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Androgen receptor gene CAG repeats length as modifier of toxicant effects on semen

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Objectives: Exposure to Persistent Organohalogen Pollutants (POP) was suggested to impair male reproductive function. A gene-environment interaction has been proposed. No genes modifying the effect of POP on reproductive organs have yet been identified. We aimed to investigate whether the CAG and GGN polymorphisms in the androgen receptor (AR) gene modify the effect of POP exposure on human sperm characteristics.

Methods: Semen and blood from 680 men (mean (SD) age 34 (10) years) from Greenland, Sweden, Warsaw (Poland) and Kharkiv (Ukraine) were collected. POP exposure was assessed by measuring serum levels of 2,2', 4,4',5,5'-hexachlorobiphenyl (CB-153) and dichlorodiphenyl dichloroethene (p,p'-DDE). Semen characteristics (volume, sperm concentration, total count, proportion of progressively motile, morphology) and DNA Fragmentation Index (DFI). CAG and GGN repeat lengths were determined by direct sequencing of leukocyte DNA.

Results: A statistically significant interaction was found between the CB-153 group and CAG repeat category in relation to sperm concentration and total sperm count ($p=0.03$ and $p=0.01$, respectively). For p,p'-DDE, in the European cohorts a significant interaction was found in relation to DFI ($p=0.01$). For CAG<20 sperm concentration and total sperm count were 35% and 42% lower, respectively, when the group with CB-153 exposure above median was compared to that below the median. DFI was 40% higher in high p,p'-DDE exposure group for CAG \leq 21.

Conclusions: This study demonstrated that AR CAG repeat length modifies the susceptibility of an individual to the adverse effects of POP exposure on semen quality. The mechanisms of action need to be elucidated in vitro.