

Litteraturgennemgang for perioden 1/4 2011 - 30/6 2011

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Humane studier ved Afdeling for Vækst og Reproduktion, Rigshospitalet

Søgning er udført på PubMed og dækker perioden 1/4/2011 - 30/6/2011

Følgende søgeprofil er benyttet: (endocrine disrupt*) AND expos* AND (human OR men OR women OR child* OR adult* OR adolescen* OR infan*)

(Bemærkning: * i slutningen af et ord betyder at man søger på alle tænkelige endelser for det givne ord. For child* betyder det for eksempel at man søger på childhood, children og child)

Limits: title/abstract, English language

Brutto resultat: der blev fundet 66 artikler via denne søgning. Det var dog de allerfærreste der blev fundet relevante, hvorfor der blev foretaget mere specifikke søgninger indenfor områderne bishenol A, PFCer og flammehæmmere. I alt er 11 artikler, primært omhandlende disse stofgrupper, inkluderet og kommenteret på.

De udvalgte studier har blandt andet fokus på eksponeringsniveauer, eksponeringsveje og betydning for pubertetsudvikling.

Environ Int. 2011 May;37(4):687-93.

Characterisation of human exposure pathways to perfluorinated compounds - comparing exposure estimates with biomarkers of exposure.

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Commercially used per- and polyfluorinated compounds (PFCs) have been widely detected in humans, but the sources of human exposure are not fully characterized. The objectives of this study were to assess the relative importance of different exposure pathways of PFCs in a group of Norwegians and compare estimated intakes with internal doses obtained through biomonitoring. Individual PFC intakes from multiple exposure sources for a study group of 41 Norwegian women were estimated using measured PFC concentrations in indoor air and house dust as well as information from food frequency questionnaires and PFC concentrations in Norwegian food. Food was generally the major exposure source, representing 67-84% of the median total intake for PFOA and 88-99% for PFOS using different dust ingestion rates and biotransformation factors of 'precursor' compounds. However, on an individual basis, the indoor environment accounted for up to around 50% of the total intake for several women. Significant positive associations between concentrations of PFCs in house dust and the corresponding serum concentrations underline the importance of indoor environment as an exposure pathway for PFCs. For breast-fed infants, breast milk was calculated to be the single most important source to PFCs by far. The estimated intakes were confirmed by comparing serum concentrations of PFOA and PFOS calculated using PK models, with the corresponding concentrations measured in serum. Even though food in general is the major source of exposure for PFCs, the indoor environment may be an important contributor to human exposure. This study provides valuable knowledge for risk assessment of PFCs and control strategies.

Environ Sci Technol. 2011 Apr 6. [Epub ahead of print]

Trends in Exposure to Polyfluoroalkyl Chemicals in the U.S. Population: 1999-2008 (†)

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Since 2002, practices in manufacturing polyfluoroalkyl chemicals (PFCs) in the United States have changed. Previous results from the National Health and Nutrition Examination Survey (NHANES) documented a significant decrease in serum concentrations of some PFCs during 1999-2004. To further assess concentration trends of perfluorooctane sulfonate (PFOS), perfluorooctanoate (PFOA), perfluorohexane sulfonate (PFHxS), and perfluorononanoate (PFNA), we analyzed 7876 serum samples collected from a representative sample of the general U.S. population ≥ 12 years of age during NHANES 1999-2008. We detected PFOS, PFOA, PFNA, and PFHxS in more than 95% of participants. Concentrations differed by sex regardless of age and we observed some differences by race/ethnicity. Since 1999-2000, PFOS concentrations showed a significant downward trend, because of discontinuing industrial production of PFOS, but PFNA concentrations showed a significant upward trend. PFOA concentrations during 1999-2000 were significantly higher than during any other time period examined, but PFOA concentrations have remained essentially unchanged during 2003-2008. PFHxS concentrations showed a downward trend from 1999 to 2006, but concentrations increased during 2007-2008. Additional research is needed to identify the environmental sources contributing to human exposure to PFCs. Nonetheless, these NHANES data suggest that sociodemographic factors may influence exposure and also provide unique information on temporal trends of exposure.

Environ Health Perspect. 2011 Apr;119(4):573-8. Epub 2010 Nov 9.

Prenatal exposure to perfluorinated chemicals and behavioral or coordination problems at age 7 years

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OBJECTIVE: Potential neurotoxic effects of perfluorinated compounds (PFCs) have been reported in highly exposed animals, but whether these chemicals are neurotoxic in humans is not known. We therefore investigated whether prenatal exposure to perfluorooctanoic acid (PFOA) or perfluorooctane sulfate (PFOS), two of the most prevalent PFCs, are associated with behavioral or coordination problems in early childhood. **METHODS:** We used data from the Danish National Birth Cohort, which enrolled mothers in early pregnancy, and we measured maternal blood levels of PFOA and PFOS using specimens drawn around 8 weeks of gestation. When the children reached 7 years of age, mothers completed the Strengths and Difficulties Questionnaire (SDQ, n=787) and the Developmental Coordination Disorder Questionnaire (DCDQ, n=526) to assess behavioral health and motor coordination of their children. SDQ scores above the 90th percentile were a priori defined to identify behavioral problems and DCDQ scores below the 10th percentile were defined as a potential DCD. **RESULTS:** The median concentrations of PFOS and PFOA in maternal blood were 34.4 ng/mL [interquartile range (IQR), 26.6-44.5] and 5.4 ng/mL (IQR, 4.0-7.1), respectively, similar to distributions reported for populations without occupational exposure. We found no association between higher SDQ scores and maternal levels of PFOS or PFOA, nor did we see any statistically significant association with motor coordination disorders. **CONCLUSION:** The findings suggest that background levels of PFOA and PFOS are not associated with behavioral and motor coordination problems in childhood. However, effects on other developmental end points, including cognitive, attentional, and clinical mental disorders not measured in this study, cannot be ruled out.

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Association of Perfluorooctanoic Acid (PFOA) and Perfluorooctane Sulfonate (PFOS) with Age of Puberty among Children Living near a Chemical Plant

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Animal studies suggest that perfluorocarbons (PFCs) may alter sexual maturation. Relationships of human PFC exposure with puberty are not clear. We conducted a cross-sectional study to investigate whether perfluorooctanoic acid (PFOA) and perfluorooctane sulfonate (PFOS) were associated with indicators of sexual maturation in a 2005-2006 survey of residents with PFOA water contamination from the Mid-Ohio Valley. Participants were 3076 boys and 2931 girls aged 8-18 years. They were classified as having reached puberty based on either hormone levels (total >50 ng/dL and free >5 pg/mL testosterone in boys and estradiol >20 pg/mL in girls) or onset of menarche. We estimated the odds of having reached puberty classified by these criteria and the fitted median age of reaching puberty in relation to serum PFOA and PFOS concentrations measured when puberty status was assigned. For boys, there was a relationship of reduced odds of reached puberty (raised testosterone) with increasing PFOS (delay of 190 days between the highest and lowest quartile). For girls, higher concentrations of PFOA or PFOS were associated with reduced odds of postmenarche (130 and 138 days of delay, respectively). In conclusion, our study showed a later age of puberty in this population correlated with PFC concentrations.

Environ Res. 2011 May;111(4):559-64.

