The potential of environmental chemicals to affect the androgen receptor function in vitro and ex vivo

Tanja Krüger, MSc

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Official opponents: Jens C. Hansen, Christine Nellemann, and Olli A. Jänne, Finland.

Tutor: Eva C. Bonefeld-Jørgensen.

Correspondence: Tanja Krüger, Afdeling for Miljø- & Arbejdsmedicin, Institut for Folkesundhed, Aarhus Universitet, Vennelyst Boulevard 6, 8000 Århus C, Denmark.

E-mail: tk@mil.au.dk

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ABSTRACT

The androgen receptor (AR) is responsible for male sexual differentiation and pubertal sexual maturation. Many xenobiotic compounds including persistent organic pollutants (POPs) and plastic components have been identified and characterized as potential (anti-)androgens. Furthermore, additive enhancement of hormone actions by xenobiotic mixtures has been reported in vitro and in vivo. Therefore, it is necessary to elucidate their effect on the AR in vitro and to monitor the actual concerted action of human serum POPs on the AR function ex vivo.

The aims were to elucidate the potential of commercial plastic components in vitro as well as human serum samples from healthy European men (Poland, Sweden, Ukraine) and Greenlandic Inuits (Nuuk, Sisimiut, Qaanaaq) ex vivo to affect the AR function.

The xenoandrogenic transactivity was determined using an AR reporter gene assay. The human serum samples were extracted and fractionated to obtain the serum POP fractions free of endogenous hormones.

The xenoandrogenic serum transactivities were evaluated for associations to serum POP markers (European: PCB153 and p,p'-DDE; Inuits: 14 PCBs and ten pesticides) and human sperm chromatin integrity assessed as DNA Fragmentation Index (%DFI).

In vitro none of 14 tested plastic components reacted as AR agonists whereas all the phenols except resorcinol and one plasticizer elicited significant AR antagonistic effects. Furthermore, a mixture of six plastic components dose-dependently antagonised the AR activity and additive effects were found using the concentration addition principle.

Ex vivo the xenoandrogenic serum transactivities significantly differed between the study groups being highest in men from Nuuk and lowest in men from Ukraine. The xenoandrogenic serum transactivities correlated negatively to p,p'-DDE and to the age-adjusted POPs for the combined European study groups and for the combined male Inuits, respectively.

For Inuits negative correlations between xenobiotic serum activities and %DFI were found, whereas for Europeans positive relations were seen. Environmental chemicals have the potential to affect the AR function in vitro as single compounds and in mixtures, and ex vivo as observed for human serum POP extracts. The differences in xenoandrogenic serum transactivity between the study groups are suggested to reflect the effect of different POP mixture profiles. Negative correlations between the xenoandrogenic transactivities and the POP markers were observed suggesting that the POPs antagonize male sex hormone transactivities.

It is recommended that future studies besides age include genetic background as well as lifestyle characteristics such as smoking and diet.