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Updating "Dataset of transcriptomic changes that occur in human preadipocytes over a 3-day course of exposure to 3,3′,4,4′,5-Pentachlorobiphenyl (PCB126)" with additional data on exposure to 2,2′,5,5′-tetrachlorobiphenyl (PCB52) or its 4-hydroxy metabolite (4-OH-PCB52)☆

Francoise A. Gourronc[a], Michael S. Chimenti[b], Hans-Joachim Lehmler[c], James A. Ankrum[d,e], Aloysius J. Klingelhutz[a,e,*]

[a] *Department of Microbiology and Immunology, University of Iowa*
[b] *Iowa Institute of Human Genetics, Bioinformatics Division, University of Iowa*
[c] *Department of Occupational and Environmental Health, University of Iowa*
[d] *Roy J. Carver Department of Biomedical Engineering, University of Iowa*
[e] *Fraternal Order of Eagles Diabetes Research Center, University of Iowa*

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* Corresponding author. 3-612 BSB, 51 Newton Road, Department of Microbiology and Immunology, University of Iowa, Iowa City, IA 52242, Tel: 319-335-7788.

E-mail address: Al-klingelhutz@uiowa.edu (A.J. Klingelhutz).

Social media: @JamesAnkrum (J.A. Ankrum)

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ABSTRACT

Polychlorinated biphenyls (PCBs) were used extensively in building materials, including those used in schools. PCBs accumulate in fat, and exposure to PCBs is associated with the development of cancer, neurodevelopmental disorders, cardiovascular disease, obesity, and diabetes. The non-dioxin-like PCB congener, PCB52 (2,2′,5,5′-tetrachlorobiphenyl), is found at one of the highest levels of any congener in school air. PCB52 is oxidized in the liver to hydroxylated forms, mainly 4-OH-PCB52 (2,2',5,5'-tetrachlorobiphenyl-4-ol). In a previous study, we reported on RNAseq data generated from exposure of human preadipocytes to the dioxin-like PCB congener, PCB126. In this new dataset, we used identical techniques to examine alterations in gene transcript levels in human preadipocytes exposed to PCB52 or 4-OH-PCB52 over a time course. This updated set of data provides a comprehensive transcriptional profile of changes that occur in preadipocytes exposed to PCB52 or 4-OH-PCB52 over time and allows for comparison of these changes between the parent compound and its hydroxy metabolite. The datasets will allow others to explore how PCB52 and 4-OH-PCB52 impact biological pathways in preadipocytes. Further studies can be performed to determine how these changes might lead to disease.

Specifications Table

Subject	Health, Toxicology and Mutagenesis
Specific subject area	Temporal gene expression changes in preadipocytes caused by exposure to PCB52 or its hydroxylated metabolite 4-OH-PCB52
Type of data	Table Figure
How the data were acquired	Same as the original data article
Data format	Raw -Fastq Analyzed – "Raw Counts after alignment" Filtered Differential Gene Expression
Description of data collection	We exposed immortalized normal human preadipocytes (NPADs) from a non-diabetic female donor to either 10 μM PCB52, 4-OH-PCB52, or DMSO as vehicle control. Cells were harvested for RNA after 9, 24, and 72 hours. Four replicates of each condition were collected and assessed for quality. RNA libraries were prepared and these were subjected to deep sequencing. Raw and processed data were deposited on a public database.
Data source location	Institution: University of Iowa City/Town/Region: Iowa City, Iowa Country: USA Latitude:41.661129 Longitude: -91.530167

(*continued on next page*)

