Center for Hormonforstyrrende Stoffer

Litteraturgennemgang for perioden 1/10 2011 - 16/12 2011

Humane studier ved Afd for Vækst og Reproduktion, Rigshospitalet

Søgning er udført på PubMed og dækker perioden 1/10/2011 - 15/12/2011

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

Det er efterhånden vores erfaring at termen (endocrine disrupt*) medfører at en række relevante studier ikke bliver fundet. I praksis erstattes (endocrine disrupt*) derfor med:

(perfluor*)
(bishenol A)
(phthalat*)
(paraben*)
(flame retardant*)

Vi er opmærksomme på at vi derved kun søger efter disse specifikke grupper.

(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 mere end 120 artikler via denne søgning. I alt er 9 artikler, hvoraf 1 omhandler phthalater, 4 bisphenol A, 2 perfluorerede forbindelser, og 2 kliniske studier af TDS forekomst, inkluderet med abstract.

Eur J Endocrinol. 2011 Oct;165(4):579-87. Epub 2011 Jul 25.
'Idiopathic' partial androgen insensitivity syndrome in 28 newborn and infant males: impact of prenatal exposure to environmental endocrine disruptor chemicals?
Gaspari L, Paris F, Philibert P, Audran F, Orsini M, Servant N, Maïmoun L, Kalfa N, Sultan C.
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OBJECTIVE: 46,XY disorders of sex differentiation (46,XY DSD) can be due to a testis determination defect, an androgen biosynthesis defect, or androgen resistance (complete or partial androgen insensitivity syndrome (PAIS), or 5α reductase deficiency). We aimed to evaluate the impact of a prenatal contamination by environmental xenoestrogens in 'idiopathic' PAIS-like phenotype.
SUBJECTS: We investigated 28 newborn/infant males with 46,XY DSD, normal androgen production, and no androgen receptor or steroid-5αR type II enzyme (SRD5A2) gene mutations.
METHODS: To exclude other genetic defects, we sequenced the steroidogenic factor 1 (SF1) and mastermind-like domain-containing 1 (MAMLD1) genes, which were recently found to be associated with the PAIS-like phenotype. Parents were interviewed about their environmental/occupational exposure to endocrine disrupting chemicals (EDCs) before/during the patients' fetal life. Total estrogenic bioactivity of patient serum was analyzed by ultrasensitive bioassay.
RESULTS: All the patients had normal SF1 sequence and one patient showed a double polymorphism of MAMLD1. Eleven (39.3%) of the 28 patients had reported parental fetal exposure to EDCs. The mean estrogenic bioactivity in these 11 patients with fetal EDC exposure (6.65 ± 8.07 pg/ml) versus 17 cases without contamination (1.27 ± 0.34 pg/ml) and controls (1.06 ± 0.44 pg/ml; $P<0.05$) was elevated.
CONCLUSIONS: Our results indicate that the 'idiopathic' PAIS-like phenotype may in some cases be related to EDC contamination during fetal life.

Hum Reprod. 2011 Nov;26(11):3155-62. Epub 2011 Aug 25.
Prenatal environmental risk factors for genital malformations in a population of 1442 French male newborns: a nested case-control study.
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Unité d'Endocrinologie-Gynécologie Pédiatrique, Service de Pédiatrie 1, Hôpita Arnaud-de-Villeneuve, CHU Montpellier et Université Montpellier 1, 34295 Montpellier, Cedex 5, France.

BACKGROUND: Over the past decades, an increasing trend in male external genital malformations such as cryptorchidism and hypospadias has led to the suspicion that environmental chemicals are detrimental to male fetal sexual development. Several environmental pollutants, including organochlorine pesticides, polychlorinated biphenyls, bisphenol A, phthalates, dioxins and furans have estrogenic and anti-androgenic activity and are thus considered as endocrine-disrupting chemicals (EDCs). Since male sex differentiation is critically dependent on the normal production and action of androgens during fetal life, EDCs may be able to alter normal male sex differentiation.
OBJECTIVE: The objective of this study was to determine the incidence of external genital malformations in a population of full-term newborn males in southern France. We also performed a case-control study to identify the risk factors for male external genital malformations, with a focus on parental occupational exposure to EDCs.
METHODS: Over a 16-month period, 1615 full-term newborn males with a birth weight above 2500 g were registered on a level-1 maternity ward, and the same pediatrician systematically examined 1442 of them (89%) for cryptorchidism, hypospadias and micropenis. For every male newborn with genital malformation, we enrolled nearly two males matched for age, parity and term. All parents of the case and control newborns were interviewed about pregnancy aspects, personal characteristics, lifestyle and their occupational exposure to EDCs using a detailed questionnaire. RESULTS We report 39 cases of genital malformation (2.70%), with 18 cases of cryptorchidism (1.25%), 14 of hypospadias (0.97%), 5 of micropenis (0.35%) and 2 of 46,XY disorders of sexual differentiation (DSD; 0.14%). We observed a significant relationship between newborn cryptorchidism, hypospadias or micropenis and parental occupational exposure to pesticides [odds ratio (OR) = 4.41; 95% confidence interval (95% CI), 1.21-16.00]. Familial clustering for male external genital malformations (OR = 7.25; 95% CI, 0.70-74.30) and medications taken by mothers during pregnancy (OR = 5.87; 95% CI, 0.93-37.00) were associated with the risk of cryptorchidism, hypospadias and micropenis, although the association was not statistically significant.
CONCLUSIONS: Although the causes of male genital malformation are multifactorial, our data support the hypothesis that prenatal contamination by pesticides may be a potential risk factor for newborn male external genital malformation and it should thus be routinely investigated in all undervirilized newborn males.

J Clin Endocrinol Metab. 2011 Nov 16. [Epub ahead of print]

Urinary Bisphenol A (BPA) Concentration Associates with Obesity and Insulin Resistance.

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Context:Bisphenol A (BPA) is one of the world's highest-volume chemicals in use today. Previous studies have suggested BPA disturbs body weight regulation and promotes obesity and insulin resistance. But epidemiological data in humans were limited.Objective:Our objective was to determine whether BPA associates with obesity and insulin resistance.Design, Setting, and Participants:This cross-sectional study included 3390 adults aged 40 yr or older, in Songnan Community, Baoshan District, Shanghai, China.Main Outcome Measures:Questionnaire, clinical and biochemical measurements, and urinary BPA concentration were determined. Generalized overweight was defined as body mass index (BMI) of 24 to less than 28 kg/m(2) and obesity was defined as BMI of 28 kg/m(2) or higher. Abdominal obesity was defined as waist circumference at least 90 cm for men and at least 85 cm for women. Insulin resistance was defined as the index of homeostasis model assessment of insulin resistance higher than 2.50.Results:The participants in the highest quartile of BPA had the highest prevalence of generalized obesity [odds ratio (OR) = 1.50; 95% confidence interval (CI) = 1.15-1.97], abdominal obesity (OR = 1.28; 95% CI = 1.03-1.60), and insulin resistance (OR = 1.37; 95% CI = 1.06-1.77). In participants with BMI under 24 kg/m(2), compared with the lowest quartile, the highest quartile of BPA increased the prevalence

of insulin resistance by 94% (OR = 1.94; 95% CI = 1.20-3.14), but this association was not observed in those with BMI of 24 kg/m(2) or higher.Conclusions:BPA was positively associated with generalized obesity, abdominal obesity, and insulin resistance in middle-aged and elderly Chinese adults.