Perfluorinated acids and hypothyroxinemia in pregnant women

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Perfluorinated acids (PFAs) are prominent and widespread contaminants of human blood. In animal studies there is evidence that suggests certain PFAs can disrupt thyroid hormone homeostasis. A commonly reported condition in exposed animals is hypothyroxinemia, whereby serum free thyroxine (fT4) is decreased despite normal thyroid stimulating hormone (TSH) concentrations. We designed an individually matched case-control study to investigate whether exposure to perfluorooctanoate (PFOA), perfluorohexane sulfonate (PFHxS), and perfluorooctane sulfonate (PFOS) was associated with hypothyroxinemia in pregnant women from Edmonton, Alberta, Canada, in 2005-2006, who underwent a "triple screen" blood test at 15-20 weeks gestation as part of ante-natal care. Thyroid hormones, fT4 and TSH, were measured in serum from 974 women, and from these we measured PFAs in the sera of 96 hypothyroxinemic cases (normal TSH, the lowest 10th percentile of fT4) and 175 controls (normal TSH, fT4 between the 50th and 90th percentiles) matched on age and referring physician. Analyses by conditional logistic regression indicated that the concentrations of PFAs in this population were not associated with hypothyroxinemia among pregnant women. The current findings do not support a causal link between PFA exposure and maternal hypothyroxinemia in the studied population.

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Assessing the Quantitative Relationships between Preschool Children's Exposures to Bisphenol A by Route and Urinary Biomonitoring

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Limited published information exists on young children's exposures to bisphenol A (BPA) in the United States using urinary biomonitoring. In a previous project, we quantified the aggregate exposures of 257 preschool children to BPA in environmental and personal media over 48-h periods in 2000-2001 at homes and daycares in North Carolina and Ohio. In the present study for 81 Ohio preschool children ages 23-64 months, we quantified the children's urinary total BPA (free and conjugated) concentrations over these same 48-h periods in 2001. Then, we examined the quantitative relationships between the children's intakes doses of BPA through the dietary ingestion, nondietary ingestion, and inhalation routes and their excreted amounts of urinary BPA. BPA was detected in 100% of the urine samples. The estimated median intake doses of BPA for these 81 children were 109 ng/kg/day (dietary ingestion), 0.06 ng/kg/day (nondietary ingestion), and 0.27 ng/kg/day (inhalation); their estimated median excreted amount of urinary BPA was 114 ng/kg/day. Our multivariable regression model showed that dietary intake of BPA ($p = 0.04$) and creatinine concentration ($p = 0.004$) were significant predictors of urinary BPA excretion, collectively explaining 17% of the variability in excretion. Dietary ingestion of BPA accounted for >95% of the children's excreted amounts of urinary BPA.

Reprod Toxicol. 2011 Mar 31. [Epub ahead of print]

In utero exposure to bisphenol-A and its effect on birth weight of offspring

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To examine the effect of in utero BPA exposure on the birth weight of offspring, a total of 587 children from families in which parent(s) did or did not have occupational exposure to BPA were examined. Their birth weights were obtained by an in-person interview of the mother. Parental BPA exposure level during the index pregnancy was determined through personal air sampling measurements and exposure history. After controlling for potential confounders, parental exposure to BPA in the workplace during pregnancy was

associated with decreased birth weight. The association was stronger for maternal exposure which is statistically significant ($P=0.02$). A dose-response relationship was observed with increased BPA exposure levels in pregnancy associated with greater magnitude of decrease of birth weight in offspring ($P=0.003$). Our findings provide the new epidemiologic evidence suggesting that in utero exposure to BPA during pregnancy may be associated with decreased birth weight in offspring.

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Urinary bisphenol A and obesity: NHANES 2003-2006

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BACKGROUND: Bisphenol A (BPA) is a chemical suspected of causing endocrine and metabolic disruption in animals and humans. In rodents, in utero exposure to low-dose BPA is associated with weight gain. Detectable levels of BPA are found in most Americans due to its widespread use in the manufacture of food and drink packaging. We hypothesized that urinary BPA concentrations would be positively associated with general and central obesity. **METHODS:** Cross-sectional analysis of urinary BPA concentrations, body mass index, and waist circumference in 2747 adults (aged 18-74), using pooled data from the 2003/04 and 2005/06 National Health and Nutrition Examination Surveys. **RESULTS:** The creatinine-adjusted geometric mean urinary BPA concentration was $2.05\mu\text{g/g}$ creatinine (25th percentile: 1.18, 75% percentile: 3.33). Relative to those in the lowest BPA quartile, participants in the upper BPA quartiles were more likely to be classified as obese (quartile 2 odds ratio (OR): 1.85, 95% confidence interval (CI): 1.22, 2.79; quartile 3 OR: 1.60, 95% CI: 1.05-2.44; quartile 4 OR: 1.76, 95% CI: 1.06-2.94). Higher BPA concentration was also associated with abdominal obesity (quartile 2 OR: 1.62, 95% CI: 1.11, 2.36; quartile 3 OR: 1.39, 95% CI: 1.02-1.90; quartile 4 OR: 1.58, 95% CI: 1.03-2.42). **CONCLUSIONS:** Higher BPA exposure is associated with general and central obesity in the general adult population of the United States. Reverse causation is of concern due to the cross-sectional nature of this study; longitudinal studies are needed to clarify the direction of the association.

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Effects of pre and postnatal exposure to low levels of polybromodiphenyl ethers on neurodevelopment and thyroid hormone levels at 4 years of age

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There are at present very few studies of the effects of polybromodiphenyl ethers (PBDEs), used as flame retardants in consumer products, on neurodevelopment or thyroid hormone levels in humans. The present study aims to examine the association between pre and postnatal PBDE concentrations and neurodevelopment and thyroid hormone levels in children at age 4 years and isolate the effects of PBDEs from those of PCBs, DDT, DDE and HCB. A prospective birth cohort in Menorca (Spain) enrolled 482 pregnant mothers between 1997 and 1998. At 4 years, children were assessed for motor and cognitive function (McCarthy Scales of Children's Abilities), attention-deficit, hyperactivity and impulsivity (ADHD-DSM-IV) and social competence (California Preschool Social Competence Scale). PBDE concentrations were measured in cord blood ($N=88$) and in serum of 4 years olds ($N=244$). Among all congeners analyzed only PBDE 47 was quantified in a reasonable number of samples ($\text{LOQ}=0.002\text{ng/ml}$). Exposure to PBDE 47 was analyzed as a dichotomous variable: concentrations above the LOQ (exposed) and concentrations below (referents). Scores for cognitive and motor functions were always lower in children pre and postnatally exposed to PBDE47 than in referents, but none of these associations was statistically significant (β coefficient (95%CI) of the total cognition score: -2.7 ($-7.0, 1.6$) for postnatal exposure, and -1.4 ($-9.2, 6.5$) for prenatal exposure). Postnatal exposure to PBDE 47 was statistically significantly related to an increased risk of symptoms on the attention deficit subscale of ADHD symptoms (RR (95%CI)= 1.8 ($1.0, 3.2$)) but not to hyperactivity symptoms. A statistically significant higher risk of poor social competence symptoms was observed as a consequence of postnatal PBDE 47 exposure (RR (95%CI)= 2.6 ($1.2, 5.9$)). Adjustment for other organochlorine compounds did not influence the results. Levels of thyroid hormones were not associated to PBDE exposure. This study highlights the importance of assessing the effects of PBDE exposure not just prenatally but also during the early years of life. In the light of current evidence a precautionary approach towards PBDE exposure of both mothers and children seems warranted.

