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Centro Interdisciplinar de Investigação Marinha e Ambiental

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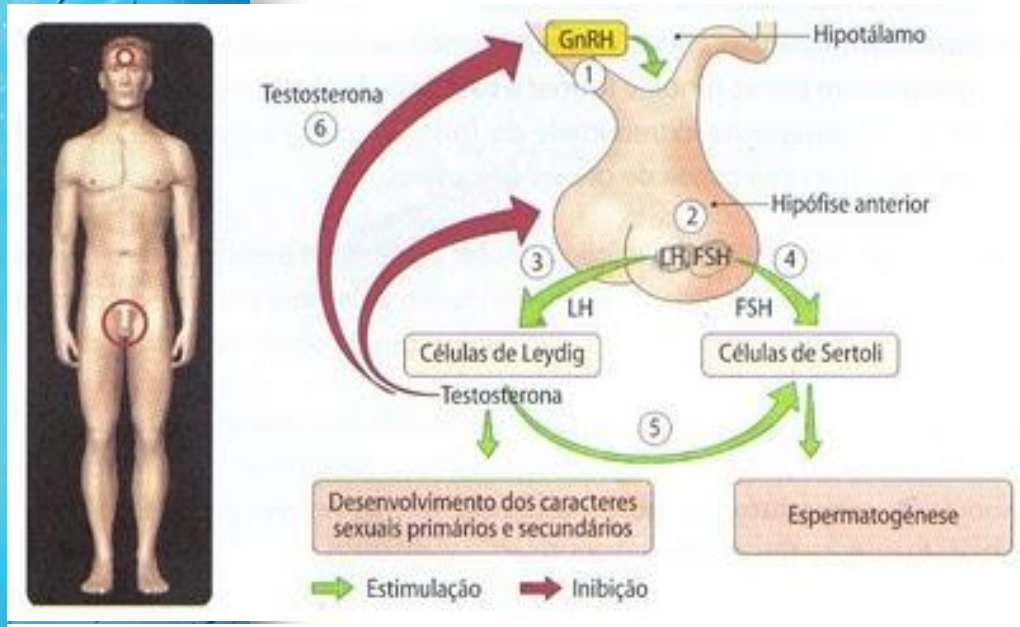
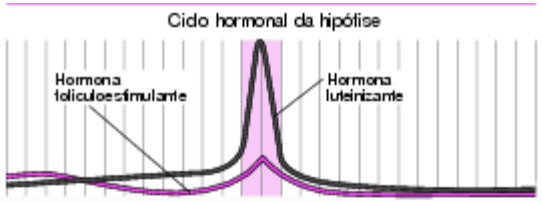
Endocrine disrupting chemicals and emerging contaminants: new challenges and perspectives

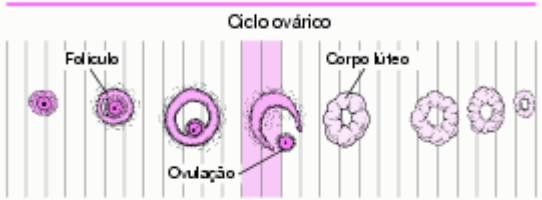
Miguel Santos – CIIMAR/FCUP
Group of Endocrine Disruptors and Emerging Contaminants

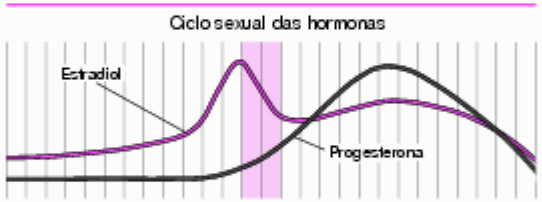
santos@ciimar.up.pt

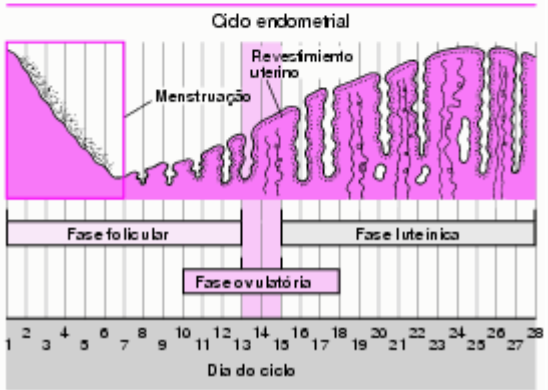
2nd Summer School on *Environmental Applications of Advanced Oxidation Processes of the European PhD School on AOPs*
NEREUS COST Action ES1403











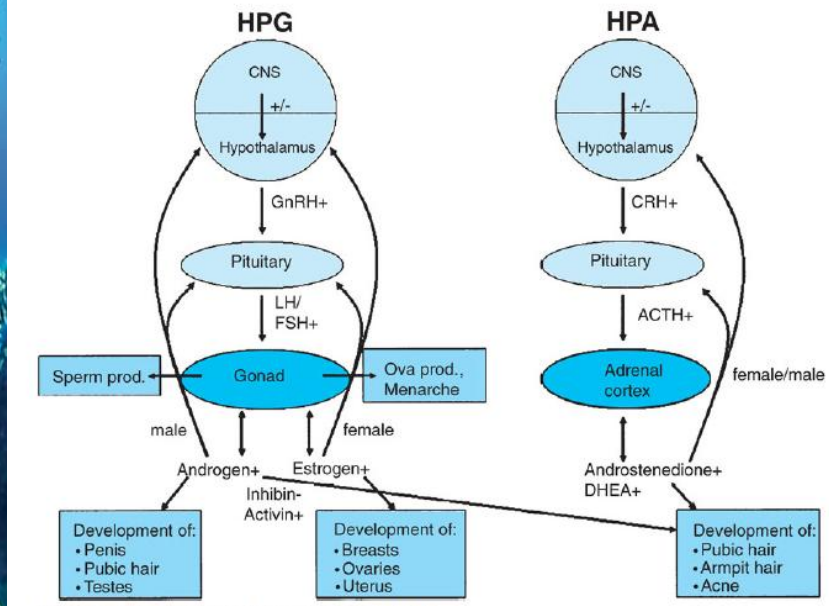
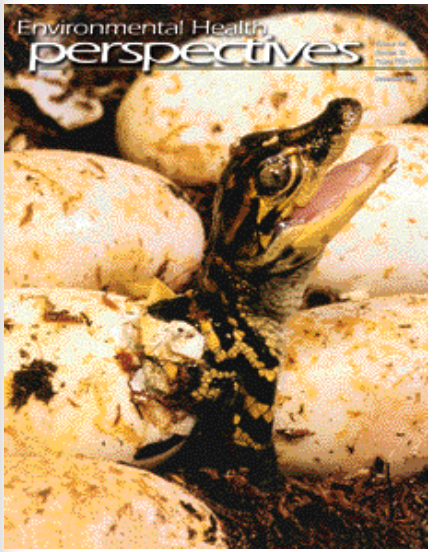


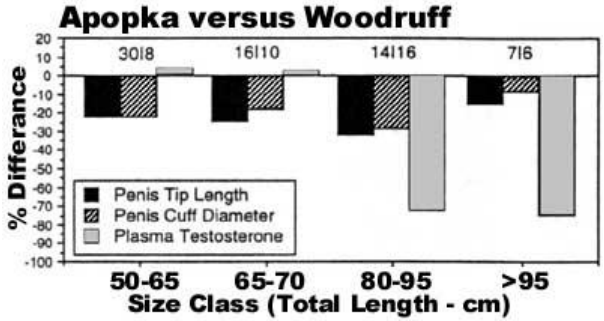
Figure 20-5. Endocrine control of puberty in males and females.

Hormones

Hormones are Chemical "messengers" controlling various activities within an organism. The hormones are secreted by the endocrine glands, and other tissues. Some act only on specific areas of the body (target cells or target organs), others are responsible for triggering a general response in the body.

Reproductive abnormalities in the 1980s in alligators from Lake Apopka, Florida DDT (dichloro-diphenyl-trichloroethane)





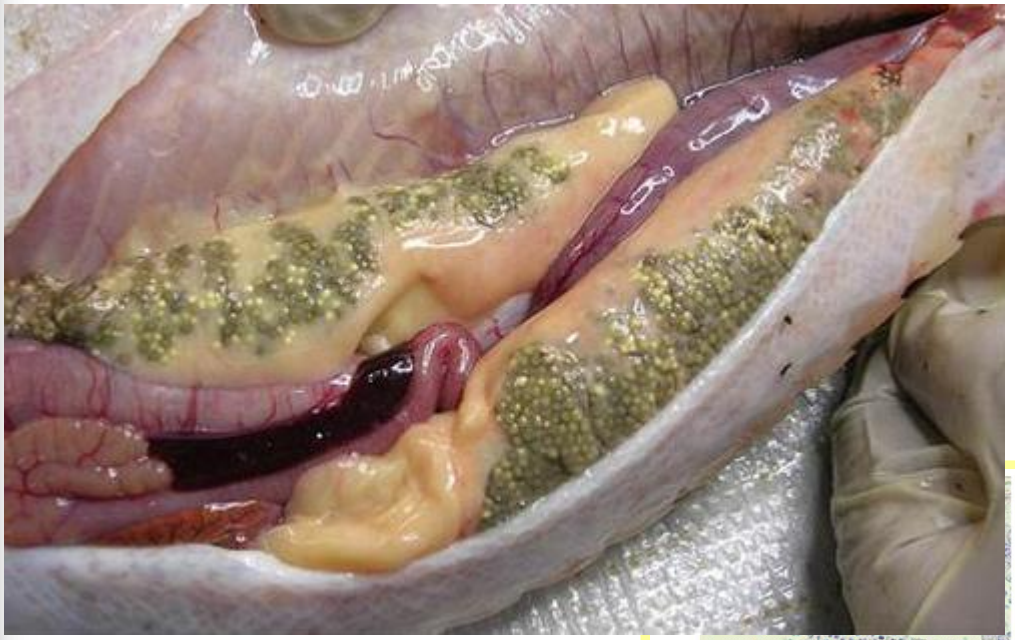
Guillette et al., 1996

Anti-androgenic effects of DDE, a DDT metabolite

Effects of DDT in prey birds

Feminization and masculinization of fish in rivers and estuaries in the 1980s.

Exposure to Estrogenic chemicals leads to male fish feminization



Male Sturgeon from Rio Missouri with intersex gonads

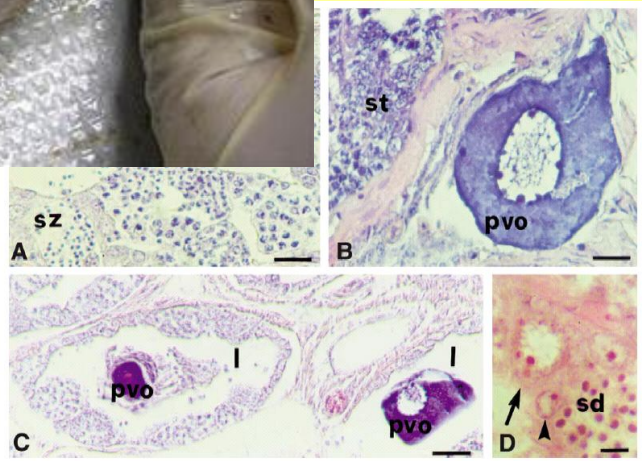
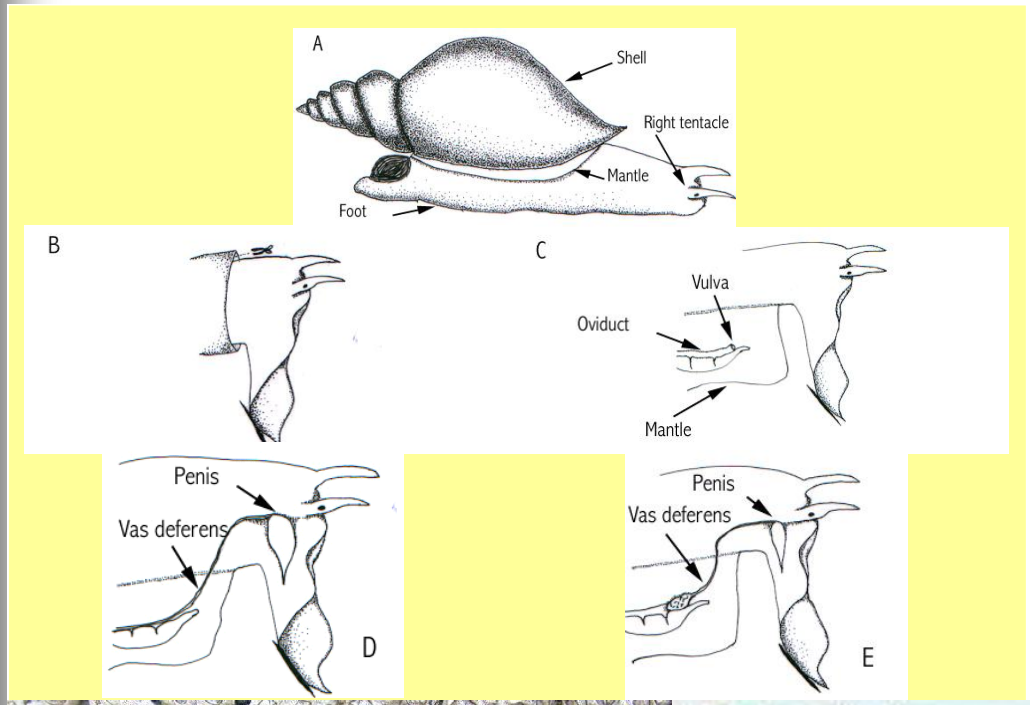


Fig. 1. (A) Testis of a maturing swordfish showing the normal testicular organization. The wall of seminipherous tubules is formed by cysts consisting in synchronously developing germ cells enveloped in Sertoli cell processes. Magnification bar = 15 μm. (B) Intersex gonad with an isolated interstitial previtellogenic oocyte. Magnification bar = 15 μm. (C) Intersex gonad with two isolated previtellogenic oocytes in the lumen of seminipherous tubules. Magnification bar = 35 μm. (D) Intersex gonad showing the presence of a putative oogonium, with a vesicular nucleus containing an eccentric nucleolus and a basophilic cytoplasm, along the wall of a seminipherous tubule. Magnification bar = 5 μm. Haematoxylin–eosin staining. Arrow: putative oogonium; arrowhead: spermatogonium; asterisk: connective stroma; l: lumen of seminipherous tubule; pvo: previtellogenic oocyte; sc: spermatocyte cyst; sd: spermatid cyst; st: seminipherous tubule; sz: sperm cyst.

