

Supporting Information Available

Toxicological assessment of polychlorinated biphenyls and their metabolites in the liver of Baikal seal (*Pusa sibirica*)

Kei Nomiyama^{†*}, Shusaku Hirakawa[‡], Akifumi Eguchi[§], Chika Kanbara[†], Daisuke Imaeda[†],
Jean Yoo[†], Tatsuya Kunisue[†], Eun-Young Kim[#], Hisato Iwata[†], Shinsuke Tanabe[†]

[†] Center for Marine Environmental Studies (CMES), Ehime University, Bunkyo-cho 2-5,
Matsuyama 790-8577, Japan

[‡] Fukuoka Institute of Health and Environmental Sciences, 39 Mukaizono, Dazaifu, Fukuoka
818-0135, Japan

[§] Chiba University, Clinical Cell Biology and Medicine: Graduate School of Medicine,
Chuo-ku Inohana 1-8-1

[#] Department of Life and Nanopharmaceutical Science and Department of Biology, Kyung
Hee University, Hoegi-Dong, Dongdaemun-Gu, Seoul 130-701, Republic of Korea

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Chemicals

Theoretically, there are 837 mono-hydroxylated PCB congeners with numbers of chlorine atoms ranging from 1 to 9, whereas 209 possible PCB congeners with numbers of chlorine substitution ranging from 1 to 10 are present. The authentic reference standards of 62 PCB (BZ number: CB1, 3, 4, 8, 10, 15, 18, 19, 22, 28, 33, 37, 44, 49, 52, 54, 70, 74, 77, 81, 87, 95, 99, 101, 104, 105, 110, 114, 118, 119, 123, 126, 128, 138, 149, 151, 153, 155, 156, 157, 158, 167, 168, 169, 170, 171, 177, 178, 180, 183, 187, 188, 189, 191, 194, 199, 201, 202, 205, 206, 208, 209) and 52 OH-PCB (tri- to octa-, methoxylated derivatives: MeO-PCBs) isomers used for identification and quantification are given in Table S2. Thirteen compounds were synthesized by thermal diazo-coupling between a chlorophenol and a chloroaniline diazonium salt (1, 2), 8 were obtained from AccuStandard, Inc. (New Haven, CT), and 31 were obtained from Wellington Laboratories Inc. (Guelph, ON, Canada).

Dichloromethane (DCM), n-hexane, methanol, ethanol, methyl tertiary-butyl ether (MTBE), decane, and silica gel (Wako-gel S1) were purchased from Wako Pure Chemical Industries (Osaka, Japan). Trimethylsilyldiazomethane (TMSDM) for derivatization was supplied by Tokyo Chemical Industry (Tokyo, Japan). Anhydrous sodium sulphate (purity >99%) and acetone were obtained from Nacalai Tesque (Kyoto, Japan). Silica gel was baked at 130°C for 3 h prior to use. Five percent hydrated silica gel (5% H₂O deactivated) was prepared by slowly adding an appropriate amount of Milli-Q water (Millipore Corp., Bedford, MA) to activated silica at room temperature.

Measurements of PCBs and OH-PCBs in the liver

A liver sample (approximately 3 g) of Baikal seal, in which ¹³C₁₂-labeled OH-PCBs (1 ng of each 4'OH-CB29, 4'OH-CB61, 4'OH-CB79, 4OH-CB107, 4'OH-CB120, 4'OH-CB159, 4'OH-CB172, and 4OH-CB187) and ¹³C₁₂-labeled PCBs (CB19, 28, 52, 95, 101, 105, 118,

138, 153, 156, 157, 159, 167, 170, 178, 180, 189, 194, 202, 208, 206, and 209) were spiked as surrogate internal standards, was denatured with 3 mL of 6 M hydrochloric acid. After adding 2-propanol (9 mL), the denatured sample was homogenized with a POLYTRON PT 2100 Homogenizer (Kinematica, Luzernerstrasse, Switzerland) (11,000 rpm, 10 min) and the target compounds were extracted three times with a 50% MTBE/hexane mixture by an ultrasonic wave method using an ultrasonic bath (220 W; 30 min) (AU-80C model, EYELA, Japan). After centrifugation, the organic phases were combined and washed with 5% NaCl solution prepared in hexane-washed water. The resulting organic phase was evaporated by a rotary evaporator and re-dissolved in hexane. Potassium hydroxide (KOH; 1 M) in 50% ethanol/water (20 mL) was added and the solution was shaken to ensure mixing. The partition step of the neutral (including PCBs) and phenolic fractions (alkaline phases including OH-PCBs) was repeated and the alkaline phases were combined.

The lipid in the organic phase containing PCBs was removed by gel permeation chromatography (GPC) with Bio-Bead S-X3 (Bio-Rad Laboratories, Hercules CA). Fifty percent dichloromethane (DCM)/hexane was used as the mobile phase at a flow rate of 5 mL min⁻¹. First fraction containing lipid was discarded, and the following fraction containing PCBs was collected, concentrated and passed through activated 4 g of silica-gel (Wako-gel DX: Wako Pure Chemical Industries Ltd., Japan) packed in a glass column. PCBs were eluted with 5% DCM/hexane (80 mL) and concentrated, and ¹³C₁₂-labeled hexabrominated diphenyl ether (BDE139) was added as a syringe spike for gas chromatography/mass spectrometry (GC/MS) analysis.

The combined alkaline phase containing OH-PCBs was acidified (pH 2) with sulfuric acid. OH-PCBs were extracted twice with 50% MTBE/hexane (60 mL). The phases were separated, and the organic phase was combined and evaporated by a rotary evaporator. Then a mixture of acetonitrile:hexane (1:1 v/v; 10 mL) was added and shaken. The partition step was repeated,

and the acetonitrile solution phases containing OH-PCBs were combined. After adding 100 mL of hexane-washed water, the solution was acidified to pH 2 with sulfuric acid. Again, OH-PCBs were extracted twice with 50% MTBE/hexane (60 mL). Subsequently, the organic phases were combined and evaporated by a rotary evaporator.

The solvent-evaporated residue was dissolved in hexane and passed through a glass column packed with 3 g hydrated silica gel (Wako-gel S-1, 5% H₂O deactivated). OH-PCBs were eluted with 50% DCM/hexane (100 mL), and the OH-PCB fraction was concentrated and dissolved in hexane (1 mL). Each treated analyte in hexane was derivatized (methylation; overnight at 20°C) using methanol and trimethylsilyldiazomethane (Tokyo Chemical Industry, Tokyo, Japan). The derivatized solution was treated by gel permeation chromatography (GPC) using a column packed with 50 g of Bio-Beads S-X3 (Bio-Rad Laboratories, Richmond, CA). Fifty percent DCM/hexane was used as the mobile phase at a flow rate of 5 mL·min⁻¹. Then the derivatized OH-PCB solution was passed through 3 g of activated silica gel packed in a glass column. Methoxylated PCBs (MeO-PCBs) were eluted with 140 mL of 10% DCM/hexane and the MeO-PCB fraction was concentrated to near dryness. Then, ¹³C₁₂-labeled CB77 and CB157 (1 ng g⁻¹) dissolved in up to 50 µL of decane were injected as surrogates for the GC/EI-HRMS analysis.

Identification and quantification of MeO-PCB isomers were performed using a HP-6890 gas chromatograph (HRGC: Agilent Technologies Inc., CA, USA) coupled with a MS-800D high-resolution mass spectrometer (JEOL, Japan). The used GC column was a DB-5MS capillary column with 0.25 µm in film thickness and 0.25 mm ID × 60 m in length (J&W Scientific). The column temperature program for the analysis of MeO-PCBs was maintained at 130 °C for 1 min, heated to 210 °C at a 1st rate of 20 °C min⁻¹ and maintained 210 °C for 1 min, heated to 260 °C at a 2nd rate of 2 °C min⁻¹, and maintained at 260 °C for 1 min, heated to 260 °C at a 3rd rate of 25 °C min⁻¹ and maintained at 300 °C for 10 min. The injection

temperature was kept at 290 °C, and the ion source temperature was maintained at 250 °C. The ionizing energy, ion current, and accelerating voltage were set at 40 eV, 500 μ A, and 10 kV, respectively. The resolution was $M/\Delta M > 10,000$ (10% valley) throughout the study, and was carried out using selected ion monitoring (SIM) mode. MeO-PCBs were monitored by SIM mode at three most intensive ions $[M+2 - \text{COCH}_3]^+$, $[M+2]^+$, and $[M+4]^+$. The peaks, which were within 15% of the theoretical ratio of two monitor ions and more than 10 times of noise ($S/N > 10$), were quantified as MeO-PCB isomers. OH-O₈CB isomers were quantified using ¹³C₁₂- labeled 4'-OH-H₇CB172 because no ¹³C₁₂-OH-O₈CB isomer was present in internal standards.

Identification and quantification of 62 native PCB isomers (BP-MS; Wellington Laboratories Inc., Canada) were performed by a GC (Agilent 6890)/MS (Agilent 5973N) using EI-SIM mode at two most intensive ions ($[M]^+$, $[M+2]^+$, and $[M+4]^+$) of the molecular ion cluster.

Quality Assurance and Quality Control

OH-PCBs and PCBs were quantified using isotope dilution method to the corresponding ¹³C₁₂-internal standards according to the formula described previously (3, 4), when the peaks met the following criteria (a~c): (a) the retention time matches that of the standard compound within ± 0.1 min, (b) the signal to noise ratio (S/N) is higher than 10 and (c) the deviation of ion intensity ratio is within 15% of that of the standard compound. Procedural blanks were analyzed simultaneously with every batch of four samples to check for interferences or contamination from solvent and glassware. For each analysis, the mean procedural blank value was used for subtraction. After blank subtraction, the limit of quantification (LOQ) was defined as the amount of target compound that resulted in a S/N of 10:1. Recoveries for the ¹³C₁₂- labeled internal standard in this analytical procedure were within 4'-OH-CB29 (64–

83%), 4'OH-CB61 (92–105%), 4'OH-CB79 (72–92%), 4'OH-CB107 (72–94%), 4'OH-CB120 (85–108%), 4'OH-CB159 (78–91%), 4'OH-CB172 (89–116%), and 4OH-CB187 (77–92%). The method repeatability was in the range of 0.6–9.8% as the relative standard deviation (RSD) for $^{13}\text{C}_{12}$ -labeled OH-PCBs. When OH-PCBs (MeO-PCBs after methylation) were analyzed using scan mode by GC/MS, OH-PCB congeners show distinctive fragment daughter ion of $[\text{M} - \text{COCH}_3]^+$ or $[\text{M} - \text{CH}_3\text{Cl}]^+$, according to the substitution position of hydroxyl group. This study re-analyzed OH-PCBs in all the samples by monitoring two intensive ions of $[\text{M} - \text{COCH}_3]^+$, $[\text{M}+2 - \text{COCH}_3]^+$, and $[\text{M}+4 - \text{COCH}_3]^+$ and of $[\text{M} - \text{CH}_3\text{Cl}]^+$, $[\text{M}+2 - \text{CH}_3\text{Cl}]^+$, and $[\text{M}+4 - \text{CH}_3\text{Cl}]^+$ by SIM mode of HRGC/HRMS, to confirm the reliability of OH-PCB peaks.