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"Novel" brominated flame retardants in Belgian and UK indoor dust: Implications for human exposure

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Concentrations of several "novel" brominated flame retardants (NBFRs) are reported in indoor dust samples from Belgian houses (n=39) and offices (n=6) and from day-care centers and schools in the West Midlands of the UK (n=36). Using a GC-ECNI/MS method, the following NBFRs were quantified: decabromodiphenyl ethane (DBDPE) (range <20-2470ngg(-1)), 1,2-bis(2,4,6-tribromophenoxy)ethane (BTBPE) (range <0.5-1740ngg(-1)), tetrabromobisphenol A-bis(2,3-dibromopropylether) (TBBPA-DBPE) (range <20-9960ngg(-1)), 2-ethylhexyl-2,3,4,5-tetrabromobenzoate (TBB) (range <2-436ngg(-1)) and bis(2-ethylhexyl)-3,4,5,6-tetrabromophthalate (TBPH) (range <2-6175ngg(-1)). Hexachlorocyclopentadienyl-dibromocyclooctane (HCDBCO), another NBFR, was below the detection limit of 2ngg(-1) dust in all dust samples. No correlation was detected between concentrations of NBFRs and PBDEs. The ratio of TBB:TBPH in the dust samples ranged from 0.01 to 4.77 (average 0.42), compared to the ratio present in the commercial flame retardant product FM 550 (TBB:TBPH=4:1). Furthermore, no correlation was detected between concentrations in dust of TBB and TBPH. This may suggest different sources of these NBFRs, or similar sources but compound-specific differences in their indoor fate and transport. Exposure via dust ingestion was estimated for both adults and toddlers under low-end (5th percentile), typical (median), and high-end (95th percentile concentrations) scenarios. These were calculated assuming 100% absorption of intake dust and using mean dust ingestion (adults=20mgd(-1); for toddlers=50mgd(-1)) and high dust ingestion (adults=50mgd(-1); for toddlers=200mgd(-1)). Typical exposure with high dust ingestion estimates for adults were 0.01, 0.2, 0.01, 0.02 and 0.08ngkg(-1) bw d(-1) and for toddlers 0.05, 1.9, 0.08, 0.4 and 1.12ngkg(-1) bw d(-1) for BTBPE, DBDPE, TBB, TBPH and TBBPA-DBPE, respectively. Our results showed that, similar to PBDEs, toddlers have higher exposure to NBFRs than adults. This study documents the presence of NBFRs in indoor environments, and emphasizes the need to evaluate the health implications of exposure to such chemicals.

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Serum PBDEs and age at menarche in adolescent girls: Analysis of the National Health and Nutrition Examination Survey 2003-2004.

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BACKGROUND: Polybrominated diphenyl ethers (PBDEs), widely used as flame retardants since the 1970s, have exhibited endocrine disruption in experimental studies. Tetra- to hexa-BDE congeners are estrogenic, while hepta-BDE and 6-OH-BDE-47 are antiestrogenic. Most PBDEs also have antiandrogenic activity. It is not clear, however, whether PBDEs affect human reproduction. **OBJECTIVES:** The analysis was designed to investigate the potential endocrine disruption of PBDEs on the age at menarche in adolescent girls. **METHODS:** We analyzed the data from a sample of 271 adolescent girls (age 12-19 years) in the National Health and Nutrition Examination Survey (NHANES), 2003-2004. We estimated the associations between individual and total serum BDEs (BDE-28, -47, -99, -100, -153, and -154, lipid adjusted) and mean age at menarche. We also calculated the risk ratios (RRs) and 95% confidence intervals (CI) for menarche prior to age 12 years in relation to PBDE exposure. **RESULTS:** The median total serum BDE concentration was 44.7ng/g lipid. Higher serum PBDE concentrations were associated with slightly earlier ages at menarche. Each natural log unit of total BDEs was related to a change of -0.10 (95% CI: -0.33, 0.13) years of age at menarche and a RR of 1.60 (95% CI: 1.12, 2.28) for experiencing menarche before 12 years of age, after adjustment for potential confounders. **CONCLUSION:** These data suggest high concentrations of serum PBDEs during adolescence are associated with a younger age of menarche.

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- 66: Frederiksen H, Jørgensen N, Andersson AM. Parabens in urine, serum and seminal plasma from healthy Danish men determined by liquid chromatography-tandem mass spectrometry (LC-MS/MS). *J Expo Sci Environ Epidemiol.* 2011 May-Jun;21(3):262-71.

In Vitro studier ved DTU - FOOD

In vitro studier ved DTU-FOOD

Søgt i Pubmed med følgende kriterier:

”Endocrine disrupt* AND in vitro* samt “Endocrine disrupt* AND expose* AND in vitro*” og ”Paraben* AND in vitro*”

Limits Activated: published in the last 180 days (April-juni 2011)

Efter at have fjernet genganger fra forrige litteraturopdateringslister, gave litteratursøgningen med de to søgekriterier tilsammen en liste med i alt 24 artikler (Bruttolisten):

Ud fra bruttolisten (se længere nede i dokumentet) er udvalgt følgende 4 artikler til engelsk abstrakt og dansk konklusion og kommentarer.

Udvalgte publikationer:

The OBELIX project: early life exposure to endocrine disruptors and obesity.

Legler J, Hamers T, van Eck van der Sluijs-van de Bor M, Schoeters G, van der Ven L, Eggesbo M, Koppe

Abstract

The hypothesis of whether early life exposure (both pre- and early postnatal) to endocrine-disrupting chemicals (EDCs) may be a risk factor for obesity and related metabolic diseases later in life will be tested in the European research project OBELIX (OBesogenic Endocrine disrupting chemicals: LInking prenatal eXposure to the development of obesity later in life). OBELIX is a 4-y project that started in May 2009 and which has the following 5 main objectives: 1) to assess early life exposure in humans to major classes of EDCs identified as potential inducers of obesity (ie, dioxin-like compounds, non-dioxin-like polychlorinated biphenyls, organochlorine pesticides, brominated flame retardants, phthalates, and perfluorinated compounds) by using mother-child cohorts from 4 European regions with different food-contaminant exposure patterns; 2) to relate early life exposure to EDCs with clinical markers, novel biomarkers, and health-effect data related to obesity; 3) to perform hazard characterization of early life exposure to EDCs for the development of obesity later in life by using a mouse model; 4) to determine mechanisms of action of obesogenic EDCs on developmental programming with in vivo and in vitro genomics and epigenetic analyses; and 5) to perform risk assessments of prenatal exposure to obesogenic EDCs in food by integrating maternal exposure through food-contaminant exposure and health-effect data in children and hazard data in animal studies.

Methoxychlor reduces estradiol levels by altering steroidogenesis and metabolism in mouse antral follicles in vitro.

Basavarajappa MS, Craig ZR, Hernández-Ochoa I, Paulose T, Leslie TC, Flaws JA.

Abstract

The organochlorine pesticide methoxychlor (MXC) is a known endocrine disruptor that affects adult rodent females by causing reduced fertility, persistent estrus, and ovarian atrophy. Since MXC is also known to target antral follicles, the major producer of sex steroids in the ovary, the present study was designed to test the hypothesis that MXC decreases estradiol (E(2)) levels by altering steroidogenic and metabolic enzymes in the antral follicles. To test this hypothesis, antral follicles were isolated from CD-1 mouse ovaries and cultured with either dimethylsulfoxide (DMSO) or

MXC. Follicle growth was measured every 24h for 96h. In addition, sex steroid hormone levels were measured using enzyme-linked immunosorbent assays (ELISA) and mRNA expression levels of steroidogenic enzymes as well as the E(2) metabolic enzyme Cyp1b1 were measured using qPCR. The results indicate that MXC decreased E(2), testosterone, androstenedione, and progesterone (P(4)) levels compared to DMSO. In addition, MXC decreased expression of aromatase (Cyp19a1), 17 β -hydroxysteroid dehydrogenase 1 (Hsd17b1), 17 α -hydroxylase/17,20-lyase (Cyp17a1), 3 β hydroxysteroid dehydrogenase 1 (Hsd3b1), cholesterol side-chain cleavage (Cyp11a1), steroid acute regulatory protein (Star), and increased expression of Cyp1b1 enzyme levels. Thus, these data suggest that MXC decreases steroidogenic enzyme levels, increases metabolic enzyme expression and this in turn leads to decreased sex steroid hormone levels.

