

ABSTRACT NUMBER: 0279

Macrophage Intracellular Fates of Monosodium Urate and Calcium Pyrophosphate Crystals: Phagocytosis, Exchanged/expulsion and Dissolution of Crystals

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SESSION INFORMATION

Date: [Saturday, November 16, 2024](#)

Session Type: Poster Session A

Title: [Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I](#)

Session Time: 10:30AM-12:30PM

Background/Purpose: Gout, due to the presence of monosodium urate crystals (**MSU**) and calcium pyrophosphate (CPP) crystal deposition disease are both responsible for recurrent inflammation flares. Both crystals stimulate interleukin-1 β production by resident macrophages. Macrophages can interact and phagocytosis both MSU and CPP crystals.

Objective: to describe the intracellular fates of MSU and CPP crystals in macrophages

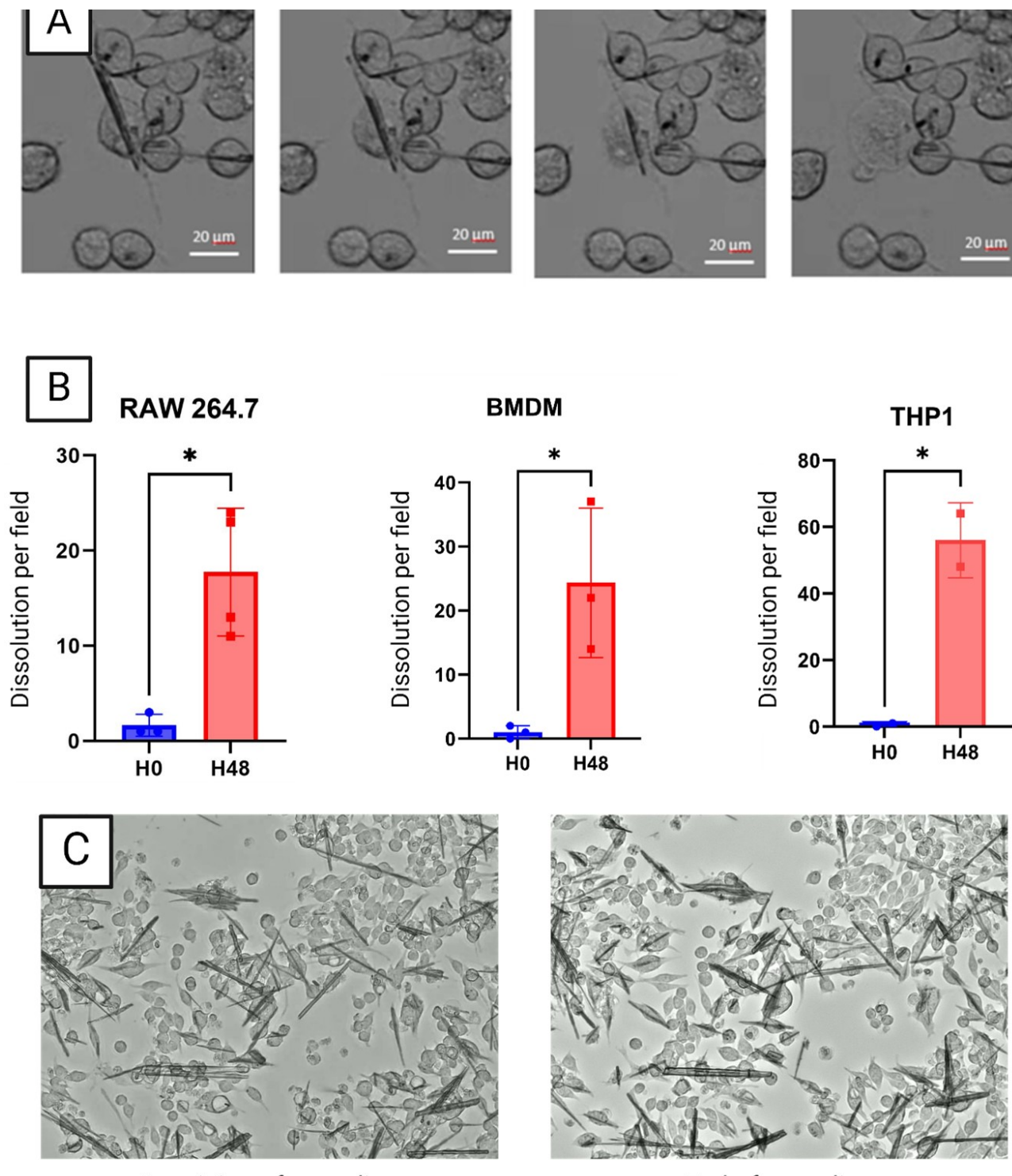
Methods: Synthetic pyrogen-free MSU and CPP crystals were used to stimulate different type of mouse (RAW 264.7 cell line, bone marrow-derived macrophages (BMDM)) and human (THP-1 cell line and peripheral blood mononuclear cells (PBMC)) macrophages. To assess crystal phagocytosis, macrophages were stimulated by MSU and CPP crystals engrafted with fluorescent organic nanoparticles (FON) and recorded during 5 days using Incucyte Live-cell Analysis instrument (Sartorius). Intracellular outcomes were assessed by 18-hours recording using apotome Zeiss microscopy. Images analysis was performed by ImageJ software.

Results: All type of macrophages including RAW 264.7, BMDM, THP-1 and PBMC, rapidly phagocytosed both MSU and CPP crystals. Crystal phagocytosis occurred within the first minutes and all crystals were phagocytosed within one hour. After phagocytosed, crystals remained mostly in the cytosol. Interestingly, in few RAW 264.7 macrophages and PBMC, phagocytosed MSU crystals were expelled into the cytosol of another macrophage. MSU crystals were dissolved after phagocytosis while CPP crystals remained undissolved even after 7 days of stimulation. MSU crystals dissolution occurred only 48 hours after phagocytosis. No dissolution was observed in the first 48 hours while all

MSU crystals were dissolved after 7 days of stimulation. Macrophages displayed different capacity to dissolve MSU crystals: after 48 hours of stimulation, 17.5% of MSU crystals (in one recording field) were dissolved in RAW 264.7 cells vs 24.3% and 56.0% for BMDM and THP-1, respectively.

Interestingly, we observed that dissolution of MSU crystals was followed by cell death and burst in RAW 264.7 macrophages and PBMC. THP-1 cells also dissolved MSU crystals but without burst nor death. Interestingly, treatment with the inhibitor of the V-ATPase pump, bafilomycin A1, completely blocked the dissolution of MSU crystals without affecting crystal phagocytosis.

Conclusion: Our result suggest that dissolution of MSU crystals is a late cellular response involving cell lysosomes and acidification. Furthers studies are ongoing to decipher the underlying mechanisms.



Beginning of recording

End of recording

Figure 1 : MSU crystal dissolution (A) Kinetic images of MSU dissolution by RAW 264.7 macrophages after 48h of incubation. (B) Dissolution potential of different types of macrophages. (C) Bafilomycin A1 inhibited crystal dissolution.

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