

Supplemental Material

Fate and complex pathogenic effects of dioxins and polychlorinated biphenyls in obese subjects before and after drastic weight loss

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Supplementary Information

Methods:

Clinical design

Preoperative evaluation included detailed medical history, physical, nutritional, metabolic, cardiopulmonary, and psychological assessments. Dietary habits were evaluated by a registered dietician who estimated the quantitative average of food consumption (kcal per day) before the surgery and during the follow-up. The subjects weight was stable (i.e. variation of less than ± 2 kg) for at least 3 months prior to the surgery. Subjects did not demonstrate evidence of acute or chronic inflammatory disease, infectious diseases, viral infection, cancer and/or known alcohol consumption (> 20 g per day). Clinical and biological parameters were carefully assessed prior to gastric bypass surgery (i.e. basal or M0) and at 1, 3, 6 and 12 months post surgery (M1, M3, M6, M12 respectively). Blood samples were also obtained for pollutants before surgery (M0) as well as at M1, M3, M6 and M12 after surgery. Oral glucose tolerance test (OGTT) was performed in non diabetic subjects and all had a glycaemia <11 mM two hours after 75 g oral glucose. According to the criteria of fasting glycaemia over 7 mM or the use of an anti-diabetic drug, 17 subjects had type 2-diabetes. Three of these individuals necessitated insulin therapy while the other 14 subjects were treated with metformin and hypolipidemic drugs (either fibrate or statins). In addition, 18 lean

female volunteers living in the same geographical area as the obese subjects were recruited as a control group in the clinical protocol. Table 1 presents the clinical characteristics of the subjects. The global design of the study and bioresources available in each obese and lean group are presented in Supplemental Material, Figure 1. The exact numbers of analysed biological samples varied in the different experimental sections because of practical considerations including for instance unexpected difficulties during collection, or insufficient sample amount or quality especially for the measurement of the targeted chemical pollutants in blood and adipose tissue. Clinical characteristics of each subgroup of subjects were similar to those of the entire group (data not shown).

The Ethics Committee of the Hôtel-Dieu Hospital approved the clinical investigations both for obese and non obese individuals. All subjects gave a written informed consent after individual explanation.

RNA preparation and real-time PCR.

RNA extraction was performed on adipose tissue using the RNeasy RNA Mini Kit (Qiagen, Courtaboeuf, France) or on whole blood using PAXgene Blood RNA Kit (Qiagen). RNA concentrations and quality were confirmed using the Agilent 2100 bioanalyzer (Agilent Technologies, Massy, France). Total RNA (1 µg) was reverse transcribed using random hexamers and Superscript II reverse transcriptase. Real-time PCRs were conducted with absolute QPCR SYBR Green Rox mix (Thermo Electron SAS, Courtaboeuf, France) on ABI Prism 7900 (Applied Biosystems, Courtaboeuf, France). mRNA values were normalized to *RPL13A* expression level. Primer sequences are available upon request.

PCDD/PCDF and PCB analysis

Reagents and Chemicals

All organic solvents (Promochem) were Picograde[®] quality. Silica (Fluka), sodium sulfate and dipotassium oxalate (Merck), acetic acid and sulfuric acid (SDS) were of superior analytical quality. Native and ¹³C-labeled standards were purchased from Cambridge Isotope Laboratories (CIL) and Wellington Laboratory. Standard solutions were prepared in toluene or iso-octane for PCDDs/PCDFs and PCBs, respectively. All reference solutions were stored in darkness at < 6 °C.

Sample preparation procedure

Before extraction, 17 ¹³C-labelled PCDDs/PCDFs and 18 ¹³C-labelled PCBs congeners were added to each sample for internal standard calibration and quantification by the isotope dilution method. Serum samples were diluted with deionized water and submitted to mechanical agitation for 30 min. The further extraction procedure included the following successive steps: addition of 20 mL aqueous saturated ammonium sulfate sodium, shaking for 1 min, extraction with 20 mL hexane, and finally extraction with 40 mL hexane. Fat samples were extracted using an ASE 300 extractor (Dionex, Sunnyvale, CA, USA) with three successive extraction cycles (5 min each) by a toluene/acetone 70:30 (v/v) mixture. Pressure and temperature were set to 100 bars and 120°C, respectively. For the two investigated biological matrices, resulting extracts (which were assimilated to the sample fat content) were evaporated to dryness (40°C), weighed, and reconstituted in hexane for further sample clean-up. Three purification steps were then performed, using successively acid silica, florisil and celite/carbon columns. After removal of fat on the first silica gel column activated with sulfuric acid, PCBs were separated from PCDDs/PCDFs on the second Florisil column. The PCDD/PCDF fraction was further cleaned up onto a third column consisting of a mixture of Carbo-pack C/Celite 545, while the separation of coplanar (non-ortho) PCBs from non-planar PCBs was achieved on an activated mixture of Florisil/ Carbo-pack C/Celite 545 (overnight at

130°C). After addition of external standards for the recovery calculation ($^{13}\text{C}_{12}$ -1,2,3,4-TCDD for PCDD/F, $^{13}\text{C}_{12}$ -PCB #111 for PCBs), final sample extracts were evaporated under a nitrogen stream to dryness and reconstituted in 5, 10 or 50 μL toluene for PCDD/Fs, coplanar PCBs and non-planar PCBs, respectively.

