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Mechanism of Phenoxy Compounds as Androgenic Endocrine Disruptors

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Phenxoy compounds, 2,4-dichlorophenol acetoxyacid (2,4-D) and 2,4-dichlorophenol (DCP), are widely used as a hormonal herbicide and intermediate for pesticide manufacturing, respectively. We have previously reported the potential of these compounds as androgenic endocrine disruptors using in vivo Hershberger assay and in vitro reporter gene assay. These compounds showed the additive effect of androgenicity by co-treatment of testosterone in hershberger assay.

To elucidate the mechanism of the additive effect on the androgenicity of testosterone by these phenoxy compounds, we studied the effect of 2,4-D and DCP on the expression of androgen receptor (AR) and their androgenicity using a reporter gene assay in prostate cancer cell lines, 22Rv1. Co-treatment of 2,4-D or DCP with 10 nM 5α -dihydrotestosterone (DHT) resulted in 1.5 to 7 fold induction of the luciferase activity compared to that of DHT alone in the 22Rv1 cells transiently transfected pMMTV-Luc. When the cells were treated 10 nM DHT alone or DHT with 2,4-D or DCP for 24 h, the expression of AR was significantly increased in western blot analysis without the increase of mRNA of AR in RT-PCR by co-treatment of DHT with. These data suggested that 2,4-D or DCP can affected the expression of AR in a post-transcriptional manner and then potentate the DHT effect. These phenoxy compounds themselves acted as androgenic endocrine disruptors. We expected that several other mechanisms may be related to these additive effects besides the expression of AR. Thus, we are studying the localization of AR using GFP-AR vector and recruitments of co-activators for elucidating the androgenic effect.

Keyword : 2,4-dichlorophenol acetoxyacid, 2,4-dichlorophenol, androgenic endocrine disruptor, reporter gene assay