Data Article

Dataset of liver proteins changed in eu- and hypothyroid female rats upon in vivo exposure to hexabromocyclododecane (HBCD)

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A B S T R A C T

Female Wistar rats with different thyroid status (eu-, hypothyroid) were exposed to 0, 3 or 30 mg/kg body weight of the flame retardant HBCD for 7 days. Changes in protein patterns obtained by 2D-DIGE were evaluated, and different animal groups compared taking into account their exposure and thyroid status. Proteins significantly altered in abundance in any of these comparisons were identified by mass spectrometry. These data, together with hormone data of the animals, are discussed in “Hexabromocyclododecane (HBCD) induced changes in the liver proteome of eu- and hypothyroid female rats” (Miller et al., 2016) [1].

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### Specifications Table

| Subject area       | Biology                        |
|--------------------|-------------------------------|
| More specific subject area | Environmental Toxicology      |
| Type of data       | Tables, image (annotated gel image) |
| How data was acquired | 2D Fluorescence Difference Gel Electrophoresis (2D-DIGE) and mass spectrometry |
| Data format        | Analyzed and filtered data    |
| Experimental factors | Liver lysates of eu- and hypothyroid female rats differently exposed to HBCD |
| Experimental features | Comparative proteomic analysis of rat liver lysates using 2D-DIGE. Proteins present in differentially abundant protein spots (regarding HBCD exposure, amount, and thyroid status) were identified using MALDI TOF/TOF analysis. |
| Data source location | Origin of samples: Wageningen University, Wageningen, The Netherlands Data collection: Luxembourg Institute of Science and Technology, Esch-sur-Alzette, Luxembourg |
| Data accessibility | MS- and regulation data is with this article as Supplementary material |

### Value of the data

- Identification of liver proteins from female rats altered due to HBCD exposure.
- Identification of liver proteins from female rats changed in hypothyroid status.
- Data showing single and combined effects (HBCD exposure, hypothyroidism).
- Identified liver proteins form the basis for further studies to achieve a more detailed understanding of involved mechanism.

### 1. Data

Two-dimensional electrophoresis of liver protein lysates showed complex patterns of about 3000 spots per gel. Patterns of 24 gels from different exposures of eu- and hypothyroid rats were evaluated quantitatively. The data from different animals groups were compared, taking different aspects into account (HBCD exposure, thyroid status). Statistically significant fold-changes of at least 30% between groups (\( P < 0.05 \) within group) were considered to be relevant.

The master gel is presented in Fig. 1, and all spots with significant abundance changes in any of the performed comparisons are labelled. Spot numbers refer to the protein identifications listed in Table 1 (peptide list in Supplemental Table 1), and to abundance changes in the various animal groups (Supplemental Table 2).

### 2. Experimental design, materials and methods

#### 2.1. Animals, treatment and experimental protocol

The animal experiment was detailed in [1] and was approved under number 2007-041 by the Animal Welfare Committee of Wageningen University. In brief, female Wistar WU (HsdCpbWU) rats with normal or reduced thyroid function (hypothyroid) were orally exposed to 0, 3 or 30 mg/kg bw/d HBCD, respectively, for 7 consecutive days. Four liver samples per group were analyzed by proteomic methods.
2.2. Proteomic analysis

Two-dimensional fluorescence difference gel electrophoresis (2D-DIGE) was performed as previously described, with minor modifications [2,3]. Rat livers were homogenized using the GE sample grinding kit in lysis buffer (urea 7 M; thiourea 2 M; CHAPS 2% w/w; tris 30 mM) containing protease inhibitor Complete Mini (Roche, Brussels, Belgium). Supernatants obtained after centrifugation (15 min at 30,000 g) were collected and stored at −20 °C until use. Protein concentration was determined according to Bradford [4]. Fifty μg per sample were labelled with CyDyes according to the manufacturer’s instructions and separated on IPGs of a non-linear 3–10 pH-range. The second dimensional SDS-PAGE was performed in 12.5% precast gels (SERVA Electrophoresis GmbH, Heidelberg, Germany). Gel images (acquired on a Typhoon 9400) were analyzed with the DeCyder 7.0 software package (both GE Healthcare, Diegem, Belgium). Gels were matched and subjected to univariate and multivariate analysis in order to highlight differentially regulated spots (fold change at least 1.3) with a P-value in the respective univariate ANOVA or two way ANOVA < 0.05.