Detection of thyroid hormone receptor disruptors by a novel stable in vitro reporter gene assay.

Freitas J, Cano P, Craig-Veit C, Goodson ML, Furlow JD, Murk AJ.

Abstract

A stable luciferase reporter gene assay was developed based on the thyroid hormone responsive rat pituitary tumor GH3 cell line that constitutively expresses both thyroid hormone receptor isoforms. Stable transfection of the pGL4CP-SV40-2xtaDR4 construct into the GH3 cells resulted in a highly sensitive cell line (GH3.TRE-Luc), which was further optimized into an assay that allowed the detection of Triiodothyronine (T(3)) and Thyroxine (T(4)) concentrations in the picomolar range after only 24 h of exposure. The greater than 20-fold induction of T(3) relative to the solvent control is illustrative of the high responsiveness of the system. The assay was validated by the quantification of the agonistic effect of the natural hormones (T(3) and T(4)), the acetic acid derivatives of T(3) (triiodothyroacetic acid, or Triac) and T(4) (tetraiodothyroacetic acid, or Tetrac), hydroxy polybrominated diphenylethers (OH-PBDEs), hydroxy polychlorinated biphenyls (OH-PCBs) and the antagonistic action of sodium arsenite (NaAsO₂). The putative antagonist Amiodarone, Bisphenol A (BPA) and its halogenated derivatives (TCBPA and TBBPA) for which effects reported in the literature are not consistent, showed comparable dose-response curves with a slight agonistic effect (5% of T(3)-max) followed by a slight antagonistic effect. The magnitude and reproducibility of the responses to various compounds confirms this assay as a promising tool for the identification and quantification of specific thyroid hormone receptor disrupting potency of compounds.

Peroxisome Proliferator-Activated Receptor γ is a Target for Halogenated Analogues of Bisphenol-A.

Riu A, Grimaldi M, le Maire A, Bey G, Phillips K, Boulahtouf A, Perdu E, Zalko D, Bourguet W, Balaguer P.

Abstract

The occurrence of halogenated analogues of the xeno-estrogen bisphenol-A (BPA) has been recently demonstrated both in environmental and human samples. These include brominated (e.g. tetrabromobisphenol-A; TBBPA) as well as chlorinated (e.g. tetrachlorobisphenol-A; TCBPA) bisphenols which are both flame retardants. Due to their structural homology with BPA, such chemicals are candidate endocrine disruptors. However, their possible target(s) within the nuclear hormone receptor (NHRs) superfamily has remained unknown.

We investigated whether BPA and halogenated analogues could be ligands of estrogen (ERs) and peroxysome proliferator-activated (PPARs) receptors and act as endocrine disrupting chemicals (EDCs).

The activity of compounds was studied using reporter cell lines expressing ERs and PPARs. The binding affinities to PPAR β were measured by competitive binding assays with [3H]-rosiglitazone. We also investigated the impact of TBBPA and TCBPA on adipocyte differentiation using NIH3T3-L1 cells. Finally, the binding mode of halogenated BPAs to PPAR β was determined by X-ray crystallography.

Two major outcomes of this study are the demonstration that TBBPA and TCBPA are human, zebrafish and xenopus PPAR β ligands and the discovery of the mechanism by which these chemicals bind to and activate PPAR β . We also provide evidence that activation of ER α , ER β and PPAR β depends on the halogenation degree of BPA analogues. The bulkier brominated BPA analogues, the greater their capability to activate PPAR β and the weaker their estrogenic potential. Our results strongly suggest that poly-halogenated bisphenols could function as obesogens by acting as agonists able to disrupt physiological functions regulated by human or animal PPAR β .

Brutto søgeresultat in vitro

1.

Application of an Integrated Testing Strategy to the US EPA Endocrine Disruptor Screening Program.

Catherine W, Bishop P, Sullivan K.

Toxicol Sci. 2011 Jun 3. [Epub ahead of print]

2.

Low-dose effects and biphasic effect profiles: Is trenbolone a genotoxicant?

Boettcher M, Kosmehl T, Braunbeck T.

Mutat Res. 2011 May 20. [Epub ahead of print]

3.

Effects of progesterone on sperm motility in fathead minnow (*Pimephales promelas*).

Murack PJ, Parrish J, Barry TP.

Aquat Toxicol. 2011 Apr 15;104(1-2):121-125. [Epub ahead of print]

4.

Analysis of environmental endocrine disrupting activities in wastewater treatment plant effluents using recombinant yeast assays incorporated with exogenous metabolic activation system.

Li J, Chen M, Wang Z, Ma M, Peng X.

Biomed Environ Sci. 2011 Apr;24(2):132-9.

5.

Pendrin mediates uptake of perchlorate in a mammalian in vitro system.

Attanasio R, Scinicariello F, Blount BC, Valentin-Blasini L, Rogers KA, Nguyen DC, Murray HE.

Chemosphere. 2011 May 6. [Epub ahead of print]

6.

Endocrine disrupting activities in sewage effluent and river water determined by chemical analysis and in vitro assay in the context of granular activated carbon upgrade.

Grover DP, Balaam J, Pacitto S, Readman JW, White S, Zhou JL.
Chemosphere. 2011 May 3. [Epub ahead of print]

7.

The OBELIX project: early life exposure to endocrine disruptors and obesity.

Legler J, Hamers T, van Eck van der Sluijs-van de Bor M, Schoeters G, van der Ven L, Eggesbo M, Koppe J, Feinberg M, Trnovec T.

Am J Clin Nutr. 2011 May 4. [Epub ahead of print]

8.

[Endocrine disruptors: hormone-active chemicals from the environment: a risk to humans?]

Klingmüller D, Alléra A.

Dtsch Med Wochenschr. 2011 May;136(18):967-972. Epub 2011 Apr 27. German.

9.

In vitro fluorescence displacement investigation of thyroxine transport disruption by bisphenol A.

Cao J, Guo LH, Wan B, Wei Y.

J Environ Sci (China). 2011;23(2):315-21.

10.

Estrogen-related receptor gamma disruption of source water and drinking water treatment processes extracts.

Li N, Jiang W, Rao K, Ma M, Wang Z, Kumaran SS.

J Environ Sci (China). 2011;23(2):301-6.

11.

Methoxychlor reduces estradiol levels by altering steroidogenesis and metabolism in mouse antral follicles in vitro.

Basavarajappa MS, Craig ZR, Hernández-Ochoa I, Paulose T, Leslie TC, Flaws JA.

Toxicol Appl Pharmacol. 2011 Jun 15;253(3):161-9. Epub 2011 Apr 14.

12.

Are cadmium and other heavy metal compounds acting as endocrine disrupters?

Kortenkamp A.

Met Ions Life Sci. 2011;8:305-17.

13.

Assessing oestrogenic effects of brominated flame retardants hexabromocyclododecane and tetrabromobisphenol A on MCF-7 cells.

Dorosh A, Děd L, Elzeinová F, Pěkníková J.

Folia Biol (Praha). 2011;57(1):35-9.

14.

The consequences of feminization in breeding groups of wild fish.

Harris CA, Hamilton PB, Runnalls TJ, Vinciotti V, Henshaw A, Hodgson D, Coe TS, Jobling S, Tyler CR, Sumpter JP.

Environ Health Perspect. 2011 Mar;119(3):306-11.