Data accessibility	Repository name: Gene Expression Omnibus (GEO) Data identification number: GSE205813 Direct URL to data: https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE205813 Code to reproduce the DEG analysis: klingelhutz_rnaseq_july2020_pcb126/rnaseq_analysis_DEseq2.Rmd
Related data article	Gourronc FA, Helm BK, Robertson LW, Chimenti MS, Lehmler HJ, Ankrum JA, Klingelhutz AJ. Dataset of transcriptomic changes that occur in human preadipocytes over a 3-day course of exposure to 3,3′,4,4′,5-Pentachlorobiphenyl (PCB126). Data Brief. 2022 Sep 1;45:108,571. doi: 10.1016/j.dib.2022.108571. PMID: 36,131,953; PMCID: PMC9483567 [1].
Related research article	Gourronc FA, Chimenti MS, Lehmler HJ, Ankrum JA, Klingelhutz AJ. Hydroxylation markedly alters how the polychlorinated biphenyl (PCB) congener, PCB52, affects gene expression in human preadipocytes. Toxicol In Vitro. 2023 Jun;89:105,568. doi: 10.1016/j.tiv.2023.105568. Epub 2023 Feb 15. PMID: 36,804,509; PMCID: PMC10081964 [2].

Value of the Data

- The updated dataset represents the first RNAseq data reported for exposure of human cells to PCB52, an important non-dioxin-like persistent organic pollutant that is present at high levels in school air, or its oxidized metabolite 4-OH-PCB52. The data can be mined to reveal novel pathways and genes activated directly or secondarily upon exposure of preadipocytes to PCB52 or 4-OH-PCB52.
- The new data adds value to and builds upon the previous report of RNAseq data for exposure of preadipocytes to PCB126, a dioxin-like PCB. This will allow for comparison of the effects of dioxin- and non-dioxin-like PCBs on human preadipocytes.

1. Data Description

Normal human preadipocytes (NPADs) derived from subcutaneous adipose tissue were exposed to 10 μM PCB52, 4-OH-PCB52, or DMSO over a time course and then subjected to RNAseq. The 10 μM concentration was chosen based on our studies demonstrating that this concentration was non-cytotoxic and studies using other PCB congeners and mixtures showing that this dose causes phenotypic changes in preadipocytes/adipocytes/adipose mesenchymal stem cells [2–4]. To define the temporal changes in gene expression that occur after PCB52 or 4-OH-PCB52 exposure, the specific time points of 9 hours, 24 hours, and 72 hours were chosen. This time frame is based on our previous findings with another congener, PCB126, demonstrating induction of genes at the early time point of 9 hours with further changes at 24 hours and 72 hours [5]. The exposures to PCB52 or 4-OH-PCB52 were done at the same time as the previously reported dataset using PCB126, and the DMSO control samples used are the same as for that dataset [1]. Table 1 outlines each raw data file and describes the treatment condition, either DMSO or 10 μM PCB52 or 4-OH-PCB52, as well as the duration of exposure to the treatment condition, 9, 24, and 72 hours. The number of aligned reads for each sample is reported in Table 2. After alignment, differentially expressed genes (DEGs) were identified by comparing the 10 μM PCB52 or 4-OH-PCB52 treated NPAD data to the DMSO treated NPAD data for each of the 3 exposure durations. The list of DEGs was filtered only to include genes that showed a log fold change $\geq$ |0.3| & FDR-adjusted p-value $\leq$ 0.05. Lists of raw counts for every gene and filtered DEG for each exposure duration and their corresponding log fold change and p-value are available in the files listed in Table 3 and can be found on GEO Accession number: GSE205813. Venn diagrams were created in iPathwayGuide to display the overlap of DEGs between PCB52- or 4-OH-PCB52-treated cells at the same time points (Fig. 1).

Table 1
List of accession numbers for each transcriptome in GEO database.

