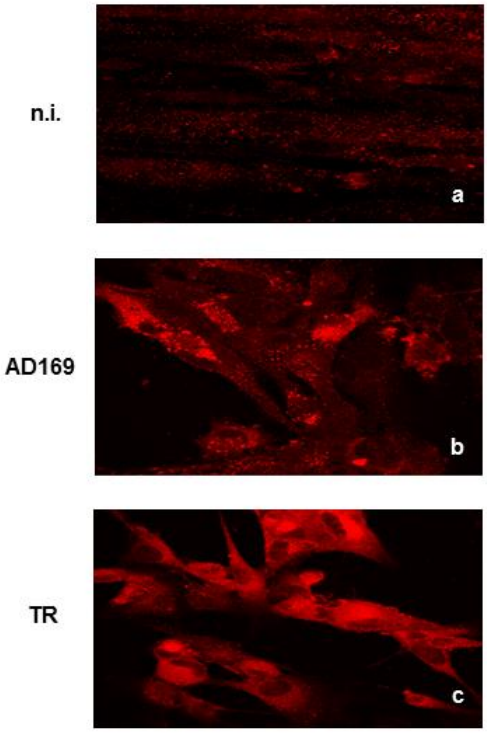
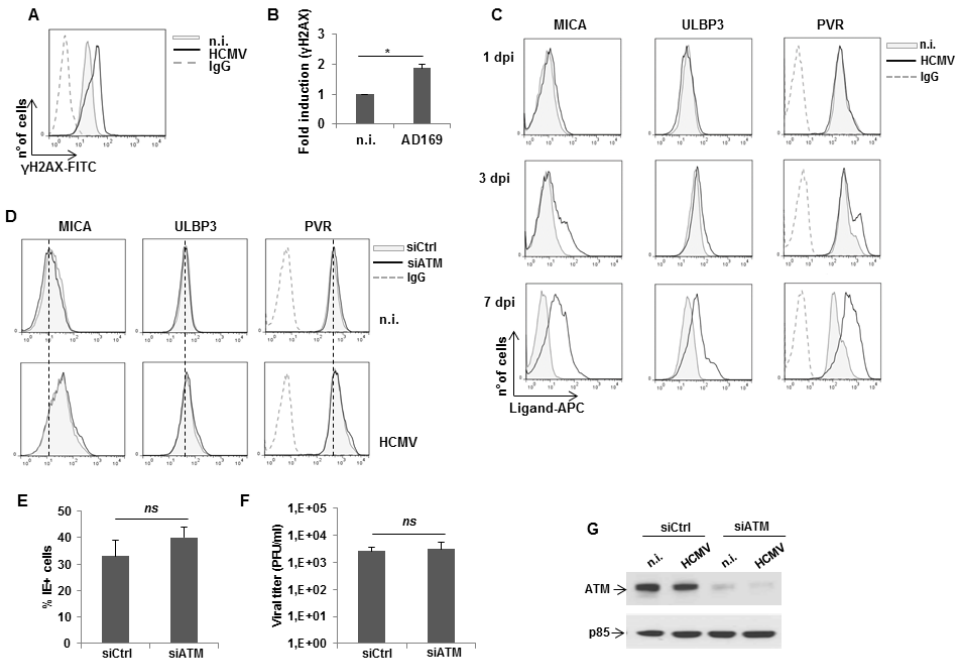
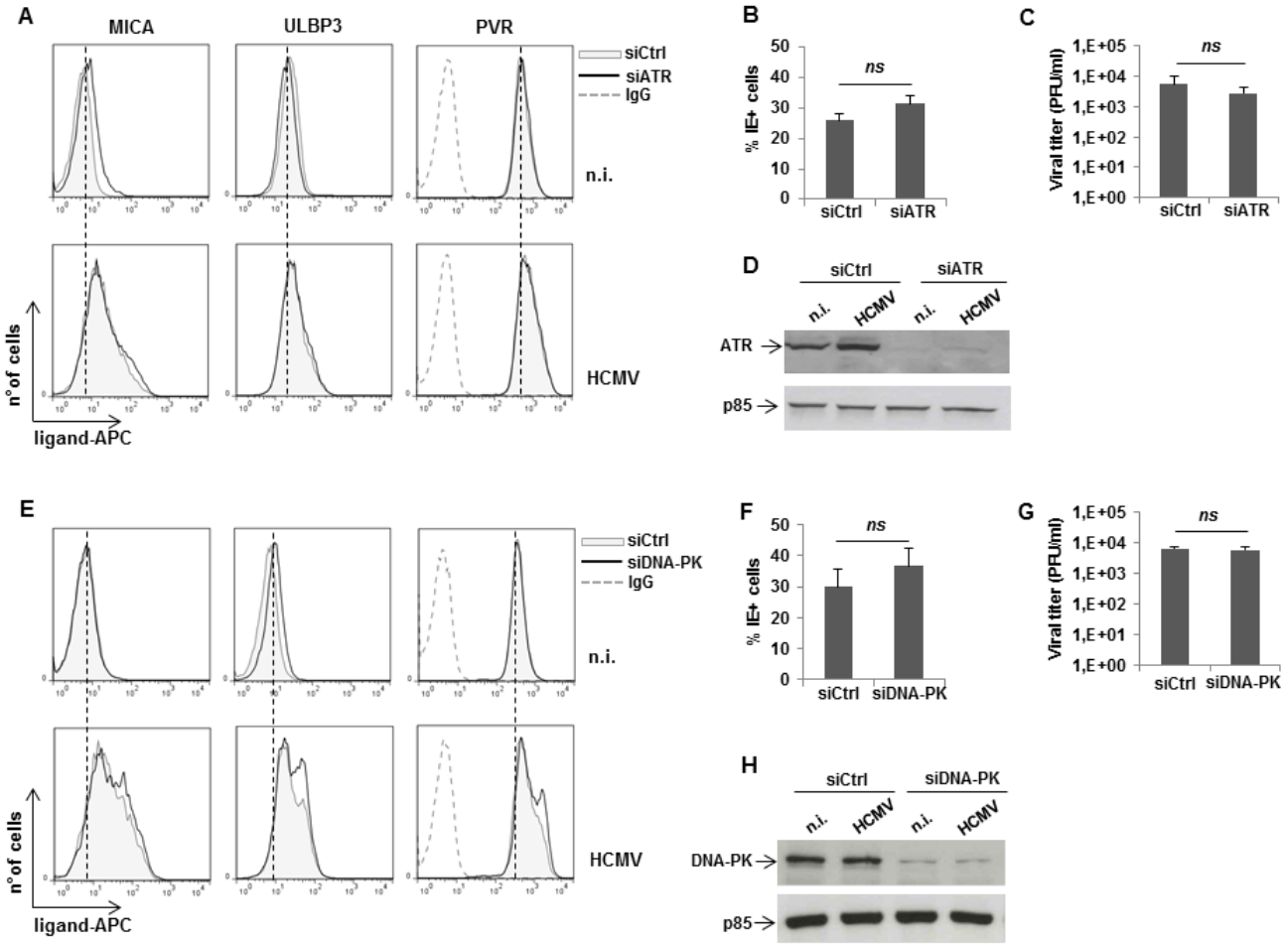