Analytical method for thyroid hormones

Total 3,3',5-triiodo-L-thyronine (T_3), 3,3',5'-triiodo-L-thyronine (rT_3), and L-thyroxine (T_4) in the Baikal seal sera were analyzed by following the LC-MS/MS procedure reported recently. (5) An aliquot of 0.5 mL of serum was placed in a 15 mL polypropylene (PP) tube. Then, 25 nanograms of stable isotope-labeled T_4 ($^{13}\text{C}_6\text{-T}_4$) were spiked as an internal standard, and 0.12 mL of antioxidant solution, containing 3 mg of each of citric acid, L-ascorbic acid and DL-dithiothreitol, were added to prevent deiodination of thyroid hormones (THs) during sample preparation. (6) After vortexing, 1 mL of cold acetone was added, vortexed, and kept at 4°C for 1 h. The mixture was centrifuged at 3000 g for 15 min. The supernatant was decanted into a new 15 mL PP tube, and the same procedure was repeated one more time by adding 1 mL of 50% acetone/de-ionize (DI) water into the residue. Acetone was evaporated with a gentle stream of N_2 , and the remaining aqueous solution was loaded onto a SampliQ[®] solid-phase extraction (SPE) cartridge (optimized polymer technology, 60 mg, 3 mL; Agilent Technologies, Santa Clara, CA) that was preconditioned sequentially with 3 mL of MeOH

and 5 mL of DI water. The cartridge was washed with 3 mL of 10% MeOH in DI water that contained 0.01% acetic acid (MeOH:water:acetic acid= 10:89.99:0.01 by volume), and THs were eluted with 3 mL of MeOH. The TH fraction was dried to 250 μ L under a gentle stream of N₂ and transferred into a 0.3 mL glass insert; the vial insert was placed in a 1.5 mL amber vial for LC-MS/MS analysis.

An API 2000 electrospray triple quadrupole mass spectrometer (ESI-MS/MS, Applied Biosystems, Foster City, CA) interfaced with an Agilent 1100 series HPLC system (Agilent Technologies, Santa Clara, CA) was used for the determination of T₃, rT₃ and T₄. Fifteen microliters of serum extract were injected into an Agilent ZORBAX Eclipse XDB-C18 (150 mm length, 2.1 mm internal diameter, 5 μ m particle diameter) chromatographic column serially connected with a guard column (Agilent ZORBAX Eclipse XDB-C8; 12.5 mm $\times$ 2.1 mm, 5 μ m) at a flow rate of 450 μ L/min. The mobile phase was 0.1% (v/v) acetic acid in MeOH (mobile phase A) and DI water (mobile phase B); the gradient started at 10% mobile phase A, was ramped up to 90% mobile phase A in 12 min, and was held for 3 min before reverting back to 10% mobile phase A. THs were monitored by the multiple reaction-monitoring (MRM) mode, using electrospray ionization (ESI) in both positive ion and negative ion modes. The MRM transitions monitored were $[M+H]^+ \rightarrow [M+H-HCOOH]^+$ (783.5 $\rightarrow$ 737.4 for ¹³C₆-T₄, 777.5 $\rightarrow$ 731.4 for T₄, 651.6 $\rightarrow$ 605.6 for T₃) in the positive ion mode (quantitation transitions), and $[M-H]^- \rightarrow I^-$ (781.5 $\rightarrow$ 126.9 for ¹³C₆-T₄, 775.5 $\rightarrow$ 126.9 for T₄, 649.6 $\rightarrow$ 126.9 for T₃) in the negative ion mode (confirmation transitions).

The analytes were quantified by an isotope (¹³C₆-T₄)-dilution method. Data processing was performed with the Analyst 1.4.1 software package. Linear regression analysis of the relative response factors of calibration standards, ranging in concentrations from 0.5 to 200 ng/mL with 50 ng/mL of ¹³C₆-T₄, showed correlation coefficients (*r*) greater than 0.9995; the linearity of the calibration standards was greater than 0.9995 for every batch of 10 samples

injected. The limits of detection (LOD), determined as 3 times the signal-to-noise ratio (S/N), were 0.45 ng/mL for T₄ and 0.30 ng/mL for T₃. The procedural recoveries of THs spiked into the serum matrix were between 97.0% and 115%, and the CVs of triplicate analyses were between 2.1% and 9.4%.

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Table S1. Sample information of Baikal seal collected analyzed in this study.

Sex	Sample ID ^a	Age (year)	Body length (cm)	Body weight (kg)	Collection date
Male	05BS-02	41.5	145.8	89	5-May-2005
	05BS-06	5.5	113.4	27.2	5-May-2005
	05BS-18	0.25	91.5	14.2	5-May-2005
	05BS-22	0.5	98.6	17.5	5-May-2005
	05BS-25	4.5	119.7	33.8	5-May-2005
	05BS-26	2.5	124.2	35	5-May-2005
	05BS-27	26.5	153	71	5-May-2005
	05BS-28	26.5	158.4	71.1	5-May-2005
	05BS-29	40.5	142	58.5	5-May-2005
	05BS-30	10.5	154.2	65.1	5-May-2005
	05BS-35	NA	128.5	54	5-Jun-2005
	05BS-41	3.5	115.5	32.9	5-Jun-2005
	05BS-43	3.5	109	28.5	5-Jun-2005
	05BS-44	13.5	140.5	63	5-Jun-2005
Female	05BS-04	8.5	124	53.5	5-May-2005
	05BS-07	2.5	102.5	26.2	5-May-2005
	05BS-08	NA	126	68.5	5-May-2005
	05BS-09	7.5	118	36.4	5-May-2005
	05BS-10	1.25	107.5	24	5-May-2005
	05BS-13	5.5	123	36.4	5-May-2005
	05BS-14	36.5	150.5	75.6	5-May-2005
	05BS-16	0.25	96	24.5	5-May-2005
	05BS-17	0.5	95.9	22.2	5-May-2005
	05BS-19	0.5	100.5	26.2	5-May-2005
	05BS-20	9.5	152	90.7	5-May-2005
	05BS-23	0.5	89.2	12.8	5-May-2005
	05BS-31	9.5	137.5	40.5	5-May-2005
	05BS-32	15.5	150.5	53	5-Jun-2005
	05BS-33	0.5	86	15.3	5-Jun-2005
	05BS-36	0.5	91	15.6	5-Jun-2005
	05BS-38	31.5	149.4	78.9	5-Jun-2005
	05BS-39	37.5	143	49.4	5-Jun-2005
	05BS-42	3.5	99.8	18.9	5-Jun-2005

a: Sample ID and sample locations are shown in the database of the Environmental Specimen Bank (*es*-BANK) of Ehime University, Japan (<http://esbank-ehime.com/>).

Table S2. The authentic reference standards of OH-PCBs.

No.	IUPAC	BZ No.	Provider
Tri-			
1	4OH-2,2',5'-trichlorobiphenyl	4'OH-CB18	Accu standard ^a
2	4OH-2',3,3'-trichlorobiphenyl	4'OH-CB20	Synthetic ^b
3	3OH-2,3',4'-trichlorobiphenyl	3OH-CB25	Synthetic
4	4OH-2',3,4'-trichlorobiphenyl	4'OH-CB25	Synthetic
5	4OH-2,3',5'-trichlorobiphenyl	4OH-CB26	Synthetic
6	4OH-2',3,5'-trichlorobiphenyl	4'OH-CB26	Accu standard
7	3OH-2',4,4'-trichlorobiphenyl	3'OH-CB28	Synthetic
8	3OH-2',4,5'-trichlorobiphenyl	3'OH-CB31	Synthetic
9	4OH-2,4',5'-trichlorobiphenyl	4OH-CB31	Synthetic
10	4OH-3,3',4'-trichlorobiphenyl	4'OH-CB35	Synthetic
Tetra-			
11	3OH-2,2',5',6'-tetrachlorobiphenyl	3'OH-CB53	Synthetic
12	4OH-2',3',4',5'-tetrachlorobiphenyl	4'OH-CB61	Accu standard
13	4OH-2',3',5',6'-tetrachlorobiphenyl	4'OH-CB65	Accu standard
14	3OH-2,3',4,4'-tetrachlorobiphenyl	3OH-CB66	Synthetic
15	4OH-2,3',4',5'-tetrachlorobiphenyl	4OH-CB70	Synthetic
16	4OH-2',3,5,5'-tetrachlorobiphenyl	4'OH-CB72	Accu standard
17	3OH-2',4,4',5'-tetrachlorobiphenyl	3'OH-CB74	Synthetic
18	4OH-3,3',4',5'-tetrachlorobiphenyl	4OH-CB79	Wellington Laboratory ^c
Penta-			
19	4'OH-2,2',3,4',5'-pentachlorobiphenyl	4'OH-CB97	Wellington Laboratory
20	4OH-2,2',4',5,5'-pentachlorobiphenyl	4'OH-CB101	Wellington Laboratory
21	4OH-2',3,3',4',5'-pentachlorobiphenyl	4'OH-CB106	Accu standard
22	4OH-2,3,3',4',5'-pentachlorobiphenyl	4OH-CB107	Wellington Laboratory
23	4'OH-2,3,3',4,5'-pentachlorobiphenyl	4'OH-CB108	Wellington Laboratory
24	2'OH-2,3,4',5,6'-pentachlorobiphenyl	2'OH-CB114	Wellington Laboratory
25	3OH-2,3',4,4',5'-pentachlorobiphenyl	3'OH-CB118	Wellington Laboratory
26	4'OH-2,3',4,5,5'-pentachlorobiphenyl	4'OH-CB120	Wellington Laboratory
27	4OH-2',3,4',5,6'-pentachlorobiphenyl	4'OH-CB121	Accu standard
28	4'OH-3,3',4,5,5'-pentachlorobiphenyl	4'OH-CB127	Wellington Laboratory
Hexa-			
29	4OH-2,2',3,3',4',5'-hexachlorobiphenyl	4'OH-CB130	Wellington Laboratory
30	4OH-2,2',3,3',5,6'-hexachlorobiphenyl	4OH-CB134	Wellington Laboratory
31	3OH-2,2',3',4,4',5'-hexachlorobiphenyl	3'OH-CB138	Wellington Laboratory
32	4OH-2,2',3,4',5,5'-hexachlorobiphenyl	4OH-CB146	Wellington Laboratory
33	3OH-2,2',4,4',5,5'-hexachlorobiphenyl	3OH-CB153	Synthetic ^d
34	4OH-2',3,3',4',5,5'-hexachlorobiphenyl	4'OH-CB159	Wellington Laboratory
35	4OH-2,3,3',4',5,5'-hexachlorobiphenyl	4OH-CB162	Wellington Laboratory
36	4OH-2,3,3',4',5,6'-hexachlorobiphenyl	4OH-CB163	Wellington Laboratory
37	4OH-2',3,3',5,5',6'-hexachlorobiphenyl	4'OH-CB165	Accu standard
Hepta-			
38	4OH-2,2',3,3',4',5,5'-heptachlorobiphenyl	4'OH-CB172	Wellington Laboratory
39	4OH-2,2',3,3',4',5,6'-heptachlorobiphenyl	4OH-CB177	Wellington Laboratory
40	4OH-2,2',3,3',5,5',6,6'-heptachlorobiphenyl	4OH-CB178	Wellington Laboratory
41	3'OH-2,2',3,4,4',5,5'-heptachlorobiphenyl	3'OH-CB180	Wellington Laboratory
42	3'OH-2,2',3,4,4',5,6'-heptachlorobiphenyl	3'OH-CB182	Wellington Laboratory
43	3OH-2,2',3',4,4',5,6'-heptachlorobiphenyl	3'OH-CB183	Wellington Laboratory
44	3'OH-2,2',3,4,4',6,6'-heptachlorobiphenyl	3'OH-CB184	Wellington Laboratory
45	4OH-2,2',3,4',5,5',6'-heptachlorobiphenyl	4OH-CB187	Wellington Laboratory
46	4OH-2,3,3',4',5,5',6'-heptachlorobiphenyl	4OH-CB193	Wellington Laboratory
Octa-			
47	4'OH-2,2',3,3',4,5,5',6'-octachlorobiphenyl	4'OH-CB198	Wellington Laboratory
48	4OH-2,2',3,3',4',5,5',6'-octachlorobiphenyl	4'OH-CB199	Wellington Laboratory
49	4'OH-2,2',3,3',4,5,6,6'-octachlorobiphenyl	4'OH-CB200	Wellington Laboratory
50	4'OH-2,2',3,3',4,5',6,6'-octachlorobiphenyl	4'OH-CB201	Wellington Laboratory
51	4OH-2,2',3,3',5,5',6,6'-octachlorobiphenyl	4OH-CB202	Wellington Laboratory
52	3'OH-2,2',3,4,4',5,5',6'-octachlorobiphenyl	3'OH-CB203	Wellington Laboratory