Sample	Treatment Condition	Exposure Duration	GEO Accession Number
Veh_1_9h	Vehicle	9 hr	GSM6231072
Veh_2_9h	Vehicle	9 hr	GSM6231073
Veh_3_9h	Vehicle	9 hr	GSM6231074
Veh_4_9h	Vehicle	9 hr	GSM6231075
52_1_9h	10 μM PCB52	9 hr	GSM6231076
52_2_9h	10 μM PCB52	9 hr	GSM6231077
52_3_9h	10 μM PCB52	9 hr	GSM6231078
52_4_9h	10 μM PCB52	9 hr	GSM6231079
52_OH_1_9h	10 μM 4-OH-PCB52	9 hr	GSM6231080
52_OH_2_9h	10 μM 4-OH-PCB52	9 hr	GSM6231081
52_OH_3_9h	10 μM 4-OH-PCB52	9 hr	GSM6231082
52_OH_4_9h	10 μM 4-OH-PCB52	9 hr	GSM6231083
Veh_1_Day1	Vehicle	24 hr	GSM6231084
Veh_2_Day1	Vehicle	24 hr	GSM6231085
Veh_3_Day1	Vehicle	24 hr	GSM6231086
Veh_4_Day1	Vehicle	24 hr	GSM6231087
52_1_Day1	10 μM PCB52	24 hr	GSM6231088
52_2_Day1	10 μM PCB52	24 hr	GSM6231089
52_3_Day1	10 μM PCB52	24 hr	GSM6231090
52_4_Day1	10 μM PCB52	24 hr	GSM6231091
52_OH_1_Day1	10 μM 4-OH-PCB52	24 hr	GSM6231092
52_OH_2_Day1	10 μM 4-OH-PCB52	24 hr	GSM6231093
52_OH_3_Day1	10 μM 4-OH-PCB52	24 hr	GSM6231094
52_OH_4_Day1	10 μM 4-OH-PCB52	24 hr	GSM6231095
Veh_1_Day3	Vehicle	72 hr	GSM6231096
Veh_2_Day3	Vehicle	72 hr	GSM6231097
Veh_3_Day3	Vehicle	72 hr	GSM6231098
Veh_4_Day3	Vehicle	72 hr	GSM6231099
52_1_Day3	10 μM PCB52	72 hr	GSM6231100
52_2_Day3	10 μM PCB52	72 hr	GSM6231101
52_3_Day3	10 μM PCB52	72 hr	GSM6231102
52_4_Day3	10 μM PCB52	72 hr	GSM6231103
52_OH_1_Day3	10 μM 4-OH-PCB52	72 hr	GSM6231104
52_OH_2_Day3	10 μM 4-OH-PCB52	72 hr	GSM6231105
52_OH_3_Day3	10 μM 4-OH-PCB52	72 hr	GSM6231106

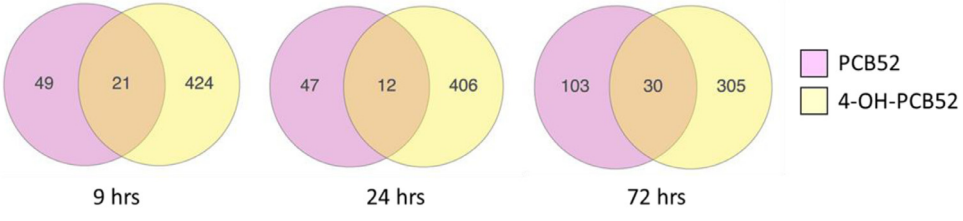

Fig. 1. Venn diagrams demonstrating overlap of filter differentially expressed genes (log fold change ≥ |0.3| & FDR-adjusted p-value ≤ 0.05) at the same time points between PCB52- and 4-OH-PCB-treated preadipocytes.

Table 2
Summary statistics of reads mapping for each sample after alignment.

Sample	# of Mapped Reads
Veh_1_9h	29,352,009
Veh_2_9h	26,035,064
Veh_3_9h	40,601,343
Veh_4_9h	29,735,917
52_1_9h	40,874,007
52_2_9h	47,215,026
52_3_9h	38,497,159
52_4_9h	33,793,144
52_OH_1_9h	34,564,996
52_OH_2_9h	34,002,685
52_OH_3_9h	31,873,220
52_OH_4_9h	31,803,449
Veh_1_Day1	29,733,576
Veh_2_Day1	36,013,685
Veh_3_Day1	33,340,688
Veh_4_Day1	35,876,505
52_1_Day1	25,978,478
52_2_Day1	44,822,922
52_3_Day1	39,570,949
52_4_Day1	37,804,878
52_OH_1_Day1	27,511,262
52_OH_2_Day1	40,918,017
52_OH_3_Day1	35,708,220
52_OH_4_Day1	36,290,154
Veh_1_Day3	29,804,511
Veh_2_Day3	31,061,250
Veh_3_Day3	34,618,101
Veh_4_Day3	25,673,758
52_1_Day3	31,000,244
52_2_Day3	34,675,517
52_3_Day3	31,885,261
52_4_Day3	36,735,258
52_OH_1_Day3	43,092,924
52_OH_2_Day3	31,148,642
52_OH_3_Day3	42,028,480

Table 3
Processed data files after alignment and differentially expressed gene analysis.