Supplementary Figure 1. HCMV AD169 and TR strains stimulate expression of cell surface MICA. HFFs were grown to subconfluence and then infected with HCMV AD169 and TR (MOI of 1 PFU/cell), or mock infected (n.i.). At 4 dpi, cells were fixed and immunostained for MICA ligand, without permeabilization. Immunofluorescence experiments were repeated three times, and representative results are presented. Magnification: 60X.



Supplementary Figure 2. Activation of DDR pathway after HCMV infection, and effect of the absence of ATM on MICA, ULBP3 and PVR cell surface expression. A) HFFs were infected with HCMV AD169 (MOI of 1 PFU/cell) or mock-infected (n.i.) and harvested at 3 dpi. Phospho-histone H2AX (γH2AX) (Ser139) expression levels were evaluated by FACS on cells stained with a specific FITC-conjugated mAb. A representative experiment of four performed at 3 dpi is shown. **B)** Data are presented as fold induction of γH2AX MFI values in HCMV-infected versus n.i. cells, set at 1. Data from four experiments ± SEs. **C)** ATM-deficient (AT-/-) fibroblasts were mock-infected (n.i.) or infected with HCMV AD169 (MOI of 1 PFU/cell). At different dpi, cells were harvested and ligand expression was analyzed as in figure 1. A representative experiment out of three is shown. **D-G)** HFFs were transiently transfected with siRNA specific for ATM (siATM) or with a non-targeting siRNA (siCtrl). 24 h later, cells were either mock-infected (n.i.) or infected with HCMV AD169 (MOI of 1 PFU/cell). At 2 dpi, cells and supernatants were harvested and assayed for ligand expression, percentage of IE+ cells, infectious virus production, and immunoblot analysis. **D)** Flow cytometry analysis of MICA, ULBP3 and PVR expression was performed as described in figure 1. Vertical dotted lines indicate the center of the peak for each ligand in not infected-siCtrl transfected cells. All panels derive from the same experiment, representative of three. **E)** The % of IE+ cells was analyzed by FACS on HCMV-infected cells stained intracellularly with a specific anti-IE mAb. **F)** Cell culture supernatants were assayed for infectious virus production by plaque assay. **G)** The levels of ATM protein expression were assayed by immunoblot analysis with a specific antibody. Immunodetection of the p85 subunit of PI-3K was used as a control of protein loading. ns: not statistically significant difference with Student's t-test.