Imposex in marine snails due to exposure to the fungicide tributilytin (TBT) used in antifouling paints



Masculinization of female snails

Intersex in crustaceans

TABLE 2.2
Sources of Endocrine Disrupting Chemicals (EDCs) Entering Watercourses

Source of EDCs	Receiving Waters	Source Method	EDCs Likely to Be Present
Domestic sewage effluent	Surface water[a]	Point	Steroid estrogens,[2] Surfactants,[3] PAEs, BPA[4]
	Groundwater	Nonpoint	
	Groundwater	Point (recharge)	
Industrial sewage effluent	Surface water	Point	Surfactants,[5,6] PAHs,[7] PCBs,[7] PBDEs,[8] pesticides,[7] PAEs,[4] BPA
	Groundwater	Nonpoint	
Industrial discharges	Surface water	Point	Dioxins, PBDEs,[8] TBBA, [9] PAEs, PCBs,[7] PAHs,[7] pesticides,[7] BPA[4]
	Groundwater	Nonpoint	
Paint applied to boats	Surface water	Point	TBT[10]
Agricultural runoff (crops)	Surface water	Nonpoint	Pesticides,[7] APs, APEs,[11] PBDEs,[12] PAHs[13,14]
	Groundwater	Nonpoint	
Agricultural runoff (animals)	Surface water	Nonpoint	Steroid estrogens[15,16]
	Groundwater	Nonpoint	
Recreational/Urban runoff	Surface water	Nonpoint	Pesticides, PAHs[7]
	Groundwater	Nonpoint	
Leachate from waste dumps	Groundwater	Nonpoint	PAHs,[17] PBDEs, TBBA,[9] BPA, PAEs
Deposition from the air	Surface water	Nonpoint	PAHs,[7] PCBs, PCDDs, PCDFs, PBDEs,[18] TBBA, pesticides
	Groundwater	Nonpoint	
Natural	Surface water	Nonpoint	PAHs, steroid estrogens (natural)[19]
	Groundwater	Nonpoint	

Phthalate acid esters (PAEs); bisphenol A (BPA); polyaromatic hydrocarbons (PAHs); polychlorinated biphenyls (PCBs); polybrominated diphenyl ethers (PBDEs); tetrabromobisphenol A (TBBA); tributyltin (TBT); polychlorinated dibenzo-*p*-dioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs)

[a]Surface waters include streams, rivers, estuaries, and seas

endocrine disruptor

An endocrine disrupter is an exogenous agent that interferes with the synthesis, secretion, transport, binding, action or elimination of natural hormones responsible for the maintenance of homeostasis, reproduction, development, and / or behavior.

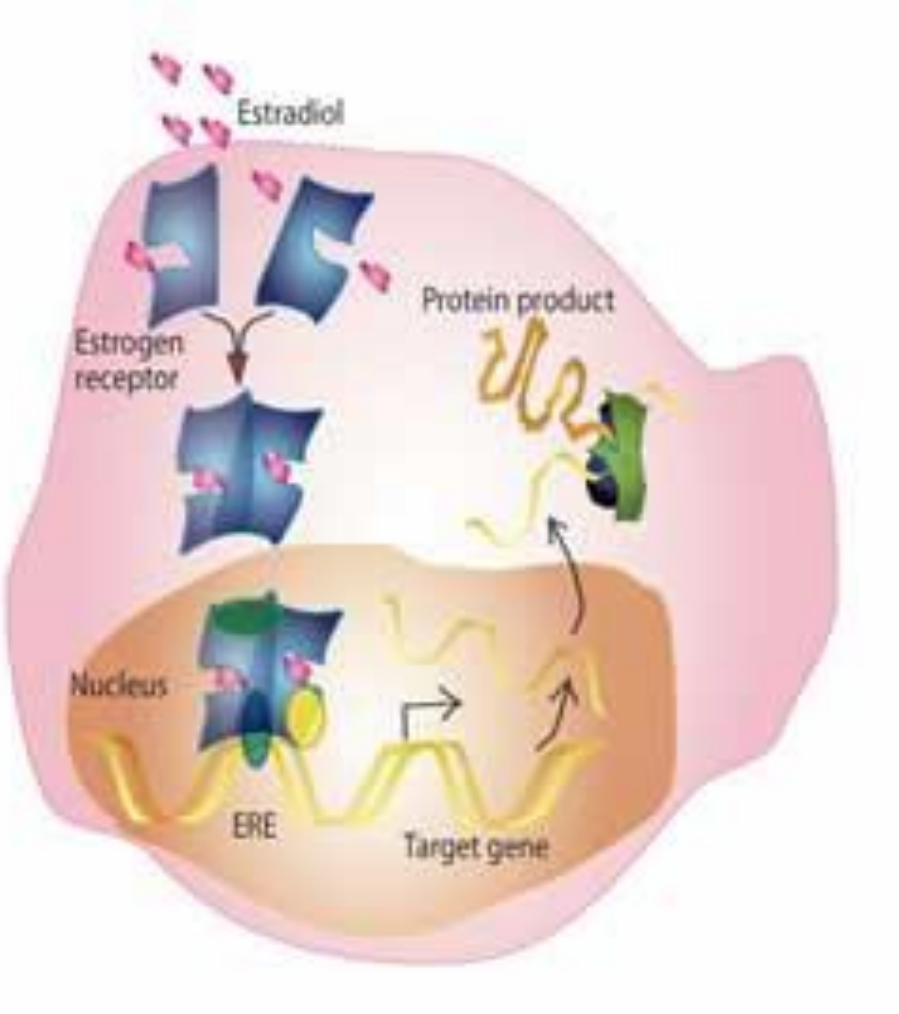
List of Compounds Classified as EDCs by Various Organizations

Compound	UKEA	USEPA	OSPAR		JEA	WWF
			vivo	vitro		
Steroids						
Ethinyl estradiol	X		X			
17β-estradiol	X		X			
Estrone	X		X			
Mestranol			X			
Diethylstilbestrol	X		X			
					X	X
Alkylphenols						
Nonylphenol	X	X	X		X	X
Nonylphenol ethoxylate	X			X		
Octylphenol	X	X	X		X	
Octylphenol ethoxylate	X					
Polyaromatic Compounds						
Polychlorinated biphenyls (PCBs)	X	X	X		X	X
Brominated flame retardants				X	X	X
Polyaromatic hydrocarbons (PAHs)		X		X		
Organic Oxygen Compounds						
Phthalates	X	X		X	X	X
Bisphenol A	X	X			X	X
Pesticides						
Atrazine	X	X		X	X	X
Simazine	X	X		X	X	X
Dichlorvos	X					
Endosulfan	X	X		X	X	X
Trifluralin	X	X				X
Demeton-*S*-methyl	X					
Dimethoate	X					X
Linuron						X
Permethrin	X	X			X	
Lindane	X	X	X			X
Chlordane	X			X	X	X
Dieldrin	X	X		X	X	X
Hexachlorobenzene	X			X	X	X
Pentachlorophenol (PCP)	X	X			X	X
Others						
Dioxins and furans	X		X		X	X
Tributyltin	X	X	X		X	

UKEA — United Kingdom Environment Agency
USEPA — United States Environmental Protection Agency
OSPAR — Oslo and Paris Commission
JEA — Japan Environment Agency
WWF — World Wildlife Fund

Endocrine-Disrupting Effects in Wildlife

Species	Contaminant/Effect
Mammals	
Panther	Hg, DDE, PCBs/cryptorchidism
Baltic seals	PCBs/sterility, adrenocortical hyperplasia
Beluga whales	PCBs, Dieldrin, 2,3,7,8-TCDD/hermaphroditism
European otter	PCBs/reproductive impairment
Dall's porpoises	PCBs, DDE/reduced testosterone levels
Birds	
Western gull	DDT compounds, methoxychlor/feminization, female–female pairing
Peregrine falcon	DDE/egg shell thinning
Fish-eating birds (U.S., Great Lakes)	PCDD, PCDF/reproductive failure, deformities
Common tern	PHAHs/reduced hatching, morphological abnormalities
Reptiles	
Snapping turtles	Organochlorine compounds/developmental abnormalities, feminization
American alligator	DDE/low hatching rates, abnormalities in males and females
Fish	
Roach	Steroid estrogens/increased vitellogenin in males, intersex
Flounder	Nonylphenol, octylphenol/vitellogenin in male fish
Flounder	Estrogens/vitellogenin in male fish
Rainbow trout	Estrogens, nonylphenol/vitellogenin in male fish



Mode of action:

- Agonists
- Antagonists
- Interfere with synthesis and/or metabolism
- Interfere with receptor number

NR are frequently impacted by EDCs

Environmental Science & Technology

Viewpoint

pubs.acs.org/est

To Bind or Not To Bind: The Taxonomic Scope of Nuclear Receptor Mediated Endocrine Disruption in Invertebrate Phyla

L. Filipe C. Castro*,†,‡ and Miguel M. Santos*,†,‡

Environmental Science & Technology Viewpoint

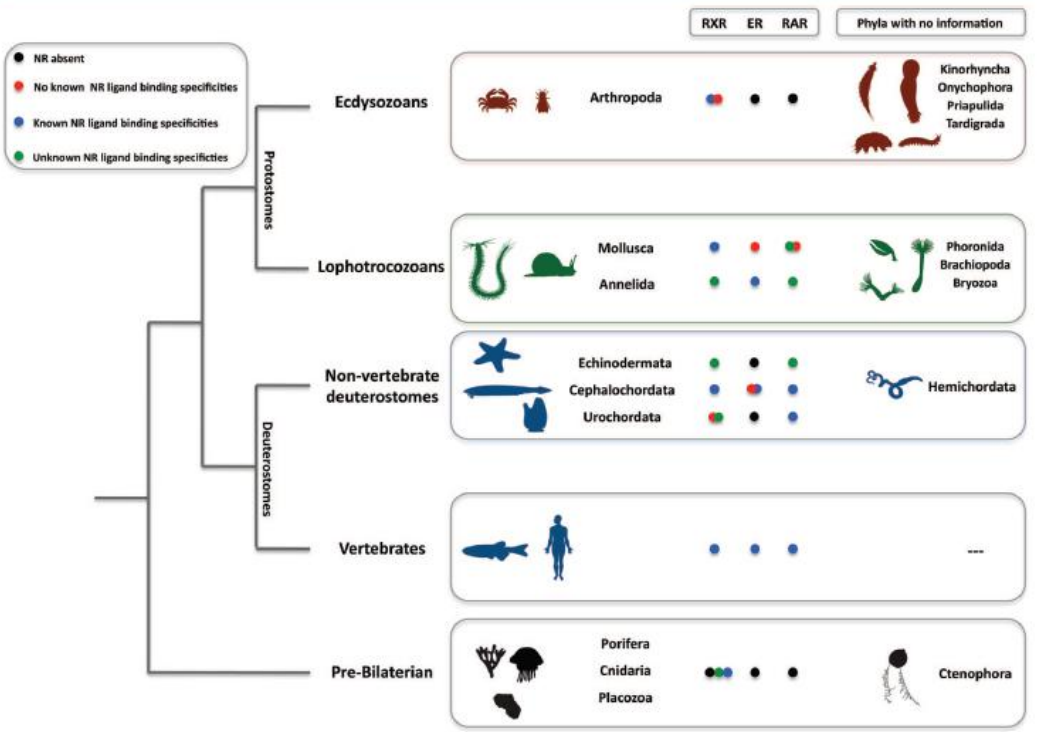
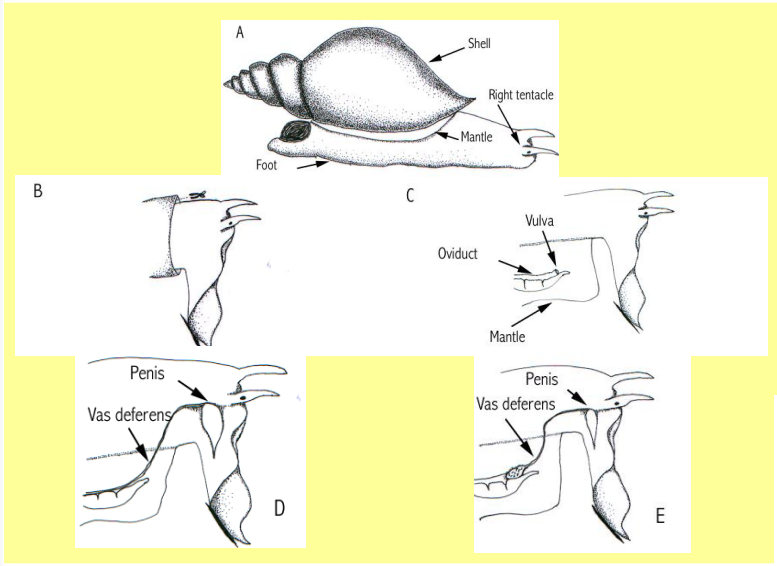
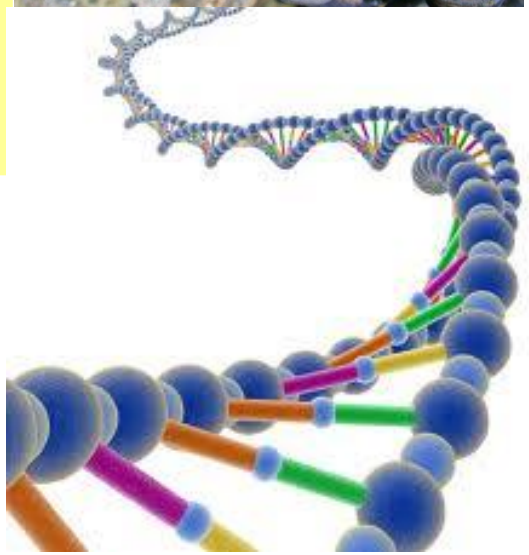


Figure 1. Phylogenetic relationships between major extant Metazoa lineages. Examples of NR repertoire (RXR, ER and RAR) and known ligand binding affinities toward endogenous compounds and/or EDCs are identified.





