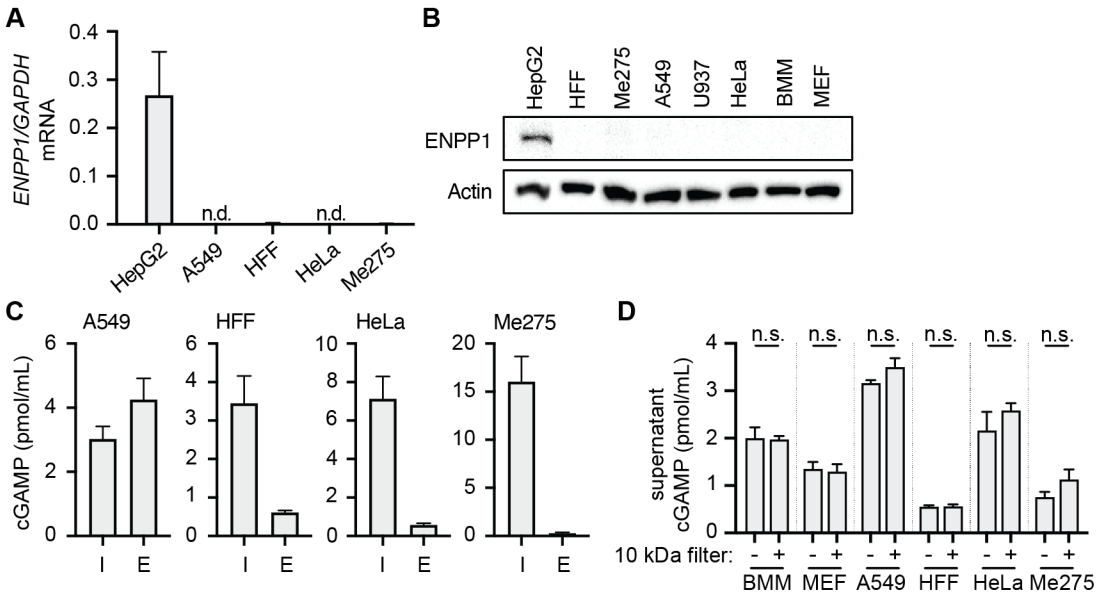
Figure S1. Quantification of ENPP1 and cGAMP, Related to Figure 1