15.
Polar compounds dominate in vitro effects of sediment extracts.
Lübcke-von Varel U, Machala M, Ciganek M, Neca J, Pencikova K, Palkova L, Vondracek J, Löffler I, Streck G, Reifferscheid G, Flückiger-Isler S, Weiss JM, Lamoree M, Brack W.
Environ Sci Technol. 2011 Mar 15;45(6):2384-90. Epub 2011 Feb 24.
16.
Specific in vitro toxicity of crude and refined petroleum products: 3. Estrogenic responses in mammalian assays.
Vrabie CM, Candido A, van den Berg H, Murk AJ, van Duursen MB, Jonker MT.
Environ Toxicol Chem. 2011 Apr;30(4):973-80. doi: 10.1002/etc.463. Epub 2011 Feb 18.
17.
The OECD validation program of the H295R steroidogenesis assay: Phase 3. Final inter-laboratory validation study.
Hecker M, Hollert H, Cooper R, Vinggaard AM, Akahori Y, Murphy M, Nellemann C, Higley E, Newsted J, Laskey J, Buckalew A, Grund S, Maletz S, Giesy J, Timm G.
Environ Sci Pollut Res Int. 2011 Mar;18(3):503-15. Epub 2010 Oct 3.
18.
Detection of thyroid hormone receptor disruptors by a novel stable in vitro reporter gene assay.
Freitas J, Cano P, Craig-Veit C, Goodson ML, Furlow JD, Murk AJ.
Toxicol In Vitro. 2011 Feb;25(1):257-66. Epub 2010 Aug 21.
19.
Effects of cigarette smoking on reproduction.
Dechanet C, Anahory T, Mathieu Daude JC, Quantin X, Reyftmann L, Hamamah S, Hedon B, Dechaud H.
Hum Reprod Update. 2011 Jan-Feb;17(1):76-95. Epub 2010 Aug 4. Review.
21.
Parabens in urine, serum and seminal plasma from healthy Danish men determined by liquid chromatography-tandem mass spectrometry (LC-MS/MS).
Frederiksen H, Jørgensen N, Andersson AM.
J Expo Sci Environ Epidemiol. 2011 May-Jun;21(3):262-71. Epub 2010 Mar 10.
22.
The role of oxidative stress in enantiomer-specific, bifenthrin-induced cytotoxicity in PC12 cells.
Lu X, Hu F, Ma Y, Wang C, Zhang Y, Zhao M.
Environ Toxicol. 2011 Jun;26(3):271-8. doi: 10.1002/tox.20553.
23.
Antiestrogenicity and estrogenicity in leachates from solid waste deposits.

Svenson A, Sjöholm S, Allard AS, Kaj L.
Environ Toxicol. 2011 Jun;26(3):233-9. doi: 10.1002/tox.20549.

Herudover er der yderligere en artikel, som ikke blev fanget af de valgte søgekriterier
Peroxisome Proliferator-Activated Receptor γ is a Target for Halogenated Analogues of Bisphenol-A.
Riu A, Grimaldi M, le Maire A, Bey G, Phillips K, Boulahtouf A, Perdu E, Zalko D, Bourguet W, Balaguer P.
Environ Health Perspect. 2011 May 11. [Epub ahead of print]

In Vivo studier ved DTU - FOOD

Søgning er udført på PubMed og dækker perioden 1/4/2011-23/6

(april – Juni 2011)

Følgende søgeprofil er benyttet: "(endocrine disrupt*) AND utero* AND (rat OR mice OR mammal*)" samt "(endocrine disrupt*) AND (rat OR mice OR mammal*)". Derudover er der også søgt på "Paraben* AND in vivo*"

Efter at have fjernet genganger fra dem vi havde med på den forrige litteraturopdateringsliste, gav litteratursøgningen tilsammen en liste med i alt 29 artikler: (Bruttolisten):

De udvalgte studier har fokus på BPA og Triclosan (den sidste vises kun abstract).

Ud fra bruttolisten (se længere nede i dokumentet) er udvalgt følgende 2 artikler til engelsk abstrakt og dansk resume og kommentarer:

Udvalgte publikationer in vivo:

Disruption of adult expression of sexually selected traits by developmental exposure to bisphenol A
Eldin Jašarević, Paizlee T. Sieli, Erin E. Twellman, Thomas H. Welsh, Jr, Todd R. Schachtman, R. Michael Roberts, David C. Geary, and Cheryl S. Rosenfeld.

PNAS. 2011 Jun www.pnas.org/cgi/doi/10.1073/pnas.1107958108

Abstract

Exposure to endocrine disrupting compounds (EDCs), such as bisphenol A (BPA), may cause adverse health effects in wildlife and humans, but controversy remains as to what traits are most sensitive to EDCs and might serve as barometers of exposure. Expression of sexually selected traits that have evolved through intrasexual competition for mates and intersexual choice of mating partner are more dependent on developmental and physical condition of an animal than naturally selected traits and thus might be particularly vulnerable to disruption by developmental exposure to EDCs. We have used the deer mouse (*Peromyscus maniculatus*) as a model to test this hypothesis. Adult male–male competition for mates in this species is supported by enhanced spatial navigational and exploratory abilities, which enable males to search for prospective, widely dispersed females. Male deer mice exposed to BPA or ethinyl estradiol (EE) through maternal diet showed no changes in external phenotype, sensory development, or adult circulating concentrations of testosterone and corticosterone, but spatial learning abilities and exploratory behaviors were severely compromised compared with control males. Because these traits are not sexually selected in females, BPA exposure predictably had no effect, although EE-exposed females demonstrated enhanced spatial navigational abilities. Both BPA-exposed and control females preferred control males to BPA-exposed males. Our demonstration that developmental exposure to BPA compromises cognitive abilities and behaviors essential for males to reproduce successfully has broad implications for other species, including our own. Thus, sexually selected traits might provide useful biomarkers to assess risk of environmental contamination in animal and human populations.

Comparison of Serum Bisphenol A Concentrations in Mice Exposed to Bisphenol A through the Diet Versus Oral Bolus Exposure

Sieli PT, Jašarević E, Warzak DA, Mao J, Eilersieck MR, Liao C, Kannan K, Collet SH, Toutain PL, Vom Saal FS, Rosenfeld CS.

Environ Health Perspect. 2011 Jun 6. [Epub ahead of print]

Abstract

Background: Bisphenol A (BPA) is a widely produced endocrine disrupting chemical. Diet is a

primary route of exposure, but internal exposure (serum concentrations) in animals and humans have only been measured after single oral bolus administration.

Objective: We compared serum concentrations of BPA over a 24 h time period after oral bolus administration or *ad libitum* feeding in mice and assessed for build-up with dietary exposure.

Methods: Adult female mice were administered BPA-*d6* as a single oral bolus (20 mg/kg BW) or fed a diet with 100 mg BPA-*d6*/kg feed weight *ad libitum* for one week. Serum concentrations were analyzed by using isotope dilution LC/MS/MS and compared between exposure groups over the first 23h and after 7 days of dietary exposure.

Results: Maximum concentration (C_{max}) for BPA-*d6* during the first 24 h was reached at 1 h and 6 h for oral bolus and diet groups, respectively. Relative BPA-*d6* bioavailability (unconjugated BPA-*d6*) was higher in diet exposed mice than the bolus group despite a relative lower absorption, a phenomenon consistent with an inhibitory effect of food on first pass hepatic metabolism. In mice with ongoing dietary exposure, unconjugated BPA-*d6* was higher on day 7 than day 1.

Conclusions: This is the first report of serum BPA concentrations in an animal model exposed to this chemical via the diet. While bolus administration of BPA-*d6* led to peak concentrations within 1 h, C_{max} for diet-exposed mice was delayed for several hours. However, bolus administration underestimates bioavailable serum BPA concentrations in animals and therefore, presumably humans than would result from dietary exposure. Exposure via diet is a more natural continuous exposure route than oral bolus exposure, and thus, a better predictor of BPA concentrations in chronically exposed animals and humans.

Triclosan: environmental exposure, toxicity and mechanisms of action.

Andrea B. Dann and Alice Hontela

J Appl Toxicol. 2011 May;31(4):285-311. doi: 10.1002/jat.1660.