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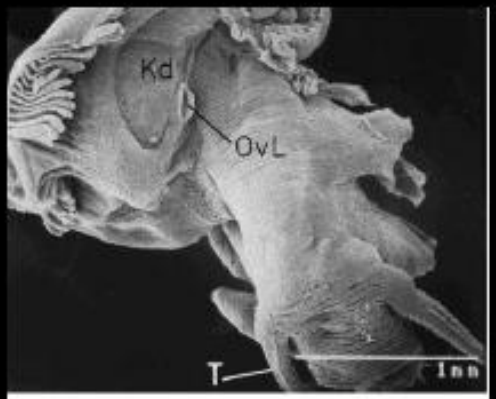
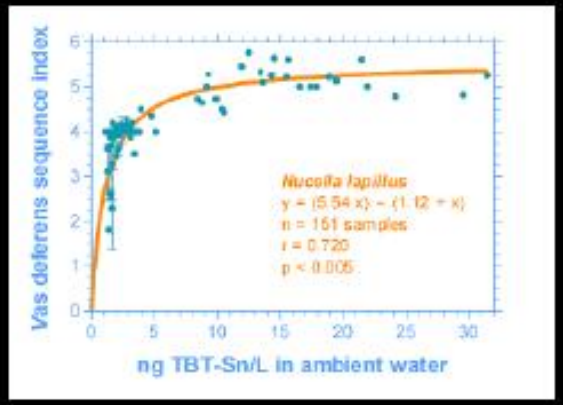
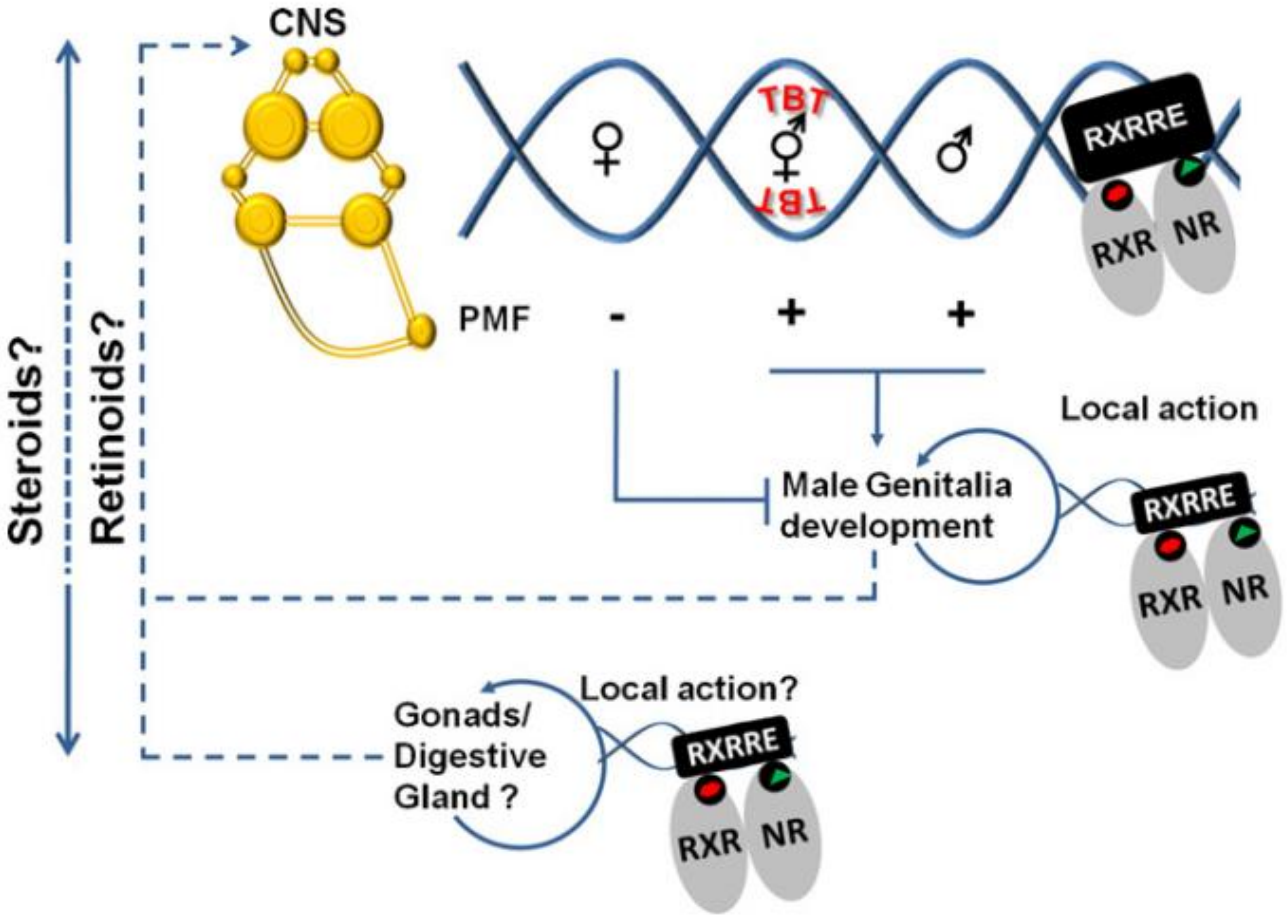
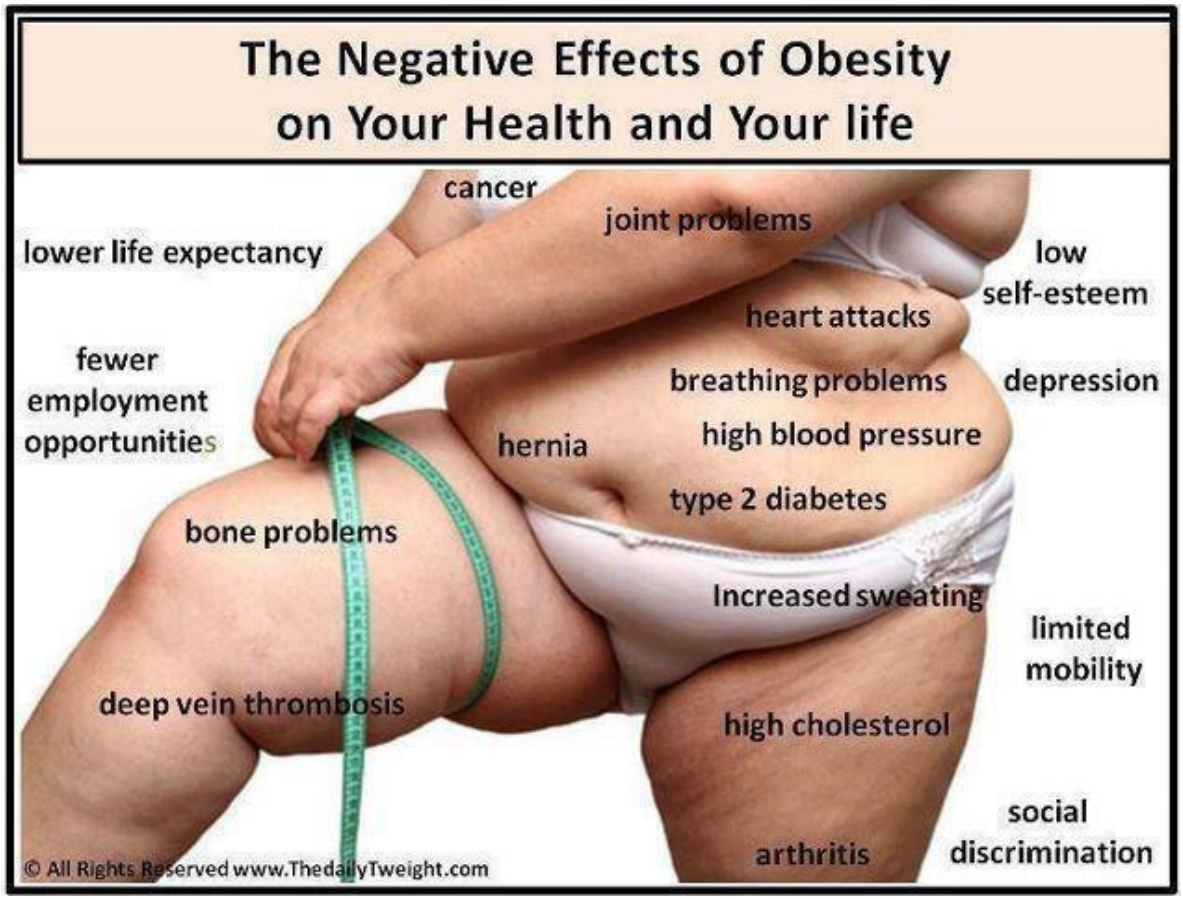




Tintas antivegetativas com organoestanhos (TBT/TPT)



Lima et al., 2011



Source: http://bodyago.com/obesity-ticking-time-bomb/

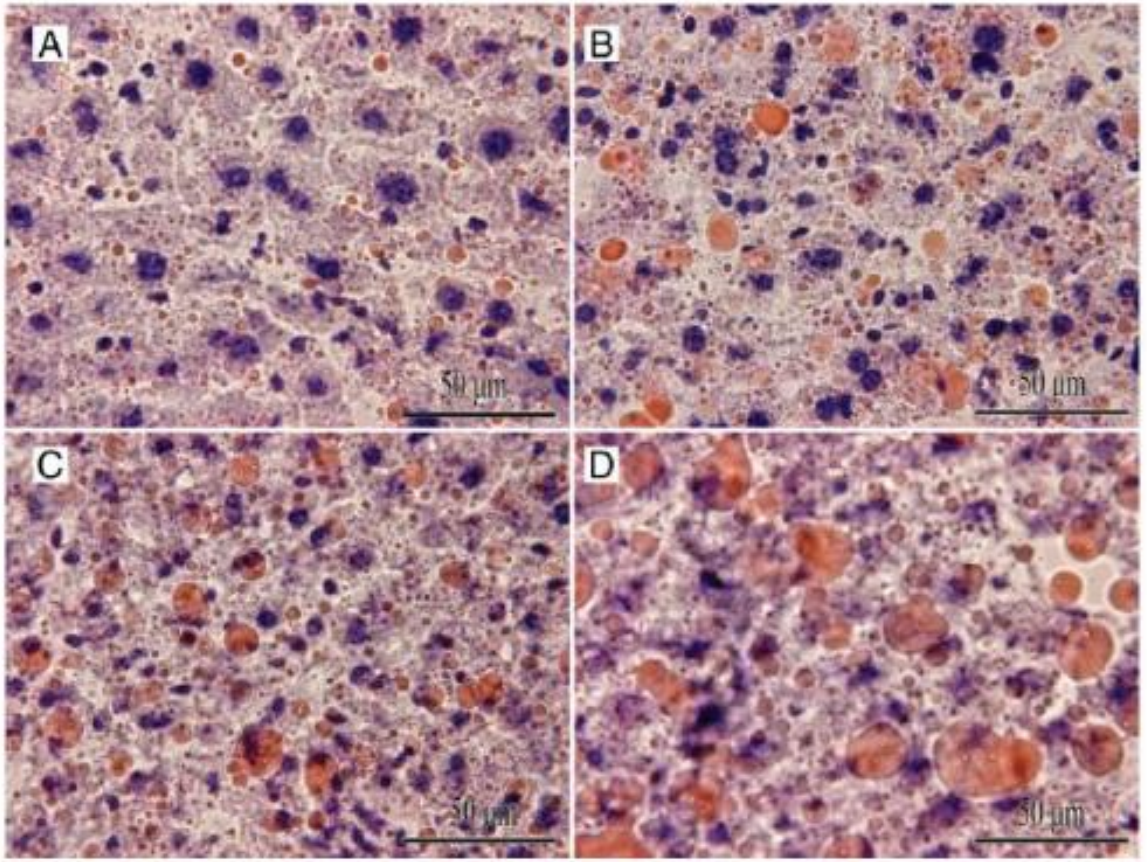


Fig. 4. Histological changes of the liver in the male mice treated with TBT for 45 days. The sections were stained with Oil Red O and counterstained with hematoxylin. (A) Control; (B) 0.5 μg/kg TBT; (C) 5 μg/kg TBT; (D) 50 μg/kg TBT. Lipid droplets revealed by orange red staining. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

Obesogens

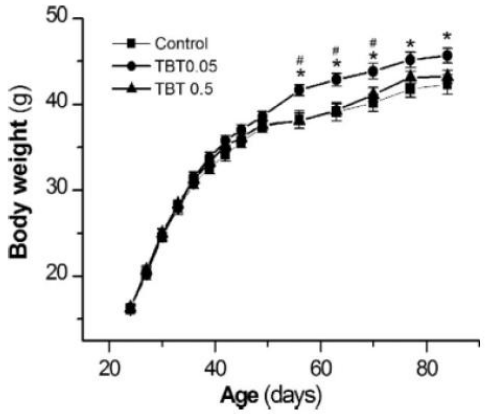
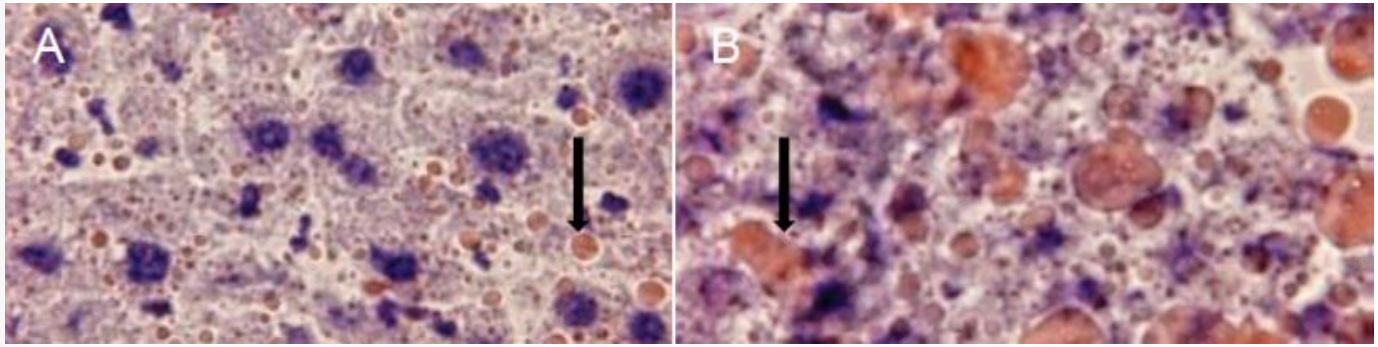


Fig. 1. Mean body weights (g) of mice from PNDs 24 to 84. Mean body weights (±SEM) of mice from PNDs 24 to 49 (n = 25), from PNDs 56 to 84 (n = 15). No significant differences in average body weight of mice between the TBTCl-treated group and the control at all time points depicted were observed from PNDs 24 to 49 ($P > 0.22$). At all time points depicted after PND 49, mice exposed to 0.05 mg/kg TBTCl were significantly heavier than control ones ($^{*}P < 0.05$). Mice treated with low-dose TBTCl were heavier than the high-dose mice on PNDs 56, 63, and 70 ($^{\#}P < 0.05$), but no significant differences in average body weight of mice between 0.5 mg/kg group and control were observed at all time points depicted.



