ASCB|EMBO 2019 Annual Meeting; December 7-11, 2019; Washington, D.C.

Abstract P589: Crosstalk Between the Hippo-YAP and Nuclear Factor-Kappa B-RELA Signaling

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Abstract

The Hippo pathway controls cell-cell interaction and organ size by regulating cell proliferation. The study aimed to determine whether Hippo/YAP and NF-kappa B/RELA signaling interact. Here, we have demonstrated that native YAP1/TEAD and RELA proteins biochemically and functionally interact with each other in human LNCaP and C4-2 cell lines. Our co-immunoprecipitation (co-IP), western blot (WB), and proximity ligation assay (PLA) showed that endogenous YAP/TEAD and RELA physically interact within the cell. Our immunofluorescence assays revealed that the expression of YAP1 and RELA proteins overlapped in the cytoplasm and the nucleus. Combined treatment of cells with RANKL (receptor activator of nuclear factor-kappa B ligand) and androgen hormone enhanced YAP1 and RELA colocalization and interaction, as demonstrated by co-IP/WB experiments. Moreover, our PLA confirmed that co-treatment of cells with androgen and SDF1a (stromal cell-derived factor 1 alpha) or RANKL increased YAP1 and RELA interaction cytoplasm and nucleus compared with controls. Our promoter-reporter assays showed that the knockdown of YAP1 by siRNA significantly reduced the activity of an NF-Kappa B responsive promoter-reporter gene. We also showed that controlled expression of MST1/STK4, a potent inhibitor of YAP1, attenuated the NF-Kappa B promoter reporter activity. Our unbiased bioinformatics analysis of the chromatin immunoprecipitation data has revealed that YAP/TEAD and NF-kappa B signaling regulates several genes. These findings suggest that interaction between the Hippo/YAP and NF-Kappa B/RELA plays a critical role in broad cellular biology.