ABSTRACT: Triclosan [5-chloro- 2- (2,4- dichlorophenoxy)phenol; TCS] is a broad spectrum antibacterial agent used in personal care, veterinary, industrial and household products. TCS is commonly detected in aquatic ecosystems, as it is only partially removed during the wastewater treatment process. Sorption, biodegradation and photolytic degradation mitigate the availability of TCS to aquatic biota; however the by-products such as methyltriclosan and other chlorinated phenols may be more resistant to degradation and have higher toxicity than the parent compound. The continuous exposures of aquatic organisms to TCS, coupled with its bioaccumulation potential, have led to detectable levels of the antimicrobial in a number of aquatic species. TCS has been also detected in breast milk, urine and plasma, with levels of TCS in the blood correlating with consumer use patterns of the antimicrobial. Mammalian systemic toxicity studies indicate that TCS is neither acutely toxic, mutagenic, carcinogenic, nor a developmental toxicant. Recently, however, concern has been raised over TCS's potential for endocrine disruption, as the antimicrobial has been shown to disrupt thyroid hormone homeostasis and possibly the reproductive axis. Moreover, there is strong evidence that aquatic species such as algae, invertebrates and certain types of fish are much more sensitive to TCS than mammals. TCS is highly toxic to algae and exerts reproductive and developmental effects in some fish. The potential for endocrine disruption and antibiotic cross-resistance highlights the importance of the judicious use of TCS, whereby the use of TCS should be limited to applications where it has been shown to be effective.

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Developmental Exposure to Di(2-ethylhexyl) Phthalate Impairs Endocrine Pancreas and Leads to Long-term Adverse Effects on Glucose Homeostasis in the Rat.
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2.
Measurement of bisphenol A, bisphenol A β -D: -glucuronide, genistein, and genistein 4'- β -D: -glucuronide via SPE and HPLC-MS/MS.
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Triclosan: environmental exposure, toxicity and mechanisms of action.

Andrea B. Dann and Alice Hontela

J Appl Toxicol. 2011 May;31(4):285-311. doi: 10.1002/jat.1660. **(abstract vises)**

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Peripubertal exposure to low doses of tributyltin chloride affects the homeostasis of serum T, E2, LH, and body weight of male mice.

Si J, Wu X, Wan C, Zeng T, Zhang M, Xie K, Li J.

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Herudover er der yderligere en artikel, som ikke blev fanget af de valgte søgekriterier

Disruption of adult expression of sexually selected traits by developmental exposure to bisphenol A
Eldin Jašarević, Paizlee T. Sieli, Erin E. Twellman, Thomas H. Welsh, Jr, Todd R. Schachtman, R.
Michael Roberts, David C. Geary, and Cheryl S. Rosenfeld. (denne er udvalgt)

PNAS. 2011 Jun www.pnas.org/cgi/doi/10.1073/pnas.1107958108

Søgningen er udført på Web of Science og dækker perioden 27/3 2011 – 27/6 2011.

Søgeprofilen kombinerer: Endocrine disrupt* og Fish*
Amphibia*
Bird* OR Avia*
Invertebrat*
Mollus*
Gastropod*
Insect*
Crustacea*
Echinoderm*
Ursus
Reptil* OR Alligator
Whal* OR seal OR dolphin

Fra bruttolisten (længere nede i dokumentet) er udvalgt 3 artikler til medtagelse af abstract og yderligere kommentarer.

Artikel 1:

Title: [Evidence suggesting that di-n-butyl phthalate has antiandrogenic effects in fish](#)

Author(s): Aoki KAA, Harris CA, Katsiadaki I, et al.

Source: ENVIRONMENTAL TOXICOLOGY AND CHEMISTRY Volume: 30 Issue: 6 Pages: 1338-1345

Abstract: Phthalate ester plasticizers are antiandrogenic in mammals. High doses of certain phthalates consistently interfere with the normal development of male offspring exposed in utero, causing disrupted sperm production, abnormal development of the genitalia, and in some cases infertility. In the environment, phthalates are considered ubiquitous and are commonly measured in aquatic ecosystems at low nanograms to micrograms per liter concentrations. Given the similarity between mammalian and teleost endocrine systems, phthalate esters may be able to cause antiandrogenic endocrine disruption in fish in the wild. In the present study, adult male three-spined sticklebacks (*Gasterosteus aculeatus*; n = 8) were exposed to di-n-butyl phthalate (DBP; 0, 15, and 35 µg DBP/L) for 22 d and analyzed for changes in nesting behavior, plasma androgen concentrations, spiggin concentrations, and steroidogenic gene expression. Plasma testosterone concentrations were significantly higher in males from the 35 µg DBP/L group compared with the solvent control, whereas plasma 11-ketotestosterone concentrations were not significantly affected. Expression of steroid acute regulatory protein and 3 beta-hydroxysteroid dehydrogenase remained unchanged. Spiggin concentrations were significantly lower in the males exposed to 35 µg DBP/L. Nest building appeared to be slower in some males exposed to DBP, but this was not statistically significant. These results suggest that DBP has antiandrogenic effects in fish. However, further research is required to firmly establish the consequences of chronic DBP exposure in fish.

Artikel 2:

Title: Endocrine-disrupting [effects of spironolactone in female western mosquitofish, *Gambusia affinis*](#)

Author(s): Raut SA, Howell WM, Angus RA

Source: ENVIRONMENTAL TOXICOLOGY AND CHEMISTRY Volume: 30 Issue: 6 Pages: 1376-1382

Abstract: The discovery of pharmaceuticals in effluent from wastewater treatment plants and drug manufacturing facilities and in receiving waters has raised environmental concern. Because these compounds are ending up in the environment, it is important to investigate the effects of these compounds on wildlife as well as humans. The present study used a fish model to investigate the endocrine-disrupting effects of spironolactone (SPL), an aldosterone antagonist used as a diuretic, but which also exhibits antiandrogenic effects in humans. A dose-response study measured the effects of SPL on anal fin ray elongation, an androgen-dependent secondary sex trait, and expression of the vitellogenin gene, an estrogen-dependent trait, in female western mosquitofish, *Gambusia affinis*. Fish were exposed to SPL in the water for 35 d at four nominal concentrations: 10, 100, 250, and 500 nM (4.2, 41.7, 104.1, and 208.3 µg/L, respectively) via the static renewal method. Masculinization of females, as evidenced by development of an

elongated and modified anal fin, was observed in the fish exposed to the three highest concentrations. Anal fin elongation was observed in the group exposed to the lowest SPL concentration, but without the development of a tip apparatus. These results confirm the results of a preliminary study that, in contrast to antiandrogenic effects seen in humans, SPL has androgenic and/or antiestrogenic activity in a fish.

Artikel 3:

Title: [Survival, development, and gonadal differentiation in *Rana dalmatina* chronically exposed to chlorpyrifos](#)

Author(s): Bernabo I, Gallo L, Sperone E, et al.

Source: JOURNAL OF EXPERIMENTAL ZOOLOGY PART A-ECOLOGICAL GENETICS AND PHYSIOLOGY

Volume: 315A Issue: 5 Pages: 314-327

Abstract: Chlorpyrifos is an organophosphate pesticide among the most widely used in the world, which is suspected to be an endocrine-disrupting compound. To determine the capacity of chlorpyrifos to affect gonadal differentiation in *Rana dalmatina*, tadpoles were exposed to this pesticide during larval development until completion of metamorphosis at ecologically relevant concentrations (0.025 and 0.05 mg/L). No effects of chlorpyrifos exposure on survival, development, or meta morphosis were observed. After a 1 month metamorphosis, the gonadal phenotype was determined by gross morphology and histological examination. Morphological and histological analysis revealed normal ovaries or testes in froglets belonging to control group, whereas testes from several froglets exposed to chlorpyrifos were interspersed with testicular oocytes in histological sections. Chlorpyrifos exposure during the entire larval period did not affect sex ratio, but reduced the percentage of males with histologically normal testes. The findings suggest that chlorpyrifos exposure has significant effects on gonadal differentiation in some animals by inducing an intersex condition and alterations to testicular morphology, and that *R. dalmatina* is sensitive to endocrine disruption. Thereby, this study provides evidence that the ecologically relevant concentrations of chlorpyrifos, although not adversely affect the survival, development, or metamorphosis, may interfere with sex differentiation and reproductive development of *R. dalmatina* via endocrine-disrupting mechanisms.