a: Accustandard, New Haven, CT, USA. b: Synthetic OH-PCBs were supplied by Dr. T. Okumura.^{1,2} c: Wellington Laboratories Inc., Guelph, ON, Canada d: 3OH-153 (3MeO-153) was synthesized according to Bergman et al.⁷

Table S3. Summary of Spearman's correlation analysis for preliminary screening ($p < 0.05$).

Concentration of total OH-PCBs	OH-PCB/PCB Ratio
CYP1A1	CYP1A1
CYP1A2	CYP1B1
CYP1B1	CYP2AA
CYP2AA	CYP2C21_1589
CYP2C21	glutathione-s-transferase-kappa-1
CYP3A	S03164-01_A13
glutathione s-transferase	S03164-01_A21
S03164-01_M11	S03164-01_C09
S03164-01_M13	S03164-01_C12
S03164-01_O01	S03164-01_C24
S03164-01_O06	S03164-01_D24
S03164-01_P06	S03164-01_E10
S03164-02_A04	S03164-01_F08
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S03164-02_N18	S03164-01_P13
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S03164-03_D13	S03164-02_C07
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S03164-03_D23	S03164-02_D19
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S03164-03_E07	S03164-02_E15
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Table S4. Concentrations (pg g⁻¹ wet wt) of OH-PCB congeners and PCBs in the liver and blood of Baikal seal.

Liver Male Med													Blood Male Med				
age	3.5	0.25	41.5	10.6	14.5	Female Med 7.5	Min 0.25	Max 41.5	Mean 13	SD 14.8	p-value *	min	Max	Female Med	Min	Max	
4'OH-CB25/4'OH-CB26/4OH-CB31	3'OH-CB28	<0.6	<0.6	<0.6	<0.6	<0.6	<0.6	1.5	<0.6	<0.6	0.003	<0.6	<0.6	<0.6	<0.6	<0.6	
	4OH-CB26	22	<0.6	180	40	47	24	<0.6	330	41	70	0.91	3.1	0.8	8.2	2.2	0.6
	4'OH-CB20	<0.6	<0.6	<0.6	<0.6	<0.6	<0.6	2.8	<0.6	0.6	0.40	<0.6	<0.6	<0.6	<0.6	<0.6	
	4'OH-CB18	<0.6	<0.6	8.2	1.3	2.2	<0.6	<0.6	2.9	<0.6	0.6	0.017	<0.6	<0.6	<0.6	<0.6	<0.6
	4OH-CB61	8.9	1.2	59	16	18	3.2	<0.6	2700	130	590	0.006	3.6	1.8	13	2.4	1.1
	4OH-CB79	<0.6	<0.6	28	1.7	6.8	<0.6	<0.6	7.7	<0.6	1.7	0.75	13	7.3	28	17	6.1
	4OH-CB70	10	3.7	84	15	19	5.1	<0.6	27	6.2	5.6	0.001	3.7	1.2	23	2.6	0.9
	3'OH-CB53	3.4	1.2	11	4.0	2.5	<0.6	<0.6	1.5	<0.6	<0.6	0.0001	<0.6	<0.6	<0.6	<0.6	<0.6
	4'OH-CB65	<0.6	<0.6	0.0	<0.6	<0.6	<0.6	<0.6	4.2	<0.6	0.9	0.12	<0.6	<0.6	<0.6	<0.6	<0.6
	4'OH-CB61	12.8	2.7	81	24	22.7	7.1	<0.6	48	11	12	0.02	<0.6	<0.6	<0.6	<0.6	<0.6
	2OH-CB114	<0.6	<0.6	97	5.7	23	<0.6	<0.6	15	1.3	4.2	0.75	<0.6	<0.6	<0.6	<0.6	<0.6
	4OH-CB97	95	<0.6	400	92	110	<0.6	<0.6	190	40	69	0.13	9.6	5.0	31	9.6	2.1
	3OH-CB118	56	27	180	64	39	38	<0.6	62	31	19	0.002	11	4.8	57	5.6	2.5
	4OH-CB120/4OH-CB101	430	250	1400	570	320	280	87	930	360	210	0.014	140	81	560	88	19
	4OH-CB108/4OH-CB107	15	<0.6	100	21	27	9.1	<0.6	61	16	16	0.75	76	41	330	51	20
	4OH-CB146	91	44	380	130	100	77	30	210	90	49	0.19	280	120	930	185	63
	4OH-CB130	12	<0.6	49	12	15	5.8	<0.6	29	9.2	10	0.85	37	18	140	27	7.6
	4OH-CB162	18	<0.6	100	30	30	12	<0.6	51	19	16	0.28	51	12	210	22	2.2
	4OH-CB134	120	<0.6	400	150	99	64	<0.6	120	63	49	0.003	41	15	150	27	8.6
	3OH-CB138	370	140	1030	420	250	300	100	470	280	110	0.08	100	46	310	67	26
	4OH-CB163	84	41	520	130	120	64	17	140	65	33	0.029	81	35	340	53	19
	3OH-CB153	98	40	400	140	97	82	31	170	80	34	0.022	32	7.5	130	17	6.7
	4OH-CB187	60	<0.6	150	59	38	46	11	120	57	34	0.91	170	68	470	175	37
	3OH-CB180	12	3.3	80	18	19	11	3.2	24	12	7.0	0.31	11	2.5	44	5.3	2.0
	4OH-CB172	30	14	120	39	29	15	4.0	70	23	17	0.026	50	12	220	23	4.3
4OH-CB193	44	17	170	56	37	23	<0.6	79	26	23	0.002	38	6.2	71	23	4.6	
4OH-CB178	17	<0.6	72	25	23	16	5.6	47	20	12	0.76	44	24	170	36	12	
4OH-CB177	19	<0.6	83	26	24	15	2.6	40	17	11	0.45	22	9.3	47	21	4.3	
3OH-CB182/3OH-CB183	25	6.6	64	25	17	19	6.0	46	18	10	0.25	24	12	79	18	6.0	
4OH-CB202	27	8.8	91	34	25	31	1.1	200	37	42	0.84	67	25	320	69	14	
4OH-CB199	15	4.2	100	31	29	14	2.1	94	24	23	0.40	57	19	170	28.8	3.9	
4OH-CB201	4.1	2.1	12	5.1	2.8	4.3	1.5	12	5.1	3.0	0.87	6.5	3.3	16	5.8	1.9	
4OH-CB200	<0.6	<0.6	3.0	0.6	0.8	0.6	<0.6	3.0	0.6	0.8	0.73	1.9	0.8	4.7	1.7	0.8	
3OH-CB203/4OH-CB198	8.7	2.8	48	12	11	9.5	1.5	30	11	8.3	1.000	27	7.6	120	15.9	5.3	
Total OH-T ₃ CBs	31	2.5	190	58	58	28	7.3	2700	170.0	590	0.55	6.0	3.4	17	3.9	0.6	
Total OH-T ₄ CBs	71	22	410	110	100	31	4.7	170	47	43	0.004	39	23	91	38	16	
Total OH-P ₃ CBs	610	400	2080	150	440	380	110	980	440	240	0.008	230	150	980	160	39	
Total OH-H ₆ CBs	790	370	2700	1010	670	630	250	1030	610	230	0.04	580	260	2100	390	160	
Total OH-H ₇ CBs	218	89	670	150	160	150	41	300	170	88	0.09	320	160	1100	340	71	
Total OH-O ₆ CBs	59	24	230	84	64	60	6.8	230	79	58	0.81	160	60	560	140	25	
Total OH-PCBs	1900	950	6060	2250	1320	1550	460	4790	1520	930	0.06	1500	710	4600	1100	310	
Total PCBs	365000	126000	2830000	675000	791000	158000	55500	764000	244000	189000	0.01	26200	6400	130000	16000	3700	

* gender difference: $p < 0.05$ Mann–Whitney U test; Total PCBs (sum of CB1, 3, 4, 8, 10, 15, 18, 19, 22, 28, 33, 37, 44, 49, 52, 54, 70, 74, 77, 81, 87, 95, 99, 101, 104, 105, 110, 114, 118, 119, 123, 126, 128, 138, 149, 151, 153, 155, 156, 157, 158, 167, 168, 169, 170, 171, 177, 178, 180, 183, 187, 188, 189, 191, 194, 199, 201, 202, 205, 206, 208 and 209). <0.6: below the LOQ. Concentrations of blood of Baikal seals used in this study was reported in our previous studies.⁸

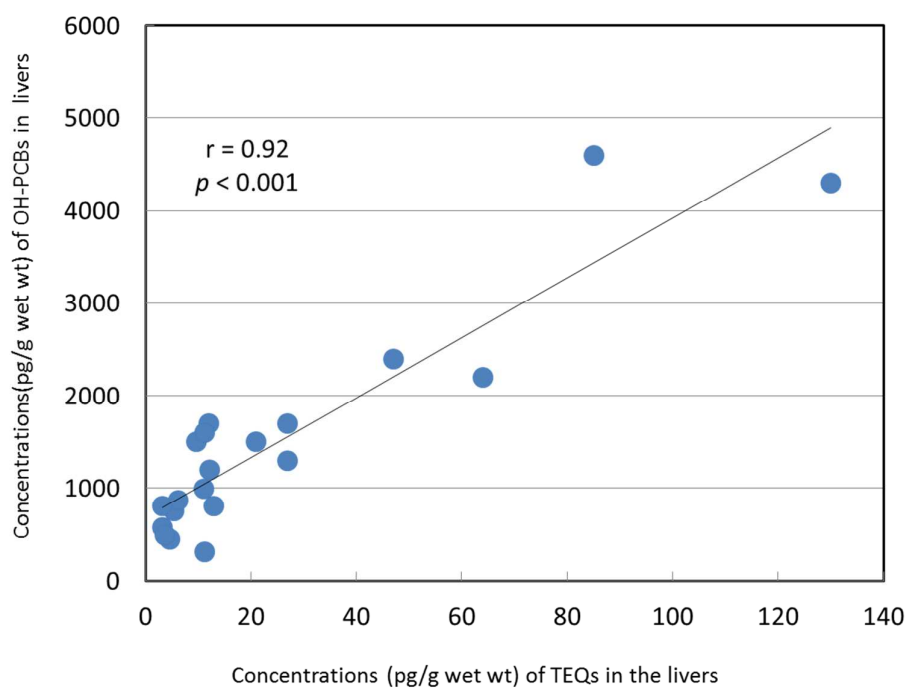


Figure S1. Correlations between the concentrations of total OH-PCBs and total TEQs in the liver of Baikal seals.

r values: Spearman's rank correlation coefficients

TEQs data: proposed by Imaeda et al., *Environ. Pollut.* **2009**, 157, 737–747.