Differentially abundant spots were automatically picked, tryptically digested and spotted on the MALDI target by the use of the Ettan Spot Handling Workstation (GE Healthcare, Diegem, Belgium). Protein identification was carried out on the Applied Biosystems MALDI-ToF-Tof 4800 Proteomics Analyser (Applied Biosystem, Gent, Belgium) as previously described [2]. Protein identification was performed by searching protein mass fingerprints (PMF) and MS/MS spectra against the SwissProt database with “Rattus norvegicus” as taxonomy. Searches were performed using the ProteinPilot software (Sciex, Nieuwerkerk aan den Ijssel, The Netherlands) and the searching algorithm MASCOT (Matrix Science, www.matrixscience.com, London, UK). For each spot one protein mass fingerprint and up to 8 MS/MS spectra were generated. Parameters for the search were set as follow: up to two
| Spot number | Protein name | Species | Swiss-Prot Acc. No. |
|-------------|--------------|---------|-------------------|
| 1063, 1065, 1067–1071, 1074–1076, 1078 | Carbamoyl-phosphate synthase[ammonia], mitochondrial | Rattus norvegicus | CPSM_RAT |
| 1072 | Murinoglobulin-2 | Rattus norvegicus | MUG2_RAT |
| 1077, 1082, 1083 | Pyruvate carboxylase, mitochondrial | Rattus norvegicus | PYC_RAT |
| 1086 | ATP-citrate synthase | Rattus norvegicus | ACLY_RAT |
| 1089 | C-1-tetrahydrofolate synthase, cytoplasmic | Rattus norvegicus | C1TC_RAT |
| 1093 | Alpha-aminoadipic semialdehyde synthase, mitochondrial | Rattus norvegicus | AASS_RAT |
| 1094, 1100 | 2-oxoglutarate dehydrogenase, mitochondrial | Rattus norvegicus | ODO1_RAT |
| 1099, 1105, 1107–1110, 1114 | Aldehyde dehydrogenase family1 member L1 | Rattus norvegicus | AL1L1_RAT |
| 1111 | Aldehyde dehydrogenase1 family, member L2 | Mus musculus | gi21961590 |
| 1112, 1115–1117, 1119 | Sarcosine dehydrogenase, mitochondrial | Rattus norvegicus | SARDH_RAT |
| 1121, 1122 | Elongation factor2 | Rattus norvegicus | EF2_RAT |
| 1123 | Cytoplasmic aconitate hydratase | Rattus norvegicus | ACOC_RAT |
| 1129 | Dimethylglycine dehydrogenase, mitochondrial | Rattus norvegicus | M2GD_RAT |
| 1135 | Serotransferrin | Rattus norvegicus | TRFE_RAT |
| 1148 | Propionyl-CoA carboxylase alpha chain, mitochondrial | Rattus norvegicus | PCCA_RAT |
| 1155 | 78kDa glucose-regulated protein | Rattus norvegicus | GRP78_RAT |
| 1161, 1165 | Heat shock cognate 71 kDa protein | Rattus norvegicus | HSP7C_RAT |
| 1163, 1164 | rCGS56002 | Rattus norvegicus | gi149036727 |
| 1169, 1172, 1173, 1181, 1186 | Serum albumin | Rattus norvegicus | ALBU_RAT |
| 1191 | Delta-1-pyrroline-5-carboxylate dehydrogenase, mitochondrial | Cricetulus griseus | gi344249754 |
| 1203 | UV excision repair protein RAD23 homolog B | Rattus norvegicus | RD23B_RAT |
| 1212 | PREDICTED: aldehyde dehydrogenase 8 family, member A1-like isoform 2 | Rattus norvegicus | gi109460389 |
| 1213 | Pyruvatekinase isozymes R/L | Rattus norvegicus | KPYR_RAT |
| 1216, 1219 | Proteindisulfide-isomerase A3 | Rattus norvegicus | PDIA3_RAT |
| 1217 | Liver carboxylesterase 4 | Rattus norvegicus | EST4_RAT |
| 1226 | Formimidoyl transferase-cyclodeaminase | Rattus norvegicus | FTCD_RAT |
| 1229 | Calreticulin | Rattus norvegicus | CALR_RAT |
| 1231 | Methylmalonate-semialdehyde dehydrogenase[acylating], mitochondrial | Rattus norvegicus | MMSA_RAT |
| 1246 | Alpha-1-antiproteinase | Rattus norvegicus | A1AT_RAT |
| 1260, 1268 | Alanine-glyoxylate aminotransferase 2, mitochondrial | Rattus norvegicus | AGT2_RAT |
| Spot number | Protein name                                           | Species          | Swiss-Prot Acc. N° |
|------------|--------------------------------------------------------|------------------|------------------|
| 1261       | Glutathione synthetase                                 | Rattus norvegicus| GSHB_RAT         |
| 1262       | 4-trimethylaminobutyaldehyde dehydrogenase             | Rattus norvegicus| AL9A1_RAT       |
| 1270, 1277 | Phenylalanine-4-hydroxylase                            | Rattus norvegicus| PH4H_RAT        |
| 1271       | Succinate-semialdehyde dehydrogenase, mitochondrial    | Rattus norvegicus| SSDH_RAT        |