Bruttoliste:

Title: [Triclosan: environmental exposure, toxicity and mechanisms of action](#)

Author(s): Dann AB, Hontela A

Source: JOURNAL OF APPLIED TOXICOLOGY Volume: 31 Issue: 4 Pages: 285-311

Title: [Use of sex ratio of bream \(*Abramis brama* L.\) as an indicator of endocrine effects: Results from the German Environmental Specimen Bank](#)

Author(s): Teubner D, Tarricone K, Veith M, et al.

Source: ECOLOGICAL INDICATORS Volume: 11 Issue: 5 Pages: 1487-1489

Title: [Apparent rapid loss of endocrine disruptors from wetlands used to store either tertiary treated sewage effluent or stormwater runoff](#)

Author(s): Norris A, Burgin S

Source: WATER AIR AND SOIL POLLUTION Volume: 219 Issue: 1-4 Pages: 285-295

Title: [Occurrence of sexual hormones in sediments of mangrove in Brazil](#)

Author(s): Froehner S, Machado KS, Stefen E, et al.

Source: WATER AIR AND SOIL POLLUTION Volume: 219 Issue: 1-4 Pages: 591-599

Title: [Ontogenetic causes and mechanisms for formation of differences in number of fish scales](#)

Author(s): Levin BA

Source: RUSSIAN JOURNAL OF DEVELOPMENTAL BIOLOGY Volume: 42 Issue: 3 Pages: 186-191

Title: [Identification of a beta\(1\) integrin isoform with restricted tissue expression in a teleost fish](#)

Author(s): Castillo-Briceno P, Cabas I, Arizcun M, et al.

Source: REPRODUCTION FERTILITY AND DEVELOPMENT Volume: 23 Issue: 5 Pages: 654-664

- Title: [Genotoxic effects in erythrocytes of *Oreochromis niloticus* exposed to nanograms-per-liter concentration of 17 beta-estradiol \(e-2\): an assessment using micronucleus test and comet assay](#)
Author(s): Sponchiado G, Reynaldo EMFD, de Andrade ACB, et al.
Source: WATER AIR AND SOIL POLLUTION Volume: 218 Issue: 1-4 Pages: 353-360
- Title: [Evidence suggesting that di-n-butyl phthalate has antiandrogenic effects in fish](#)
Author(s): Aoki KAA, Harris CA, Katsiadaki I, et al.
Source: ENVIRONMENTAL TOXICOLOGY AND CHEMISTRY Volume: 30 Issue: 6 Pages: 1338-1345
- Title: Endocrine-disrupting [effects of spironolactone in female western mosquitofish, *Gambusia affinis*](#)
Author(s): Raut SA, Howell WM, Angus RA
Source: ENVIRONMENTAL TOXICOLOGY AND CHEMISTRY Volume: 30 Issue: 6 Pages: 1376-1382
- Title: [Chronic perchlorate exposure causes morphological abnormalities in developing stickleback](#)
Author(s): Bernhardt RR, von Hippel FA, O'Hara TM
Source: ENVIRONMENTAL TOXICOLOGY AND CHEMISTRY Volume: 30 Issue: 6 Pages: 1468-1478
- Title: [beta-Blockers as endocrine disruptors: The potential effects of human beta-blockers on aquatic organisms](#)
Author(s): Massarsky A, Trudeau VL, Moon TW
Source: JOURNAL OF EXPERIMENTAL ZOOLOGY PART A-ECOLOGICAL GENETICS AND PHYSIOLOGY Volume: 315A Issue: 5 Pages: 251-265
- Title: [Are toxicological responses in laboratory \(inbred\) zebrafish representative of those in outbred \(wild\) populations? - a case study with an endocrine disrupting chemical](#)
Author(s): Brown AR, Bickley LK, Le Page G, et al.
Source: ENVIRONMENTAL SCIENCE & TECHNOLOGY Volume: 45 Issue: 9 Pages: 4166-4172
- Title: [Daphnia response to biotic stress is modified by PCBs](#)
Author(s): Bernatowicz P, Pijanowska J
Source: ECOTOXICOLOGY AND ENVIRONMENTAL SAFETY Volume: 74 Issue: 4 Pages: 711-718
- Title: [Elucidating the mechanism of action of tributyltin \(TBT\) in zebrafish](#)
Author(s): McGinnis CL, Crivello JF
Source: AQUATIC TOXICOLOGY Volume: 103 Issue: 1-2 Pages: 25-31
- Title: [Cadmium-mediated disruption of cortisol biosynthesis involves suppression of corticosteroidogenic genes in rainbow trout](#)
Author(s): Sandhu N, Vijayan MM
Source: AQUATIC TOXICOLOGY Volume: 103 Issue: 1-2 Pages: 92-100
- Title: [Ontogenetic expression and 17 beta-estradiol regulation of immune-related genes in early life stages of Japanese medaka \(*Oryzias latipes*\)](#)
Author(s): Sun LW, Shao XL, Wu YD, et al.
Source: FISH & SHELLFISH IMMUNOLOGY Volume: 30 Issue: 4-5 Pages: 1131-1137
- Title: [Effect of 4-nonylphenol on the sperm dynamic parameters, morphology and fertilization rate of *Bufo raddei*](#)
Author(s): Feng MY, Chen P, Wei X, et al.
Source: AFRICAN JOURNAL OF BIOTECHNOLOGY Volume: 10 Issue: 14 Pages: 2698-2707
- Title: [Estrogenic activity of tropical fish food can alter baseline vitellogenin concentrations in male fathead minnow \(*Pimephales promelas*\)](#)
Author(s): Beresford N, Brian JV, Runnalls TJ, et al.
Source: ENVIRONMENTAL TOXICOLOGY AND CHEMISTRY Volume: 30 Issue: 5 Pages: 1139-1145
- Title: [Proteomics in aquatic amphipods: can it be used to determine mechanisms of toxicity and interspecies responses after exposure to atrazine?](#)

Author(s): Ralston-Hooper KJ, Sanchez BC, Adamec J, et al.
Source: ENVIRONMENTAL TOXICOLOGY AND CHEMISTRY Volume: 30 Issue: 5 Pages: 1197-1203

Title: [A method for the determination of genetic sex in the fathead minnow, *Pimephales promelas*, to support testing of endocrine-active chemicals](#)

Author(s): Olmstead AW, Villeneuve DL, Ankley GT, et al.
Source: ENVIRONMENTAL SCIENCE & TECHNOLOGY Volume: 45 Issue: 7 Pages: 3090-3095

Title: [Transcriptional responses in the brain, liver and gonad of Japanese ricefish \(*Oryzias latipes*\) exposed to two anti-estrogens](#)

Author(s): Sun LW, Shao XL, Chi JA, et al.
Source: COMPARATIVE BIOCHEMISTRY AND PHYSIOLOGY C-TOXICOLOGY & PHARMACOLOGY
Volume: 153 Issue: 4 Pages: 392-401

