Suppression of androgen receptor transactivation and prostate cancer cell growth by heterogeneous nuclear ribonucleoprotein A1 via interaction with androgen receptor coregulator ARA54.

張育嘉

Yang Z;Chang YJ;Miyamoto H;;Yeh S;Yao JL;;di Sant'Agnese PA;;Tsai MY;Chang C

摘要

Abstract

The androgen receptor (AR) requires coregulators for its optimal transactivation. Whether AR coregulators also need interacting proteins to modulate their function remains unclear. Here we describe heterogeneous nuclear ribonucleoprotein (hnRNP) A1 as an associated negative modulator for the AR coregulator ARA54. hnRNP A1 selectively suppressed ARA54-enhanced wild-type and mutant AR transactivation via interruption of AR-ARA54 interaction and ARA54 homodimerization. Stable transfection of hnRNP A1 in the LNCaP cells suppressed AR-mediated cell growth and the expression of prostate-specific antigen, and this suppressive effect was abolished by the addition of ARA54-small interfering RNA. Small interfering RNA knockdown of endogenous hnRNP A1 enhanced cell growth and prostate-specific antigen expression in LNCaP cells. These results not only suggest that the loss of hnRNP A1 expression might activate the ARA54-enhanced cell growth and contribute to the prostate cancer progression, but also demonstrate the dual functional roles for ARA54 as an AR coregulator directly and as a mediator for the suppressive effect of hnRNP A1 indirectly. The novel finding that a protein can modulate AR function without direct interaction with AR might provide a new therapeutic approach to battle prostate cancer by targeting AR indirectly with fewer side effects