Table S5. List of genes correlated positively with OH-PCB concentrations in the liver of Baikal seals by stepwise multiple linear regressions

Gene library ID	Seq. Description positive	Estimate	Std.Error	t-value	Pr(> t)	p
CYP2C21	cytochrome family subfamily polypeptide 18	0.000355719	0.000118295	3.007059	0.007934	**
S03164.02_F02_450	t-complex protein eta subunit (tcp-1-eta) (cct-eta) (hiv-1 nef interacting protein) isoform 4	8.96003E-05	3.39E-05	2.643074	0.017085	*
S03164.03_B13_543	cold inducible rna binding protein	0.000105649	4.46411E-05	2.36662	0.030087	*
S03164.03_C11_347	cytochrome b5	7.47304E-05	2.30791E-05	3.238012	0.004835	**
S03164.03_D23_454	ribosomal protein l8	8.11151E-05	3.69043E-05	2.197987	0.042091	*
S03164.03_E04_336	11-beta-hydroxysteroid dehydrogenase 1	0.000154119	6.93114E-05	2.22357	0.040022	*
S03164.03_P13_362	chromosome 10 open reading frame 97	9.26633E-05	2.20555E-05	4.201374	0.0006	***
S03164.04_J22_237	Raichu-1237X [synthetic construct]	4.9354E-05	2.11447E-05	2.334109	0.032118	*
S03164.04_N09_243	fth1 protein	0.000122812	4.40248E-05	2.789602	0.012578	*
S03164.05_B10_293	proteasome (macropain) beta type 3	6.80699E-05	2.05556E-05	3.311502	0.004126	**
S03164.05_C07_452	fatty acid binding protein 3	0.000225314	5.07485E-05	4.43981	0.000359	***
S03164.05_L20_441	peroxiredoxin 1	0.000153639	4.6766E-05	3.285281	0.004367	**
S03164.05_P04_504	fth1 protein	0.000164824	6.85288E-05	2.405181	0.027833	*
S03164.06_H20_81	translocase of inner mitochondrial membrane 13 homolog	0.000113679	4.45885E-05	2.549511	0.020731	*
S03164.06_M01_385	mitochondrial ribosomal protein s24	6.08597E-05	2.44481E-05	2.489348	0.023453	*
S03164.07_A23_478	neural precursor cell developmentally down-regulated 8	6.95988E-05	2.22178E-05	3.13257	0.006066	**
S03164.07_C10_491	cytochrome b5	0.000141376	5.48015E-05	2.579789	0.019477	*
S03164.07_E20_330	nucleolar protein family member 2	6.70303E-05	0.00003151	2.127271	0.048334	*
S03164.07_G01_363	stress-induced-phosphoprotein 1 (hsp70 hsp90-organizing protein)	0.00013646	4.95138E-05	2.755991	0.018689	*
S03164.07_K01_461	cytochrome family subfamily polypeptide 1	0.000103344	4.55348E-05	2.269561	0.040902	*
S03164.07_K13_469	proteasome (macropain) alpha 7	0.000068408	2.33946E-05	2.924088	0.009466	**
S03164.08_D19_78	cd63 antigen	8.26206E-05	3.66334E-05	2.255338	0.037583	*
S03164.08_I08_166	proteasome (macropain) alpha 3	0.000137477	5.89674E-05	2.331406	0.032293	*
S03164.09_A07_24	ferritin l subunit	0.000169615	7.80459E-05	2.173271	0.044183	*
S03164.09_D04_220	als2 c-terminal like	0.000111465	5.11706E-05	2.178296	0.04375	*
S03164.10_A11_478	cofilin 1 (non-muscle)	0.000109321	4.60202E-05	2.3755	0.029553	*
S03164.10_G21_215	profilin 1	5.08608E-05	2.12173E-05	2.397143	0.028289	*
S03164.10_K09_88	glyceraldehyde-3-phosphate dehydrogenase	8.27858E-05	3.08596E-05	2.682664	0.015734	*
S03164.10_L10_272	protein phosphatase methylesterase 1	6.68617E-05	1.8978E-05	3.523127	0.003074	**
S03164.10_L13_5	ferritin l subunit	0.000193475	5.89197E-05	3.283707	0.004381	**
S03164.11_A01_500	proteasome (macropain) alpha 3	0.000145205	3.97742E-05	3.65074	0.001979	**
S03164.11_G01_518	fth1 protein	0.000173028	6.67162E-05	2.593494	0.018933	*
S03164.11_H18_91	biliverdin reductase b (flavin reductase)	0.000126168	3.78043E-05	3.337406	0.003902	**
S03164.12_C08_339	biliverdin reductase b (flavin reductase)	0.0001571	4.73688E-05	3.316525	0.004082	**
S03164.12_C17_219	proteasome (macropain) alpha 3	0.000111655	4.58822E-05	2.43352	0.026279	*
S03164.12_G18_389	williams beuren syndrome chromosome region 22	6.98378E-05	2.11061E-05	3.308885	0.00415	**
S03164.12_P14_253	ribosomal protein s3	7.21883E-05	2.0639E-05	3.497666	0.002758	**
S03164.13_K05_428	fth1 protein	0.000166296	6.78386E-05	2.451341	0.025344	*
S03164.14_A07_469	proteasome (macropain) beta 4	9.28029E-05	3.69681E-05	2.510355	0.022466	*
S03164.14_A20_370	als2 c-terminal like	5.28327E-05	2.42052E-05	2.1827	0.043374	*

S03164.14_A23_371	ribosomal protein s16	6.03182E-05	2.44035E-05	2.471702	0.024314	*
S03164.14_G02_397	glutathione s-transferase pi	0.000103492	3.70662E-05	2.792082	0.012512	*
S03164.14_H24_364	immunoglobulin member 4c	4.64677E-05	2.01305E-05	2.308324	0.03382	*
S03164.07_M07_383	steroid dehydrogenase homolog	6.23903E-05	2.46751E-05	2.52847	0.021647	*
S03164.07_N20_47	chromosome 3 open reading frame 10	6.11611E-05	2.76908E-05	2.20872	0.041211	*
S03164.09_P07_513	heavy polypeptide 1	0.000149746	5.74614E-05	2.606025	0.018449	*
S03164.03_I14_324	thioredoxin reductase 1	0.000382779	0.000110088	3.477038	0.003111	**
S03164.03_O02_456	triosephosphate isomerase 1	0.000340092	0.000124361	2.734722	0.014688	*
S03164.03_O08_280	type ii	0.000459105	0.000120053	3.824179	0.002108	**
S03164.04_A07_280	phosphonoformate immuno-associated protein 5	9.26633E-05	2.20555E-05	4.201374	0.0006	***
S03164.02_N18_332	fatty acid-binding epidermal (e-fabp) (psoriasis-associated fatty acid-binding protein homolog) (pa-fabp)	0.000382078	0.000111887	3.414839	0.003547	**
S03164.02_O24_366	proteasome (macropain) beta 7	0.000186288	7.00499E-05	2.659363	0.017139	*
S03164.04_M06_194	general transcription factor polypeptide 30kda	0.000235007	6.84366E-05	3.433932	0.003407	**
S03164.07_O15_248	40s ribosomal protein s2	0.000269746	5.68282E-05	4.746691	0.000219	***
S03164.08_A15_216	ww domain binding protein 4 (formin binding protein 21)	0.000228091	7.69867E-05	2.962727	0.009164	**
S03164.10_A02_498	proteasome (macropain) beta 2	0.000206089	5.43256E-05	3.793584	0.001594	**
S03164.10_K01_432	ubiquitin-conjugating enzyme e2l 3	0.000182881	5.53918E-05	3.301581	0.004504	**
S03164.10_K12_265	proteasome (macropain) alpha 7	0.000164704	4.02721E-05	4.08979	0.000855	***
S03164.14_A22_377	coiled-coil-helix-coiled-coil-helix domain containing 2	0.000200438	7.60082E-05	2.637061	0.017936	*
S03164.14_E13_254	myosin regulatory light chain mrc13	0.000353936	9.51246E-05	3.720762	0.00205	**
S03164.14_I23_347	von hippel-lindau binding protein 1	0.000164603	6.78001E-05	2.427769	0.027362	*
S03164.03_E07_366	dolichyl-phosphate mannosyltransferase polypeptide catalytic subunit	0.000247913	8.53355E-05	2.905159	0.01033	*
S03164.06_G01_232	tumor rejection antigen 1	0.000375426	0.000155911	2.407947	0.028465	*
S03164.09_M24_282	zinc finger protein 229	0.000361369	0.00013506	2.675612	0.0202	*
S03164.10_H01_380	ribosomal protein p2	0.000217942	6.5185E-05	3.343436	0.004124	**
S03164.14_M02_318	mof4 family associated protein 1	0.000293257	0.000110779	2.647214	0.017569	*
S03164.14_N20_358	yip1 domain member 4	0.000231896	8.97547E-05	2.583661	0.019993	*
S03164.14_O15_323	eukaryotic translation elongation factor 1 beta 2	0.000364754	0.000147502	2.47288	0.025	*

p-value: <0.001 = ‘***’, <0.01, = ‘**’, <0.05 = ‘*’

Table S6. List of genes correlated negatively with OH-PCB concentrations in the liver of Baikal seals by stepwise multiple linear regressions