Title: [Effects of the UV-filter 2-ethyl-hexyl-4-trimethoxycinnamate \(EHMC\) on expression of genes involved in hormonal pathways in fathead minnows \(*Pimephales promelas*\) and link to vitellogenin induction and histology](#)

Author(s): Christen V, Zucchi S, Fent K
Source: AQUATIC TOXICOLOGY Volume: 102 Issue: 3-4 Pages: 167-176

Title: [Natural mixtures of POPs affected body weight gain and induced transcription of genes involved in weight regulation and insulin signaling](#)

Author(s): Lyche JL, Nourizadeh-Lillabadi R, Karlsson C, et al.
Source: AQUATIC TOXICOLOGY Volume: 102 Issue: 3-4 Pages: 197-204

Title: [A transcriptomics-based biological framework for studying mechanisms of endocrine disruption in small fish species \(vol 98, pg 230, 2010\)](#)

Author(s): Wang RL, Bencic D, Villeneuve DL, et al.
Source: AQUATIC TOXICOLOGY Volume: 102 Issue: 3-4 Pages: 232-235

Title: [Endpoint sensitivity in fish endocrine disruption assays: Regulatory implications](#)

Author(s): Dang ZC, Li K, Yin HW, et al.
Source: TOXICOLOGY LETTERS Volume: 202 Issue: 1 Pages: 36-46

Title: [Quantification of 2-hydrazinopyridine derivatized steroid hormones in fathead minnow \(*Pimephales promelas*\) blood plasma using LC-ESI+/MS/MS](#)

Author(s): Hala D, Overturf MD, Petersen LH, et al.
Source: JOURNAL OF CHROMATOGRAPHY B-ANALYTICAL TECHNOLOGIES IN THE BIOMEDICAL AND LIFE SCIENCES Volume: 879 Issue: 9-10 Pages: 591-598

Title: Disrupted [stress endocrine axis in wild fish from polluted california marine environments. characterization studies](#)

Author(s): Causey DR, Reyes JA, Waggoner CM, et al.
Conference Information: Annual Meeting of the Society-for-Integrative-and-Comparative-Biology, JAN 03-07, 2011 Salt Lake City, UT
Source: INTEGRATIVE AND COMPARATIVE BIOLOGY Volume: 51 Pages: E22-E22 Supplement: Suppl. 1

Title: [Health risk characterisation for environmental pollutants with a new concept of overall risk probability](#)

Author(s): Cao QM, Yu QM, Connell DW
Source: JOURNAL OF HAZARDOUS MATERIALS Volume: 187 Issue: 1-3 Pages: 480-487

Title: [Effects of estrogens and antiestrogens on gene expression of fathead minnow \(*Pimephales promelas*\) early life stages](#)

Author(s): Johns SM, Denslow ND, Kane MD, et al.
Source: ENVIRONMENTAL TOXICOLOGY Volume: 26 Issue: 2 Pages: 195-206

Title: [Fate and developmental effects of dietary uptake of methylmercury in *Silurana tropicalis* tadpoles](#)

Author(s): Davidson MA, Croteau MC, Millar CS, et al.

Source: JOURNAL OF TOXICOLOGY AND ENVIRONMENTAL HEALTH-PART A-CURRENT ISSUES
Volume: 74 Issue: 6 Pages: 364-379

Title: [Simultaneous determination of several natural steroids in blood plasma from perch \(*Perca fluviatilis*\) by GC-HRMS](#)

Author(s): Widell B, Noaksson E, Balk L, et al.

Source: INTERNATIONAL JOURNAL OF ENVIRONMENTAL ANALYTICAL CHEMISTRY Volume: 91
Issue: 4 Pages: 303-318

Title: [Effects of triclocarban, triclosan, and methyl triclosan on thyroid hormone action and stress in frog and mammalian culture systems](#)

Author(s): Hinthner A, Bromba CM, Wulff JE, et al.

Source: ENVIRONMENTAL SCIENCE & TECHNOLOGY Volume: 45 Issue: 12 Pages: 5395-5402

Title: [Survival, development, and gonadal differentiation in rana dalmatina chronically exposed to chlorpyrifos](#)

Author(s): Bernabo I, Gallo L, Sperone E, et al.

Source: JOURNAL OF EXPERIMENTAL ZOOLOGY PART A-ECOLOGICAL GENETICS AND PHYSIOLOGY Volume: 315A Issue: 5 Pages: 314-327

Title: [Agricultural intensity in ovo affects growth, metamorphic development and sexual differentiation in the Common toad \(*Bufo bufo*\)](#)

Author(s): Orton F, Routledge E

Source: ECOTOXICOLOGY Volume: 20 Issue: 4 Pages: 901-911

Title: [Effect of 4-nonylphenol on the sperm dynamic parameters, morphology and fertilization rate of *Bufo raddei*](#)

Author(s): Feng MY, Chen P, Wei X, et al.

Source: AFRICAN JOURNAL OF BIOTECHNOLOGY Volume: 10 Issue: 14 Pages: 2698-2707

Title: [Intersex frogs concentrated in suburban and urban landscapes](#)

Author(s): Skelly DK, Bolden SR, Dion KB

Source: ECOHEALTH Volume: 7 Issue: 3 Pages: 374-379

Title: [Effect of low dose exposure to the herbicide atrazine and its metabolite on cytochrome P450 aromatase and steroidogenic factor-1 mRNA levels in the brain of premetamorphic bullfrog tadpoles \(*Rana catesbeiana*\)](#)

Author(s): Gunderson MP, Veldhoen N, Skirrow RC, et al.

Source: AQUATIC TOXICOLOGY Volume: 102 Issue: 1-2 Pages: 31-38

Title: [Altered pairing behaviour and reproductive success in white ibises exposed to environmentally relevant concentrations of methylmercury](#)

Author(s): Frederick P, Jayasena N

Source: PROCEEDINGS OF THE ROYAL SOCIETY B-BIOLOGICAL SCIENCES Volume: 278 Issue: 1713 Pages: 1851-1857

Title: [Pollutants affect development in nestling starlings *Sturnus vulgaris*](#)

Author(s): Markman S, Muller CT, Pascoe D, et al.

Source: JOURNAL OF APPLIED ECOLOGY Volume: 48 Issue: 2 Pages: 391-397

Title: [Global trends and diversity in pentachlorophenol levels in the environment and in humans: a meta-analysis](#)

Author(s): Zheng WW, Wang X, Yu H, et al.

Source: ENVIRONMENTAL SCIENCE & TECHNOLOGY Volume: 45 Issue: 11 Pages: 4668-4675

Title: [Anthropogenic organic contaminants in water, sediments and benthic organisms of the mangrove-fringed Segara Anakan Lagoon, Java, Indonesia](#)

Author(s): Dsikowitzky L, Nordhaus I, Jennerjahn TC, et al.

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Title: [Endocrine disrupting effects, at different temperatures, on *Moina micrura* \(Cladocera: Crustacea\) induced by carbendazim, a fungicide](#)

Author(s): Miracle MR, Nandini S, Sarma SSS, et al.

Source: HYDROBIOLOGIA Volume: 668 Issue: 1 Pages: 155-170

Title: [Potential mechanisms of phthalate ester embryotoxicity in the abalone *Haliotis diversicolor supertexta*](#)

Author(s): Zhou J, Cai ZH, Xing KZ

Source: ENVIRONMENTAL POLLUTION Volume: 159 Issue: 5 Special Issue: Sp. Iss. SI Pages: 1114-1122

Title: [Organotin pollution at Arraial do Cabo, Rio de Janeiro state, Brazil: Increasing levels after the TBT ban](#)

Author(s): Toste R, Fernandez MA, Pessoa ID, et al.

Source: BRAZILIAN JOURNAL OF OCEANOGRAPHY Volume: 59 Issue: 1 Pages: 111-117

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