could become a relatively weaker AR coactivator in other cells, such as PC-3 cells or HeLa cells. In summary, it will be very important to compare systematically the relative strength of different coactivators under the same conditions.

Comparing AR, glucocorticoid receptor (GR) and progesterone receptor (PR), our results indicated that ARA70 exhibits relatively high specificity to AR in the prostate cancer DU145 cells. On the other hand, ARA55 was able to enhance most of the classic steroid receptors except ER.[19] As transfection conditions and cell environments may influence the coactivator effects, we may expect different specificity patterns to occur when we replace DU145 cells with other cells. Furthermore, as our data only compares the coactivator specificity among classic steroid receptors, the potential coactivator effect on many new members of steroid receptor superfamily, such as orphan receptors, remains unclear. Indeed, preliminary data indicate that ARA70 can also function as a coactivator to enhance the transactivation of the peroxisome proliferator-activated receptor in DU145 cells.[40] Together, the distinct specificity of each coactivator in different cells may provide cell-specificity for each steroid receptor.

Androgens and AR function in the control of the proliferation of prostate cells. The functional study of AR cofactors and AR transactivation may help us to gain better understanding of the mechanism of prostate cancer process. To date, prostate cancer has become the most frequently diagnosed neoplasm in the United States and the second leading cause of cancer-related death in American men. So far, the only effective treatment for metastatic prostate cancer is androgen ablation therapy. But the main problem in androgen ablation therapy is that the median duration of response is only 18–36 months. While both HF and casodex are effective antiandrogens for treatment of prostate cancer, they will gradually lose their therapeutic effect after long term treatment. Several studies have tried to provide the explanation at the molecular level of why an antiandrogen eventually loses its antagonist effect on AR and then resurfaces as an agonist after a certain period of treatment.

In this review, we have discussed the results that may provide some clues to this phenomenon. The results shown here suggest that some selective AR cofactors, such as ARA70 and ARA55, have a unique ability to modulate the partial agonist activity of the antiandrogens in human prostate cancer DU145 cells. Further studies on the expression patterns of these AR coactivators in different stages of prostate cancer, both before and after antiandrogen treatment, may further strengthen the roles of these AR cofactors in the progression of prostate cancer from an androgen dependant to an androgen independent stage.

In summary, the identification of cofactors that can enhance AR transactivation and change the agonist/antagonist activity may allow us to better understand the mechanism of AR function and to develop better antiandrogens to battle the prostate cancer.

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