# 3rd Nordic Autophagy Society (NAS) Conference

## Utrecht, May 22nd-24th 2019

Venue: St. Bartholomeus Gasthuis, Lange Smeestraat 40, 3511 PZ Utrecht
(https://www.bartholomeusgasthuis.nl/)

**Local organizers**

Paul Coffer (University Medical Center Utrecht)
Muriel Mari (University Medical Center Groningen)
Fulvio Reggiori (University Medical Center Groningen)

## Nordic Autophagy Society (NAS)


https://nordicautophagy.org/

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## A23: MAP kinase-dependent autophagy is involved in phorbol myristate acetate differentiation of HL-60 leukemia cells

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We investigated the mechanism and the role of autophagy in phorbol myristate acetate (PMA)-induced myeloid differentiation of human acute myeloid leukemia HL-60 cells. The mRNA levels of myeloid differentiation markers colony stimulating factor 1 receptor (CSF1R), early growth response protein 1 (EGR1), and interleukin 8 (IL-8), were assessed by real-time RT-PCR. Cell cycle arrest and the expression of surface myeloid marker CD11b were analyzed by flow cytometry. Autophagy was monitored by acridine orange staining, RT-PCR analysis of autophagy-related (ATG) gene expression, LC3-II/p62 immunoblotting, Beclin-1/Bcl-2 interaction, nuclear translocation of transcription factor EB (TFEB). The activation of MAP kinases extracellular signal-regulated kinase (ERK) and c-Jun-N terminal kinase (JNK) was assessed by immunoblotting. Pharmacological inhibition and RNA interference (RNAi) were used to determine the role of MAP kinases in autophagy and HL60 cell differentiation, while the role of autophagy in HL60 differentiation was analyzed using RNAi-mediated knockdown of ATG5 and p62. Results: PMA-induced differentiation of HL-60 cells into macrophage-like cells was confirmed by cell-cycle arrest accompanied by elevated expression of p21, CD11b, CSF1R, EGR1, and IL-8. The induction of autophagy was demonstrated by the accumulation of LC3-II, the increase in autophagic flux, the increase in expression of ATG genes, nuclear translocation of TFEB and dissociation of Beclin1from Bcl-2. The suppression of autophagy by RNAi–mediated knockdown of ATG5 or p62 counteracted myeloid differentiation of HL60 cells. Both ERK and JNK were activated by PMA, and their pharmacological and genetic inhibition decreased PMA-induced autophagy and differentiation of HL60 cells. Conclusion: Our study revealed the involvement of JNK and ERK in autophagy-dependent myeloid differentiation of HL60 cells, indicating MAP kinase-mediated autophagy as a possible target for the treatment of acute myeloid leukemia.