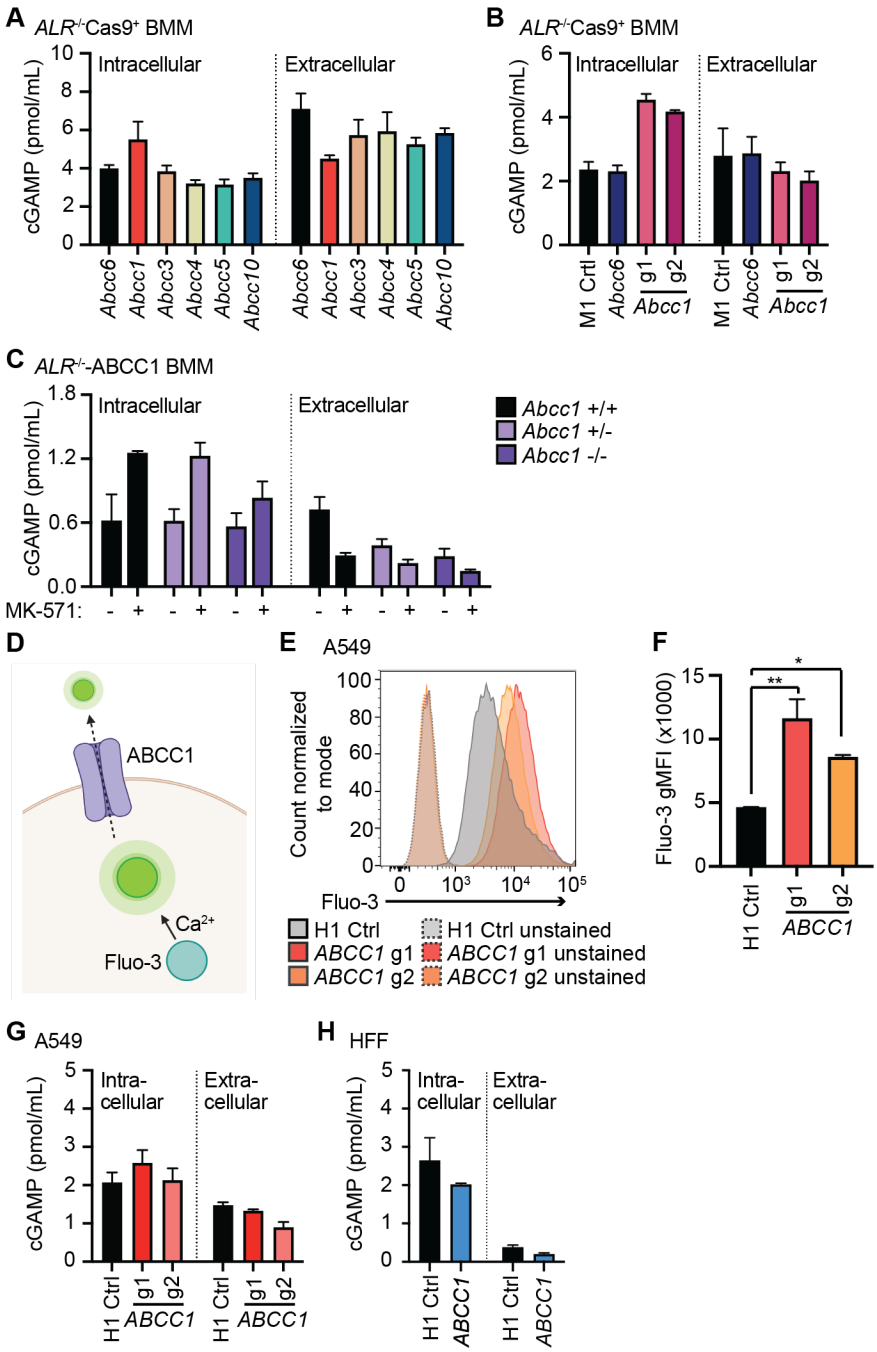
(**A**) Quantification of *ENPP1* mRNA transcript in indicated cell types by RT-qPCR. HepG2 cells are used as control for *ENPP1* expression.

(**B**) Quantification of ENPP1 protein by Western blot. HepG2 cells are used as control for ENPP1 expression.

(**C**) Quantification of intracellular and extracellular cGAMP from indicated cell types following CT DNA transfection for 8 hours.

(**D**) Quantification of extracellular cGAMP from the indicated cell types, before and after filtration through a 10 kDa filter for exosome removal. Error bars represent mean ± SD of three biological replicates per group. All data shown are derived from a single representative experiment. Comparative results were obtained across three independent experiments.

Figure S2. cGAMP and Fluo-3 measurements, Related to Figure 3



(**A, B**) Quantification of intracellular and extracellular cGAMP from indicated targeted lines of BMMs following CT DNA transfection for 8 hours.

(**C**) Quantification of intracellular and extracellular cGAMP from indicated genotypes following CT DNA transfection for 8 hours. Cells were pretreated with 25 μM MK-571 or mock.

(**D**) Schematic of Fluo-3AM staining and export.
(**E**) *ABCC1*- or H1 control-targeted A549 cells were stained with Fluo-3AM and incubated for 1 hour at 37 C, followed by flow cytometric quantification of Fluo-3AM staining intensity.
(**F**) gMFI quantification of flow cytometry data from (E).
(**G, H**) Quantification of intracellular and extracellular cGAMP from indicated cell types following CT DNA transfection for 8 hours. Error bars represent mean ± SD of three biological replicates per group. Statistical analysis in (E) was performed using a one-way ANOVA comparing all groups to H1 control and corrected for multiple comparisons using the Holm-Sidak method. *p<0.05, **p<0.01. All data shown are derived from a single representative experiment. Comparative results were obtained across two (C-E) or three (A, B, F, G) independent experiments.