GC-HRMS measurement

PCDD/F and PCB measurements were performed by Gas Chromatography coupled to High resolution Mass Spectrometry (GC-HRMS) using an HP-5890 gas chromatograph (Hewlett Packard, Palo Alto, CA, USA) coupled to a JMS 700D or a JMS 800D double electromagnetic sector high resolution mass spectrometers (Jeol, Tokyo, Japan). A DB5MS (30 m x 0.25 mm x 0.25 μm) capillary column (J&W) was used in splitless mode. The GC temperature program for PCDD/F analysis was the following: 120 °C (3 min), 20 °C/min to 170 °C (0 min) and 3 °C/min to 275 °C (7 min). The GC program for PCB was 120 °C (3 min), 20 °C/min to 170 °C (0 min), 3 °C/min to 245 °C (0 min) and finally 20 °C/min to 275 °C (7 min). Ionisation was achieved in the electron impact mode (38 and 42 eV electron energy for PCDD/Fs and PCB respectively). The spectrometric resolution was set at 10,000, and the signal acquisition was performed in the Single Ion Monitoring (SIM) mode focusing on the two most abundant signals from each target molecular ion (^{35}Cl and ^{37}Cl isotopic contributions). Signals were integrated by JEOL Diok software (v.2). Toxic Equivalent Quotient values (TEQ) were calculated according to the 1998 World Health Organization Toxic Equivalency Factors (1998-WHO-TEF) and basically expressed on a lipid weight basis. However, additional results expressed on a fresh weight basis (for serum) or reported to the total body burden (for serum and fat) were also calculated. All these procedures integrated quality control parameters to fulfil the requirements of the Commission Directive 2002/69/EC and 2002/70/EC of July 2002 laying down the sampling methods and the methods of analysis

for the official control of dioxins and the determination of dl-PCBs in foodstuffs and feedingstuffs respectively. Moreover, all analyses were performed upon a double quality management system associating an accreditation according to the ISO 17025 standard and a certification according to the ISO 9001:2000 standard.

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Supplementary Material Table 1: relationships between various POPs and a set of phenotypical parameter in obese individuals

Parameter	dl-PCB blood pRs	dl-PCB blood pval.	dl-PCB AT pRs	dl-PCB AT pval.	dl-PCB TBB pRs	dl-PCB TBB pval.	i-PCB blood pRs	i-PCB blood pval.	i-PCB AT pRs	i-PCB AT pval.	i-PCB TBB pRs	i-PCB TBB pval.	PCDD/F blood pRs	PCDD/F blood pval.	PCDD/F AT pRs	PCDD/F AT pval.	PCDD/F TBB pRs	PCDD/F TBB pval.
Weight (kg)	-0.001	NS	-0.077	NS	0.069	NS	0.012	NS	-0.071	NS	0.114	NS	-0.037	NS	-0.312	1.21E-02	0.100	NS
BMI (kg/m ²)	-0.071	NS	-0.070	NS	0.144	NS	-0.136	NS	-0.165	NS	0.037	NS	-0.198	NS	-0.247	4.87E-02	0.254	4.81E-02
Fat mass (kg)	-0.053	NS	-0.101	NS	0.208	NS	-0.145	NS	-0.100	NS	0.125	NS	-0.095	NS	-0.148	NS	0.367	3.61E-03
Fat mass (% of weight)	-0.081	NS	0.040	NS	0.232	NS	-0.256	NS	-0.099	NS	0.036	NS	-0.083	NS	0.149	NS	0.451	2.63E-04
Fat free mass (kg)	0.017	NS	-0.191	NS	-0.075	NS	0.101	NS	-0.012	NS	0.071	NS	-0.011	NS	-0.339	7.52E-03	-0.137	NS
Fat free mass (% of weight)	0.019	NS	-0.108	NS	-0.262	4.12E-02	0.184	NS	0.080	NS	-0.038	NS	0.004	NS	-0.169	NS	-0.428	5.83E-04
Adipocyte diameter (µm)	-0.550	9.17E-04	-0.144	NS	-0.112	NS	-0.503	2.87E-03	-0.039	NS	-0.007	NS	-0.292	NS	-0.021	NS	0.054	NS
Adipocyte volume (nL)	-0.225	NS	-0.071	NS	-0.041	NS	-0.110	NS	-0.021	NS	0.017	NS	-0.059	NS	-0.100	NS	-0.030	NS
Adipocyte weight (ng)	-0.224	NS	-0.072	NS	-0.042	NS	-0.112	NS	-0.022	NS	0.016	NS	-0.060	NS	-0.099	NS	-0.029	NS
Leptin	-0.142	NS	0.080	NS	0.200	NS	-0.137	NS	0.140	NS	0.216	NS	-0.111	NS	0.168	NS	0.269	4.10E-02
Adiponectin	-0.035	NS	-0.076	NS	-0.079	NS	0.024	NS	-0.125	NS	-0.148	NS	0.084	NS	0.090	NS	0.035	NS
SGPT (IU/L)	0.222	NS	-0.096	NS	-0.116	NS	0.404	1.60E-02	-0.002	NS	-0.002	NS	0.347	4.41E-02	-0.181	NS	-0.204	NS
SGOT (IU/L)	0.410	1.44E-02	0.020	NS	-0.034	NS	0.453	6.28E-03	0.021	NS	-0.002	NS	0.360	3.68E-02	-0.119	NS	-0.203	NS
GGT (IU/L)	0.495	2.50E-03	0.527	7.75E-06	0.569	1.73E-06	0.581	2.54E-04	0.673	1.14E-09	0.664	5.29E-09	0.388	2.35E-02	0.316	1.10E-02	0.302	1.81E-02
Steatosis amount	-0.540	2.54E-02	-0.445	1.21E-02	-0.394	3.45E-02	-0.418	NS	-0.246	NS	-0.225	NS	-0.204	NS	-0.318	NS	-0.269	NS
Total cholesterol (mmol/L)	0.394	1.92E-02	0.068	NS	0.196	NS	0.337	4.81E-02	0.080	NS	0.162	NS	0.410	1.61E-02	0.156	NS	0.328	9.83E-03
Triglycerides (mmol/L)	0.599	1.42E-04	-0.046	NS	-0.081	NS	0.636	4.05E-05	-0.088	NS	-0.065	NS	0.533	1.18E-03	-0.118	NS	-0.088	NS
HDL cholesterol (mmol/L)	0.046	NS	0.166	NS	0.234	NS	-0.027	NS	0.141	NS	0.174	NS	0.047	NS	0.183	NS	0.272	3.40E-02

Supplementary Material Table 1 (continued):