PLoS One. 2011;6(10):e26868. Epub 2011 Oct 26.
Urinary bisphenol A and type-2 diabetes in U.S. adults: data from NHANES 2003-2008.
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OBJECTIVE: Bisphenol A (BPA) is found in plastics and other consumer products; exposure may lead to insulin resistance and development of type-2 diabetes mellitus (T2DM) through over-activation of pancreatic β-cells. Previous studies using data from the National Health and Nutrition Examination Survey (NHANES) showed an inconsistent association between prevalence of self-reported T2DM and urinary BPA. We used a different diagnosis method of T2DM (hemoglobin A1c (HbA1c)) with a larger subset of NHANES.
METHODS AND FINDINGS: We analyzed data from 4,389 adult participants who were part of a sub-study of environmental phenol measurements in urine from three NHANES cycles from 2003 to 2008. T2DM was defined as having a HbA1c ≥ 6.5% or use of diabetes medication. The weighted prevalence of T2DM was 9.2%. Analysis of the total sample revealed that a two-fold increase in urinary BPA was associated with an odds ratio (OR) of 1.08 of T2DM (95% confidence interval (CI), 1.02 to 1.16), after controlling for potential confounders. However, when we examined each NHANES cycle individually, we only found a statistically significant association in the 2003/04 cycle (n = 1,364, OR = 1.23 (95% CI, 1.07 to 1.42) for each doubling in urinary BPA). We found no association in either the NHANES cycle from 2005/06 (n = 1,363, OR = 1.05 (95% CI, 0.94 to 1.18)); or 2007/08 (n = 1,662, OR = 1.06 (95% CI, 0.91 to 1.23)). Similar patterns of associations between BPA and continuous HbA1c were also observed.
CONCLUSIONS: Although higher urinary BPA was associated with elevated HbA1c and T2DM in the pooled analysis, it was driven by data from only one NHANES cycle. Additional studies, especially of a longitudinal design with repeated BPA measurements, are needed to further elucidate the association between BPA and T2DM.

JAMA. 2011 Nov 23;306(20):2218-20.
Canned soup consumption and urinary bisphenol A: a randomized crossover trial.
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(Eftersom der ikke er noget abstract, og den fulde tekst er overskuelig og yderst informativ, er den indsat nedenfor)

To the Editor: Human exposure to bisphenol A (BPA) is widespread.1 In adults, urinary BPA concentrations are positively associated with cardiovascular disease and diabetes.2 Exposure occurs primarily through the diet.3 Bisphenol A has been quantified in many canned goods,4,5 where it is present as a by-product of interior epoxy coatings used to prevent corrosion. We hypothesized that canned soup consumption would increase urinary BPA concentrations relative to fresh soup consumption
Methods: In 2010, we recruited Harvard School of Public Health (HSPH) student and staff volunteers (aged >18 years) via informational fliers and e-mail. The study was approved by the HSPH institutional review board. Written informed consent was obtained. We used a randomized, single-blinded, 2 × 2 crossover design. For the first 5-day period (October 25-29, 2010), one group consumed a 12-ounce serving of fresh soup (prepared without canned ingredients) daily between 12:15 and 2 PM; the other group consumed a 12-ounce serving of canned soup (from 18.5-ounce Progresso brand) per the same schedule. After a 2-day washout, treatment assignments were reversed (November 1-5, 2010). We used 5 different varieties of vegetarian soup per treatment and repeated them in the same order the following week. Participants were not restricted in their consumption of other foods. Donation of spot urine samples took place between 3 and 6 PM on the fourth and fifth days of each phase. Urine was collected in polyethylene containers and stored in polypropylene cryogenic vials. When urine was donated both days,

combined urine samples were created to minimize within-person variation. The specific gravity (SG) of the urine was measured using a handheld refractometer; total (free plus conjugated species) urinary BPA concentration was measured at the Centers for Disease Control and Prevention using online solid-phase extraction coupled to isotope dilution high-performance liquid chromatography–tandem mass spectrometry.6
Urinary BPA concentrations were adjusted for dilution by multiplying values (in μg/L) by [(1.014 − 1)/(SG − 1)]. In the absence of a period effect, we used a paired *t* test to examine mean absolute change in SG-adjusted untransformed urinary BPA concentrations (BPAcanned − BPAfresh) because differences were normally distributed, and we calculated confidence intervals for the mean using SAS version 9.2. Statistical tests were 2-sided and performed at the .05 level of significance.
Results: Of 84 volunteers, 75 (89%) completed the study. Median age was 27 years and 51 (68%) were female; median treatment adherence was 100% (Table). Bisphenol A was detected in 77% (n = 58) of samples after fresh soup consumption and 100% (n = 75) of samples after canned soup consumption. The SG-adjusted geometric mean concentration of BPA was 1.1 μg/L (95% CI, 0.9-1.4 μg/L) after fresh soup consumption (unadjusted: 0.9 μg/L; 95% CI, 0.7-1.2 μg/L) and 20.8 μg/L (95% CI, 17.9-24.1 μg/L) after canned soup consumption (unadjusted: 17.5 μg/L; 95% CI, 14.1-21.8 μg/L). Stratification by treatment sequence revealed similar values (Figure). Following canned soup consumption, SG-adjusted urinary BPA concentrations were, on average, 22.5 μg/L higher (95% CI, 19.6-25.5 μg/L) than those measured after a week of fresh soup consumption ($P < .001$), representing a 1221% increase.
Comment: Consumption of 1 serving of canned soup daily over 5 days was associated with a more than 1000% increase in urinary BPA. Generalizability is limited due to selection of participants from 1 school and testing of a single soup brand; however, generalizability to canned goods with similar BPA content is expected. The increase in urinary BPA concentrations following canned soup consumption is likely a transient peak of yet uncertain duration. The effect of such intermittent elevations in urinary BPA concentration is unknown. The absolute urinary BPA concentrations observed following canned soup consumption are among the most extreme reported in a nonoccupational setting. For comparison, the 95th percentile unadjusted urinary BPA in the 2007-2008 National Health and Examination Survey was 13.0 μg/L (95% CI, 10.0-15.4 μg/L).1 The observed increase in urinary BPA concentrations following canned soup consumption, even if not sustained, may be important, especially in light of available or proposed alternatives to epoxy resins linings for most canned goods