Gene library ID	Seq. Description negative	Estimate	Std.Error	t-value	Pr(> t)	p
S03164.01_O06_343	tetraspanin 4	-4.35574E-05	1.57408E-05	-2.76717	0.013185	*
S03164.02_A04_364	cd36 antigen	-8.33287E-05	3.69242E-05	-2.25675	0.037478	*
S03164.02_A19_459	zinc finger and btb domain containing 8 opposite strand	-7.77595E-05	3.14435E-05	-2.47299	0.02425	*
S03164.02_F01_486	alpha polypeptide isoform 2	-0.00028069	0.000103474	-2.71266	0.014779	*
S03164.02_N10_295	solute carrier family member 39	-5.57141E-05	2.63688E-05	-2.11288	0.050677	.
S03164.03_E23_458	afamin	-7.56528E-05	3.35781E-05	-2.25304	0.037755	*
S03164.06_D02_313	gnas complex locus	-9.14833E-05	3.00956E-05	-3.03976	0.007399	**
S03164.06_J10_227	transcription elongation factor a 1	-0.000103275	4.26599E-05	-2.42089	0.026961	*
S03164.07_C22_367	poliovirus receptor-related 3 isoform alpha	-0.000126645	4.45363E-05	-2.84362	0.011224	*
S03164.07_D09_362	tho complex 5	-4.78123E-05	1.69378E-05	-2.82282	0.011728	*
S03164.08_A22_449	apolipoprotein c-iii	-8.97719E-05	3.78921E-05	-2.36914	0.029934	*
S03164.08_C16_91	PREDICTED: hypothetical protein [Bos taurus]	-7.21884E-05	2.58591E-05	-2.7916	0.012525	*
S03164.08_L10_162	serpine1 mrna binding protein isoform cra_d	-0.00016799	7.369E-05	-2.27969	0.035808	*
S03164.08_P03_338	metallothionein isoform cra_a	-0.000589389	0.000175151	-3.36504	0.003675	**
S03164.09_E04_343	inter-alpha inhibitor h1	-0.000157323	3.85695E-05	-4.07894	0.000782	**
S03164.12_C02_503	vitamin d-binding protein	-0.000158275	3.74159E-05	-4.23016	0.000564	**
S03164.12_I10_383	wd repeat domain 61	-4.53809E-05	1.62139E-05	-2.79889	0.012334	*
S03164.12_K02_286	erythrocyte protein band	-8.41836E-05	2.75501E-05	-3.05566	0.00801	**
S03164.13_A15_206	fibulin 1	-0.000138617	5.90952E-05	-2.34566	0.031382	*
S03164.13_B16_187	novel protein	-0.000136962	6.35134E-05	-2.15643	0.045663	*
S03164.13_C05_313	cyclin-dependent kinase 5	-7.60743E-05	2.38838E-05	-3.18519	0.006612	**
S03164.14_K05_273	proteolipid protein	-7.12079E-05	3.20888E-05	-2.21909	0.040377	*
S03164.04_F02_255	reticulin 1	-5.54361E-05	2.42462E-05	-2.28638	0.038327	*
S03164.12_A07_510	destrin	-8.99266E-05	3.40974E-05	-2.63734	0.017289	*
S03164.03_I06_229	transmembrane protein 141	-0.00032913	7.88651E-05	-4.17333	0.000717	**
S03164.05_M16_431	beta 4	-0.000253472	6.4243E-05	-3.94552	0.001157	**
S03164.03_D13_235	inter-alpha globulin inhibitor h2 polypeptide	-0.000488749	0.000129819	-3.76484	0.001694	**
S03164.05_H13_415	chromosome 16 open reading frame 57	-0.000119096	4.1914E-05	-2.84144	0.011788	*
S03164.06_B13_200	n-acetylglucosamine-1- gamma subunit	-0.000115603	3.89878E-05	-2.9651	0.009119	**
S03164.08_G04_473	unnamed protein product [Tetraodon nigroviridis]	-0.000558727	0.000181202	-3.08346	0.007122	**
S03164.12_G12_585	cytochrome oxidase subunit iii	-0.000639457	0.000166726	-3.83537	0.00146	**
S03164.13_F09_369	actin related protein 2 3 subunit 21kda	-0.000166273	5.23524E-05	-3.17604	0.005866	**
S03164.14_C03_397	protein kinase (camp- catalytic) inhibitor beta	-0.000273337	8.24866E-05	-3.31371	0.004391	**
S03164.14_D15_460	fetal and adult testis expressed transcript protein	-0.00028201	7.62098E-05	-3.70045	0.001941	**
S03164.04_O05_381	nadh dehydrogenase subunit 5	-0.000646083	0.000277306	-2.32985	0.033233	*
S03164.07_I09_358	eh-domain containing 1	-0.000270523	8.94767E-05	-3.02339	0.008076	**
S03164.07_M19_619	cytochrome oxidase subunit ii	-0.000377904	0.000150204	-2.51594	0.022927	*
S03164.08_N14_442	vitronectin	-0.000348266	0.000116723	-2.98369	0.008773	**
S03164.10_K19_490	tyrosine 3-monooxygenase tryptophan 5-monooxygenase activation zeta polypeptide	-0.000257378	9.07648E-05	-2.83566	0.01193	*

p-value: <0.001 = '***', <0.01, = '**', <0.05 = '*'

Table S7. List of genes correlated positively with PCB/OH-PCB concentration ratios in the liver of Baikal seals by stepwise multiple linear regressions

Gene library ID	Seq. Description positive	Estimate	Std.Error	t-value	Pr(> t)	p
CYP2AA_1412	cytochrome p450 2a13	97.13465	12.24102	7.935	4.08E-07	***
S03164.01_A13_456	fibrinogen gamma polypeptide	64.753428	16.952336	3.82	0.00151	**
S03164.01_O06_343	tetraspanin 4	12.27822	4.37824	2.804	0.0122	*
S03164.01_O11_81	golgi phosphoprotein 2	14.1773	6.1787	2.295	0.0348	*
S03164.02_A19_459	zinc finger and btb domain containing 8 opposite strand	20.45937	8.95878	2.284	0.03552	*
S03164.02_B19_84	serpin peptidase clade a (alpha-1 antitrypsin) member isoform cra_a	15.15544	8.55288	1.772	0.0943	.
S03164.02_C20_268	fibrinogen alpha-e subunit	61.731605	18.847213	3.275	0.00476	**
S03164.02_D19_447	nucleolin-related protein	34.007444	11.587629	2.935	0.009713	**
S03164.02_E20_431	cd9 antigen	24.87958	9.19795	2.705	0.015	*
S03164.02_F01_486	alpha polypeptide isoform 2	121.40982	18.16012	6.686	3.83E-06	***
S03164.02_M23_436	heterogeneous nuclear ribonucleoprotein u (scaffold attachment factor a)	33.06448	13.53698	2.443	0.0258	*
S03164.03_A16_348	actin binding 1b	56.44199	13.5583	4.163	0.000652	***
S03164.03_B21_265	clusterin	59.56358	19.38739	3.072	0.0069	**
S03164.03_D06_355	annexin a5	24.00087	10.9409	2.194	0.042449	*
S03164.03_M23_346	protein disulfide isomerase associated 6	53.58664	16.05595	3.337	0.0039	**
S03164.03_N08_448	chaperonin subunit 6a	19.5359	7.72479	2.529	0.021624	*
S03164.04_I16_259	c3orf6 protein	49.9944	19.2325	2.599	0.0187	*
S03164.04_N21_93	c-reactive protein precursor	124.5901	32.2278	3.866	0.00124	**
S03164.04_O18_85	ribosomal protein l27a	9.46228	4.08125	2.318	0.0331	*
S03164.05_A03_557	ceruloplasmin isoform 1	136.423134	37.317901	3.656	0.00213	**
S03164.05_D14_424	adenosine kinase	61.5196	21.8191	2.82	0.01181	*
S03164.05_I10_447	mannose-binding 2-like	11.49388	5.25154	2.189	0.0429	*
S03164.05_I24_261	protein phosphatase 2 (formerly 2a) regulatory subunit a (pr 65) alpha isoform	12.20761	4.96982	2.456	0.0251	*
S03164.05_K11_292	signal sequence gamma	33.86476	11.63945	2.909	0.00976	**
S03164.06_C02_390	fibrinogen-like 1	90.9133	31.6852	2.869	0.0106	*
S03164.06_C20_227	heavy polypeptide non-muscle	82.4816	24.4962	3.367	0.00366	**
S03164.06_I22_82	fibrinogen a-alpha chain	95.9227	16.1028	5.957	1.56E-05	***
S03164.06_J10_227	transcription elongation factor a 1	33.72605	11.13628	3.028	0.00758	**
S03164.07_A20_300	selenoprotein s	27.502892	11.612397	2.368	0.0308	*
S03164.07_C16_487	extracellular superoxide dismutase	24.6032	8.87839	2.771	0.0131	*
S03164.07_D09_362	tho complex 5	11.5616	5.001	2.312	0.0336	*
S03164.07_D17_237	b chain crystallographic and kinetic studies of human mitochondrial acetoacetyl-coa thiolase : the importance of potassium and chloride for its structure and function	30.03915	11.22459	2.676	0.0159	*
S03164.07_J20_452	complement component factor h	65.96864	15.95325	4.135	0.000692	***
S03164.07_K20_342	cytochrome family subfamily polypeptide 1	129.6114	39.0955	3.315	0.00409	**
S03164.07_N16_243	alpha (gene sequence 28)	23.78505	7.03133	3.383	0.00354	**
S03164.08_A17_473	c1 inhibitor	65.2251	15.7299	4.147	0.000675	***
S03164.08_B24_74	heterogeneous nuclear ribonucleoprotein k	39.983437	8.341667	4.793	0.000199	***
S03164.08_G20_239	tropomyosin gamma isoform 8	43.3767	11.19248	3.876	0.00121	**
S03164.08_L10_162	serpine1 mrna binding protein isoform cra_d	52.8231	19.7235	2.678	0.01588	*
S03164.08_N04_482	hemopexin	43.6953	16.2949	2.682	0.01577	*
S03164.09_E05_231	selective lim-binding factor wimple	17.09642	7.88214	2.169	0.0446	*