| 1273       | Hydroxymethylglutaryl-CoA synthase, mitochondrial      | Rattus norvegicus| HMCS2_RAT       |
| 1275       | Alpha-enolase                                          | Rattus norvegicus| ENOA_RAT        |
| 1296       | Ifi47 protein                                          | Rattus norvegicus| gi44890246      |
| 1298, 1301, 1310 | Betaine–homocysteine S-methyltransferase 1 | Rattus norvegicus| BHMT1_RAT      |
| 1300       | Eukaryotic initiation factor 4A-II                    | Rattus norvegicus| IF4A2_RAT      |
| 1314       | 3-ketoacyl-CoA thiase, mitochondrial                   | Rattus norvegicus| THIM_RAT       |
| 1323, 1326 | Argininosuccinate synthase                             | Rattus norvegicus| ASSY_RAT       |
| 1332       | Keratin, type I cytoskeletal 18                        | Rattus norvegicus| K1C18_RAT      |
| 1337       | Aspartate aminotransferase, cytoplasmic                | Rattus norvegicus| AATC_RAT       |
| 1341, 1345, 1354 | Actin, cytoplasmic 1                          | Rattus norvegicus| ACTB_RAT       |
| 1344       | Creatinekinase B-type                                  | Rattus norvegicus| KCRB_RAT       |
| 1356       | Aspartate aminotransferase, mitochondrial              | Rattus norvegicus| AATM_RAT       |
| 1357       | Serum paraoxonase/arylesterase 2                      | Rattus norvegicus| PON2_RAT       |
| 1363, 1365 | Fructose-bisphosphate aldolase B                       | Rattus norvegicus| ALDOB_RAT      |
| 1366       | Serum paraoxonase/lactonase 3                         | Rattus norvegicus| PON3_RAT       |
| 1370, 1371, 1374, 1378, 1384 | Fructose-1,6-bisphosphatase 1 | Rattus norvegicus| F16P1_RAT     |
| 1381       | Adipocyte plasmamembrane-associated protein            | Rattus norvegicus| APMAP_RAT      |
| 1388       | Farnesyl pyrophosphate synthase                        | Rattus norvegicus| FPPS_RAT       |
| 1391, 1393 | Arginase-1                                              | Rattus norvegicus| ARGI1_RAT      |
| 1404, 1417 | 3-oxo-5-beta-steroid 4-dehydrogenase                   | Rattus norvegicus| AK1D1_RAT      |
| 1406       | Glyceraldehyde-3-phosphate dehydrogenase               | Rattus norvegicus| G3P_RAT       |
| 1412       | 3-alpha-hydroxy steroid dehydrogenase                  | Rattus norvegicus| DIDH_RAT      |
| 1420, 1429 | Glycerol-3-phosphate dehydrogenase[NAD+], cytoplasmic  | Rattus norvegicus| GPDA_RAT      |
| 1422       | L-lactate dehydrogenase A chain                        | Rattus norvegicus| LDHA_RAT      |
| 1428       | Beta-lactamase-like protein 2                           | Rattus norvegicus| LACB2_RAT     |
| Spot number | Protein name                                                                 | Species                     | Swiss-Prot Acc. No. |
|-------------|------------------------------------------------------------------------------|-----------------------------|---------------------|
| 1433        | Ester hydrolase C11 orf 54 homolog                                           | Rattus norvegicus           | CK054_RAT           |
| 1438        | Sulotransferase 1A1                                                          | Rattus norvegicus           | ST1A1_RAT           |
| 1441, 1443  | Thiosulfate sulfurtransferase                                                | Rattus norvegicus           | THTR_RAT            |
| 1445        | Guanine nucleotide-binding protein subunit beta-2-like1                      | Rattus norvegicus           | GBLP_RAT            |
| 1447        | Reguacalcin                                                                  | Rattus norvegicus           | RGN_RAT             |
| 1449        | D-beta-hydroxybutyrate dehydrogenase, mitochondrial                         | Rattus norvegicus           | BDH_RAT             |
| 1450        | Hydroxacyl-coenzyme A dehydrogenase, mitochondrial                         | Rattus norvegicus           | HCDH_RAT            |
| 1460        | Nitrilase homolog 1                                                          | Rattus norvegicus           | NIT1_RAT            |
