Exposure to chlordecone leads to transgenerational effects in murine prostate tissue

Prostate cancer is one of the most frequently diagnosed cancers and it is the cause of 250,000 deaths in the world every year. It is suggested that genetic and epigenetic alterations can induce cancerous transformations. It has been proposed that occupational exposures may play a role in prostate cancer development. Chlordecone (CD) has been used as pesticide for banana plantations in French West Indies. Although banned since 1978 in the United States of America (IARC, 1979), CD was detected in drinking water, plant and aquatic organisms in 2005. In French West Indies CD was banned in 2004, however, it is estimated that CD pollution in soil will last for centuries. This is a major concern for the population about the potential health implications. It was discovered that exposure to CD associates with high risk of prostate cancer development (Multigner et al., 2010). In order to reveal the mechanistic actions of CD on prostate tissue and to understand whether the effects of CD could be transgenerational, we used the outbred mouse model and gestational exposure to low doses of CD (100 or 250 ug/kg/day). The male progeny of exposed were crossed for three generations. We found the morphological changes in prostate tissue in F3 generation males. To reveal the molecular mechanisms of CD we used RNA-seq technique using 3 biological replicates per condition and we found that 84 genes (FC2, FDR5%) were differentially expressed in F3 generation males. Among altered genes there are genes associated with extracellular matrix, development and signal transduction functions. Several genes (Upk1a, Sprr11a, Hoxa7) are known to be implicated in cancer development. Our data suggest that developmental exposure to low dose of chlordecone leads to changes in prostate tissue in several generations after treatment.

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