Pediatrics. 2011 Nov;128(5):873-82. Epub 2011 Oct 24.
Impact of early-life bisphenol A exposure on behavior and executive function in children.
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OBJECTIVES: To estimate the impact of gestational and childhood bisphenol A (BPA) exposures on behavior and executive function at 3 years of age and to determine whether child gender modified those associations.
METHODS: We used a prospective birth cohort of 244 mothers and their 3-year-old children from the greater Cincinnati, Ohio, area. We characterized gestational and childhood BPA exposures by using the mean BPA concentrations in maternal (16 and 26 weeks of gestation and birth) and child (1, 2, and 3 years of age) urine samples, respectively. Behavior and executive function were measured by using the Behavior Assessment System for Children 2 (BASC-2) and the Behavior Rating Inventory of Executive Function-Preschool (BRIEF-P).
RESULTS: BPA was detected in >97% of the gestational (median: 2.0 μg/L) and childhood (median: 4.1 μg/L) urine samples. With adjustment for confounders, each 10-fold increase in gestational BPA concentrations was associated with more anxious and depressed behavior on the BASC-2 and poorer emotional control and inhibition on the BRIEF-P. The magnitude of the gestational BPA associations differed according to child gender; BASC-2 and BRIEF-P scores increased 9 to 12 points among girls, but changes were null or negative among boys. Associations between childhood BPA exposure and neurobehavior were largely null and not modified by child gender.
CONCLUSIONS: In this study, gestational BPA exposure affected behavioral and emotional regulation domains at 3 years of age, especially among girls. Clinicians may advise concerned patients to reduce their exposure to certain consumer products, but the benefits of such reductions are unclear.

Environ Health. 2011; 10: 88. Published online 2011 October 6.

Perfluorinated compounds are related to breast cancer risk in greenlandic inuit: A case control study

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Background: Breast cancer (BC) is the most common cancer for women in the western world. From very few cases an extraordinary increase in BC was observed in the Inuit population of Greenland and Canada although still lower than in western populations. Previous data suggest that exposure to persistent organic pollutants (POPs) might contribute to the risk of BC. Rat studies showed that perfluorinated compounds (PFCs) cause significantly increase in mammary fibroadenomas. This study aimed at evaluating the association between serum levels of POPs/PFCs in Greenlandic Inuit BC cases and their controls, and whether the combined POP related effect on nuclear hormone receptors affect BC risk.
Methods: Thirty-one BC cases and 115 controls were sampled during 2000-2003 from various Greenlandic districts. The serum levels of POPs, PFCs, some metals and the combined serum POP related effect on estrogen- (ER), androgen- (AR) and Ah-receptor (AhR) transactivity were determined. Independent student t-test was used to compare the differences and the odds ratios were estimated by unconditional logistic regression models.
Results: We observed for the very first time a significant association between serum PFC levels and the risk of BC. The BC cases also showed a significantly higher concentration of polychlorinated biphenyls at the highest quartile. Also for the combined serum POP induced agonistic AR transactivity significant association to BC risk was found, and cases elicited a higher frequency of samples with significant POP related hormone-like agonistic ER transactivity. The AhR toxic equivalent was lowest in cases.
Conclusions: The level of serum POPs, particularly PFCs, might be risk factors in the development of BC in Inuit. Hormone disruption by the combined serum POP related xenoestrogenic and xenoandrogenic activities may contribute to the risk of developing breast cancer in Inuit. Further investigations are needed to document these study conclusions.

Environ Health Perspect. 2011 Oct;119(10):1466-71. Epub 2011 Jun 10.

Serum perfluorinated compound concentration and attention deficit/hyperactivity disorder in children 5-18 years of age.

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Background: Perfluorinated compounds (PFCs) are persistent environmental pollutants. Toxicology studies demonstrate the potential for perfluorooctanoic acid (PFOA) and other PFCs to affect human growth and development. Attention deficit/hyperactivity disorder (ADHD) is a developmental disorder with suspected environmental and genetic etiology.
Objectives: We examined the cross-sectional association between serum PFC concentration and parent or self-report of doctor-diagnosed ADHD with and without current ADHD medication.
Methods: We used data from the C8 Health Project, a 2005–2006 survey in a Mid-Ohio Valley community highly exposed to PFOA through contaminated drinking water, to study non-Hispanic white children 5–18 years of age. Logistic regression models were adjusted for age and sex.
Results: Of the 10,546 eligible children, 12.4% reported ADHD and 5.1% reported ADHD plus ADHD medication use. We observed an inverted J-shaped association between PFOA and ADHD, with a small increase in prevalence for the second quartile of exposure compared with the lowest, and a decrease for the highest versus lowest quartile. The prevalence of ADHD plus medication increased with perfluorohexane sulfonate (PFHxS) levels, with an adjusted odds ratio of 1.59 (95% confidence interval, 1.21–2.08) comparing the highest quartile of exposure to the lowest. We observed a modest association between perfluorooctane sulfonate and ADHD with medication.
Conclusions: The most notable finding for PFOA and ADHD, a reduction in prevalence at the highest exposure level, is unlikely to be causal, perhaps reflecting a spurious finding related to the geographic determination of PFOA exposure in this population or to unmeasured behavioral or physiologic correlates of exposure and outcome. Possible positive associations between other PFCs and ADHD, particularly PFHxS, warrant continued investigation.

Environ Health Perspect. 2011 Nov 23. [Epub ahead of print]

Association between Pregnancy Loss and Urinary Phthalate Levels around the Time of Conception.

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Background: Animal studies indicate that some phthalate metabolites may harm female reproductive function.
Objectives: We assessed the associations between exposure to phthalate metabolites and pregnancy loss.
Methods: In a previously established cohort of first pregnancy planners, we analyzed four primary and two oxidized secondary phthalate metabolites in urine samples collected on day 10 after the first day of the last menstrual period before conception occurred (n=128) and during the previous cycle (if any, n=111). Subclinical embryonal loss was identified by repeated urinary hCG measurements and information on clinical spontaneous abortions was obtained by telephone interview with the mother.
Results. Pregnancy loss (n = 48) was increased among women with urinary concentration of monoethylhexyl phthalate (MEHP) in the upper tertile in the conception sample compared with women in the lowest tertile [adjusted odds ratio 2.9; 95% confidence interval (CI) 1.1; 7.6]. The corresponding odds ratio for subclinical embryonal loss (n=32) was 40.7 (CI 4.5; 369.5). **Conclusions**. The phthalate metabolite MEHP was associated with higher occurrence of pregnancy loss. Since this is the first human study to show this association and the sample size is small, the findings need to be corroborated in independent studies.