Parameter	dl-PCB blood pRs	dl-PCB blood pval.	dl-PCB AT pRs	dl-PCB AT pval.	dl-PCB TBB pRs	dl-PCB TBB pval.	i-PCB blood pRs	i-PCB blood pval.	i-PCB AT pRs	i-PCB AT pval.	i-PCB TBB pRs	i-PCB TBB pval.	PCDD/F blood pRs	PCDD/F blood pval.	PCDD/F AT pRs	PCDD/F AT pval.	PCDD/F TBB pRs	PCDD/F TBB pval.
HOMA-B	-0.231	NS	-0.033	NS	-0.104	NS	-0.308	NS	0.031	NS	-0.027	NS	-0.210	NS	-0.045	NS	-0.155	NS
HOMA-S	-0.030	NS	0.133	NS	0.095	NS	0.037	NS	0.059	NS	0.037	NS	0.077	NS	0.170	NS	0.130	NS
HOMA-IR	0.281	NS	-0.065	NS	-0.060	NS	0.171	NS	-0.081	NS	-0.072	NS	0.105	NS	-0.143	NS	-0.156	NS
CRPus (mg/L)	-0.188	NS	-0.113	NS	-0.109	NS	-0.089	NS	-0.053	NS	-0.063	NS	-0.263	NS	-0.045	NS	-0.053	NS
Fibrinogen (g/L)	0.092	NS	0.092	NS	0.136	NS	0.059	NS	-0.017	NS	0.033	NS	0.079	NS	0.154	NS	0.291	3.27E-02
Interleukin 1 beta (serum)	-0.405	4.44E-02	-0.420	3.68E-02	-0.390	NS	-0.311	NS	-0.223	NS	-0.220	NS	-0.448	2.80E-02	-0.328	NS	-0.273	NS
Interleukin 1 beta (AT)	-0.450	NS	-0.686	9.58E-03	-0.640	1.86E-02	-0.668	1.26E-02	-0.843	2.91E-04	-0.535	NS	-0.173	NS	-0.448	NS	-0.303	NS
Interleukin 6 (serum)	-0.036	NS	-0.026	NS	0.006	NS	0.044	NS	-0.004	NS	0.019	NS	0.111	NS	-0.006	NS	0.022	NS

This table contains detailed results of linear regression models used to explore relationships between various POPs congeners and a set of phenotypical parameters. In all models age and sex were considered as confounding factors.

For each couple of variables including a POP congener (columns) and a phenotypical parameter (rows) two values are provided: a partial correlation coefficient (pRs) and a statistical significance p-value (pval.).

Blood - indicates serum concentration of the respective POP congener. AT - indicates adipose tissue concentration of the respective POP congener. NS: non significant relation. TBB: total body burden of respective POP congener.

Supplementary Material Table 2: relationships between various POPs and a set of phenotypical parameters during weight loss (not adjusted for fat mass)

Parameter	dl-PCB blood pRs	dl-PCB blood pval.	dl-PCB AT pRs	dl-PCB AT pval.	i-PCB blood pRs	i-PCB blood pval.	i-PCB AT pRs	i-PCB AT pval.	PCDD/F blood pRs	PCDD/F blood pval.	PCDD/F AT pRs	PCDD/F AT pval.
Weight (kg)	-0.279	3.26E-03	-0.280	2.00E-03	-0.300	5.10E-03	-0.247	NS	-0.367	6.95E-04	-0.462	5.80E-03
BMI (kg/m ²)	-0.333	6.72E-05	-0.326	2.69E-04	-0.416	8.73E-05	-0.346	4.71E-02	-0.441	6.91E-06	-0.505	1.27E-02
Fat mass (kg)	-0.344	2.30E-05	-0.344	7.91E-06	-0.443	1.03E-05	-0.332	4.05E-03	-0.409	8.46E-06	-0.494	1.00E-02
Fat mass (% of weight)	-0.310	NS	-0.310	9.86E-08	-0.467	NS	-0.355	6.79E-07	-0.337	6.54E-07	-0.422	2.49E-02
Fat free mass (kg)	-0.123	NS	-0.171	1.01E-02	-0.061	NS	-0.073	NS	-0.200	NS	-0.285	1.08E-02
Fat free mass (% of weight)	0.279	NS	0.275	NS	0.414	NS	0.320	NS	0.286	2.98E-03	0.383	NS
Adipocyte diameter (µm)	-0.333	6.03E-06	-0.264	2.10E-02	-0.322	2.90E-05	-0.250	NS	-0.272	1.80E-03	-0.274	NS
Adipocyte volume (nL)	-0.328	NS	-0.314	3.33E-03	-0.338	2.34E-02	-0.251	7.07E-02	-0.316	5.37E-02	-0.427	4.94E-02
Adipocyte weight (ng)	-0.326	NS	-0.313	3.40E-03	-0.337	2.40E-02	-0.250	7.07E-02	-0.315	5.67E-02	-0.427	5.02E-02
Leptin	-0.252	NS	-0.220	NS	-0.314	3.47E-02	-0.190	NS	-0.291	2.62E-02	-0.301	NS
Adiponectin	0.153	NS	0.202	NS	0.197	4.07E-02	0.148	NS	0.297	4.35E-03	0.387	1.84E-02
SGPT (IU/L)	-0.179	NS	-0.143	NS	-0.040	NS	-0.042	NS	-0.069	NS	-0.124	NS
SGOT (IU/L)	-0.153	4.04E-02	-0.084	NS	-0.091	1.99E-02	-0.031	NS	-0.047	NS	-0.065	NS
GGT (IU/L)	0.057	3.64E-03	0.242	1.34E-02	0.106	1.94E-04	0.362	4.86E-06	0.006	3.16E-02	-0.015	4.90E-02
Total cholesterol (mmol/L)	0.355	3.84E-03	0.076	3.82E-02	0.302	5.51E-04	0.053	6.21E-03	0.303	8.57E-05	0.005	1.70E-03
Triglycerides (mmol/L)	0.215	1.87E-04	-0.145	NS	0.184	5.81E-05	-0.162	NS	0.145	4.59E-03	-0.219	NS
HDL cholesterol (mmol/L)	0.230	4.11E-02	0.200	1.48E-02	0.202	1.82E-02	0.173	4.11E-03	0.238	5.01E-02	0.244	1.05E-03
HOMA-B	0.043	NS	0.101	NS	0.045	NS	0.066	3.53E-02	0.117	NS	0.101	NS
HOMA-S	0.368	2.32E-03	0.369	9.86E-10	0.485	9.95E-05	0.330	6.57E-14	0.490	7.25E-04	0.629	9.89E-17
HOMA-IR	-0.122	NS	-0.218	4.01E-02	-0.203	NS	-0.211	NS	-0.199	NS	-0.314	NS
Interleukin 6 (serum)	-0.059	NS	-0.053	NS	-0.037	NS	-0.049	NS	-0.009	NS	-0.084	NS

This file contains detailed results of LME regression models used to explore relationships between various POPs congeners and a set of phenotypical parameters.