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29 **Supplementary Figure 3. ATR or DNA-PK silencing does not affect MICA, ULBP3 and PVR expression.**
30 HFFs were transfected with siRNA specific for ATR (siATR) (panels A-D), DNA-PK (siDNA-PK) (panels E-H),
31 or a non-targeting siRNA (siCtrl), and then infected and harvested as described in Fig. S3. **A) and E)** Flow
32 cytometry analysis of MICA, ULBP3 and PVR expression was performed as described in figure 1. Vertical dotted
33 lines indicate the center of the peak for each ligand in not infected-siCtrl transfected cells. All panels in A) or E)
34 derive from the same experiment, representative of three. **B) and F)** The % of IE+ cells was analyzed by FACS on
35 HCMV-infected cells stained intracellularly with a specific anti-IE mAb. **C) and G)** Cell culture supernatants were
36 assayed for infectious virus production by plaque assay. **D) and H)** The levels of ATR or DNA-PK protein
37 expression were assayed by immunoblot analysis with a specific antibody. Immunodetection of the p85 subunit of
38 PI-3K was used as a control of protein loading. ns: not statistically significant difference with Student's t-test.

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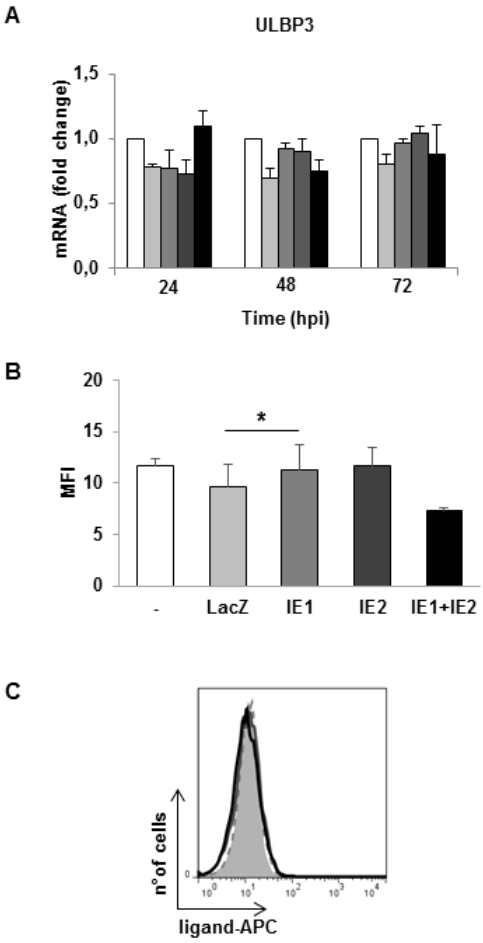

Supplementary Figure 4. Adenoviral-mediated overexpression of IE1 and IE2 proteins does not affect mRNA and cell surface expression of ULBP3. HFFs were transduced with adenoviral vectors (AdV) expressing IE1, IE2, or LacZ as a control, alone or in combination (total MOI 4 PFU/cell). Cells were harvested 24 h, 48 h or 72 h later, and analyzed for ligand mRNA and surface expression. **A)** Real-time PCR. Data from four experiments ± SEs, expressed as fold change units**,** were normalized with GAPDH and referred to not-transduced cells (-), considered as calibrators and set at 1. **B)** Cell surface expression levels of ULBP3 at 72 hpi, measured by FACS, are presented as MFI. Data from three experiments ± SEs. **C)** ULBP3 cell surface expression from a representative experiment performed at 72 hpi.