S03164.10_F19_320	pyridoxal kinase	34.81884	13.92241	2.501	0.0229	*
S03164.10_O24_412	complement component 3	62.26215	16.52449	3.768	0.00153	**
S03164.10_P01_424	protein phosphatase regulatory subunit 15a	16.39385	7.08623	2.313	0.0335	*
S03164.11_A09_187	cytochrome family subfamily polypeptide 6	55.99908	11.7231	4.777	0.000175	***
S03164.12_K10_350	complement component s subcomponent	28.32641	6.46797	4.379	0.000409	***
S03164.12_M06_311	sec61 gamma subunit	32.2685	11.90647	2.71	0.0149	*
S03164.12_N13_436	general transcription factor polypeptide 74kda	37.07453	11.79246	3.144	0.00592	**
S03164.13_A02_383	retinoic acid receptor responder (tazarotene induced) 2	77.843911	19.684722	3.955	0.00114	**
S03164.13_B16_187	novel protein	49.8923	15.9491	3.128	0.00612	**
S03164.13_C21_198	mortality factor 4 like 1	25.55258	10.50382	2.433	0.0263	*
S03164.13_D09_310	ribonucleic acid binding protein s1	28.17144	9.03887	3.117	0.00628	**
S03164.13_D19_418	complement component r subcomponent	48.21881	12.99866	3.71	0.001741	**
S03164.13_G24_353	transgelin	25.19332	10.03238	2.511	0.0224	*
S03164.14_C03_397	protein kinase (camp- catalytic) inhibitor beta	29.5594	9.429	3.135	0.00604	**
S03164.14_C23_407	complement factor h-related 1	69.3713	22.7243	3.053	0.0072	**
S03164.14_E12_426	haptoglobin	71.3733	22.5252	3.169	0.00561	**
S03164.14_E14_267	glycine n-methyltransferase	42.64225	16.17672	2.636	0.0173	*
S03164.14_F18_269	alpha (gene sequence 28)	37.0474	11.00692	3.366	0.00367	**
S03164.14_H02_494	alpha-1-antichymotrypsin precursor	106.4042	28.7377	3.703	0.00177	**
S03164.14_I01_432	gamma 1	27.37585	11.58653	2.363	0.0303	*
S03164.14_K21_269	fk506 binding protein 19 kda	26.67191	10.0092	2.665	0.01633	*
S03164.14_N15_264	vitamin k epoxide reductase subunit 1	23.89464	9.94041	2.404	0.0279	*
S03164.02_N10_295	solute carrier family member 39	19.98451	8.33237	2.398	0.029	*
S03164.03_I19_279	transcriptional co-repressor sin3a	28.88397	13.3397	2.165	0.04582	*
S03164.03_P14_308	calnexin	41.18805	13.50432	3.05	0.00764	**
S03164.04_C08_309	adp-ribosyltransferase 3	23.73257	4.68425	5.066	0.000139	***
S03164.04_F02_255	reticulon 1	24.27199	7.37538	3.291	0.00536	**
S03164.05_J20_326	calnexin	35.44393	8.19156	4.327	0.000521	***
S03164.07_G09_286	sialidase 1 (lysosomal sialidase)	18.88444	5.90587	3.198	0.00561	**
S03164.07_K21_490	histidine triad nucleotide binding protein 3	23.06122	9.3925	2.455	0.025898	*
S03164.07_L07_267	cross-immune reaction antigen pcia1	26.89256	9.9323	2.708	0.01621	*
S03164.09_L19_288	wdr82 protein	30.25506	12.31699	2.456	0.0277	*
S03164.10_A14_521	gamma 1	32.88953	11.95106	2.752	0.0156	*
S03164.10_A22_568	myotrophin	27.86156	10.45111	2.666	0.01762	*
S03164.10_G20_517	transcobalamin ii precursor	18.63381	5.73456	3.249	0.00503	**

p-value: <0.001 = '***', <0.01, = '**', <0.05 = '*'

Table S8. List of genes correlated negatively with PCB/OH-PCB concentration ratios in the liver of Baikal seals by stepwise multiple linear regressions

Gene library ID	Seq. Description negative	Estimate	Std.Error	t-value	Pr(> t)	p
CYP1A1_2374	cytochrome p450 1a1	-1.33E+02	3.52E+01	-3.782	0.00163	**
CYP1A2_1347	cytochrome p450 1a2	-77.945238	25.89835	-3.01	0.00831	**
CYP2C21_1589	cytochrome family subfamily polypeptide 18	-83.8892	35.4747	-2.365	0.0302	*
S03164.05_N12	glutathione.s.transferase.kappa.1	-27.42494	8.87915	-3.089	0.00666	**
S03164.01_M03_93	arp3 actin-related protein 3 homolog	-17.27463	6.455178	-2.676	0.016	*
S03164.01_N10_212	phosphoglycerate kinase 1	-46.2579	16.0571	-2.881	0.0104	*
S03164.02_E02_380	thioredoxin-like 5	-39.74649	9.26961	-4.288	0.000498	***
S03164.02_L01_334	isoform cra_b	-13.78101	5.38718	-2.558	0.0204	*
S03164.02_N23_478	transmembrane protein 59	-31.71085	12.65879	-2.505	0.022712	*
S03164.02_O20_268	ferritin l subunit	-41.28232	18.63872	-2.215	0.0407	*
S03164.02_P14_78	split hand foot malformation type 1	-10.85688	4.76706	-2.277	0.036	*
S03164.03_J01_536	esterase d formylglutathione hydrolase	-36.015	15.7553	-2.286	0.0354	*
S03164.04_K02_246	comm domain containing 10	-23.783	8.2935	-2.868	0.01067	*
S03164.04_N13_356	serine incorporator 1	-44.572668	13.358999	-3.337	0.00418	**
S03164.04_O10_342	nadh dehydrogenase 1 alpha 39kda	-36.6844	12.314	-2.979	0.00842	**
S03164.05_C04_311	phytanoyl- hydroxylase	-47.535059	19.878848	-2.391	0.0294	*
S03164.05_N12_488	glutathione s-transferase kappa 1	-27.42494	8.87915	-3.089	0.00666	**
S03164.05_P04_504	fth1 protein	-51.518	18.301	-2.815	0.0119	*
S03164.06_H20_81	translocase of inner mitochondrial membrane 13 homolog	-31.24561	12.52925	-2.494	0.0232	*
S03164.06_M01_385	mitochondrial ribosomal protein s24	-20.23136	6.289	-3.217	0.00506	**
S03164.06_M06_299	methylcrotonoyl-coenzyme a carboxylase 2	-27.09441	10.24354	-2.645	0.017	*
S03164.06_N11_376	hcv f-transactivated protein 1	-31.4716	14.1211	-2.229	0.0396	*
S03164.07_D13_300	voltage-dependent anion channel 3	-27.96875	8.43728	-3.315	0.004096	**
S03164.07_E21_410	peroxiredoxin 5	-21.92251	9.33902	-2.347	0.03127	*
S03164.07_F23_388	phosphatidic acid phosphatase 2a	-26.57897	5.37786	-4.942	0.000124	***
S03164.07_P07_371	phenol sulfotransferase	-82.012082	23.724366	-3.457	0.00325	**
S03164.07_P22_92	ribosomal protein s10	-35.75717	14.181882	-2.521	0.0227	*
S03164.08_I08_166	proteasome (macropain) alpha 3	-48.21413	14.87504	-3.241	0.0048	**
S03164.08_L15_276	coiled-coil domain containing 124	-13.1829	4.4408	-2.969	0.00861	**
S03164.08_N17_169	s-phase kinase-associated protein 1a	-24.3029	10.1854	-2.386	0.028931	*
S03164.08_P08_414	cytochrome c oxidase subunit iv isoform 1	-24.6091	11.2505	-2.187	0.043	*
S03164.09_A07_24	ferritin l subunit	-52.5458	21.0907	-2.491	0.0234	*
S03164.09_F01_96	glyceraldehyde-3-phosphate dehydrogenase	-18.2263	6.17063	-2.954	0.008889	**
S03164.10_E01_476	lysozyme c precursor	-22.05081	10.30463	-2.14	0.0472	*
S03164.10_I01_361	apolipoprotein e	-41.715	17.9601	-2.323	0.0329	*
S03164.10_I02_586	s-phase kinase-associated protein 1a	-27.39557	11.65279	-2.351	0.031	*
S03164.10_K09_88	glyceraldehyde-3-phosphate dehydrogenase	-26.3534	8.0557	-3.271	0.0045	**
S03164.10_O03_369	ubiquitin fusion degradation 1-like	-70.548317	15.70011	-4.493	0.000368	***
S03164.11_A08_357	heme binding protein 1	-55.998266	9.159108	-6.114	1.49E-05	***
S03164.11_G01_518	fth1 protein	-50.828	18.2394	-2.787	0.0127	*
S03164.12_C17_219	proteasome (macropain) alpha 3	-36.71001	11.92382	-3.079	0.00681	**

S03164.12_O12_292	growth hormone inducible transmembrane protein	-29.92073	8.90748	-3.359	0.00372	**
S03164.12_O22_473	basigin	-27.15448	11.95771	-2.271	0.0364	*
S03164.13_C01_583	6-pyruvoyl-tetrahydropterin synthase dimerization cofactor of hepatocyte nuclear factor 1 alpha	-31.299746	7.819369	-4.003	0.000922	***
S03164.13_H08_373	glutamic-pyruvate transaminase	-53.92629	21.603351	-2.496	0.0239	*
S03164.13_H24_344	cystatin b	-40.42269	13.63285	-2.965	0.00868	**
S03164.13_K05_428	fth1 protein	-53.664	17.7917	-3.016	0.00778	**
S03164.13_K07_208	growth hormone inducible transmembrane protein	-36.0718	14.8462	-2.43	0.0265	*
S03164.13_L09_251	40s ribosomal protein sa (34 67 kda laminin receptor) (colon carcinoma laminin-binding protein) (nem 1chd4) (multidrug resistance-associated protein mgr1-ag) isoform 2	-24.21646	10.06954	-2.405	0.0278	*
S03164.13_M01_464	superoxide dismutase soluble	-31.56	14.3192	-2.204	0.0416	*
S03164.13_M10_41	isoform cra_b	-33.04365	10.2603	-3.221	0.00502	**
S03164.14_A20_370	zinc finger protein 250	-20.83672	5.74276	-3.628	0.00208	**
S03164.14_A23_371	ribosomal protein s16	-17.21502	6.76202	-2.546	0.0209	*
S03164.14_B05_247	ribosomal p1	-27.42098	9.37707	-2.924	0.00946	**
S03164.14_G02_397	glutathione s-transferase pi	-24.01514	11.06406	-2.171	0.0444	*
S03164.14_G07_222	biphenyl hydrolase-like (serine hydrolase breast epithelial mucin-associated antigen)	-30.1572	14.0419	-2.148	0.0465	*
S03164.14_H13_331	nadh dehydrogenase 1 beta 18kda	-13.89064	6.55771	-2.118	0.049192	*
S03164.14_K09_321	atp h+ mitochondrial f0 subunit c1 (subunit 9)	-35.48568	15.62551	-2.271	0.0364	*
S03164.14_P22_86	glyceraldehyde-3-phosphate dehydrogenase	-38.46662	9.63155	-3.994	0.00094	***
S03164.01_D24_249	ww domain binding protein 2	-19.12655	8.77896	-2.179	0.0457	*
S03164.04_I09_238	wd repeat domain 41	-27.32927	10.76984	-2.538	0.0228	*
S03164.09_K05_72	macrophage erythroblast attacher	-22.42813	6.44001	-3.483	0.00334	**
S03164.10_K16_371	selenoprotein 1	-39.61955	13.12682	-3.018	0.00816	**
S03164.10_L10_272	protein phosphatase methylesterase 1	-18.08286	5.29855	-3.413	0.00386	**

p-value: <0.001 = '***', <0.01, = '**', <0.05 = '*'

