Supplementary Information

Health hazard of the Methylammonium Lead Iodide based perovskite: cytotoxicity studies

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Supplementary figure S1. MAPbI$_3$ solubility in cell culture media.

(a) MAPbI$_3$ solubility in DMEM (left) and DMEM:F12 (right) at a concentration of 100 mg/ml (stock solution). The vials with the purple colored liquid contain the reference cell culture media. The orange colored vials show the MAPbI$_3$–cell culture media dispersions after 6 days of soaking. Note the purple-to-orange color change and the appearance of a white/yellow precipitate in both cell culture media at a concentration as high as 100 mg/ml. The pH of the dispersions were 6.68 and 7.70, respectively; (b) Addition of MAPbI$_3$ at the highest concentration used in our study (200 µg/ml) did not change significantly the pH of the cell culture media; (c) Concentration levels of lead and iodine in MAPbI$_3$ solution in DMEM:F12 cell culture medium after filtration.
Supplementary figure S2. Elemental analysis of the white/yellow solid precipitate formed by reacting MAPbI$_3$ powder with cell culture media (DMEM, DMEM:F12).

(a) The elemental composition of the solid decomposition by products of the MAPbI$_3$ dispersed in cell culture media DMEM and DMEM:F12 were analyzed by Energy-dispersive X-ray spectroscopy (EDS); (b) The elemental analysis revealed that the white, solid precipitate (Fig. S1 a) contains significant amounts of Pb, Ca and P. The yellow/white solid precipitate is presumably a mixture of lead (II) hydroxide, lead (II) carbonate, and lead (II) phosphate compounds, which were formed by the reaction of Pb$^{2+}$ with the carbonate, phosphate and hydroxide anions of the cell culture media. Note that the toxicity effect of this solid precipitate is out of the scope of the present study.
Supplementary figure S3. Flow cytometry plots of the cytotoxicity assay (Sytox Green) performed in SH-SY5Y cells. Flow cytometry dot plots: SSCA vs. FSCA with a gate on the population of interest (upper panels) and Sytox Green fluorescence histograms (lower panels) of SH-SY5Y cells for the following concentrations of MAPbI₃: non-treated (NT), exposed to non-treated (NT), exposed to 50 µg/ml (50), 100 µg/ml (100) and 200 µg/ml (200).
Supplementary figure S4. MAPbI$_3$ affects SH-SY5Y cell density without the activation of caspase 8.

SH-SY5Y cells were plated in 24 wells then treated with increasing concentrations of MAPbI$_3$ (50, 100 and 200 μg/ml). Living cells were counted and caspase 8 activity was evaluated.

(a) Variation of the cellular density evaluated using a Neubauer hemocytometer; (b) SH-SY5Y neuroblastoma cells were harvested 5 days post-treatment and caspase 8 activity was measured using fluorogenic assay combined to flow cytometry quantification.

All the histograms show an average of at least 3 independent repeats (each condition in triplicate). Bars are means ± S.D. One-way ANOVA test followed by a Tukey-Kramer post-hoc test were performed (non-treated vs MAPbI$_3$ treated conditions), **p<0.001, ***p<0.0005.
Supplementary figure S5. MAPbI$_3$ does not induce necrotic cell death in SH-S5Y5 or in A549 cells. Dot plots show the fluorescence of FLICA-Caspase3 and propidium iodide using flow cytometry of SH-S5Y5 cells (A) or A549 cells (B) exposed to MAPbI$_3$: non treated cells (a), cells treated with 50 µg/ml (b), 100 µg/ml (c) and 200 µg/ml (d). Dot plots are divided in 4 quadrants (Q1, Q2, Q3 and Q4) that show the respective distribution expressed as a
percentage of the healthy cells [negative for PI and for caspase 3 activity (Q4)], the cells undergoing apoptosis but not yet dead [negative for PI but showing caspase 3 activity (Q3)], the apoptotic dead cells [positive for PI and for caspase 3 activity (Q2)] or the necrotic dead cells [positive for PI but negative for caspase 3 activity (Q1)].

The overall meaning of these plots (A and B) confirms that necrotic cell death was not induced in SH-S5Y5 cells (A) or A549 cells (B) or exposed to MAPbI$_3$. Under these conditions, only SH-S5Y5 cells died via apoptotic signaling pathways.
Supplementary figure S6. Flow cytometry plots of the cytotoxicity assay (Sytox Green) performed in A549 cells. Flow cytometry dot plots: SSCA vs. FSCA with a gate on the population of interest (upper panels) and Sytox Green fluorescence histograms (lower panels) of A549 cells for the following concentrations of MAPbI$_3$: non-treated (NT), exposed to 50 µg/ml (50), 100 µg/ml (100) and 200 µg/ml (200).
Supplementary figure S7. Effects of lead-containing solutions on SH-SY5Y (left panel) and A549 cells (right panel) measured by the uptake of Sytox green using flow cytometry. Assay performed on non-treated cells (NT, blue bar), and cells exposed to: MAPbI\textsubscript{3} at 100 μg/ml; Pb(CH\textsubscript{3}CO\textsubscript{2})\textsubscript{2}.3H\textsubscript{2}O (Sigma Aldrich, Switzerland) (lead salt, orange bar); Hydroiodic acid 57 wt. % in H\textsubscript{2}O + Pb(CH\textsubscript{3}CO\textsubscript{2})\textsubscript{2}.3H\textsubscript{2}O (Sigma Aldrich, Switzerland) (lead iodine, green bar); CH\textsubscript{3}NH\textsubscript{2} 40wt. % in H\textsubscript{2}O + Pb(CH\textsubscript{3}CO\textsubscript{2})\textsubscript{2}.3H\textsubscript{2}O (Sigma Aldrich, Switzerland) (Methylamine lead, light blue bar). The solution of MAPbI\textsubscript{3} at 100 μg/ml has a molecular weight percent of lead, iodine and methylamine of respectively 33.42, 61.41 and 5.17%. The lead-containing solutions used in this figure contain the same percentage of lead as in a solution of MAPbI\textsubscript{3} at 100 μg/ml. All the histograms show an average of at least 3 independent repeats (each condition in triplicate). Bars are means ± S.D. One-way ANOVA test followed by a Tukey-Kramer post-hoc test were performed (non-treated vs. MAPbI\textsubscript{3} treated conditions), *p<0.05, **p<0.005 ***p<0.0001.