INTRODUCTION

- Persistent organic pollutants (POPs) are defined as organic chemicals
  - resistant to degradation in the environment
  - bioaccumulate and biomagnify in living organisms
  - have potential harmful impacts on humans and wildlife

- Humans are exposed to POP mixtures.
  - However, most available scientific data focus on:
    - the effect of single compounds at a time
    - do not address the cocktail/mixture effect of mixtures of POPs

This study aims to determine in vitro the cocktail effect of a mixture of POPs in reporter cell lines at the level of the Aryl hydrocarbon Receptor (AhR) function.

*AhR is a key receptor regulating the metabolism of xenobiotics including POPs.

MATERIALS AND METHODS

- Dioxin Responsive and luciferase gene transformed rat hepatoma DR-H4IE
- Induced light production will be in proportion with the concentration of AhR ligands.

- POP Mixture = Mixture of 29 tested POPs belonging to 3 groups of perfluorinated, brominated and chlorinated compounds

POPs and Early Menopause in U.S. Women

http://t.co/ycXekUG2AA

POPs: Perchloroethylene, Perfluorooctanoic acid, Perfluorooctane sulfonyl fluoride, Perfluorooctane sulfonate, Perfluorodecanoic acid, Perfluorobutanoic acid, Perfluorobutane sulfonate, Perfluorocaproic acid, Perfluorododecanoic acid, Perfluoroheptanoic acid, Perfluorononanoic acid, Perfluoroundecanoic acid

RESULTS

- Only 4 out of the 29 compounds showed AhR agonistic activities on DR-H4IE cells

Table 1: EC50, efficiency and potency values for the 5 AhR agonistic compounds in DR-H4IE cells.

<table>
<thead>
<tr>
<th>POP Mixture</th>
<th>EC50 (µM)</th>
<th>Efficiency</th>
<th>Potency</th>
</tr>
</thead>
<tbody>
<tr>
<td>PBOE 47</td>
<td>0.07 ± 0.02</td>
<td>0.01 ± 0.003</td>
<td>0.014 ± 0.020</td>
</tr>
<tr>
<td>PCB 28</td>
<td>0.02 ± 0.004</td>
<td>0.025 ± 0.019</td>
<td>0.018 ± 0.007</td>
</tr>
<tr>
<td>HBCD</td>
<td>0.01 ± 0.002</td>
<td>0.005 ± 0.001</td>
<td>0.003 ± 0.001</td>
</tr>
<tr>
<td>PCB 99</td>
<td>0.005 ± 0.001</td>
<td>0.001 ± 0.000</td>
<td>0.0005 ± 0.0001</td>
</tr>
<tr>
<td>HCB</td>
<td>0.001 ± 0.000</td>
<td>0.0001 ± 0.0000</td>
<td>0.00001 ± 0.00000</td>
</tr>
</tbody>
</table>

- In contrast, 19 out of 29 compounds showed AhR antagonistic activities on DR-H4IE cells

Table 2: IC50 and efficiency values of the POP Mixture and 19 AhR antagonistic compounds in DR-H4IE cells.

<table>
<thead>
<tr>
<th>POP Mixture</th>
<th>IC50 (µM)</th>
<th>Efficiency</th>
</tr>
</thead>
<tbody>
<tr>
<td>PC8 28</td>
<td>0.08 ± 0.04</td>
<td>0.06 ± 0.03</td>
</tr>
<tr>
<td>PCB 99</td>
<td>0.03 ± 0.02</td>
<td>0.02 ± 0.01</td>
</tr>
<tr>
<td>HCB</td>
<td>0.01 ± 0.00</td>
<td>0.005 ± 0.002</td>
</tr>
<tr>
<td>PCB 28</td>
<td>0.005 ± 0.001</td>
<td>0.001 ± 0.0001</td>
</tr>
<tr>
<td>HCB</td>
<td>0.0005 ± 0.0001</td>
<td>0.0001 ± 0.00001</td>
</tr>
</tbody>
</table>

- POP Mixture effect: antagonistic

Figure 1: Dose-response curves of the POP Mixture (POPs), GNF-351 (a typical AhR agonistic) and PBDE 47 (the most efficiency AhR agonistic in the mixture) on DR-H4IE cells co-exposed with 15 µM TCDD.

- The effect starts increasing significantly when the mixture concentration is 75 times higher than their levels in the human blood.
- According to the addition concentration model (Payne et al., 2000):
  \[ \text{Calculated IC50} = 16.8 \mu M < \text{Measured IC50} = 5.07 \pm 0.02 \mu M \]

DISCUSSIONS AND CONCLUSIONS

- The POP Mixture is an AhR antagonist in DR-H4IE cells.
- The compounds in the POP Mixture could act additively or even synergically as AhR antagonists in DR-H4IE cells.
- Extrapolating from in vitro to in vivo, we could say that a contamination incident leading to an increase of the POP mixture blood concentration up to 75 times the background level could result in an inhibition of the AhR transactivation activities.

REFERENCES