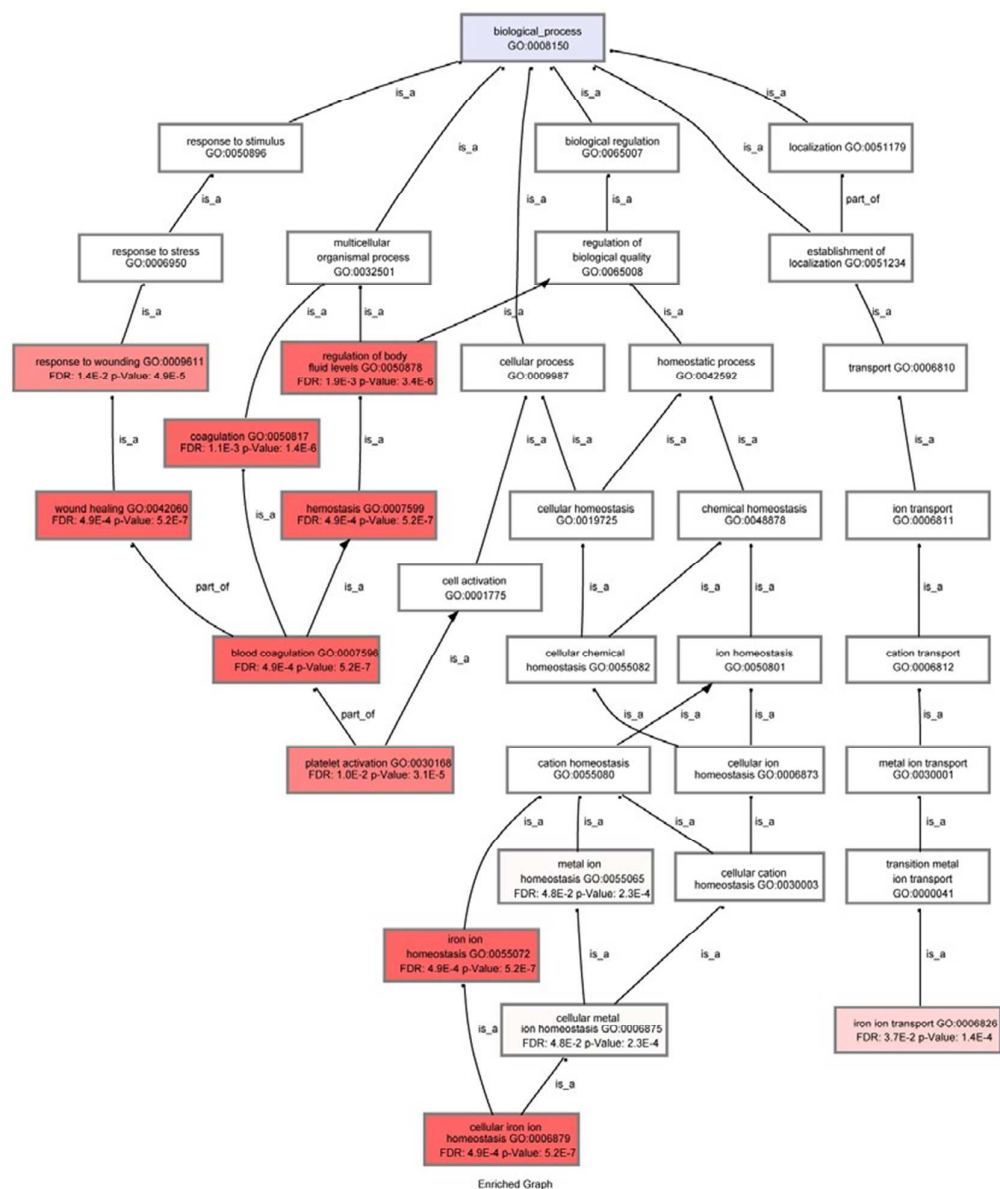


Figure S2a. Signaling pathways with OH-PCBs significantly enriched in the liver of Baikal seal

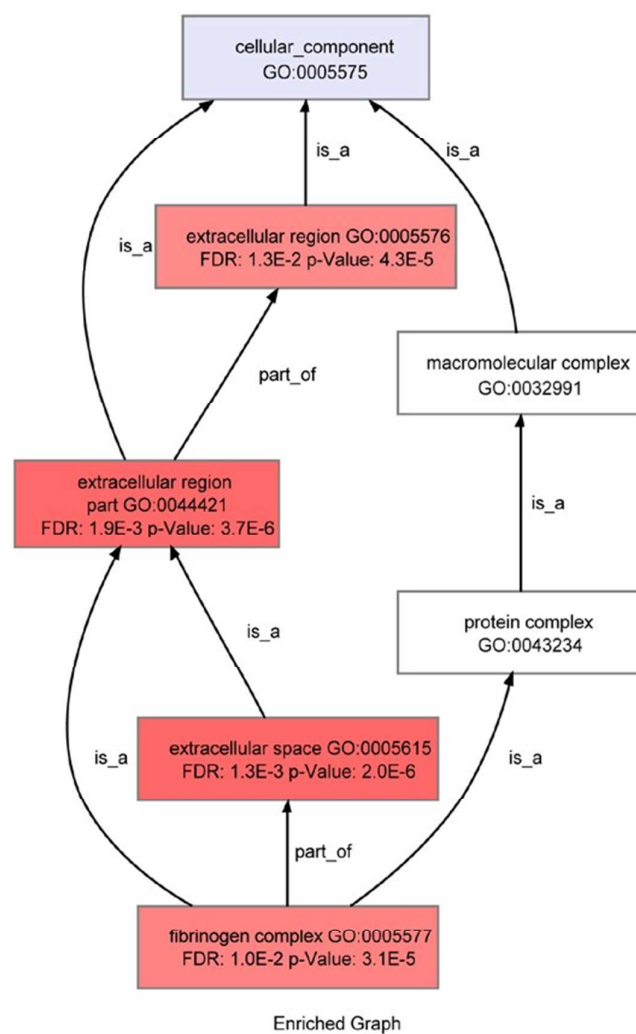
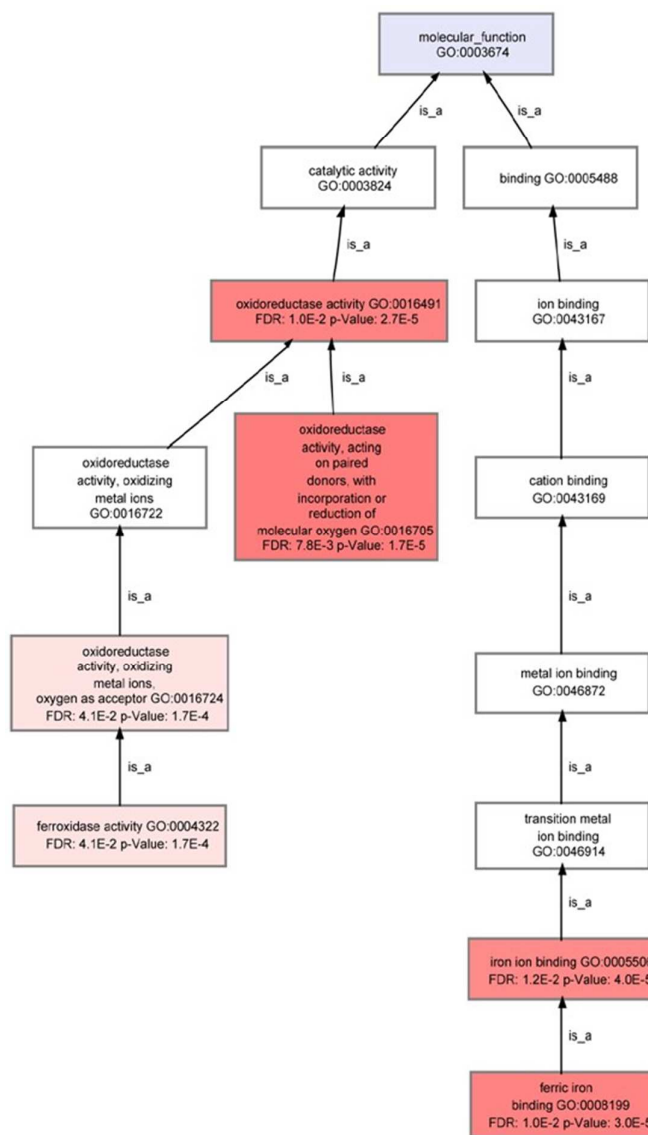


Figure S2b. Signaling pathways with OH-PCBs significantly enriched in the liver of Baikal seals



Enriched Graph

Figure S2c. Signaling pathways with OH-PCBs significantly enriched in the liver of Baikal seals

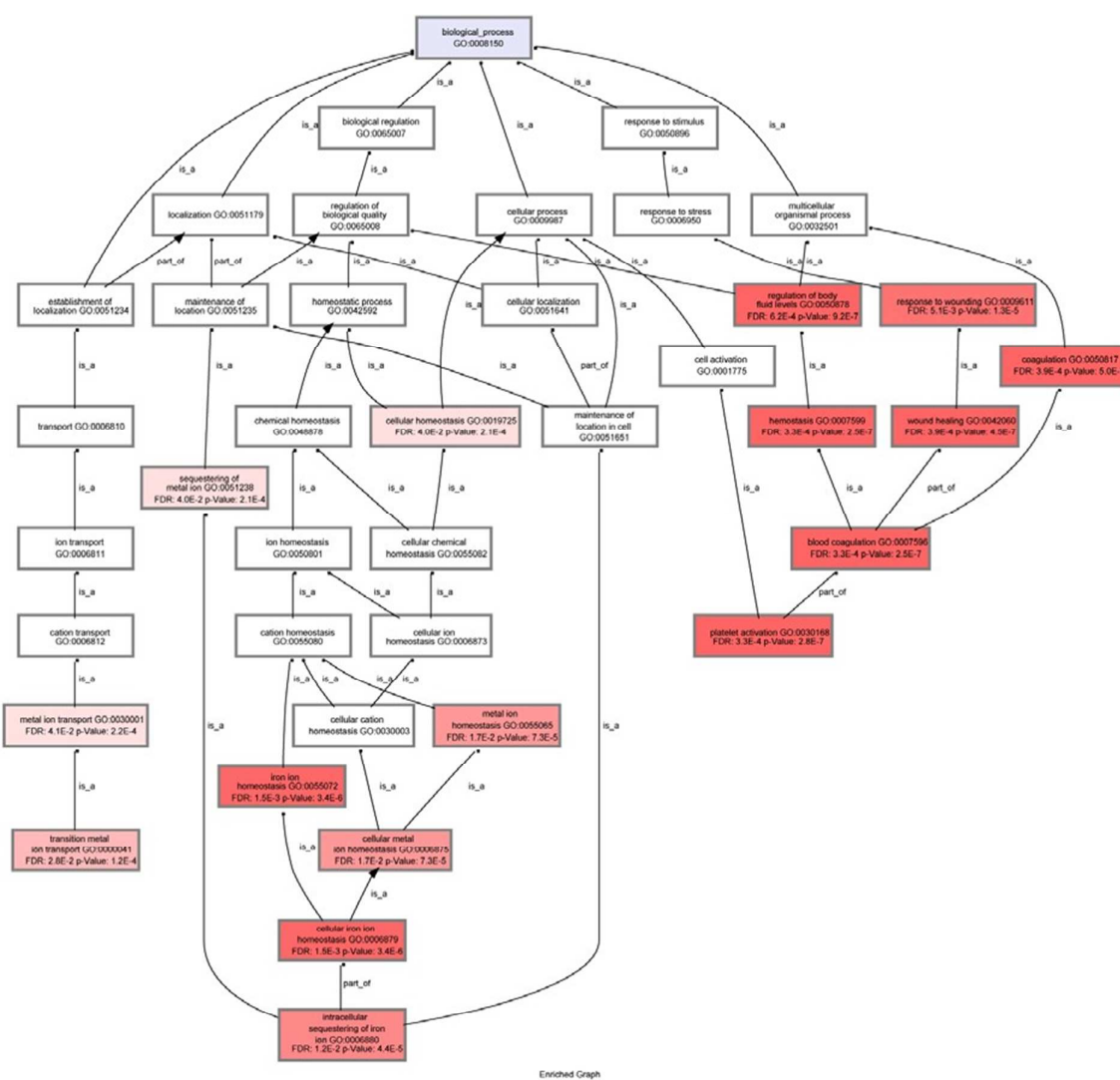


Figure S2d. Signaling pathways with OH-PCB/PCB ratios significantly enriched in the liver of Baikal seals

