The potential of environmental chemicals to affect the aryl hydrocarbon receptor

A molecular and cellular study in vitro and ex vivo

Manhai Long, MB

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Official opponents: Torben Sigsgaard, Magnus Engwall, Sweden, and Greet Schoeters, Belgium.

Tutor: Eva Cecilie Bonefeld-Jørgensen.

Correspondence: Manhai Long, Department of Environmental & Occupational Medicine, Institute of Public Health, University of Aarhus, Vennelyst Boulevard 6, 8000 Århus C, Denmark.

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ABSTRACT

The aryl hydrocarbon receptor (AhR) is involved in most of the toxic and biological effects of the persistent organic pollutants (POPs) such as dioxin and dioxin-like compounds (DLCs). Chemicals found in the environment and food have been shown to interfere with the function of AhR. Therefore, it is necessary to identify possible AhR ligands in the environment and biota as well as personal care products and to monitor the actual concerted dioxin-like (DL)- activity in humans as well as elucidate their in vitro and ex vivo effects.

To elucidate the potential of commercial compounds like pesticides currently used in Denmark and plasticizers widely used in many products as well as biological samples including human breast milk form Denmark and human plasma/serum from Greenlandic Inuits, and inhabitants from Sweden, Poland, Ukraine to affect the AhR function.

A reporter gene bioassay using recombinant human or rat or mouse cell lines were used to detect the DL-activity of samples.

Results: Three pesticides (iprodione, chlorpyrifos and prochloraz) elicited significant dose-dependent induction of AhR effect. Furthermore, a cell line specific weak agonistic and/or antagonistic effect of few other pesticides was also observed. Six of sixteen tested plasticizers and mixtures of selected plasticizers exhibited weak but significant induction of AhR activity in the mouse cell line.

District-dependent differences of serum DL-toxic potential among the Greenlandic Inuits and Europeans were observed. The Greenlandic Inuits having relatively high POP burden elicited lower DL-toxic potential than the Caucasians from Sweden, Poland and Ukraine. The serum DL-toxic potential was negatively correlated to age, intake of marine food and POPs in Greenlandic Inuits. However, in Europeans the DL-toxic potential was positively correlated to age and POP marker. Furthermore, a negative correlation between DL-activity in serum and sperm DNA damage was found for in Inuits, whereas for European Caucasians a positive correlation was observed.

Some commercial compounds may contribute to the AhR action and might influence the toxic potential and thus human health risk. The serum toxic potential is suggested to reflect the different profiles of POPs and other fatty soluble chemicals of different populations. Whether the higher DL-toxic potential of Europeans is due to the DLCs sources need further study. Genetic background and life style such as diet and age must be taken into consideration in the future epidemiological-mechanistic study design for determining DL-toxic potential in relation to chemical exposure.