Impact over several generations without exposure

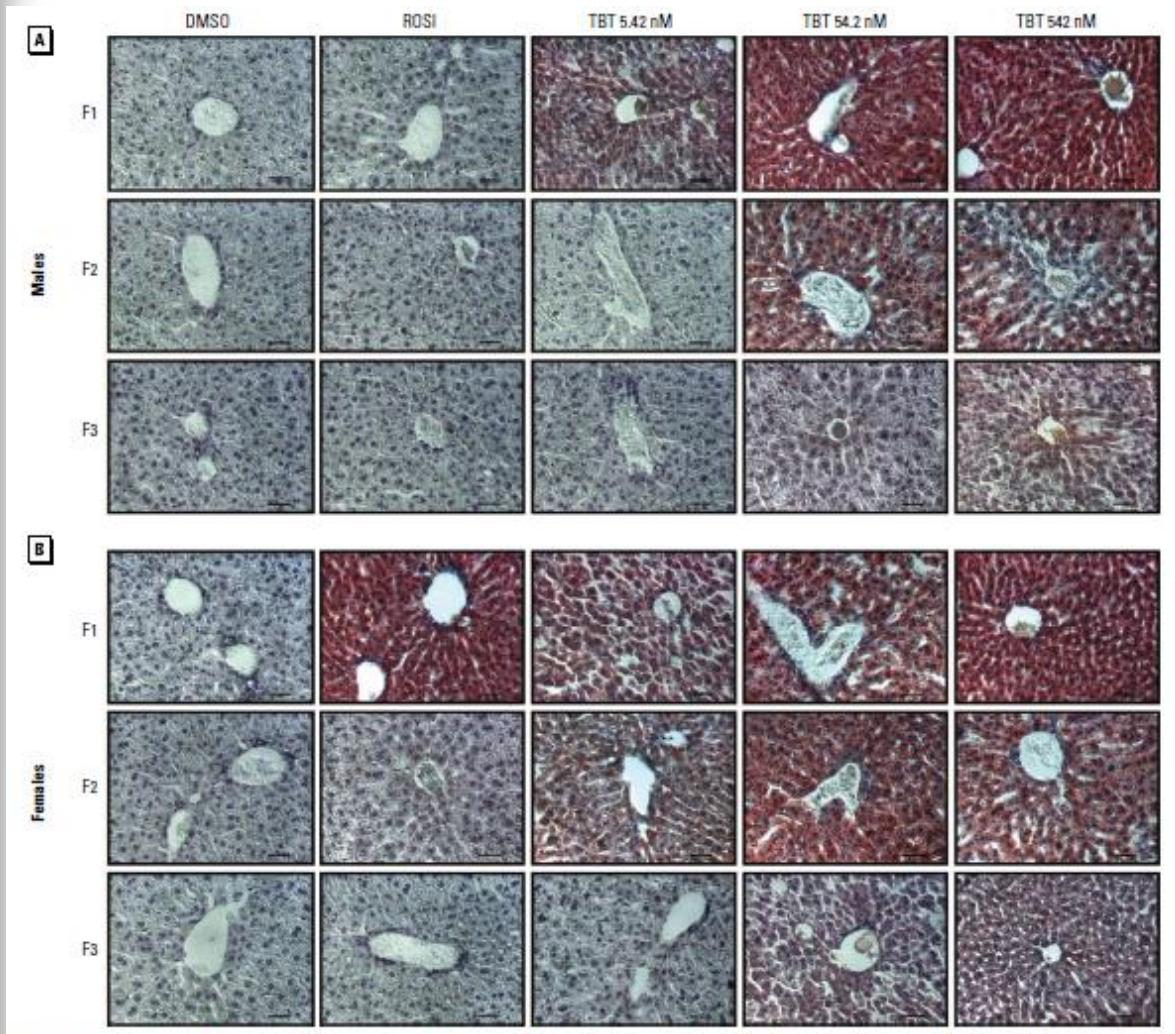


Figure 3. Transgenerational effects of DMSO (vehicle), ROSI, or TBT (5.42, 54.2, or 542 nM) on hepatic lipid accumulation in F1, F2, and F3 male (*A*) and female (*B*) mice. Histological sections of frozen livers were stained with Oil Red O and hematoxylin; at least five animals per exposure group were analyzed, and representative photomicrographs are shown. Bars = 50 µm.

Chamorro-Garcia et al., 2013

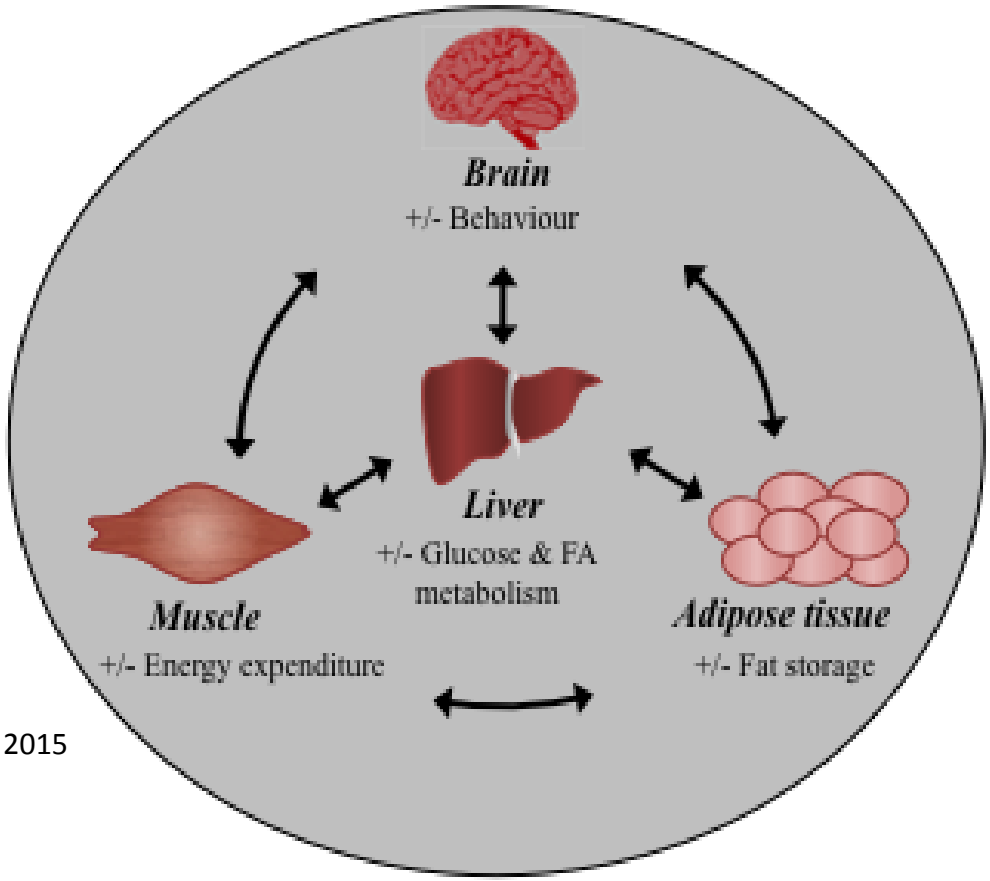
PLOS | ONE

RESEARCH ARTICLE

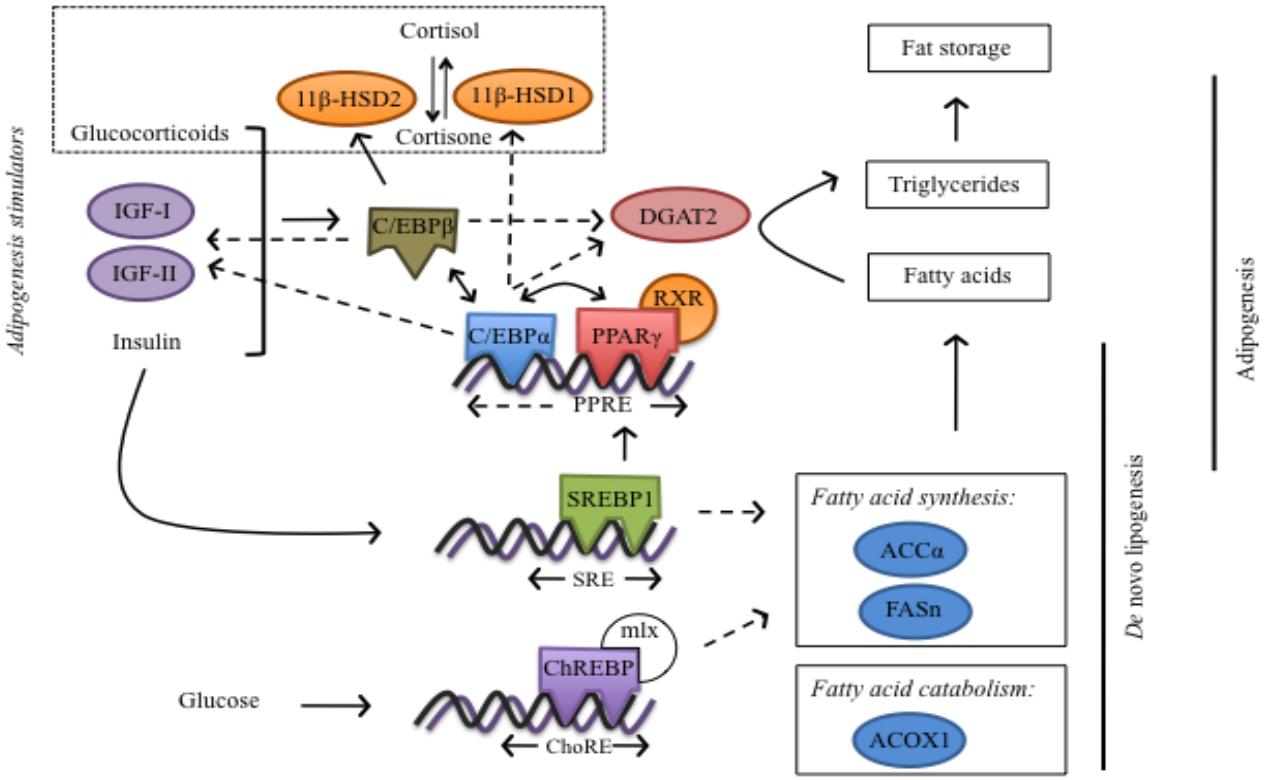
The Mammalian "Obesogen" Tributyltin Targets Hepatic Triglyceride Accumulation and the Transcriptional Regulation of Lipid Metabolism in the Liver and Brain of Zebrafish

Angeliki Lyssimachou[1]*, Joana G. Santos[1], Ana André[1], Joana Soares[1], Daniela Lima[1], Laura Guimarães[1], C. Marisa R. Almeida[1], Catarina Teixeira[1], L. Filipe C. Castro[1]*, Miguel M. Santos[1,2]*

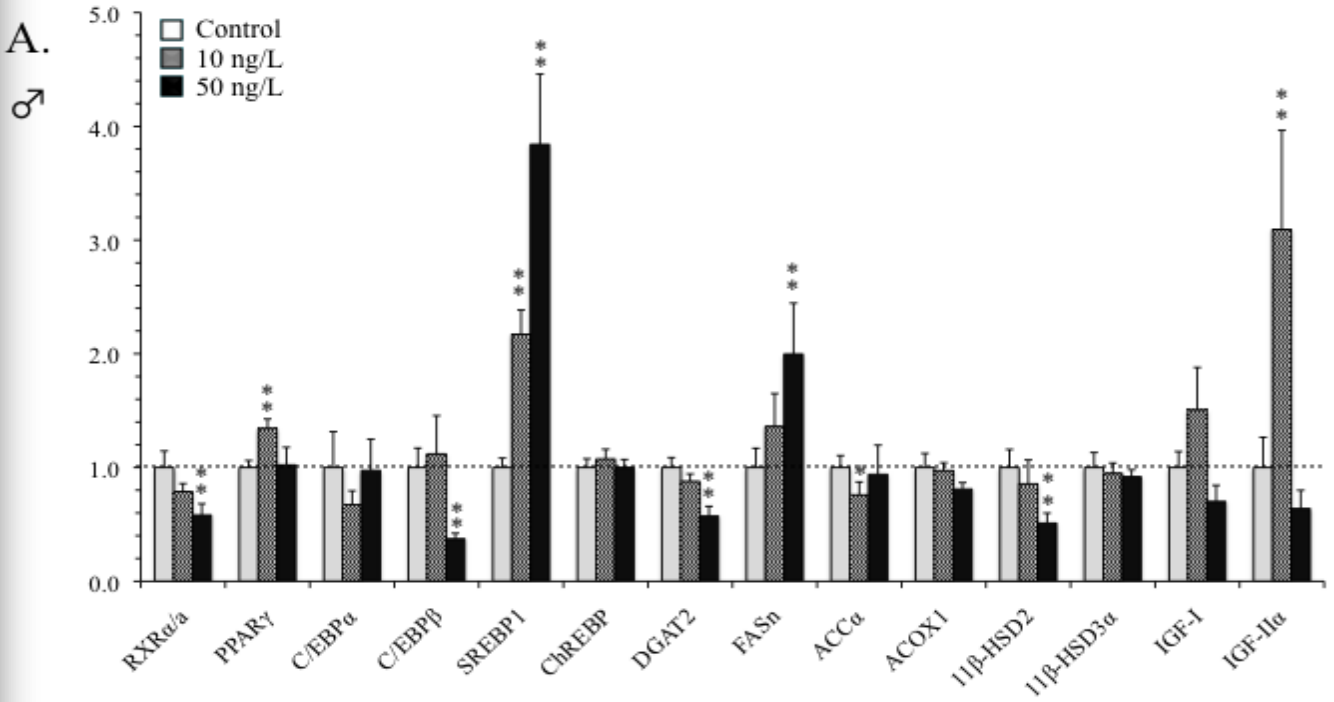
1 CIMAR/CIIMAR-AL, Interdisciplinary Centre of Marine and Environmental Research, Rua dos Bragas 289, 4050–123, Porto, Portugal, 2 FCUP–Department of Biology, Faculty of Sciences, University of Porto, Porto, Portugal



