Trends in **Molecular Biology** • Special issue

# Abstract Book

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CoMBoS2

# Content

# WELCOME SPEECH

Professor Dušanka **Savić-Pavićević**
President of the Serbian Society
for Molecular Biology

Dr. Melita **Vidaković**
President of the Steering Committee
of the Serbian Society for Molecular Biology

Dear colleagues and friends,

On behalf of the Serbian Society for Molecular Biology (MolBioS), we warmly welcome you to Belgrade for the Second Congress of Molecular Biologists of Serbia (CoMBoS2).

The congress is gathering almost 250 participants from 13 countries (Sweden, United Kingdom, Italy, Switzerland, USA, Australia, Hungary, Czech Republic, Romania, Montenegro, Croatia, Bosnia and Herzegovina, and Serbia).

The program covers various fields of Molecular Biology, including Molecular Biomedicine, Molecular Biotechnology and Molecular Cell Biology, and consists of plenary and invited lectures, the MolBioS award winner lecture, poster sessions and the project corner. Special attention is paid to students and young scientists through the MolBioS Student Session, flash presentations and workshops on state-of-the-art molecular biology methods.

We wish you to be inspired by exciting and outstanding lectures given by renowned scientists and experts, exchange ideas, find opportunities for new collaborations, and have good fun.

**WELCOME TO**

CoMBoS2

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# MAP KINASES ACTIVATE TFEB/FOXO-DEPENDENT AUTOPHAGY INVOLVED IN PHORBOL MYRISTATE ACETATE-INDUCED MACROPHAGE DIFFERENTIATION OF HL-60 LEUKEMIA CELLS

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**Introduction:** Autophagy has been shown to participate in the differentiation of hematopoietic and leukemic cells. We investigated the mechanisms of autophagy action in the differentiation induced by PKC activator phorbol myristate acetate (PMA) in HL-60 acute myeloid leukemia cells.

**Methods:** The macrophage markers CD11b, CD13, CD14, CD45, EGR1, CSF1R, and IL-8 were assessed by flow cytometry and RT-qPCR. Autophagy was monitored by RT-qPCR analysis of autophagy-related (*ATG*) gene expression, LC3-II/p62 immunoblotting, beclin-1/Bcl-2 interaction, nuclear translocation of TFEB and FOXO1/3. The activation of MAP kinases, ERK and JNK was assessed by immunoblotting. Pharmacological inhibition and RNA interference were used to determine the role of MAP kinases and autophagy in HL60 cell differentiation.

**Results:** PMA-triggered differentiation of HL-60 cells into macrophage-like cells was confirmed by elevated expression of macrophage markers CD11b, CD13, CD14, CD45, EGR1, CSF1R, and IL-8. The induction of autophagy was demonstrated by accumulation/punctuation of LC3-II, and the increase in autophagic flux. PMA also increased nuclear translocation of TFEB, FOXO1/3, as well as the expression of several *ATG* genes in HL-60 cells. PMA stimulated the phosphorylation of ERK and JNK via PKC-dependent mechanism. Pharmacological or genetic inhibition of ERK or JNK suppressed PMA-triggered nuclear translocation of TFEB and FOXO1/3, *ATG* expression, dissociation of beclin-1 from Bcl-2, autophagy induction, and differentiation of HL-60 cells into macrophage-like cells.

**Conclusion:** Our study revealed the involvement of ERK and JNK in TFEB/FOXO-dependent autophagy and differentiation of HL60 cells, indicating MAP kinase-mediated autophagy as a possible target in differentiation therapy of AML.

Key words: leukemia; autophagy; differentiation; ERK; JNK

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