In all models age and sex were considered as confounding factors. Body fat mass was not considered as confounding factor in these LME models (please see supplementary data file SDF3 for the results obtained after adjusting for body fat mass).

For each couple of variables including a POP congener (columns) and a phenotypical parameter (rows) two values are provided: a partial correlation coefficient (pRs) and a LME significance p-value (pval.).

Blood - indicates serum concentration of the respective POP congener. AT - indicates adipose tissue concentration of the respective POP congener. NS - non significant relation

Supplementary Material Table 3: relationships between various POPs and a set of phenotypical parameters during weight loss (adjusted for fat mass)

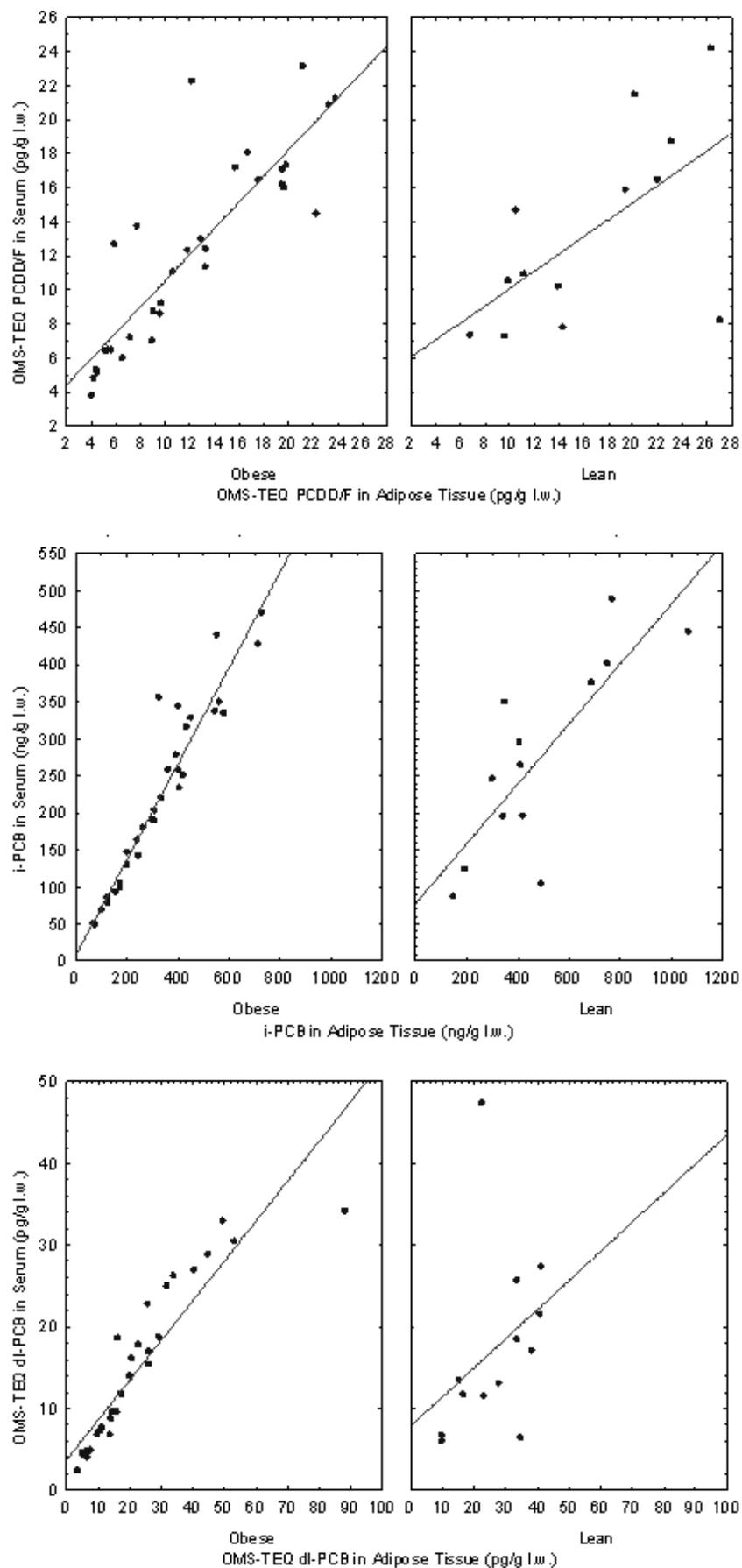
Parameter	dl-PCB blood pRs	dl-PCB blood pval.	dl-PCB AT pRs	dl-PCB AT pval.	i-PCB blood pRs	i-PCB blood pval.	i-PCB AT pRs	i-PCB AT pval.	PCDD/F blood pRs	PCDD/F blood pval.	PCDD/F AT pRs	PCDD/F AT pval.
Weight (kg)	0.011	NS	-0.030	NS	0.132	5.72E-02	0.077	NS	-0.056	NS	-0.108	NS
BMI (kg/m ²)	-0.037	NS	-0.085	NS	-0.014	NS	-0.114	NS	-0.181	NS	-0.149	NS
Fat mass (kg)	-	-	-	-	-	-	-	-	-	-	-	-
Fat mass (% of weight)	-0.086	NS	-0.079	8.84E-03	-0.230	NS	-0.168	1.36E-04	-0.055	2.20E-02	-0.079	NS
Fat free mass (kg)	0.015	NS	-0.029	NS	0.138	NS	0.080	NS	-0.047	NS	-0.095	8.84E-02
Fat free mass (% of weight)	0.059	NS	0.038	NS	0.166	1.23E-02	0.122	NS	0.004	NS	0.038	NS
Adipocyte diameter (µm)	-0.232	5.90E-05	-0.131	NS	-0.177	2.82E-04	-0.118	NS	-0.134	8.73E-03	-0.062	NS
Adipocyte volume (nL)	-0.160	NS	-0.126	NS	-0.081	NS	-0.051	NS	-0.082	NS	-0.158	NS
Adipocyte weight (ng)	-0.158	NS	-0.125	NS	-0.080	NS	-0.050	NS	-0.081	NS	-0.158	NS
Leptin	-0.065	NS	-0.005	NS	-0.067	NS	0.034	9.60E-03	-0.072	NS	0.007	1.94E-02
Adiponectin	0.077	NS	0.126	NS	0.102	6.08E-02	0.058	NS	0.225	7.78E-03	0.296	1.51E-02
SGPT (IU/L)	-0.193	NS	-0.127	NS	-0.050	NS	-0.011	NS	-0.078	NS	-0.101	NS
SGOT (IU/L)	-0.192	NS	-0.109	NS	-0.144	NS	-0.045	NS	-0.087	NS	-0.107	NS
GGT (IU/L)	0.167	8.48E-05	0.339	1.53E-02	0.274	3.31E-06	0.460	6.77E-06	0.144	2.10E-03	0.099	4.01E-02
Total cholesterol (mmol/L)	0.433	4.75E-06	0.162	1.04E-03	0.408	1.06E-06	0.132	2.83E-04	0.400	2.91E-07	0.124	2.63E-04
Triglycerides (mmol/L)	0.258	4.73E-05	-0.113	NS	0.244	3.51E-05	-0.114	NS	0.195	2.52E-03	-0.157	NS
HDL cholesterol (mmol/L)	0.167	1.31E-02	0.156	3.20E-03	0.119	6.20E-03	0.123	1.34E-03	0.167	1.22E-02	0.184	4.07E-04
HOMA-B	0.121	NS	0.156	NS	0.164	NS	0.121	3.56E-02	0.223	1.55E-02	0.204	NS
HOMA-S	0.286	1.07E-03	0.291	2.72E-10	0.374	1.21E-05	0.240	5.01E-16	0.402	2.54E-04	0.539	3.92E-19
HOMA-IR	0.024	NS	-0.120	NS	0.005	NS	-0.100	NS	-0.021	NS	-0.157	NS
IL6	0.036	NS	0.015	NS	0.100	9.21E-02	0.021	NS	0.109	2.99E-02	0.017	NS