Bruttoliste

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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 (slut Sep.-December 2011)
Efter at have fjernet gengangere, fra dem vi havde med på de forrige litteraturopdateringslister, gav **litteratursøgningen, med de angivne søgekriterier, tilsammen en liste med i alt 21 artikler.**

Ud fra bruttolisten (se længere nede i dokumentet) er udvalgt følgende 3 artikler med engelsk abstrakt

Udvalgte publikationer:

A comparison of two human cell lines and two rat gonadal cell primary cultures as **in vitro** screening tools for aromatase modulation.
Quignot N, Desmots S, Barouki R, Lemazurier E.

Abstract
Environmental toxicants are a serious health concern, and numerous studies have been devoted to studying the effects of environmental Endocrine Disrupting Chemicals (EDCs). The balance between androgens and estrogens controls the function of many EDC-sensitive organs, and the aromatase enzyme plays a key role in maintaining this balance. In vitro studies have suggested that aromatase expression and activity is a promising biomarker for initial screenings of putative hormonal disrupting compounds. To further validate the aromatase biomarker, we tested several EDCs (atrazine, bisphenol A, methoxychlor, methoxychlor metabolite HPTE, vinclozolin, vinclozolin metabolite M2) in four different models (human cell lines H295R and JEG-3, rat primary cultures of granulosa and leydig cells). We evaluated the similarities/differences in the chemical impact on aromatase mRNA levels and enzymatic activity for the different species and cell types. Aromatase gene expression was assessed by q-RT-PCR, and enzymatic activity was assessed via a tritiated water method with either intact cells or isolated microsomes. The aromatase gene mRNA levels and cellular enzymatic activity varied between the four different models tested, which suggests that the EDC effect varies among different cell types. However, regulation of microsomal aromatase activity appeared to be conserved across all the species and cell types tested. These results suggest that several well characterized complementary cellular models are required to fully characterize the effects of putative EDCs and predict the in vivo effects.

Mechanistic profiling of the cAMP-dependent steroidogenic pathway in the **H295R** endocrine disrupter screening system: New endpoints for toxicity testing.
Vanparys C, Hectors T, Blust R, De Coen W.

Abstract
The need for implementation of effects on steroid synthesis and hormone processing in screening batteries of endocrine disruptive compounds is widely acknowledged. In this perspective, hormone profiling in the H295R adrenocortical cell system is extensively examined and recently OECD validated (TG 456) as a replacement of the minced testis assay. To further elucidate the complete mechanisms and endocrine responsiveness of this cell system, microarray-based gene expression profiling of the cAMP response pathway, one of the major pathways in steroidogenesis regulation, was examined in H295R cells. Next to the steroid synthesis pathway, a broader lipid metabolic pathway, including cholesterol uptake/biosynthesis, hormone metabolization and many hormone and nuclear receptors, are sensitive towards cAMP stimulation in this cell system. Moreover, these pathways were clearly dose and time responsive, indicating early regulation (10h) of cholesterol uptake and mobilization genes and later expression (24-48h) of cholesterol biosynthesis and steroid synthesis. Transcription network analysis suggested several important transcription factors that could be involved in regulation of the steroid hormone pathway, of which HNF4α, a broader lipid metabolism related transcription factor, might indicate some new transcription regulation patterns in this cell line. Overall we can conclude that the time dependent gene expression patterns of the strongly coordinated cholesterol supply and steroidogenesis pathways in the H295R cell system seem to reflect well the in vivo ACTH/cAMP signalling cascade in adrenal cells. Moreover, the completeness of the steroidogenic related pathways in terms of gene expression sensitivity indicates the H295R cell line as a promising cell line in omics-based endocrine disruption screening.

An improved **thyroid hormone reporter assay** to determine the **thyroid hormone**-like activity of amiodarone, bithionol, closantel and rafoxanide.
Matsubara K, Sanoh S, Ohta S, Kitamura S, Sugihara K, Fujimoto N.

Abstract
A number of environmental chemicals have been reported to exhibit thyroid hormone-like activity. Since thyroid hormones play a crucial role in development, it is important to identify chemicals in the environment that are capable of endocrine disruption of thyroid hormone homeostasis. In order to detect thyroid hormone-like activity, the growth of pituitary cell lines has been commonly used as a sensitive marker, albeit with limited specificity to thyroid hormones. Reporter gene assays using the thyroid hormone responsive element (TRE) connected to the luciferase reporter gene, have also been developed. Thus far however, this type of assay appears to have limited sensitivity compared to cell growth assays. In the present study, we developed a highly sensitive TRE reporter gene assay by using a pituitary cell line, MtT/E-2, and by culturing cells in a serum-free medium. Our assay was developed in order to detect T3 activity at a concentration of 10(-11)M. This assay identified thyroid hormone-like activity from the antiarrhythmic drug, amiodarone, and from three anti-parasitic drugs, bithionol, closantel and rafoxanide, all commonly used in veterinary medicine. Thyroid hormone-like activity of these compounds was further confirmed by the induction of BCL3 gene expression in MtT/E-2, which is known to be regulated by thyroid hormones. Our improved assay was proved to be a sensitive tool for assessing thyroid hormone-like activity of environmental chemicals.

Bruttolisten

1.
Gene expression is altered after Bisphenol A exposure in human fetal oocytes **in vitro**.
Brieño-Enríquez MA, Reig R, Cabero L, Toran N, Martínez F, Roig I, Garcia Caldés M.
Mol Hum Reprod. 2011 Nov 25. [Epub ahead of print]

2.
A comparison of two human cell lines and two rat gonadal cell primary cultures as **in vitro** screening tools for aromatase modulation.
Quignot N, Desmots S, Barouki R, Lemazurier E.
Toxicol **In Vitro**. 2011 Nov 18. [Epub ahead of print]

3.
Enantioselectivity in estrogenicity of the organochlorine insecticide acetofenate in human trophoblast and MCF-7 cells.
Chen F, Zhang Q, Wang C, Lu Y, Zhao M.
Reprod Toxicol. 2011 Nov 18. [Epub ahead of print]

4.
Endocrine Disruptors, Polychlorinated Biphenyls-Induced gC1qR-Dependent Apoptosis in Human Trophoblast Cell Line HTR-8/SVneo.
Gu PQ, Gao LJ, Li L, Liu Z, Luan FQ, Peng YZ, Guo XR.
Reprod Sci. 2011 Nov 18. [Epub ahead of print]

5.
In Vitro Acute Exposure to DEHP Affects Oocyte Meiotic Maturation, Energy and Oxidative Stress Parameters in a Large Animal Model.
Ambruosi B, Filioli Uranio M, Sardanelli AM, Pocar P, Martino NA, Paternoster MS, Amati F, Dell'aquila ME.
PLoS One. 2011;6(11):e27452. Epub 2011 Nov 4.