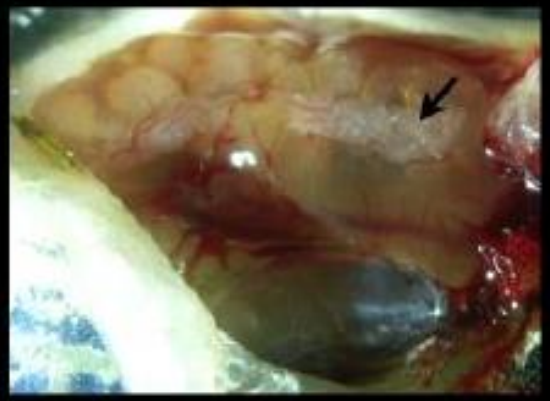
Lyssimachou et al., 2015

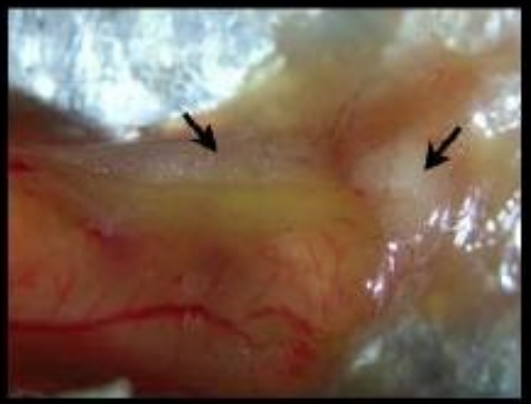


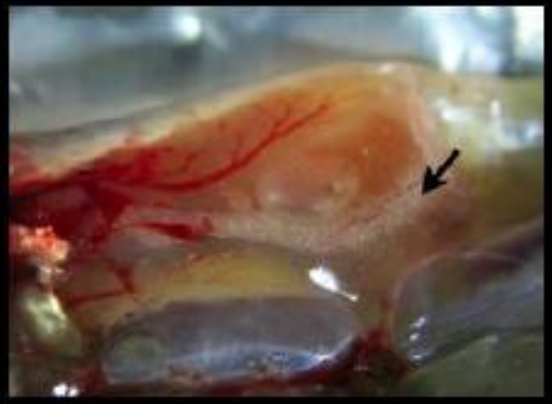
Lyssimachou et al., 2015

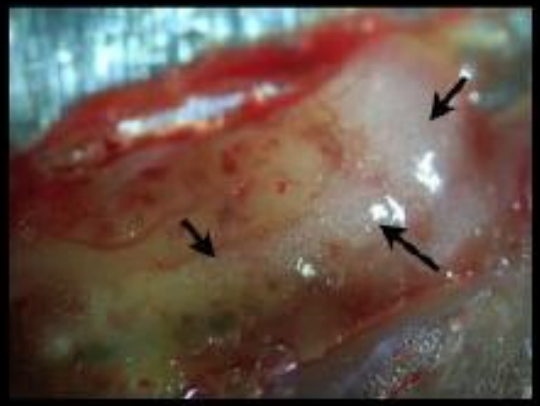


Lyssimachou et al., 2015









Lyssimachou et al., 2015

Arrows indicate adipocites

PROCEEDINGS OF THE ROYAL SOCIETY B

Proc. R. Soc. B (2011) 278, 1626–1632
doi:10.1098/rspb.2010.1890
Published online 24 November 2010

Canaries in the coal mine: a cross-species analysis of the plurality of obesity epidemics

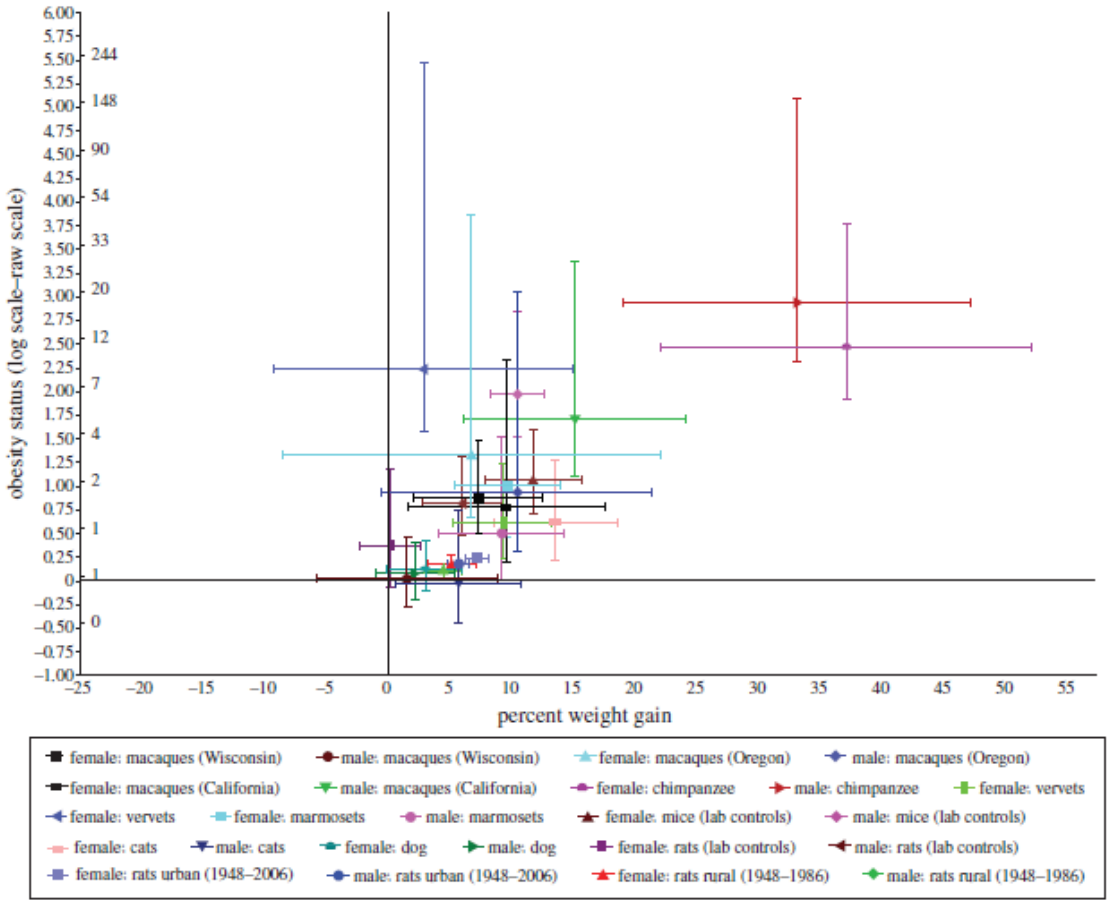
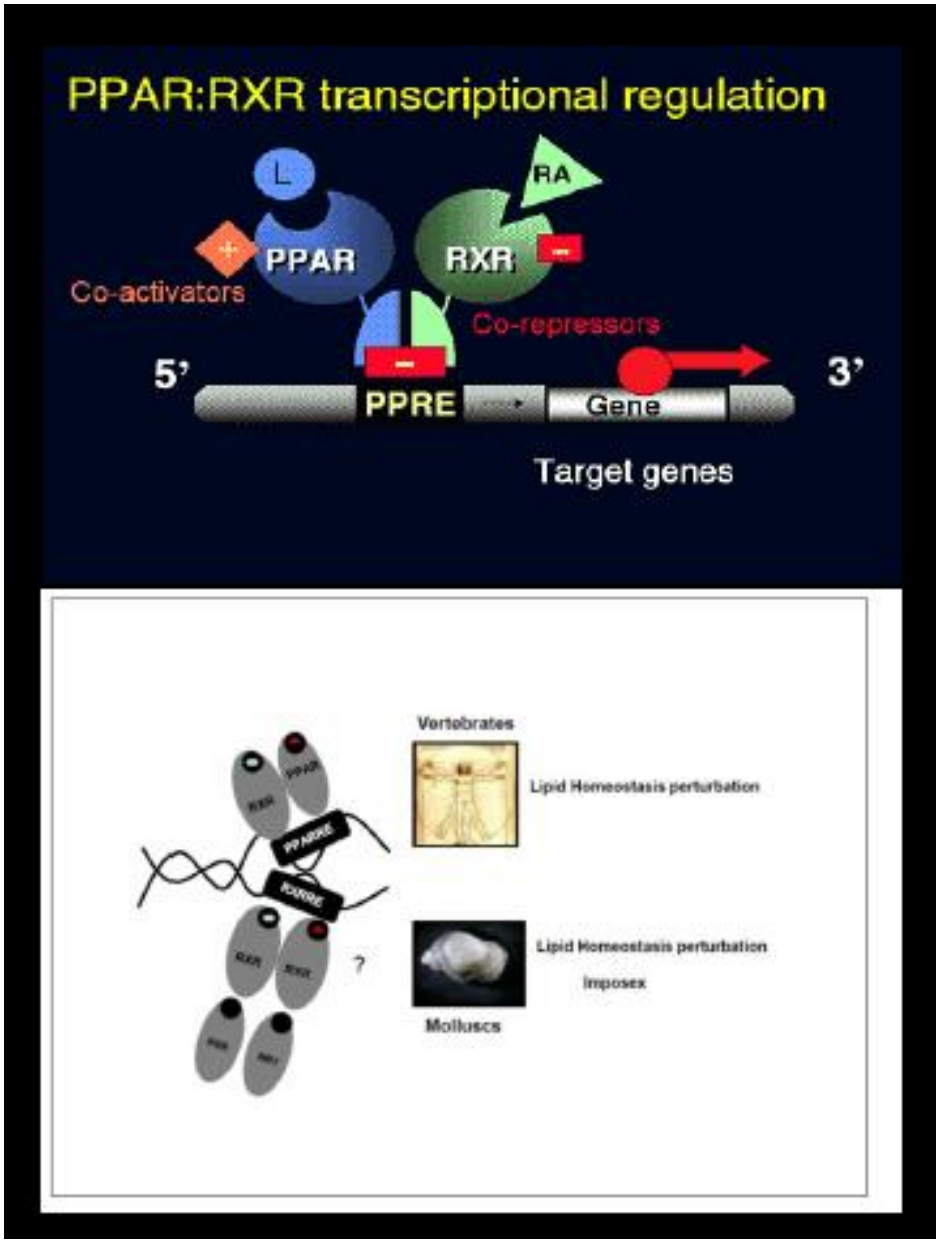


Figure 1. Mean and ±1 s.e. of per cent weight gain and obesity status by decade. The left side of the *y*-axis refers to the raw scale of obesity status, and the right side refers to the log scale of obesity status.


PPAR:RXR transcriptional regulation
L
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PPAR
RXR
Co-activators
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5'
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Target genes
Vertebrates
Lipid Homeostasis perturbation
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Lipid Homeostasis perturbation
Imposex
Molluscs

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Estimating Burden and Disease Costs of Exposure to Endocrine-Disrupting Chemicals in the European Union

Table 4. Evaluations of Exposure-Outcome Relationships

Exposure	Outcome	Strength of Human Evidence	Strength of Toxicological Evidence	Probability of Causation, %	Base Estimate, €	Low Estimate, €	High Estimate, €
PBDEs	IQ loss and intellectual disability	Moderate-to-high	Strong	70–100	9 587 571 420	1 577 449 522	22 356 864 892
Organophosphate pesticides	IQ loss and intellectual disability	Moderate-to-high	Strong	70–100	146 178 556 566	46 760 988 423	194 850 545 761
DDE	Childhood obesity	Moderate	Moderate	40–69	24 610 041	24 610 041	86 448 264
DDE	Adult diabetes	Low	Moderate	20–39	834 741 170	834 741 170	16 694 823 393
Di-2-ethylhexylphthalate	Adult obesity	Low	Strong	40–69	15 610 612 091	15 610 612 091	15 610 612 091
Di-2-ethylhexylphthalate	Adult diabetes	Low	Strong	40–69	606 944 344	606 944 344	606 944 344
BPA	Childhood obesity	Very low-to-low	Strong	20–69	1 537 177 463	1 537 177 463	1 537 177 463
PBDEs	Testicular cancer	Very low-to-low	Weak	0–19	1 695 951 864	626 359 671	1 695 951 864
PBDEs	Cryptorchidism	Low	Strong	40–69	259 614 654	233 683 168	233 683 168
Benzyl and butyl phthalates	Male infertility, resulting in increased assisted reproductive technology	Low	Strong	40–69	4 714 114 146	4 714 114 146	4 714 114 146
Phthalates	Low T, resulting in increased early mortality	Low	Strong	40–69	7 958 358 238	7 958 358 238	7 958 358 238
Multiple exposures	ADHD	Low-to-moderate	Strong	20–69	1 743 332 686	1 212 298 027	2 861 405 410
Multiple exposures	Autism	Low	Moderate	20–39	199 339 876	79 735 951	398 679 753

Abbreviation: ADHD, attention-deficit hyperactivity disorder.

Results: Expert panels achieved consensus for probable (>20%) EDC causation for IQ loss and associated intellectual disability, autism, attention-deficit hyperactivity disorder, childhood obesity, adult obesity, adult diabetes, cryptorchidism, male infertility, and mortality associated with reduced T. Accounting for probability of causation and using the midpoint of each range for probability of causation, Monte Carlo simulations produced a median cost of €157 billion (1.23% of EU gross domestic product) annually across 1000 simulations. Notably, using the lowest end of the probability range for each relationship in the Monte Carlo simulations produced a median range of €119 billion that differed modestly from base case probability inputs.