This file contains detailed results of LME regression models used to explore relationships between various POPs congeners and a set of phenotypical parameters.

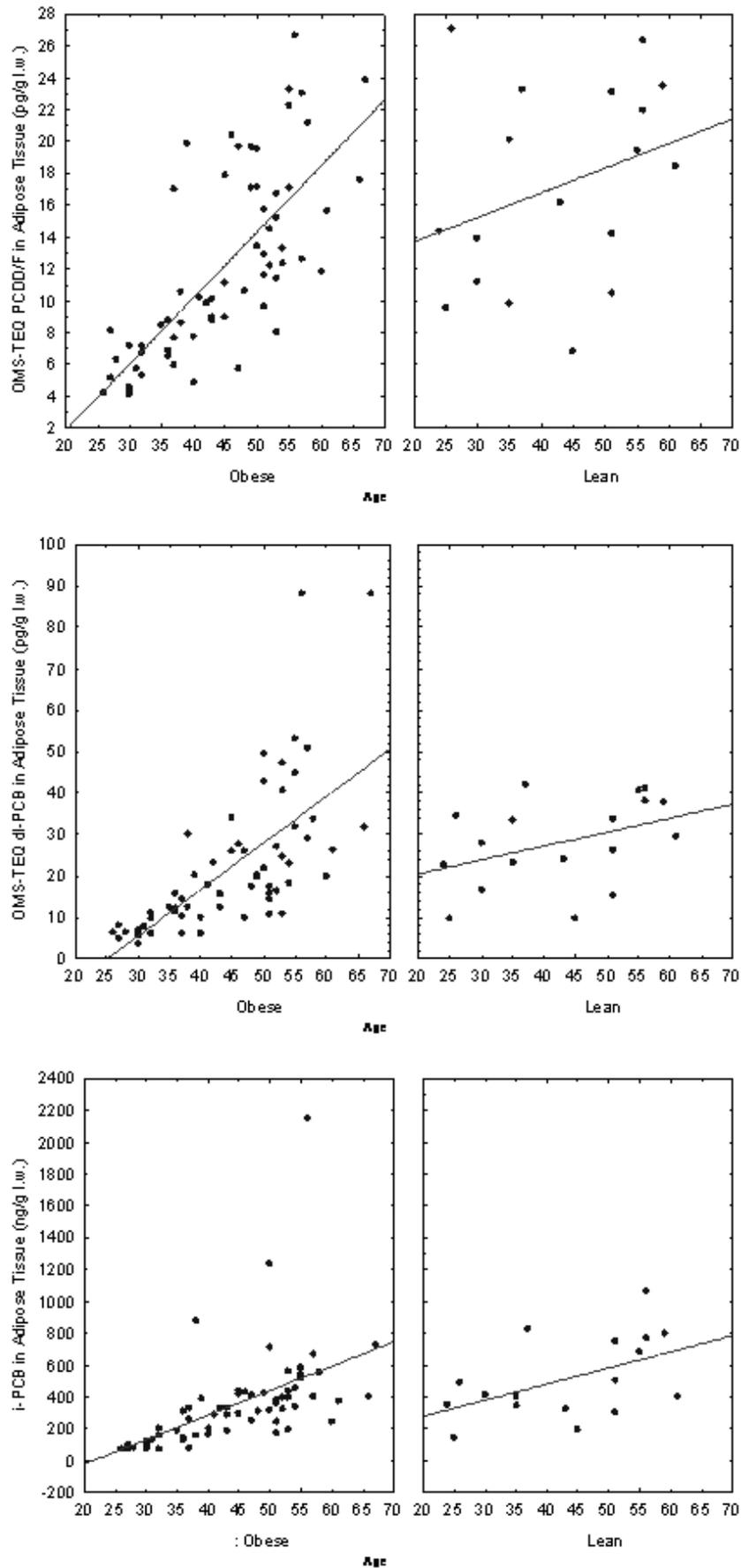
In all models age, sex and body fat mass (expressed in kg of body weight) were considered as confounding factors. For each couple of variables including a POP congener (columns) and a phenotypical parameter (rows) two values are provided: a partial correlation coefficient (pRs) and a LME significance pvalue (pval.). Blood - indicates serum concentration. AT - indicates adipose tissue concentration.