Figure S3. ENPP1, Fluo-3, and cGAMP measurements, Related to Figure 4

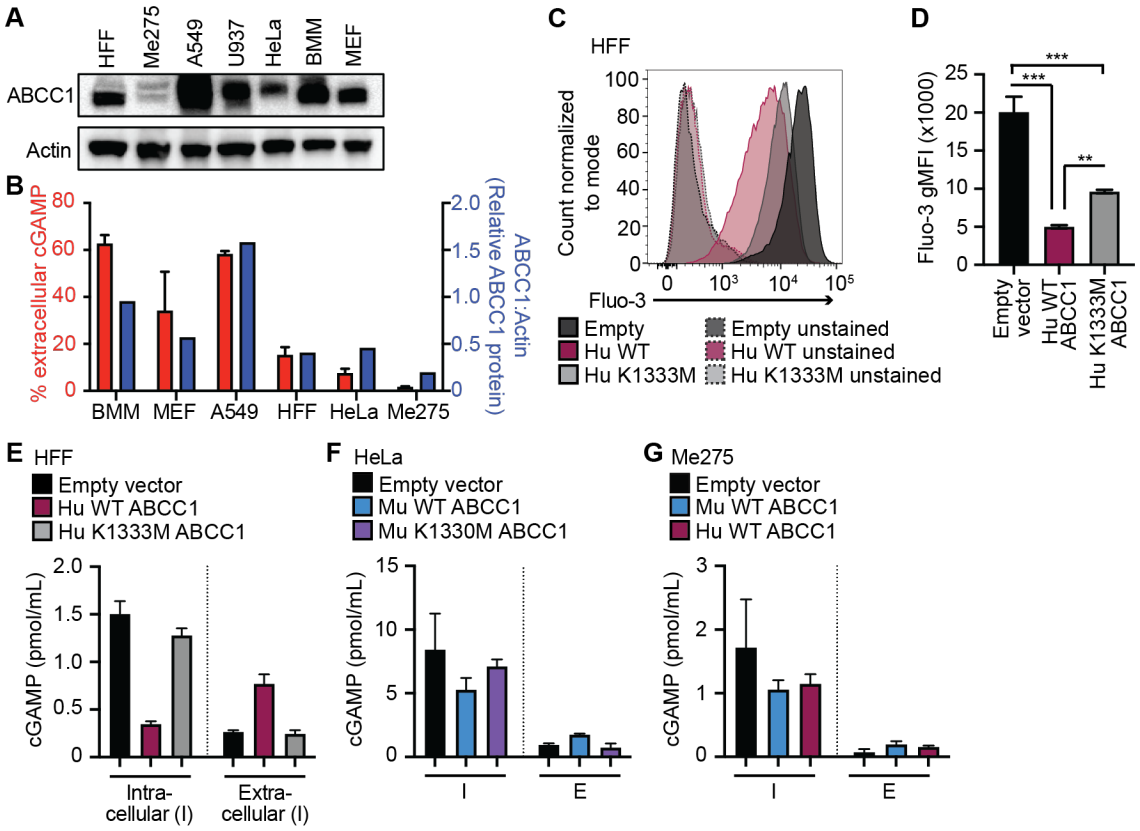


Figure S3, refers to Figure 4

(**A**) Western blot analysis of indicated cells for ABCC1 protein expression.

(**B**) cGAMP export efficiency calculated in Fig. 1E overlayed with densitometry from (A) for ABCC1 protein expression normalized to Actin expression.

(**C**) Cells from Fig. 4A were stained with Fluo-3AM and incubated for 1 hour, followed by flow cytometric quantification of Fluo-3AM staining intensity.

(**D**) Quantification of gMFI from (C).

(**E-G**) Quantification of intracellular and extracellular cGAMP from indicated cell types following CT DNA transfection for 8 hours. Error bars represent mean ± SD of three biological replicates per group. Statistical analysis in (D) was performed using a one-way ANOVA comparing the mean of each group to the mean of every other group, corrected for multiple comparisons using the Holm-Sidak method. **p<0.01, ***p<0.001. All data shown are derived from a single representative experiment. Comparative results were obtained across three independent experiments (C-G).