Conclusions: EDC exposures in the EU are likely to contribute substantially to disease and dysfunction across the life course with costs in the hundreds of billions per year. These estimates represent only those EDCs with the highest probability of causation; a broader analysis would have produced greater estimates of burden of disease and costs. (*J Clin Endocrinol Metab* 100: 0000–0000, 2015)

OECD Conceptual Framework for Testing and Assessment of Endocrine Disrupters (as revised in 2012)

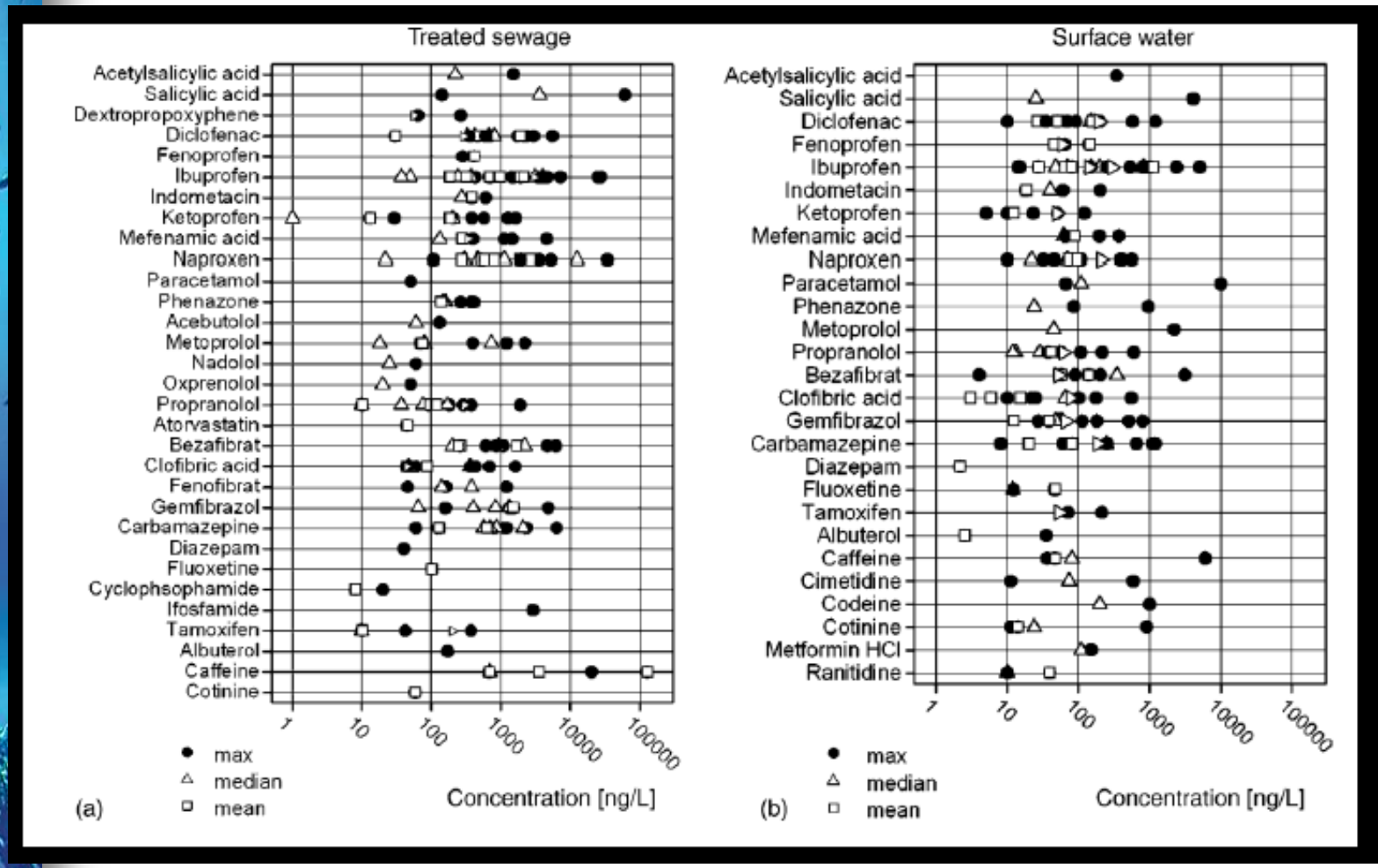
	Mammalian and non mammalian Toxicology
Level 1 Existing Data and Non-Test Information	• Physical & chemical properties, e.g., MW reactivity, volatility, biodegradability • All available (eco)toxicological data from standardized or non-standardized tests. • Read across, chemical categories, QSARs and other *in silico* predictions, and ADME model predictions
Level 2 *In vitro* assays providing data about selected endocrine mechanism(s) / pathways(s) (Mammalian and non mammalian methods)	• Estrogen or androgen receptor binding affinity • Estrogen receptor transactivation (OECD TG 455 – OECD TG 457) • Androgen or thyroid transactivation (If/when TGs are available) • Steroidogenesis in vitro (OECD TG 456) • MCF-7 cell proliferation assays (ER ant/agonist) • Other assays as appropriate

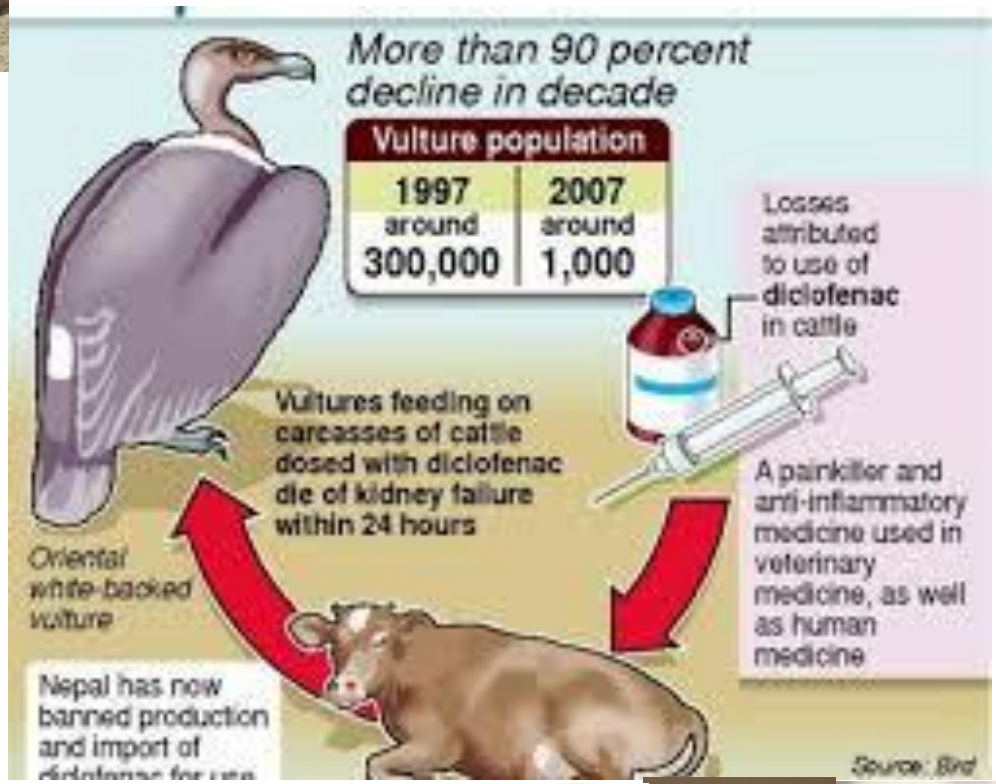
	Mammalian Toxicology	Non-Mammalian Toxicology
Level 3 *In vivo* assays providing data about selected endocrine mechanism(s) / pathway(s)[1]	• Uterotrophic assay (OECD TG 440) • Hershberger assay (OECD TG 441)	• Xenopus embryo thyroid signalling assay (When/if TG is available) • Amphibian metamorphosis assay (OECD TG 231) • Fish Reproductive Screening Assay (OECD TG 229) • Fish Screening Assay (OECD TG 230) • Androgenized female stickleback screen

Level 4 *In vivo* assays providing data on adverse effects on endocrine relevant endpoints [2]	• Repeated dose 28-day study (OECD TG 407) • Repeated dose 90-day study (OECD TG 408) • 1-generation reproduction toxicity study (OECD TG 415) • Male pubertal assay (see GD 150, Chapter C4.3)[3] • Female pubertal assay (see GD 150, Chapter C4.4)[3] • Intact adult male endocrine screening assay (see GD 150, Chapter Annex 2.5) • Prenatal developmental toxicity study (OECD TG 414) • Chronic toxicity and carcinogenicity studies (OECD TG 451-3) • Reproductive screening test (OECD TG 421 if enhanced) • Combined 28-day/reproductive screening assay (OECD TG 422 if enhanced) • Developmental neurotoxicity (OECD TG 426)	• Fish sexual development test (OECD TG 234) • Fish Reproduction Partial Lifecycle Test (when/If TG is Available) • Larval Amphibian Growth & Development Assay (when TG is available) • Avian Reproduction Assay (OECD TG 206) • Mollusc Partial Lifecycle Assays (when TG is available) [4] • Chironomid Toxicity Test (TG 218-219) [4] • Daphnia Reproduction Test (with male induction) (OECD TG 211) [4] • Earthworm Reproduction Test (OECD TG 222) [4] • Enchytraeid Reproduction Test (OECD TG 220) [4] • Sediment Water Lumbriculus Toxicity Test Using Spiked Sediment (OECD TG 225) [4] • Predatory mite reproduction test in soil (OECD TG 226) [4] • Collembolan Reproduction Test in Soil (TG OECD 232) [4]
Level 5 *In vivo* assays providing more	• Extended one-generation reproductive toxicity study (OECD TG 443)[5]	• FLCTT (Fish LifeCycle Toxicity Test) (when TG is available)

Level 5 *In vivo* assays providing more	• Extended one-generation reproductive toxicity study (OECD TG 443)[5]	• FLCTT (Fish LifeCycle Toxicity Test) (when TG is available)
comprehensive data on adverse effects on endocrine relevant endpoints over more extensive parts of the life cycle of the organism [2]	• 2-Generation reproduction toxicity study (OECD TG 416 most recent update)	• Medaka Multigeneration Test (MMGT) (when TG is available) • Avian 2 generation reproductive toxicity assay (when TG is available) • Mysid Life Cycle Toxicity Test (when TG is available)[4] • Copepod Reproduction and Development Test (when TG is available)[4] • Sediment Water Chironomid Life Cycle Toxicity Test (OECD TG 233) [4] • Mollusc Full Lifecycle Assays (when TG is available) [4] • Daphnia Multigeneration Assay (if TG is available) [4]

Emerging pollutants


Treated sewage
Acetylsalicylic acid
Salicylic acid
Dextropropoxyphene
Diclofenac
Fenoprofen
Ibuprofen
Indometacin
Ketoprofen
Mefenamic acid
Naproxen
Paracetamol
Phenazone
Acebutolol
Metoprolol
Nadolol
Oxprenolol
Propranolol
Atorvastatin
Bezafibrat
Clofibric acid
Fenofibrat
Gemfibrazol
Carbamazepine
Diazepam
Fluoxetine
Cyclophsophamide
Ifosfamide
Tamoxifen
Albuterol
Caffeine
Cotinine
1
10
100
1000
10000
100000
max
median
mean
(a)
Concentration [ng/L]
Surface water
Acetylsalicylic acid
Salicylic acid
Diclofenac
Fenoprofen
Ibuprofen
Indometacin
Ketoprofen
Mefenamic acid
Naproxen
Paracetamol
Phenazone
Metoprolol
Propranolol
Bezafibrat
Clofibric acid
Gemfibrazol
Carbamazepine
Diazepam
Fluoxetine
Tamoxifen
Albuterol
Caffeine
Cimetidine
Codeine
Cotinine
Metformin HCl
Ranitidine
1
10
100
1000
10000
100000
max
median
mean
(b)
Concentration [ng/L]


More than 90 percent decline in decade
Vulture population
1997 around 300,000
2007 around 1,000
Losses attributed to use of diclofenac in cattle
Vultures feeding on carcasses of cattle dosed with diclofenac die of kidney failure within 24 hours
A painkiller and anti-inflammatory medicine used in veterinary medicine, as well as human medicine
Oriental white-backed vulture
Nepal has now banned production and import of
Source: Bird


Voltaren
Schmerzgel
120 g Gel


Dyfoject
Diclofenac


MELOXICAM
INJECTION
MELONEX
DISIC-VET
NEOVET

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Aquatic Toxicology

journal homepage: www.elsevier.com/locate/aquatox

Hypocholesterolaemic pharmaceutical simvastatin disrupts reproduction and population growth of the amphipod *Gammarus locusta* at the ng/L range

Teresa Neuparth[a,*], Carla Martins[c], Carmen B. de los Santos[a], Maria H. Costa[c], Irene Martins[d], Pedro M. Costa[c], Miguel M. Santos[a,b,*]

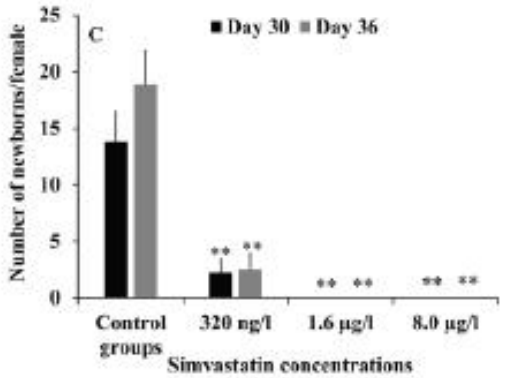

Fig. 3. Chronic effects of SIM on *Gammarus locusta* females reproductive endpoints in bioassay 2. (A) Percentage of ovigerous females; (B) Number of stadium I–II embryos per female; (C) number of newborns per female. Error bars indicate the standard errors; * and ** indicate significant differences from control groups ($p < 0.05$ and $p < 0.01$, respectively).

