

## **WDR5, ASH2L, and RBBP5 control the efficiency of FOS transcript processing**

### **Abstract**

H3K4 trimethylation is strongly associated with active transcription. The deposition of this mark is catalyzed by SET-domain methyltransferases, which consist of a subcomplex containing WDR5, ASH2L, and RBBP5 (the WAR subcomplex); a catalytic SET-domain protein; and additional complex-specific subunits. The ERK MAPK pathway also plays an important role in gene regulation via phosphorylation of transcription factors, co-regulators, or histone modifier complexes. However, the potential interactions between these two pathways remain largely unexplored. We investigated their potential interplay in terms of the regulation of the immediate early gene (IEG) regulatory network. We found that depletion of components of the WAR subcomplex led to increased levels of unspliced transcripts of IEGs that did not necessarily reflect changes in their mature transcripts. This occurs in a manner independent from changes in the H3K4me3 levels at the promoter region. We focused on FOS and found that the depletion of WAR subcomplex components affected the efficiency of FOS transcript processing. Our findings show a new aspect of WAR subcomplex function in coordinating active transcription with efficient pre-mRNA processing.