Study in mice of the transcriptional effects of PCB118 and PCB153 in liver, adipose tissue, muscle and colon: Highlighting of Glut4 and Lipin 1 as main target genes for PCB induced metabolic disorders

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Abstract

Epidemiological studies have associated environmental exposure to PCB with an increased risk of type 2 diabetes, but little is known concerning underlying mechanisms involved in metabolic side-effects of PCB.

The aim of our study performed in mice, was to evaluate in various tissues (liver, visceral adipose tissue, muscle, and colon) the transcriptional effects of subchronic exposures (gavage at Day0 and Day15 with either 10, or 100 $\mu$mol/Kg bw) to PCB118 (dioxin-like PCB), or to PCB153 (nondioxin-like PCB), or to an equimolar mixture of PCB118 and PCB153.

Our results showed that short term exposure to PCB118, or to PCB153, or to a mixture of PCB118 and PCB153 enhances triglyceride circulating levels, but glycemia remains unaffected. Among the studied tissues, we did not observed any modification of the expression of genes involved in inflammation, such as cytokines or chemokines. The main transcriptional effects were observed in visceral adipose tissue and in liver. We demonstrated a downregulation of lipin1 and glut4 expression in these two target organs. In adipose tissue, we also showed a downregulation of Agpat2, Slc25a1, and Fasn. All these genes are involved in lipid metabolism and are associated to insulin resistance. In muscles, we observed an induction of CnR1 and Foxo3 expression which could also be involved at least in part in the reduction of insulin sensitivity.

In summary, our results suggested that adipocytes are the main target in metabolic disorders induced by PCB, but further studies are required to fully elucidate the involved mechanisms.