6.
Endocrine disruptor & nutritional effects of heavy metals in ovarian hyperstimulation.
Dickerson EH, Sathyapalan T, Knight R, Maguiness SM, Killick SR, Robinson J, Atkin SL.
J Assist Reprod Genet. 2011 Nov 10. [Epub ahead of print]

7.
Selective activation of zebrafish estrogen receptor subtypes by chemicals by using stable reporter gene assay developed in a zebrafish liver cell line.
Cosnefroy A, Brion F, Maillot-Maréchal E, Porcher JM, Pakdel F, Balaguer P, Aït-Aïssa S.

Toxicol Sci. 2011 Nov 1. [Epub ahead of print]

8.
Bioluminescent yeast estrogen assay (BLYES) as a sensitive tool to monitor surface and drinking water for estrogenicity.
Di Dea Bergamasco AM, Eldridge M, Sanseverino J, Sodré FF, Montagner CC, Pescara IC, Jardim WF, Umbuzeiro GD.
J Environ Monit. 2011 Oct 31. [Epub ahead of print]

9.
Xenoestrogenic chemicals effectively alter sperm functional behavior in mice.
Park YJ, Mohamed ES, Kwon WS, You YA, Ryu BY, Pang MG.
Reprod Toxicol. 2011 Oct 20;32(4):418-424. [Epub ahead of print]

10.
17α-Ethynylestradiol alters the immune response of the teleost gilthead seabream (Sparus aurata L.) both in vivo and **in vitro**.
Cabas I, Liarte S, García-Alcázar A, Meseguer J, Mulero V, García-Ayala A.
Dev Comp Immunol. 2011 Oct 10. [Epub ahead of print]

11.
Metalloestrogenic effects of quantum dots.
Jain MP, Vaisheva F, Maysinger D.
Nanomedicine (Lond). 2011 Oct 20. [Epub ahead of print]

12.
Identification of Major Dioxin-Like Compounds and Androgen Receptor Antagonist in Acid-Treated Tissue Extracts of High Trophic-Level Animals.
Suzuki G, Tue NM, van der Linden S, Brouwer A, van der Burg B, van Velzen M, Lamoree M, Someya M, Takahashi S, Isobe T, Tajima Y, Yamada TK, Takigami H, Tanabe S.
Environ Sci Technol. 2011 Nov 8. [Epub ahead of print]

13.
Identification of Di-isononyl Phthalate Metabolites for Exposure Marker Discovery Using **In Vitro/In** Vivo Metabolism and Signal Mining Strategy with LC-MS Data.
Hsu JF, Peng LW, Li YJ, Lin LC, Liao PC.
Anal Chem. 2011 Nov 15;83(22):8725-31. Epub 2011 Oct 27.

14.
Development of an **in vitro** binding assay for ecdysone receptor of mysid shrimp (Americamysis bahia).
Yokota H, Eguchi S, Nakai M.
Aquat Toxicol. 2011 Oct;105(3-4):708-16. Epub 2011 Sep 17.

15.
Effects of 4-nonylphenol on proliferation of AGS gastric cells.
Manente L, Sellitti A, Lucariello A, Laforgia V, De Falco M, De Luca A.
Cell Prolif. 2011 Oct;44(5):477-85. doi: 10.1111/j.1365-2184.2011.00774.x.

16.
Thyroid effects of **endocrine disrupting** chemicals.
Boas M, Feldt-Rasmussen U, Main KM.
Mol Cell Endocrinol. 2011 Sep 10. [Epub ahead of print]

17.
In vitro induction of apoptosis, necrosis and genotoxicity by cosmetic preservatives: application of flow cytometry as a complementary analysis by NRU.
de Carvalho CM, de Menezes PF, Letenski GC, de Oliveira Praes CE, Feferman IH, Lorencini M.
Int J Cosmet Sci. 2011 Nov 28. doi: 10.1111/j.1468-2494.2011.00698.x. [Epub ahead of print]

18.
In vitro analyses of the effect of heparin and **parabens** on Candida albicans biofilms and planktonic cells.
Miceli MH, Bernardo SM, Ku TS, Walraven C, Lee SA.
Antimicrob Agents Chemother. 2011 Oct 10. [Epub ahead of print]

19.
The suitability of concentration addition for predicting the effects of multi-component mixtures of up to 17 anti-androgens with varied structural features in an **in vitro** AR antagonist assay.
Ermler S, Scholze M, Kortenkamp A.
Toxicol Appl Pharmacol. 2011 Dec 1;257(2):189-97. Epub 2011 Sep 16.

20.
A comprehensive evaluation of the toxicology of cigarette ingredients: aromatic and aliphatic alcohol compounds.
Coggins CR, Frost-Pineda K, Smith DC, Oldham MJ.
Inhal Toxicol. 2011 Jun;23 Suppl 1:141-56.

21.
Dual modulation of GIP and glucagon action by the low molecular weight compound 4-hydroxybenzoic acid 2-bromobenzylidene hydrazide.
Franklin ZJ, McDonnell B, Montgomery IA, Flatt PR, Irwin N.
Diabetes Obes Metab. 2011 Aug;13(8):742-9. doi: 10.1111/j.1463-1326.2011.01401.x.

Herudover er der yderligere 2 artikel, som ikke blev fanget af de valgte søgekriterier
Mechanistic profiling of the cAMP-dependent steroidogenic pathway in the **H295R** endocrine disrupter screening system: New endpoints for toxicity testing.
Vanparys C, Hectors T, Blust R, De Coen W.
Toxicol Lett. 2011 Oct 31. [Epub ahead of print]

An improved **thyroid hormone reporter assay** to determine the **thyroid hormone**-like activity of amiodarone, bithionol, closantel and rafoxanide.
Matsubara K, Sanoh S, Ohta S, Kitamura S, Sugihara K, Fujimoto N.
Toxicol Lett. 2012 Jan 5;208(1):30-5. Epub 2011 Oct 13.