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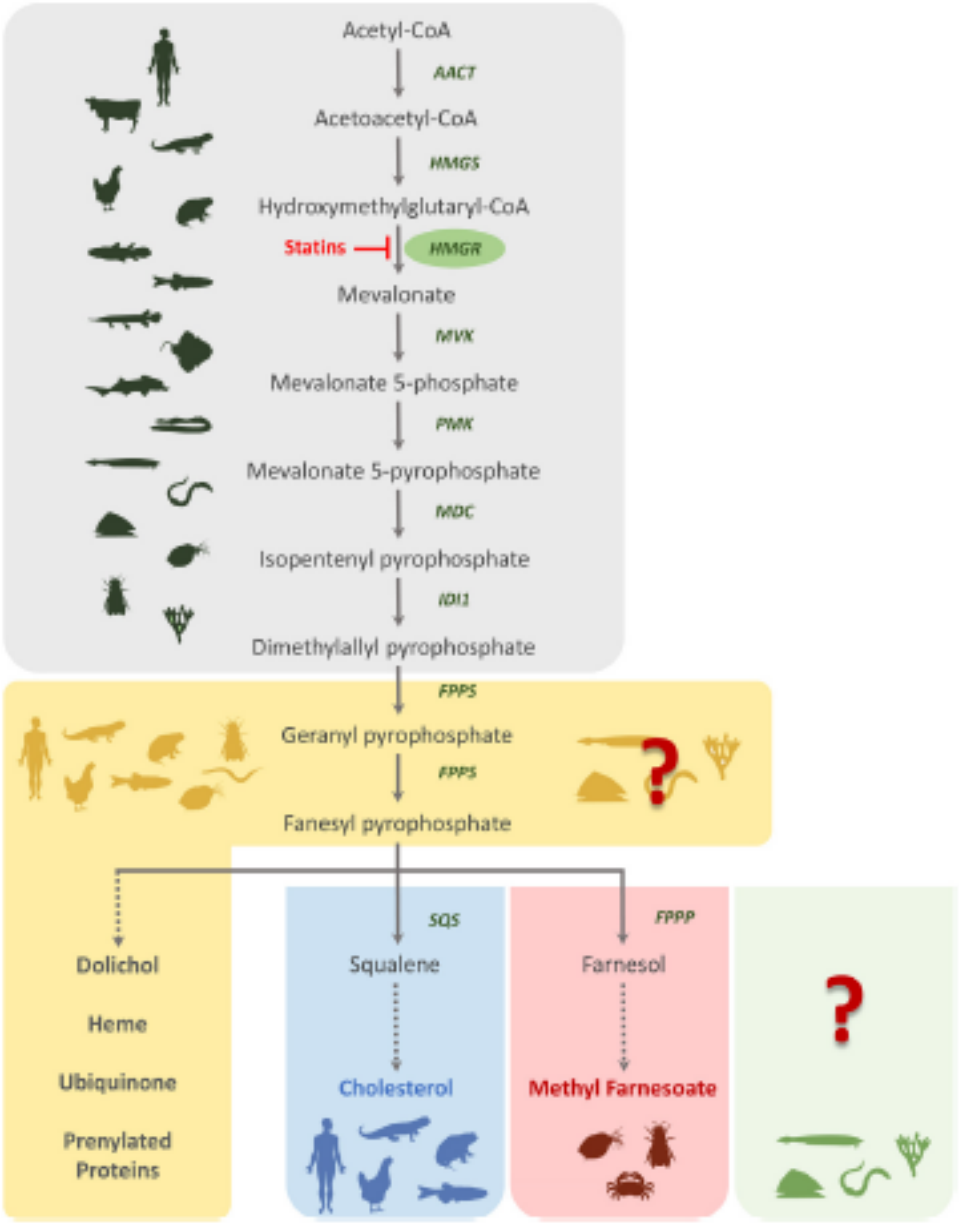
Statins: An undesirable class of aquatic contaminants?

Miguel M. Santos[a,b,*], Raquel Ruivo[a], Mónica Lopes-Marques[a,c], Tiago Torres[a], Carmen B. de los Santos[a], L. Filipe C. Castro[a,b], Teresa Neuparth[a]

MEVALONATE PATHWAY



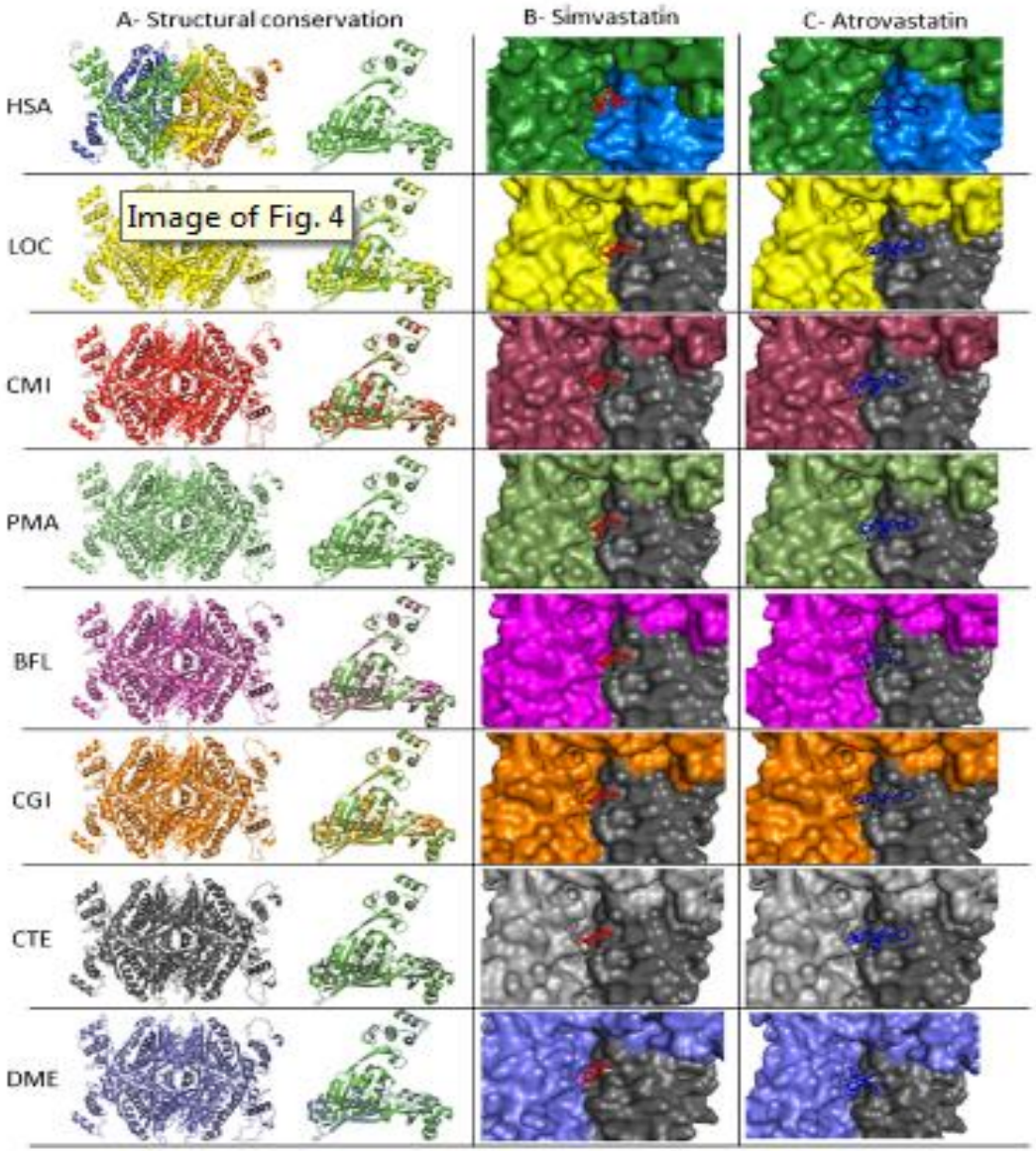


Fig. 4. Comparative homology models and human crystal structure 1HWI in line 1, Column A—structural conservation analysis, on the left predicted quaternary structure, on the right structural alignment of one monomer from each model to one monomer from 1HWI. Column B—best predicted docking poses for Simvastatin. Column C—best predicted docking poses for Atrovastatin. HSA-*Homo sapiens*, LOC-*Leptosynapta ocnalata*, CMI-*Callorhinchus milii*, PMA-*Petromyzon marinus*, BFL-*Branchiostoma floridae*, CGI-*Crassostrea gigas*, CTE- *Capitella teleta*, DME-*Drosophila melanogaster*.

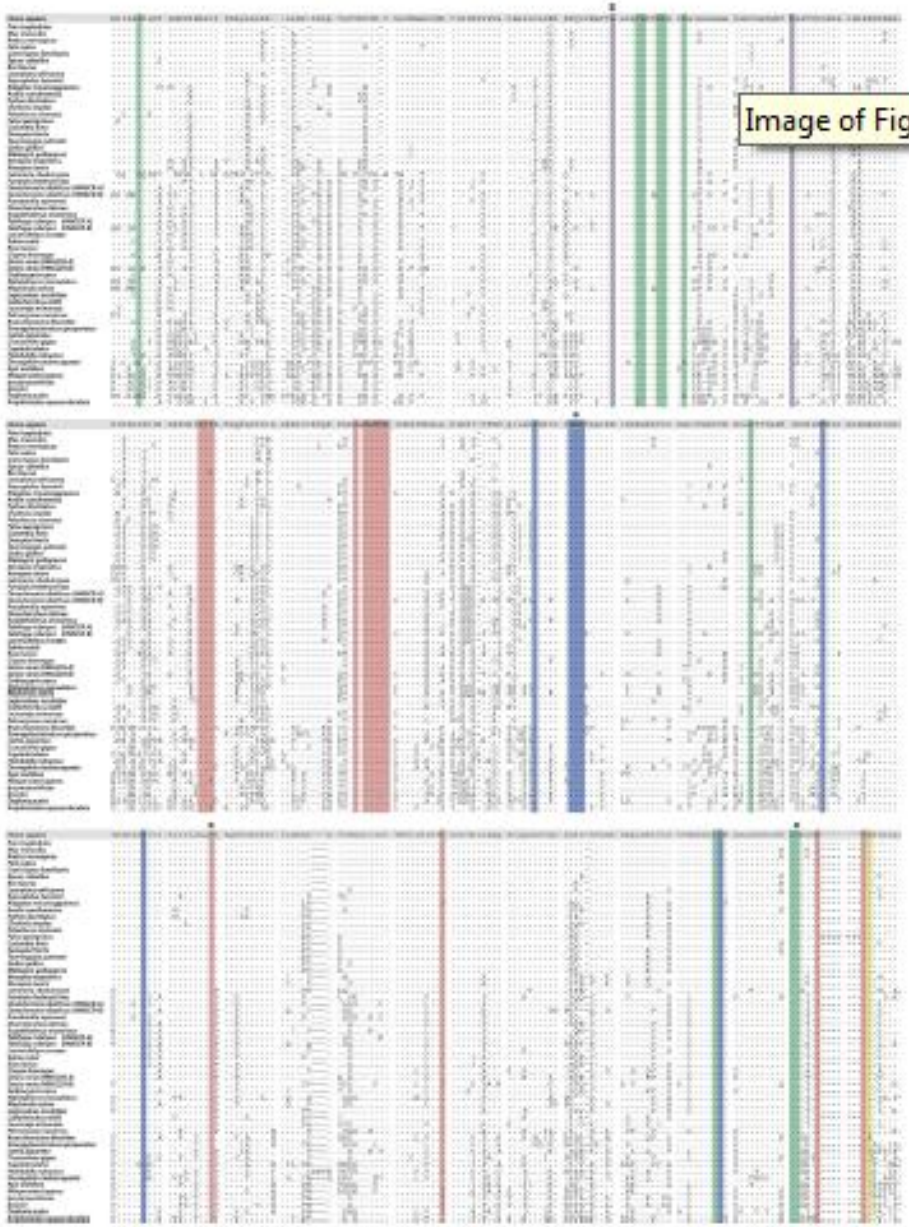
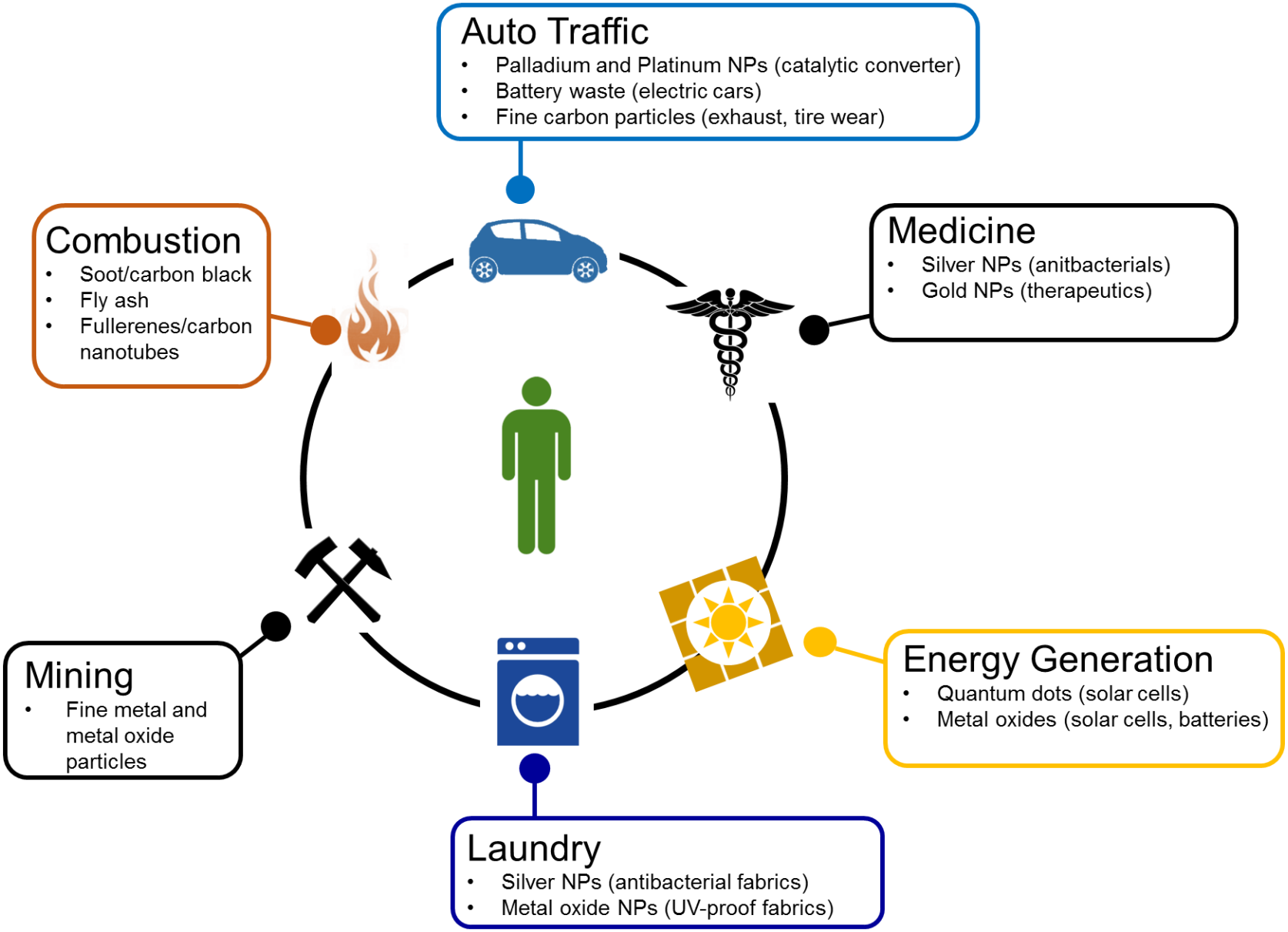