		Obese Subjects (71)	Lean Subjects (18)
Mesure of POPs concentration	<u>Adipose tissue</u>		
	Basal	65	18 (12 with DXA)
	Kinetic	26	NA
	<u>Serum</u>		
	Basal	35	17
	Kinetic	26	NA
Mesure of gene expression of POPs target genes	<u>Adipose tissue</u>		
	Basal	9	7
	Kinetic	15	NA
	<u>Blood cells</u>		
	Basal	28	16
	Kinetic	27	NA

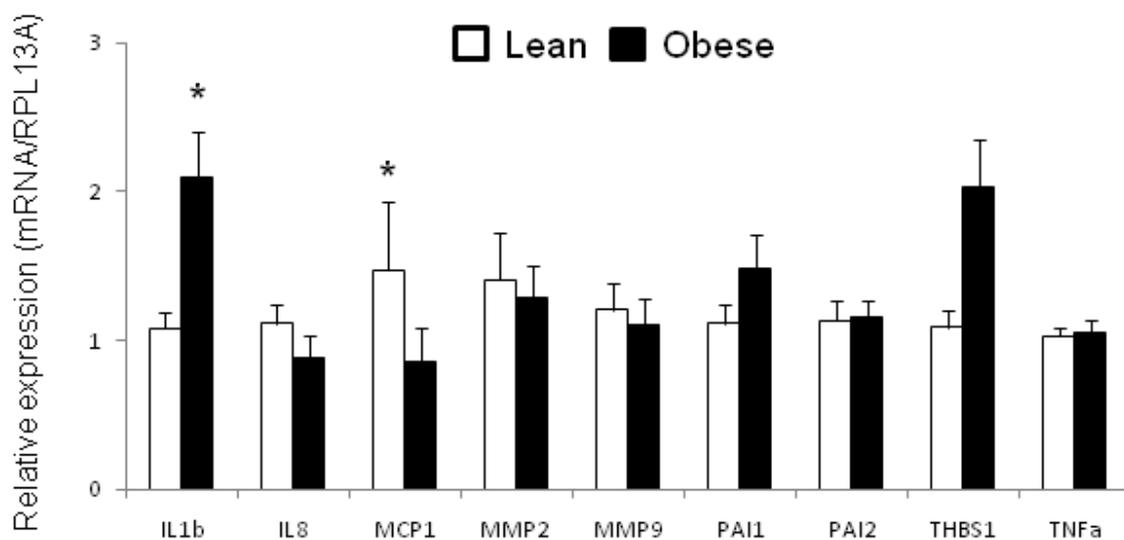
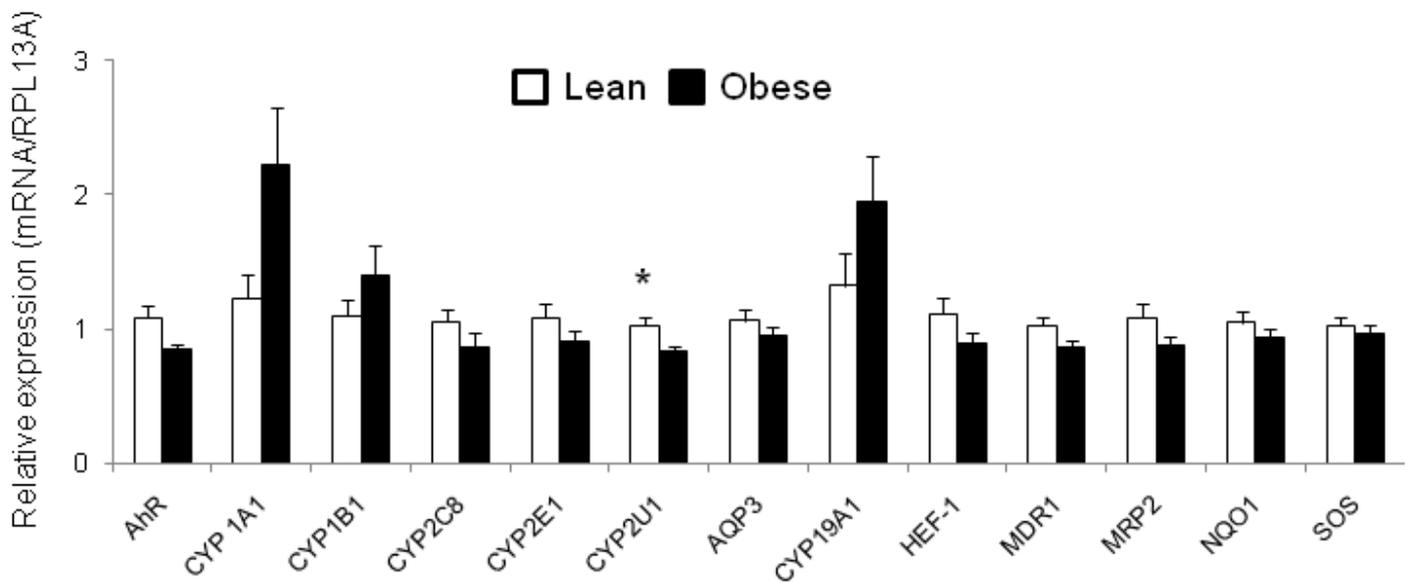
Supplementary Material, Figure 1: Scheme of the study design and resources available for each subject.



Supplementary Material, Figure 2: Correlations between the contamination levels measured in adipose tissue versus serum for obese individuals before surgery (n=32) and lean (n=13) subjects.



