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Polycomb group protein SCML2 interacts with the Hippo pathway effector YAP1

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Abstract:
Sex comb on midleg-like-2 (SCML2), a conserved polycomb group protein, functions as a transcriptional repressor. SCML2 binds monomethylated lysine residues on histones and regulates homeotic gene expression during development in mammals and the fly. Using proteomic approaches, we have identified SCML2 as a binding partner of the YAP1 protein complexes isolated from nuclei of prostate cancer cell lines. Both SCML2 and YAP1 are known to regulate basic cellular biology, including stem cell maintenance and carcinogenesis. Our western blot analysis showed that, unlike androgen receptor (AR)-negative cancerous and non-cancerous prostate epithelium, AR-positive cell lines express the high levels of SCML2, suggesting a possible link between androgen hormonal signaling and SCML2. In addition, our immunofluorescence imaging revealed that androgen hormone signaling promoted the subcellular localization of SCML2 and YAP1 proteins compared with mock control. Enzalutamide, a potent pharmacological inhibitor of AR, significantly prevented the subcellular distribution of YAP1 and SCML2 proteins. Consistent with this observation, our proximity ligation assay demonstrated that androgen also regulated the physical interaction between SCML2 and YAP1 proteins that occurred primarily in cell nuclei. Enzalutamide also prevented protein-protein interaction between YAP and SCML2. Besides, our GST-pulldown assay revealed that SCML2 and YAP proteins physically interact with each other in the test tube. Furthermore, our promoter-reporter assay showed that transfection of two different SCML2 siRNA enhanced the activation of the YAP-responsive promoter-reporter gene by four-fold compared to mock siRNA control. These observations suggest that the interaction between SCML2 and YAP1 is biologically functional and crucial in human physiology and disease.

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