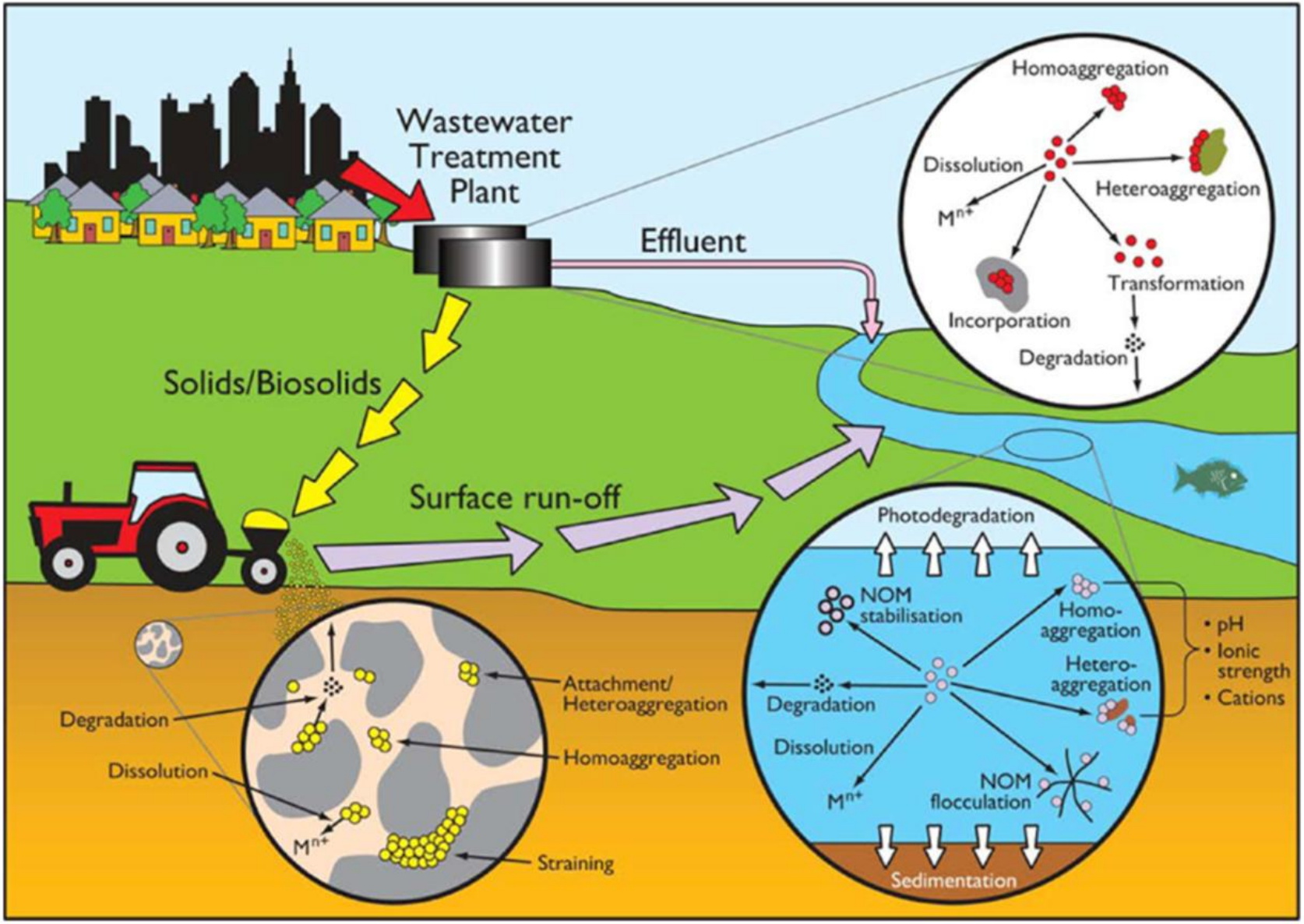
Image of Fig. 3

Fig. 3. Partial alignment of the catalytic domain of HMGR. Human HMGR catalytic and substrate-binding residues are highlighted (Istvan and Deisenhofer, 2000, 2001). The catalytic tetrad is denoted by grey dots. In green, residues involved in CoA binding. Co-factor (NADP+)-binding residues are highlighted in red. In blue, residues interacting with the hydroxymethylglutaryl (HMG) moieties of both HMG-CoA and statins. Residues shared by NADP+ and HMG are in purple. A phosphorylation site is also shown (yellow) (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article).

Personal Care Products (PCPs)

Nanoparticles





GRAEME et al., 2013

Effects potentially associated with exposure to nanoparticles

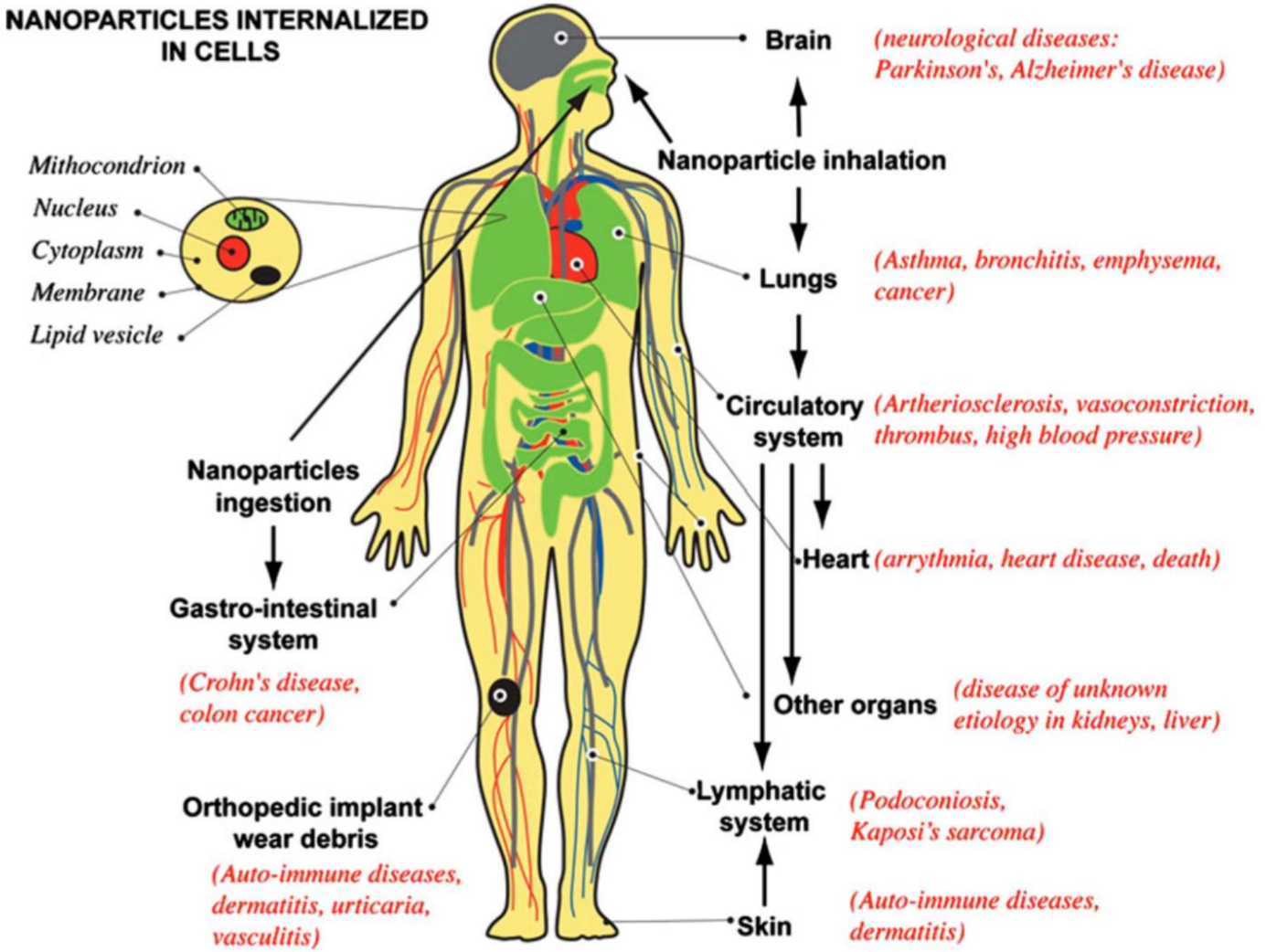


FIG. 7. Schematics of human body with pathways of exposure to nanoparticles, affected organs, and associated diseases from epidemiological, *in vivo* and *in vitro* studies.

Aquatic Ecosystems

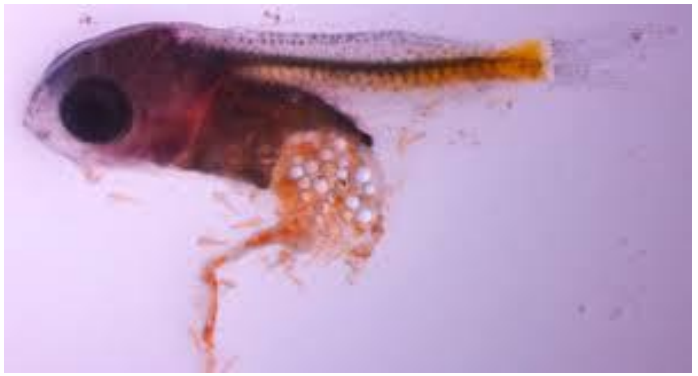
TABLE 1. Estimated Environmental Concentrations of Manufactured Nanomaterials Compared to Predicted No Effects Concentrations

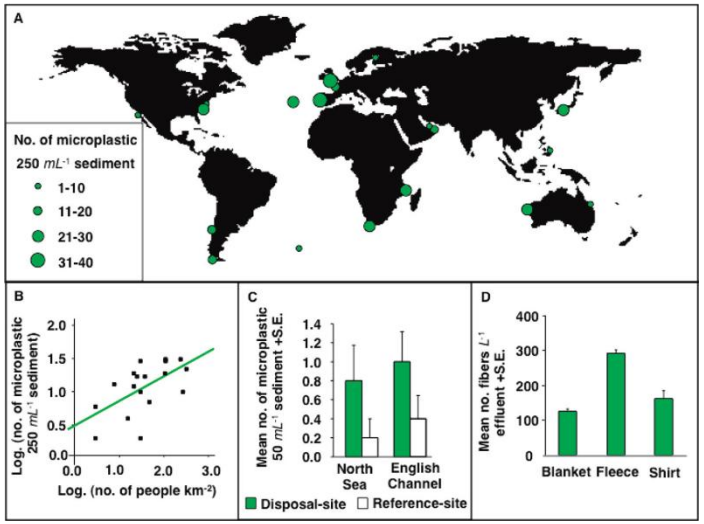
nanomaterial	PEC, μg/L	water body	ref	PNEC, μg/L	ref
TiO_2	0.7–16	freshwater	41	40	61
	<5–15	WWTP effluent	51	50	in 46
	1–10	freshwater	45		
	<8	Swiss rivers	47		
n-C_{60}	0.0005–19	WWTP effluent	62	7.9	61
CNT	0.0005–0.0008	freshwater	41		
Ag	0.03–0.08	freshwater	41	40	41
	0.04–0.32	freshwater	45	1	in 46
	<0.03	Swiss rivers	47		
CeO_2	0.1–1	freshwater	45	3000	in 46

Overview

- For several compounds the information for calculating PNECs is still limited.
- The PECs, in most cases, are several orders of magnitude below the concentrations that induce effects in ecotoxicological trials.
- Further studies are needed to evaluate NOECs.
- Need for chronic toxicity studies involving environmentally relevant levels.
- Evaluation of bioconcentration;
- Effects on parameters that are relevant from an environmental point of view;

Microplastics





Overview

Considering the high concentrations of microplastics observed in different areas, (2) the fact that plastics are extremely persistent in the environment, (3) the microplastics in the environment have their origin in several sources, strategies should be developed to mitigate their presence and better understand their ecological effects.

How to better improve risk assessment of Emerging Contaminants acting as EDCs?

Diversity is a key aspect

If we aim to improve risk assessment of EDCs and emerging pollutants at an ecosystems scale, and understand their mode of action (MOA), we must establish a framework to include a broad phylogenetic sampling of Metazoans taking advantage of all tools available.

This includes data on available genomes/transcriptomes, functional characterized NR/enzymatic assays, laboratory-established life cycles of representative *taxa*, OECD toxicity testing protocols. The development of these tools across metazoans will allow the implementation of this step-wise procedure to prioritize chemicals to assess their potential risk as EDCs.

Obrigado !