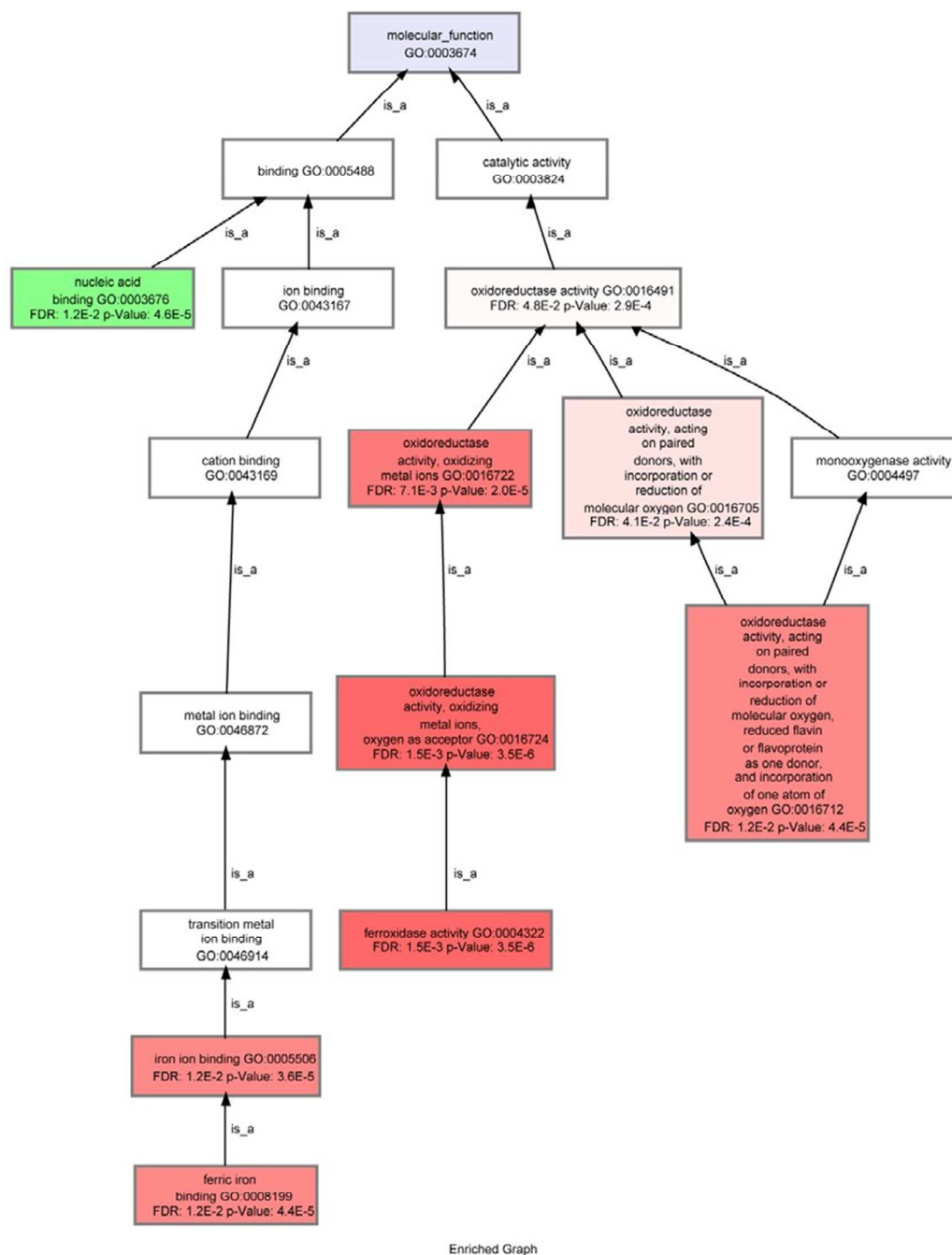


Figure S2e. Signaling pathways with OH-PCB/PCB ratios significantly enriched in the liver of Baikal seals

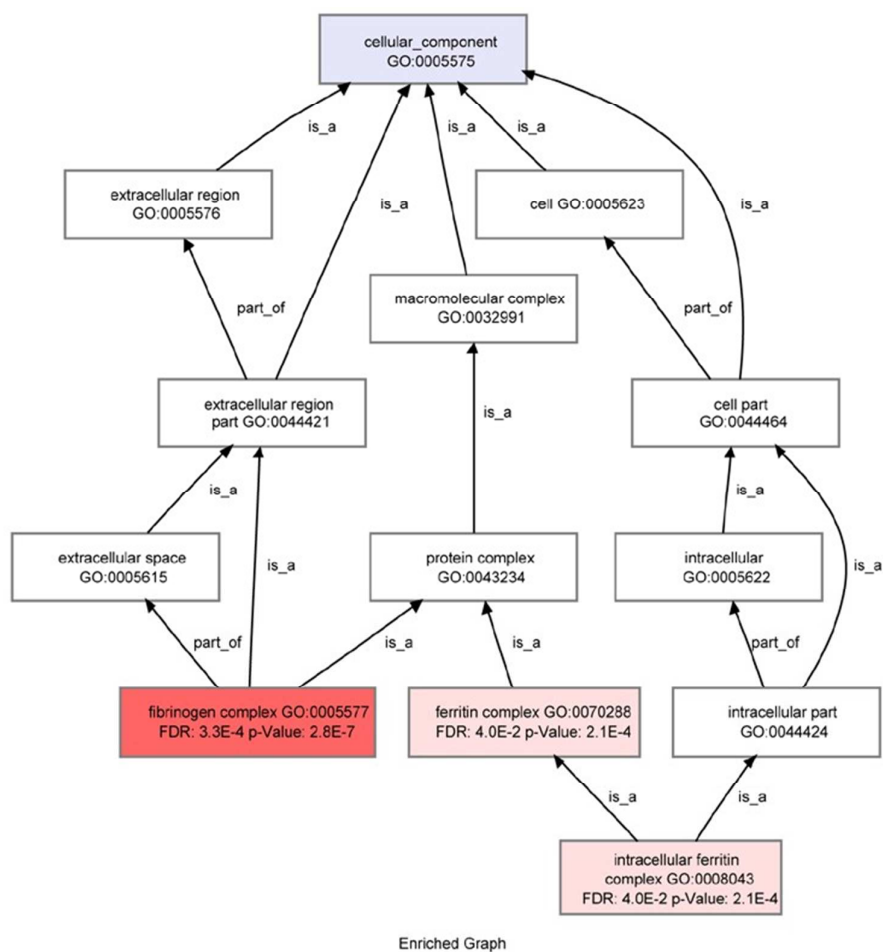


Figure S2f. Signaling pathways with OH-PCB/PCB ratios significantly enriched in the liver of Baikal seals

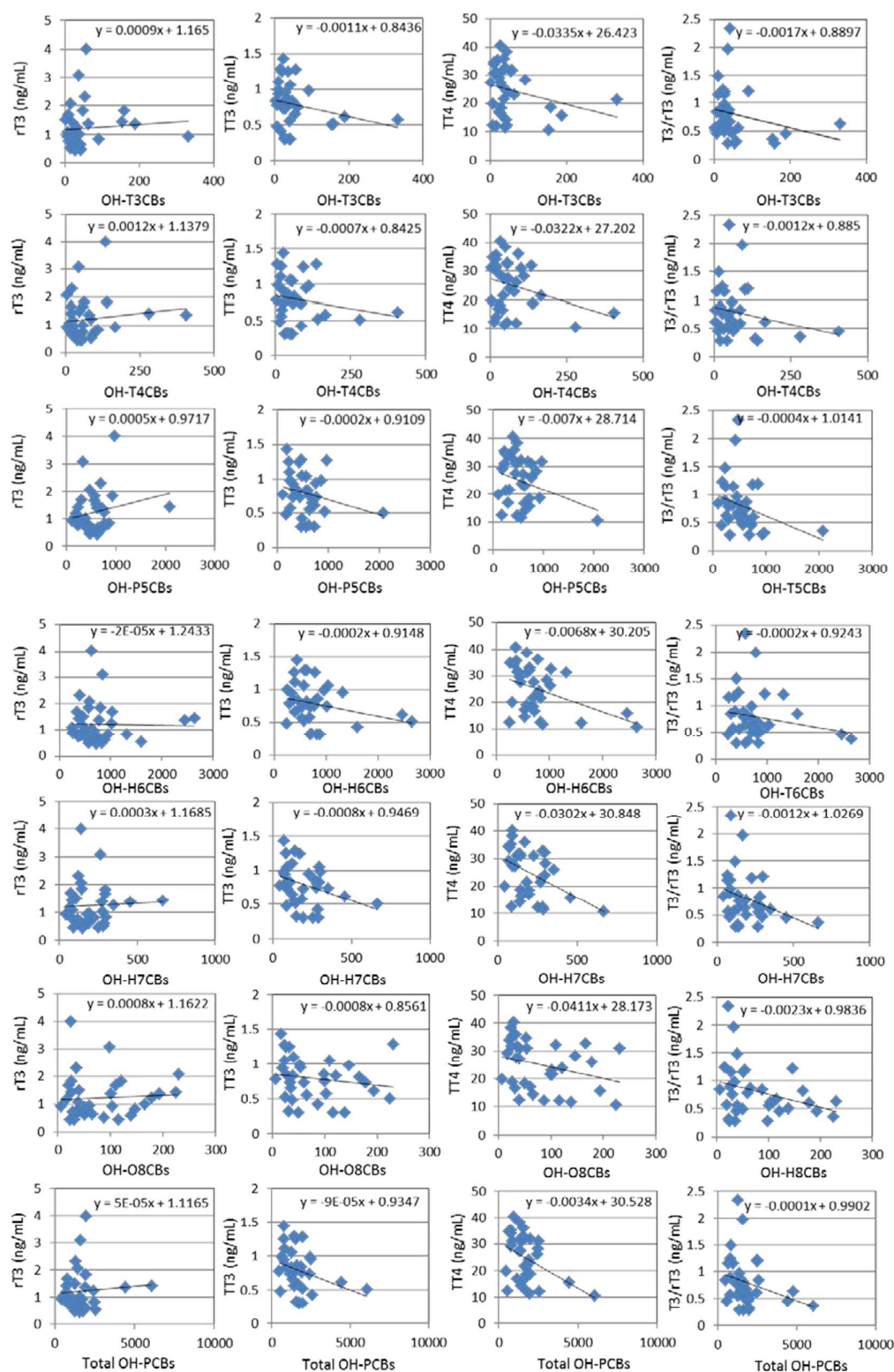


Figure S3. Linear regression between hepatic OH-PCB concentrations and serum thyroid hormone levels in Baikal seals