In Vivo studier ved DTU - FOOD

Søgning er udført på PubMed og dækker perioden 23/9/2011-7/12 2011
(Slutn. September-December 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 17 artikler (Bruttolisten):
De udvalgte studier har fokus på: Genistein, 4-tert-octylphenol, kviksølv og PFOA

Ud fra bruttolisten (se længere nede i dokumentet) er udvalgt følgende 3 artikler med engelsk abstrakt

Udvalgte publikationer:

Xenoestrogenic chemicals effectively alter sperm functional behavior in mice.
Park YJ, Mohamed el-SA, Kwon WS, You YA, Ryu BY, Pang MG.
Reprod Toxicol. 2011 Dec;32(4):418-24. Epub 2011 Oct 20. **(kun abstract)**

Abstract
Xenoestrogenic compounds (XCs) can disrupt endogenous hormone function and affect sperm function by binding to receptors on sperm membrane. Albeit spermatozoa are potentially a useful model for screening estrogenic activities of endocrine disruptors, high-quality *in vitro* test system that examination of the XCs effects on sperm function is required. The objective of this study was to compare the effects of XCs (genistein and 4-tert-octylphenol) to those of steroids (estrogen and progesterone) and heparin on *in vitro* capacitation and acrosome reaction (AR) in mouse spermatozoa. Mouse spermatozoa were incubated with various concentrations (0.001–100 μM) of each chemical for 15 or 30 min, and then capacitation and AR were assessed using chlortetracycline. All chemicals studied effectively alter capacitation and/or AR in mouse spermatozoa with different manner. Therefore, we believed that our system will provide a good *in vitro* model system to characterize the physiological effect of XCs especially when compared with steroids

Maternal Thimerosal Exposure Results in Aberrant Cerebellar Oxidative Stress, Thyroid Hormone Metabolism, and Motor Behavior in Rat Pups; Sex- and Strain-Dependent Effects.
Sulkowski ZL, Chen T, Midha S, Zavacki AM, Sajdel-Sulkowska EM.
Cerebellum. 2011 Oct 21. [Epub ahead of print]

Abstract
Methylmercury (Met-Hg) and ethylmercury (Et-Hg) are powerful toxicants with a range of harmful neurological effects in humans and animals. While Met-Hg is a recognized trigger of oxidative stress and an endocrine disruptor impacting neurodevelopment, the developmental neurotoxicity of Et-Hg, a metabolite of thimerosal (TM), has not been explored. We hypothesized that TM exposure during the perinatal period impairs central nervous system development, and specifically the cerebellum, by the mechanism involving oxidative stress. To test this, spontaneously hypertensive rats (SHR) or Sprague–Dawley (SD) rat dams were exposed to TM (200 μg/kg body weight) during pregnancy (G10–G15) and lactation (P5–P10). Male and female neonates were evaluated for auditory and motor function; cerebella were analyzed for oxidative stress and thyroid metabolism. TM exposure resulted in a delayed startle response in SD neonates and decreased motor learning in SHR male (22.6%), in SD male (29.8%), and in SD female (55.0%) neonates. TM exposure also resulted in a significant increase in cerebellar levels of the oxidative stress marker 3-nitrotyrosine in SHR female (35.1%) and SD male (14.0%) neonates. The activity of cerebellar type 2 deiodinase, responsible for local intra-brain conversion of thyroxine to the active hormone, 3′,3,5-triiodothyronine (T3), was significantly decreased in TM-exposed SHR male (60.9%) pups. This coincided with an increased (47.0%) expression of a gene negatively regulated by T3, Odf4 suggesting local intracerebellar T3 deficiency. Our data thus demonstrate a negative neurodevelopmental impact of perinatal TM exposure which appears to be both strain- and sex-dependent.

Endocrine disrupting properties of perfluorooctanoic acid.
White SS, Fenton SE, Hines EP.
J Steroid Biochem Mol Biol. 2011 Oct;127(1-2):16-26. Epub 2011 Mar 21.

Abstract
Perfluoroalkyl acids (PFAAs) have attracted attention in recent years for their environmental ubiquity, as well as their toxicity. Several PFAAs are found in human tissues globally, as humans are exposed on a daily basis through intake of contaminated food, water, and air, irrespective of proximity to industry. Perfluorooctanoic acid (PFOA) is a PFAA shown to be developmentally toxic in mice, with broad and varied health consequences that may include long-lasting effects in reproductive tissues and metabolic reprogramming. To date, the only demonstrated mode of action by which the health effects of PFOA are mediated is via the activation of the peroxisome proliferator-activated receptor alpha (PPARα). The endogenous roles for this receptor, as well as the adverse outcomes of activation by exogenous agents during development, are currently under investigation. Recent studies suggest that PFOA may alter steroid hormone production or act indirectly, via ovarian effects, as a novel means of endocrine disruption. Here we review the existing literature on the known health effects of PFOA in animal models, focusing on sensitive developmental periods. To complement this, we also present epidemiologic health data, with the caveat that these studies largely address only associations between adult exposures and outcomes, rarely focusing on endocrine-specific endpoints, susceptible subpopulations, or windows of sensitivity. Further research in these areas is needed.

Bruttolisten in vivo

1. A comparison of two human cell lines and two rat gonadal cell primary cultures as in vitro screening tools for aromatase modulation.
Quignot N, Desmots S, Barouki R, Lemazurier E.
Toxicol In Vitro. 2011 Nov 18. [Epub ahead of print]

2. Synergistic effects of octylphenol and isobutyl paraben on the expression of calbindin-D9k in GH3 rat pituitary cells.
Kim YR, Jung EM, Choi KC, Jeung EB.
Int J Mol Med. 2012 Feb;29(2):294-302. doi: 10.3892/ijmm.2011.823. Epub 2011 Nov 7.

3. Xenoestrogenic chemicals effectively alter sperm functional behavior in mice.
Park YJ, Mohamed el-SA, Kwon WS, You YA, Ryu BY, Pang MG. (**valgt abstract**)
Reprod Toxicol. 2011 Dec;32(4):418-24. Epub 2011 Oct 20.

4. Lactocrine programming of female reproductive tract development: Environmental connections to the reproductive continuum.
Bartol FF, Bagnell CA.
Mol Cell Endocrinol. 2011 Oct 19. [Epub ahead of print]

5. Synergistic effects of parabens on the induction of calbindin-D9k gene expression act via a progesterone receptor-mediated pathway in GH3 cells.
Yang H, Nguyen TT, An BS, Choi KC, Jeung EB.
Hum Exp Toxicol. 2011 Oct 25. [Epub ahead of print]

6. Maternal Thimerosal Exposure Results in Aberrant Cerebellar Oxidative Stress, Thyroid Hormone Metabolism, and Motor Behavior in Rat Pups; Sex- and Strain-Dependent Effects.
Sulkowski ZL, Chen T, Midha S, Zavacki AM, Sajdel-Sulkowska EM. (**valgt**)
Cerebellum. 2011 Oct 21. [Epub ahead of print]

7. Metalloestrogenic effects of quantum dots.
Jain MP, Vaisheva F, Maysinger D.
Nanomedicine (Lond). 2011 Oct 20. [Epub ahead of print]

8. Comparative developmental biology of the uterus: Insights into mechanisms and developmental disruption.
Spencer TE, Dunlap KA, Filant J.
Mol Cell Endocrinol. 2011 Oct 8. [Epub ahead of print]

9. Identification of major dioxin-like compounds and androgen receptor antagonist in Acid-treated tissue extracts of high trophic-level animals.
Suzuki G, Tue NM, van der Linden S, Brouwer A, van der Burg B, van Velzen M, Lamoree M, Someya M, Takahashi S, Isobe T, Tajima Y, Yamada TK, Takigami H, Tanabe S.
Environ Sci Technol. 2011 Dec 1;45(23):10203-11. Epub 2011 Nov 8.

