"The F-box protein FBXL16 upregulates the stability of the atypical MAPK ERK3"

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11:00 AM

Blackboard Collaborate
https://us.bbcollab.com/guest/63a1b38f991a44808125ab87d4766c20

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Abstract Title:

F-box proteins are essential components of the SCF (SKP1-CUL1-F-box) E3 ubiquitin ligases as they are responsible for substrate recognition. F-box proteins bind to SKP1 through the F-box motif and bring the substrate to the E3 ligase complex for ubiquitination. FBXL16 is a poorly studied F-box protein, which was shown to be a transcriptional target of E2F1. FBXL16 doesn’t interact with Cul1 and might not form a functional SCF-E3 ligase complex. By data mining, we found that FBXL16 is highly upregulated in many cancers, and its upregulation is often associated with poor survival, indicating that FBXL16 may play important roles in cancers. We recently found that FBXL16 upregulates oncoproteins targeted by SCF-E3 ligases, such as SRC-3 and c-myc, by antagonizing FBW7 activity. Here, we found that FBXL16 interacts with and stabilizes the atypical MAPK ERK3. Little is known about ERK3 protein regulation and so far, no E3 ligase involved in ERK3 ubiquitination has been identified. In this study, we found that FBXL16 decreases ERK3 ubiquitination and identified FBW7 as a potential E3 ligase targeting ERK3. Besides, we found that FBXL16 binds to and decreases FBW7 stability. Taken together, our findings reveal that FBXL16 acts as a unique F-box protein by downregulating another F-box protein, FBW7, a major tumor suppressor, leading to the upregulation of ERK3 and other oncoproteins.