File Name	Description of Analysis	Exposure Duration
GSE205813_raw_counts_GRCh38.p13_NCBI.tsv.gz	Raw Counts after alignment	All
GSE205813_DEG_pcb52_dayzero_vs_veh.xlsx	Differential Gene Expression	9 hr
GSE205813_DEG_pcb52OH_dayzero_vs_veh.xlsx	between DMSO and PCB52	9 hr
GSE205813_DEG_pcb52_dayone_vs_veh.xlsx	treated cells. Filtered to include	24 hr
GSE205813_DEG_pcb52OH_dayone_vs_veh.xlsx	genes with log fold change $\geq$	24 hr
GSE205813_DEG_pcb52OH_daythree_vs_veh.xlsx	$\|0.3\|$ & p-value ≤ 0.05	72 hr
GSE205813_DEG_pcb52OH_daythree_vs_veh.xlsx		72 hr

2. Experimental Design, Materials and Methods

PCB52 was synthesized by reduction of 2,2′,5,5′-tetrachlorobenzidine with hypophosphorous acid [6] and authenticated as described previously [7,8]. 4-OH-PCB52 was synthesized by the Suzuki-coupling reaction of 2,5-dichloro-4-iodoanisole and 2,5-dichlorobenzene boronic acid followed by deprotection of the methoxy group with boron tribromide [9]. The Synthesis core of the Iowa Superfund Research Program provided the study compounds.

We used immortalized human preadipocytes called NPADs (Normal PreADipocytes) and cultured them as previously described [1,2,10,11]. Cells were treated as described previously [1,2,11] using dimethyl sulfoxide (DMSO), 10 μM PCB52, or 10 μM 4-OH-PCB52 dissolved in DMSO. The level of DMSO was held constant in all conditions at a level of 0.1% (v/v). The DMSO or toxicant-containing media remained on the cells until RNA harvesting. RNA was isolated as previously described [2,11]. Treatment conditions and treatment durations were repeated 4 times to provide biological replicates. RNA quality was assessed by using an Agilent Bioanalyzer. Any samples with RNA integrity numbers below 8 were excluded from further analysis. This resulted in one sample of 4-OH-PCB52 treated cells at the Day 3 time point to be eliminated from further analysis.

RNA library preparation, RNA sequencing, data processing, and differential gene expression analysis were performed exactly as described previously in the original Data in Brief article [1]. To generate Venn diagrams, DEGs were exported to iPathwayGuide (Advaita). Meta-Analysis in the iPathwayGuide software was used to determine what DEGs overlapped between treatments and time points to generate Venn diagrams.

Ethics Statements

This manuscript complies with ethical publishing guidelines and does not involve human subjects. The NPAD cell line utilized in this study is an immortal cell line that has been previously published [9] and was developed from de-identified primary preadipocytes that were obtained by consent and purchased from Lonza.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data Availability

Human Preadipocyte Response to PCB52 or 4-OH-PCB52 (Original data) (Gene Expression Omnibus).

CRediT Author Statement

Francoise A. Gourronc: Conceptualization, Methodology, Investigation, Data curation, Writing – original draft; **Michael S. Chimenti:** Data curation, Writing – original draft; **Hans-Joachim Lehmler:** Resources, Funding acquisition; **James A. Ankrum:** Conceptualization, Writing – original draft, Funding acquisition; **Aloysius J. Klingelhutz:** Conceptualization, Methodology, Investigation, Data curation, Writing – original draft, Supervision, Funding acquisition.

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