10. Bisphenol A and 17β-estradiol promote arrhythmia in the female heart via alteration of calcium handling.
Yan S, Chen Y, Dong M, Song W, Belcher SM, Wang HS.
PLoS One. 2011;6(9):e25455. Epub 2011 Sep 27.
11. Inhibition of human and rat testicular steroidogenic enzyme activities by bisphenol A.
Ye L, Zhao B, Hu G, Chu Y, Ge RS.
Toxicol Lett. 2011 Nov 30;207(2):137-42. Epub 2011 Sep 8.

11. Enantioselective endocrine-disrupting effects of bifenthrin on hormone synthesis in rat ovarian cells.
Liu J, Yang Y, Zhuang S, Yang Y, Li F, Liu W.
Toxicology. 2011 Nov 28;290(1):42-9. Epub 2011 Aug 19.

12. Melatonin ameliorates bisphenol A-induced biochemical toxicity in testicular mitochondria of mouse.
Anjum S, Rahman S, Kaur M, Ahmad F, Rashid H, Ansari RA, Raisuddin S.
Food Chem Toxicol. 2011 Nov;49(11):2849-54. Epub 2011 Aug 5.

13. Benzo[a]pyrene Reduces Testosterone Production in Rat Leydig Cells via a Direct Disturbance of Testicular Steroidogenic Machinery.
Chung JY, Kim YJ, Kim JY, Lee SG, Park JE, Kim WR, Yoon YD, Yoo KS, Yoo YH, Kim JM.
Environ Health Perspect. 2011 Nov;119(11):1569-74. Epub 2011 Jul 7.

14. Effect of 2,2',4,4'-tetrahydroxybenzophenone (BP2) on steroidogenesis in testicular Leydig cells.
Kim Y, Ryu JC, Choi HS, Lee K.
Toxicology. 2011 Oct 9;288(1-3):18-26. Epub 2011 Jun 24.

15. Endocrine disrupting properties of perfluorooctanoic acid.
White SS, Fenton SE, Hines EP. (**valgt**)
J Steroid Biochem Mol Biol. 2011 Oct;127(1-2):16-26. Epub 2011 Mar 21.

16. Molecular mechanisms of induction of persistent changes by estrogenic chemicals on female reproductive tracts and external genitalia. Review
Miyagawa S, Sato M, Iguchi T.
J Steroid Biochem Mol Biol. 2011 Oct;127(1-2):51-7. Epub 2011 Mar 21.

17. Early changes induced by short-term low-dose cadmium exposure in rat ventral and dorsolateral prostates.
Lacorte LM, Delella FK, Porto Amorim EM, Justulin LA Jr, Godinho AF, Almeida AA, Felipe Pinheiro PF, Amorim RL, Felisbino SL.
Microsc Res Tech. 2011 Nov;74(11):988-97. doi: 10.1002/jemt.20985. Epub 2011 Feb 1.

Wildlife studier ved Biologisk Institut, Syddansk Universitet (SDU)

Søgningen er udført på Web of Science og dækker perioden 23/9 2011 -9/12 2011.

Søgeprofilen kombinerer: Endocrinedisrupt* 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 tre artikler til medtagelse af abstract. Alle tre artikler omhandler studier på mollusker (bløddyr). På grund af deres mangfoldighed og økologiske betydning har mollusker de seneste år haft øget opmærksomhed med henblik på anvendelse som testorganismer i økotoksikologiske tests. Der mangler dog standardiserede testprotokoller for forsøg med mollusker. OECD har derfor taget initiativ til udviklingen af standardiserede tests med mollusker inden for "conceptualframework" til vurdering af hormonforstyrrende kemikalier. Danmark deltager også i dette arbejde støttet af Miljøstyrelsen. De tre beskrevne artikler bidrager til en større viden om molluskers endokrine systemsamt deres respons på hormonforstyrrende stoffer, hvilket der kan drages nytte af ved udviklingen af standardiserede tests.

Artikel 1:

Abidli,S., Santos,M.M., Lahbib,Y., Castro,L.F.C., Reis-Henriques,M.A., and El Menif,N.T., 2012. Tributyltin (TBT) effects on Hexaplextrunculus and Bolinusbrandaris (Gastropoda: Muricidae): Imposex induction and sex hormone levels insights. Ecological Indicators 13, 13-21.

Tributyltin (TBT)-induced imposex in gastropods is often cited as a prime example of environmental endocrine disruption. Several endocrine-related hypotheses have been proposed to define possible mechanismsby which TBT causes imposex. Recently, it has been demonstrated that mollusks have the abilityto control endogenous steroid levels (i.e., testosterone and estradiol) by esterification with fatty acid and TBT may impact this metabolic pathway. Hence, this study was designed to investigate the presence and levels of sexual steroids (testosterone and estradiol) in the two TBT sensitive Muricids species Hexaplextrunculus and Bolinusbrandaris, and to clarify the sex related impact of TBT in free and esterified steroid levels. Two months exposure to TBT (5 and 50 ng TBT L^{-1}) induced imposex and led to a significant increase in the severity of the phenomenon in the high TBT exposure group but statistical tests failed to detect an effect in 5 ng TBT L^{-1} treatment. The steroid levels found in both sexes revealed that testosteroneand estradiol were present in the free and esterified forms in the digestive gland-gonad complex.Both hormones were predominantly found in the esterified form, although clear sex differences werenot observed. In females of B. brandaris, 2 months exposure to TBT at 50 ng TBT L^{-1} induced a significantelevation of free testosterone and a decrease in the esterified fraction. In females of H. trunculus, TBT ledto a significant elevation of both free and esterified testosterone. In contrast, TBT had no effect in male'stestosterone levels, although it led to an increased trend in penis lengths. Free and esterified estradiol levels were not affected by TBT in both sexes of B. brandaris but free estradiol was increased in females of H. trunculus. Overall, the present study demonstrates that TBT exposure leads to steroid imbalance in both species, with a boost of free testosterone levels in females. Although TBT increases male penis length, no effects in male steroid levels were recorded in both species. Hence, TBT impacts in testosterone and estradiol metabolism is sex dependent, and does not seem to be associated with the increase of male penis length observed in TBT exposed animals.