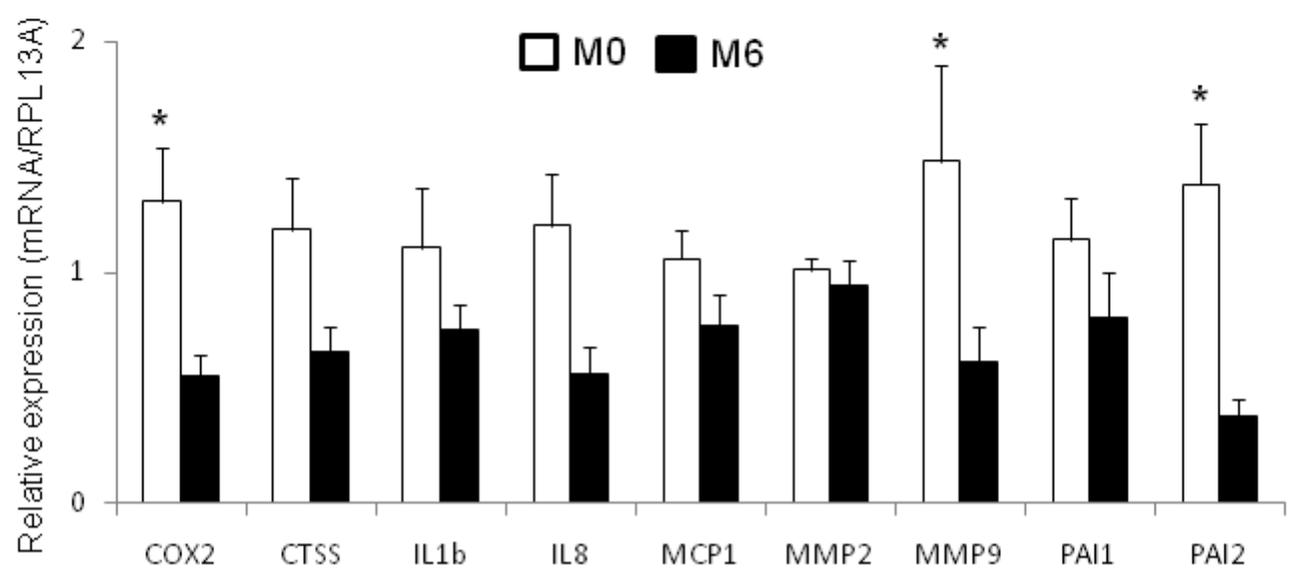
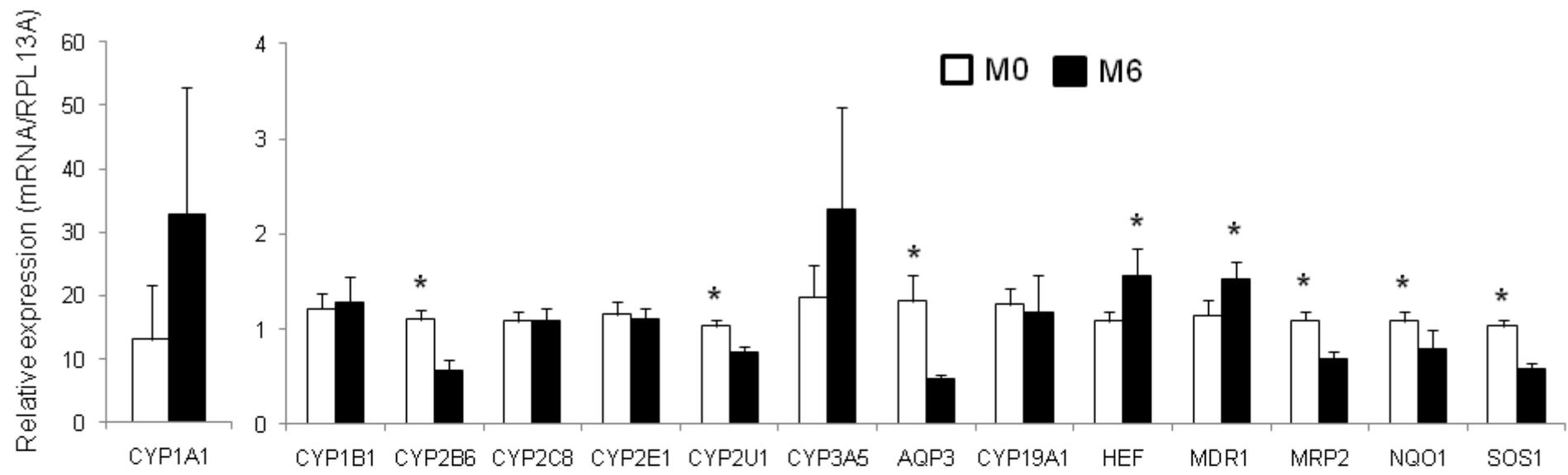
Supplementary Material, Figure 3: Correlations between the contamination levels measured in adipose tissue versus age for obese before surgery (n=65) and lean (n=18) subjects