| 1463        | Proteasome activator complex subunit1                                       | Rattus norvegicus           | PSME1_RAT           |
| 1471        | Nicotinate-nucleotide pyrophosphorylase [carboxylating]                      | Rattus norvegicus           | NADC_RAT            |
| 1473        | Thiopurine S-methyltransferase                                               | Rattus norvegicus           | TPMT_RAT            |
| 1477, 1483  | Electron transfer flavoprotein subunit beta                                  | Rattus norvegicus           | ETFB_RAT            |
| 1480        | Isoamyl acetate-hydrolyzing esterase 1 homolog                              | Rattus norvegicus           | IAH1_RAT            |
| 1486        | Glutathione S-transferase Mu2                                                | Rattus norvegicus           | GSTM2_RAT           |
| 1488        | Glutathione S-transferase alpha-5                                            | Rattus norvegicus           | GSTA5_RAT           |
| 1489        | Peroxiredoxin-4                                                             | Rattus norvegicus           | PRDX4_RAT           |
| 1495        | protein ETHE1, mitochondrial                                                | Rattus norvegicus           | gi|157819563         |
| 1496, 1509, 1510 | Carbonic anhydrase 3                                                                 | Rattus norvegicus           | CAH3_RAT           |
| 1504        | Endoplasmic reticulum resident protein 29                                   | Rattus norvegicus           | ERP29_RAT           |
| 1506        | Glutathione S-transferase alpha-1                                            | Rattus norvegicus           | GSTA1_RAT           |
| 1507        | Glutathione S-transferase alpha-2                                            | Rattus norvegicus           | GSTA2_RAT           |
| 1508        | Glutathione S-transferase alpha-3                                            | Rattus norvegicus           | GSTA3_RAT           |
| 1512        | Glutathione S-transferase alpha-4                                            | Rattus norvegicus           | GSTA4_RAT           |
| 1514        | NADH dehydrogenase [ubiquinone] flavoprotein 2, mitochondrial              | Rattus norvegicus           | NDUV2_RAT           |
| 1522        | Glutathione S-transferase P                                                  | Rattus norvegicus           | GSTP1_RAT           |
| 1523        | biliverdin reductase B (flavinreductase(NADPH)) (predicted), isoform CRA_c   | Rattus norvegicus           | gi|149056527         |
| 1524        | Peroxiredoxin-1                                                             | Rattus norvegicus           | PRDX1_RAT           |
| 1528, 1530  | Abhydrolase domain-containing protein 14B                                    | Rattus norvegicus           | ABHEB_RAT           |
| 1540        | Peptidyl-prolyl cis-trans isomerase F, mitochondrial                         | Rattus norvegicus           | PPIF_RAT            |
| 1543        | Coflin-1                                                                     | Rattus norvegicus           | COF1_RAT            |
missed cleavages allowed, 100 ppm tolerance in PMF, 0.75 Da mass tolerance for precursor ion mass, carbamidomethyl cysteine as fixed modification, oxidation of methionine and oxidation of tryptophan (single oxidation, double oxidation and kynurenin) as variable modifications. Identifications were considered to be significant when the combined MOWSE score had $P < 0.05$.

Statistics, including univariate analysis (ANOVA and $t$-test) and multivariate analysis (two way ANOVA), was performed using the Extended Data Analysis (EDA) module, which is present inside the Decyder 7.0 software package.

Appendix A. Supplementary material

Supplementary data associated with this paper can be found in the online version at http://dx.doi.org/10.1016/j.dib.2016.02.047.

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