Artikel 2:

Sieratowicz,A., Stange,D., Schulte-Oehlmann,U., and Oehlmann,J., 2011. Reproductive toxicity of bisphenol A and cadmium in Potamopyrgusantipodarum and modulation of bisphenolA effects by different test temperature. Environmental Pollution 159, 2766-2774.

Abstract: An OECD initiative for the development of mollusc-based toxicity tests for endocrine disrupters and other chemicals has recommended three test species with respective test designs for further standardisation. Preparing a subsequent pre-validation study we performed a reproduction test with Potamopyrgus antipodarum, determining the concentration range of the selected test substances, bisphenol A(BPA) and cadmium (Cd). At 16 °C, the

recommended test temperature, the number of embryos in thebrood pouch was increased by BPA and decreased by Cd (NOEC: 20 mg BPA/L and 1 mg Cd/L). CoinstantaneousBPA tests at 7 °C and 25 °C demonstrated a temperature dependency of the response,resulting in lower NOECs (5 mg/L respectively). As expected, reproduction in control groups significantlyvaried depending on temperature. Additional observations of the brood stock showed seasonal fluctuationsin reproduction under constant laboratory conditions. The recommended temperature range andtest conditions have to be further investigated.

Artikel 3:

Stange,D., Sieratowicz,A., Horres,R., and Oehlmann,J., 2012. Freshwater mudsnail (Potamopyrgusantipodarum) estrogen receptor: Identification and expression analysis under exposure to (xeno-)hormones. Ecotoxicology and Environmental Safety 75, 94-101.

Abstract: Molluscs are raising attention as ecotoxicological test organisms due to their high diversity and ecologicalimportance. The ovoviviparous prosobranch gastropod Potamopyrgusantipodarum (freshwater mudsnail)responds very sensitively to xenobiotics and has therefore been proposed as OECD standard test organism.Endocrine disrupting chemicals influence the reproduction of P. antipodarum, which can be assessed byembryo numbers in the brood pouch. However, the knowledge about the endocrine system of P. antipodarum is rather limited. The aim of this study was to identify an estrogen receptor in the endocrine system of P. antipodarum and to investigate if this receptor is differentially expressed under exposure to (xeno-)hormones (17a-ethinylestradiol, bisphenol A and 17a-methyltestosterone). The DNA-binding domain of the identified ER-like transcript has an amino acid identity of 92 percent compared to the ER of the gastropod Nucella lapillus (84 percent to human ERa) and 83 percent in the ligand binding domain (38 percent to human ERa). Furthermore, the P. antipodarum ER is transcriptionally regulated as shown by quantitative real-time PCRs of (xeno-)hormone exposed snails. 17a-ethinylestradiol andbisphenol A exposure resulted in a transitory ER-mRNA increase while17a-methyltestosterone caused a transitory reduction of ER-mRNA. In addition the solvent dimethyl sulfoxide had also a modulating effect on the receptor.

Bruttoliste:

Abidli,S., Santos,M.M., Lahbib,Y., Castro,L.F.C., Reis-Henriques,M.A., and El Menif,N.T., 2012. Tributyltin (TBT) effects on Hexaplextrunculus and Bolinusbrandaris (Gastropoda: Muricidae): Imposex induction and sex hormone levels insights. Ecological Indicators 13, 13-21.

Aoki,J., Hatsuyama,A., Hiramatsu,N., and Soyano,K., 2011. Effects of ethynylestradiol on vitellogenin synthesis and sex differentiation in juvenile grey mullet (Mugilcephalus) persist after long-term exposure to a clean environment. Comparative Biochemistry and Physiology C-Toxicology & Pharmacology 154, 346-352.

Aufartova,J., Mahugo-Santana,C., Sosa-Ferrera,Z., Santana-Rodriguez,J.J., Novakova,L., and Solich,P., 2011. Determination of steroid hormones in biological and environmental samples using green rnicroextraction techniques: An overview. AnalyticaChimicaActa 704, 33-46.

Baek,H.J., Hwang,I.J., Lee,Y.D., and Kim,H.B., 2011. Effects of nonylphenol and 3,3',4,4',5-pentachlorobiphenyl on in vitro oocyte steroidogenesis in redlip mullet, Chelonhaematocheilus. Animal Cells and Systems 15, 189-196.

Barber,L.B., Brown,G.K., Nettesheim,T.G., Murphy,E.W., Bartell,S.E., and Schoenfuss,H.L., 2011. Effects of biologically-active chemical mixtures on fish in a wastewater-impacted urban stream.Science of the Total Environment 409, 4720-4728.

Cabas,I., Chaves-Pozo,E., Alcazar,A.G., Meseguer,J., Mulero,V., and Garcia-Ayala,A., 2011. Dietary intake of 17 alpha-ethinylestradiol promotes leukocytes infiltration in the gonad of the hermaphrodite gilthead seabream. Molecular Immunology 48, 2079-2086.

Colosi,J.C. and Kney,A.D., 2011. A Yeast Estrogen Screen Without Extraction Provides Fast, Reliable Measures of Estrogenic Activity. Environmental Toxicology and Chemistry 30, 2261-2269.

Delgado,V.S., Lopes,P.F.I., Podratz,P.L., and Graceli,J.B., 2011. Triorganotin as a compound with potential reproductive toxicity in mammals. Brazilian Journal of Medical and Biological Research 44, 958-965.

Fernandes,D., Schnell,S., and Porte,C., 2011. Can pharmaceuticals interfere with the synthesis of active androgens in male fish? An in vitro study.Marine Pollution Bulletin 62, 2250-2253.

Han,Z.H., Jiao,S.J., Kong,D.Y., Shan,Z.J., and Zhang,X.W., 2011. Effects of Beta-Endosulfan on the Growth and Reproduction of Zebrafish (DanioRerio). Environmental Toxicology and Chemistry 30, 2525-2531.

Hayes,T.B., Anderson,L.L., Beasley,V.R., de Solla,S.R., Iguchi,T., Ingraham,H., Kestemont,P., Kniewald,J., Kniewald,Z., Langlois,V.S., Luque,E.H., Mccoy,K.A., Munoz-de-Toro,M., Oka,T., Oliveira,C.A., Orton,F., Ruby,S., Suzawa,M., Tavera-Mendoza,L.E., Trudeau,V.L., Victor-Costa,A.B., and Willingham,E., 2011. Demasculinization and feminization of male gonads by atrazine: Consistent effects across vertebrate classes. Journal of Steroid Biochemistry and Molecular Biology 127, 64-73.

Ishihara,A., Makita,Y., and Yamauchi,K., 2011. Gene Expression Profiling to Examine the Thyroid Hormone-Disrupting Activity of Hydroxylated Polychlorinated Biphenyls in Metamorphosing Amphibian Tadpole. Journal of Biochemical and Molecular Toxicology 25, 303-311.

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