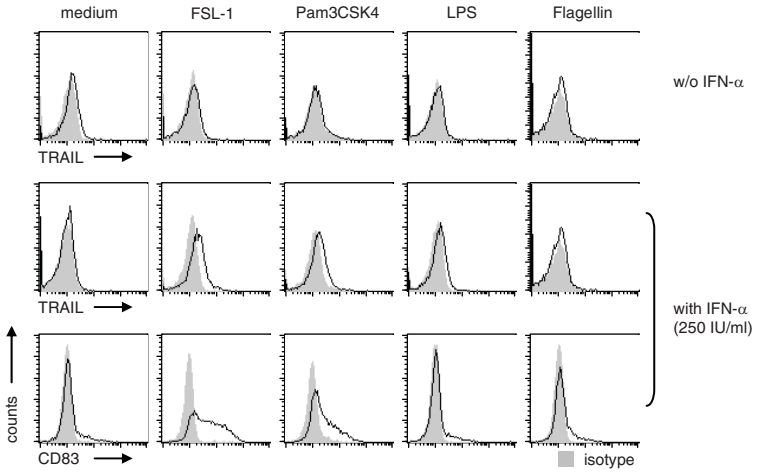
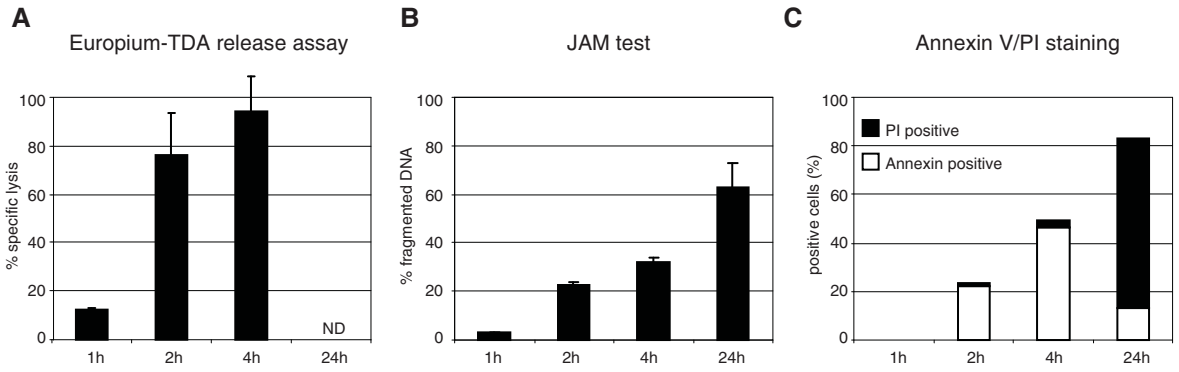
**Supplemental Fig. 1**



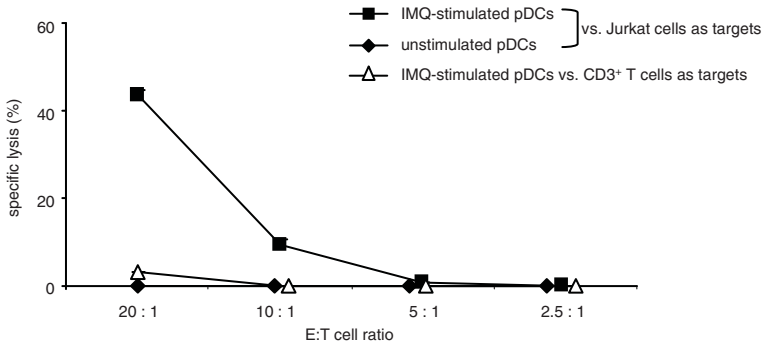

**Supplemental Fig. 1. Ligands to TLR2/1 and TLR2/6, but not TLR4 or TLR5, induce TRAIL expression on pDCs in the presence of suboptimal/physiological doses of IFN-α.** Purified pDCs were stimulated with the TLR ligands FSL-1 (TLR2/6), Pam3CSK4 (TLR2/1), LPS (TLR4) and FLA-ST (TLR5) with or without suboptimal doses of IFN-α (250 IU/ml). The surface expression of TRAIL and the activation marker CD83 were assessed by FACS analysis (n=1).

**Supplemental Fig. 2**



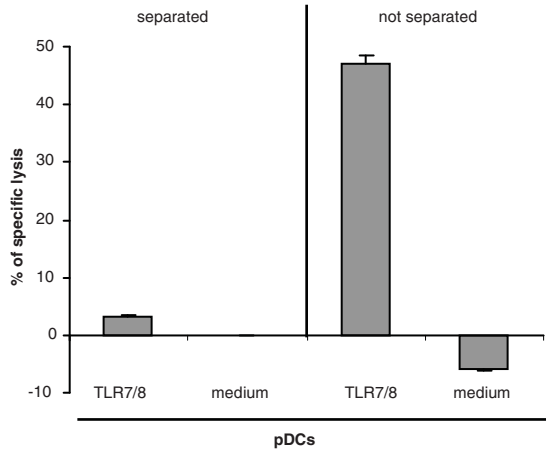

**Supplemental Fig. 2. Signs of cell lysis or apoptosis mediated by TRAIL are already detectable after 1-2 h.** Jurkat cells were treated with skTRAIL (100 ng/ml) for up to 24h. The extent of cell death was evaluated using 3 different assays: *(A)* the Europium-TDA release cytotoxicity assay (described in Materials & Methods), *(B)* the JAM test, which measures DNA fragmentation and *(C)* flow cytometric Annexin V/Propidium iodide (PI) staining, detecting early and late apoptotic cells, respectively. Data in *A* and *B* represent mean of duplicates of specific lysis/DNA fragmentation ± SD (n=1-2). ND, not done (technical reasons – high background).

**Supplemental Fig. 3**




**Supplemental Fig. 3. TLR7/8-activated TRAIL$^+$ pDCs do not lyse autologous CD3$^+$ T cells.** Cytotoxic activity of IMQ-activated (5 µg/ml) pDCs or pDCs that were left unstimulated overnight was determined after 2 h. Jurkat cells and unstimulated CD3$^+$ T cells isolated from the same donor as effector pDCs were used as target cells. Data represent mean of duplicates of specific lysis ± SD and one representative example is shown (n=3).

**Supplemental Fig. 4**




**Supplemental Fig. 4. TLR7/8-activated TRAIL$^+$ pDCs do not lyse tumor cells if separated by a transwell.** Cytotoxic activity of TLR7/8-activated pDCs against BATDA-labeled Jurkat cells that were either cocultured in the same well or separated by a 1 μm transwell (Corning) was determined after 2 h. Data represent mean of duplicates of specific lysis ± SD of one experiment.