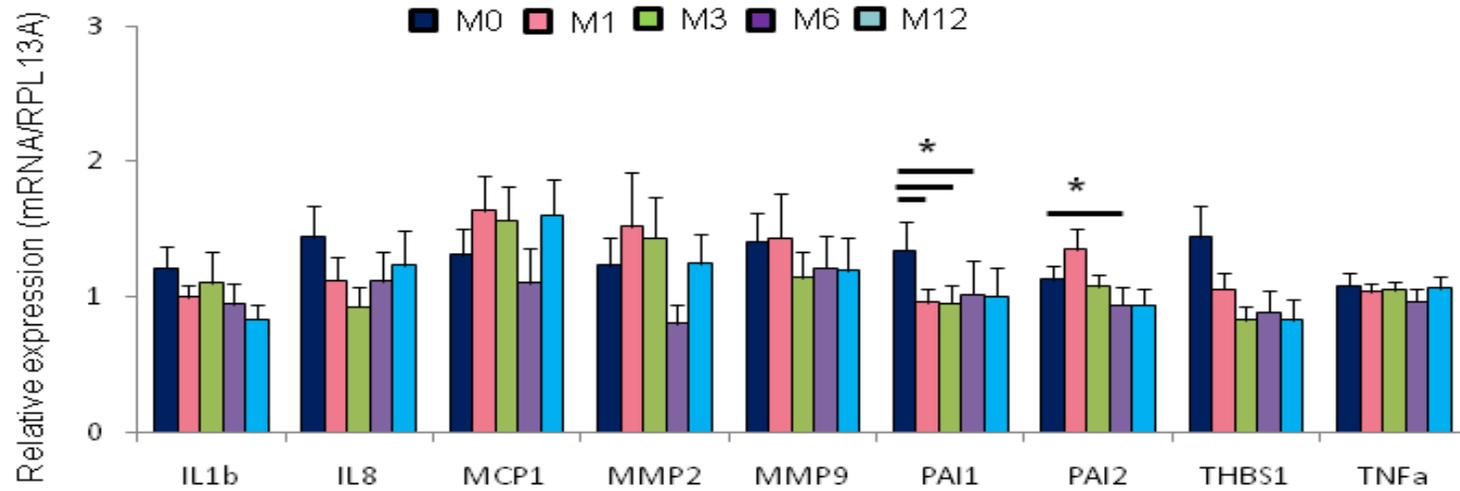
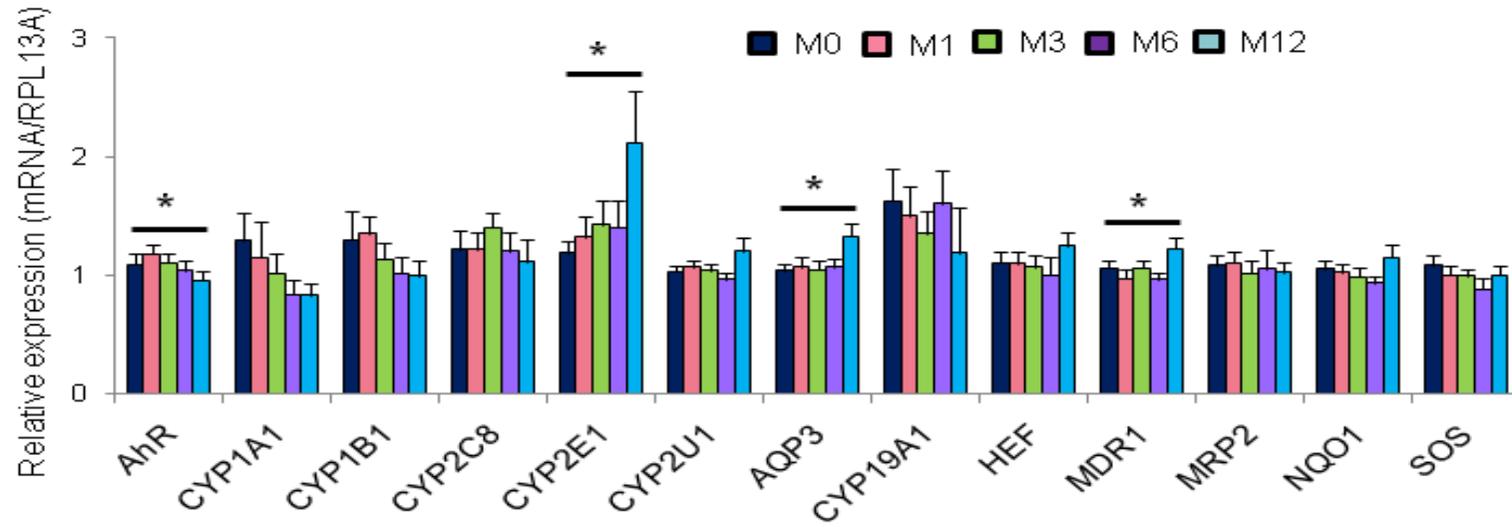
Supplementary Material, Figure 4: Expression of pollutant target genes in blood cells of lean and obese subjects:

mRNAs were measured in blood cells of lean (n=16) and obese (n=28) subjects by RTqPCR using the $\Delta\Delta C_t$ method by reporting C_t of target gene of each subject to mean C_t of lean subjects and by using *RPL13A* as reference gene. Data are expressed as mean \pm SEM. A (upper panel): *AhR*, phase I xenobiotic metabolizing CYP genes and other targets of the xenobiotic receptors, B (lower panel): targets of the xenobiotic receptors involved in obesity-associated low-grade inflammation. For each gene, data for obese and lean subjects were statistically compared by Wilcoxon Rank Sum test. *: $p < 0.05$

5A



5B



Supplementary Material, Figure 5: Pollutant target gene expression in blood cells and adipose tissue of obese patients before and after gastric bypass.

5A: POP target gene expression in adipose tissue of obese patients before and after gastric bypass. The amounts of mRNAs in adipose tissue of obese patients (n=15) were assessed before (M0) and 6 months (M6) after gastric bypass by RTqPCR. The relative expression was obtained by $\Delta\Delta\text{Ct}$ method by reporting Ct of target gene of each subject to mean Ct of obese subjects at M0 and by using *RPL13A* as reference gene. Data are expressed as mean \pm SEM. A: *AhR*, phase I xenobiotic metabolizing CYP genes and other targets of the xenobiotic receptors, B: targets of the xenobiotic receptors involved in obesity-associated low-grade inflammation. For each gene, data for M0 and M6 of obese subjects were statistically compared by Wilcoxon Rank Sum test *: $p < 0.05$

5B: Pollutant target gene expression in blood cells of obese patients before and after gastric bypass. mRNAs were measured in blood cells of obese patients (n=27) before (M0) and 1 (M1), 3 (M3), 6 (M6) and 12 (M12) months after gastric bypass by RTqPCR using $\Delta\Delta\text{Ct}$ method by reporting Ct of target gene of each subject to mean Ct of obese subjects at M0 and by using *RPL13A* as reference gene. Data are expressed as mean \pm SEM. A (upper panel): *AhR*, phase I xenobiotic metabolizing CYP genes and other targets of the xenobiotic receptors, B (lower panel): targets of the xenobiotic receptors involved in obesity-associated low-grade inflammation. For each gene, data were statistically compared by Friedman test and if significant differences were found Wilcoxon Rank Sum test was applied between M1, M3, M6, M12 vs M0 *: $p < 0.05$