Environmental Signaling and Epigenetics

Endocrine Disruption as a Case Study

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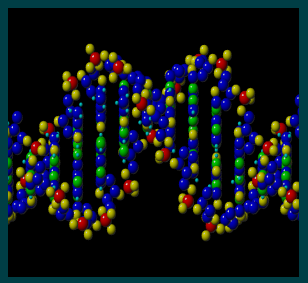
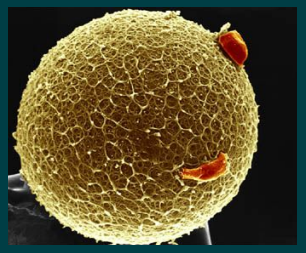
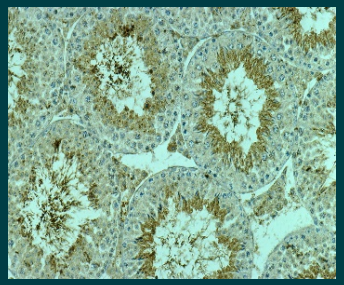
The World of Environmental Health







Laboratory-based Studies

Molecular

↑ seconds

Cellular

↑ minutes

Tissue

↑ hours

Organ

Biosphere

↑ eons

Ecosystem

↑ centuries

Community

↑ decades

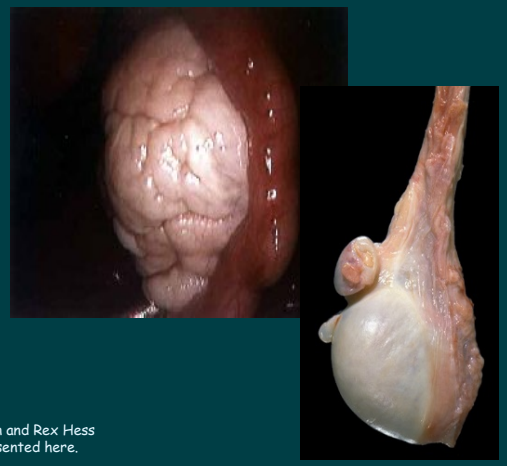
Population

Field-based Studies

Organism

years

Lab or Field-based Studies

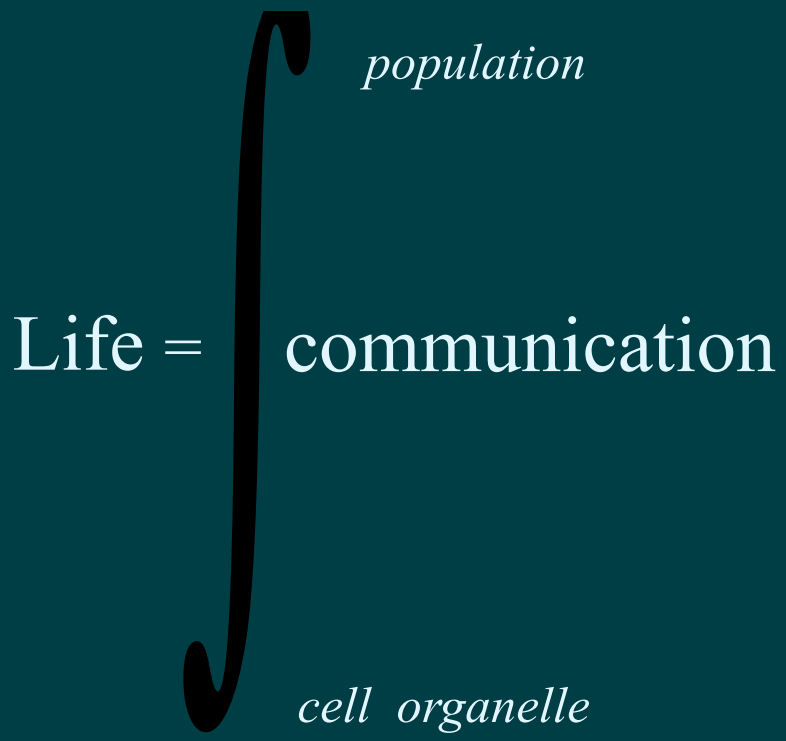


Thanks to John Moran and Rex Hess
for use of photos presented here.

From Louis Guillette

Definition of *Signal*

- Signal (noun)
  - A gesture, action or sound that is used to convey information or instructions, typically by prearrangement between the parties concerned



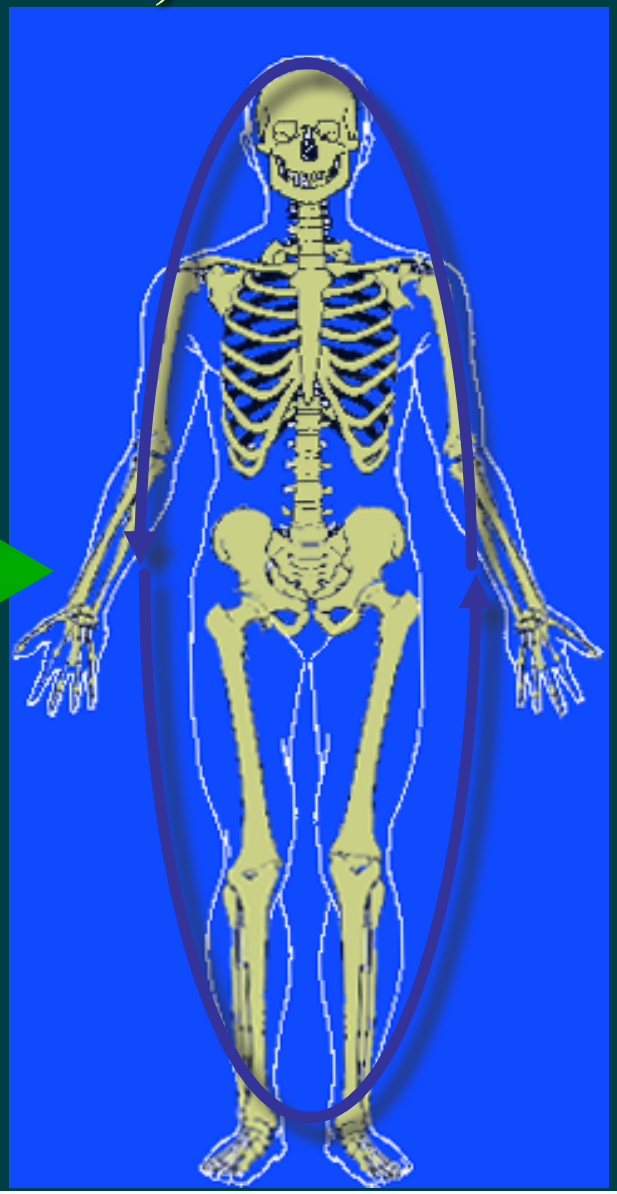
de Loof, Int. j. biochem. 25:1715,1993

via Howard Bern, 1999

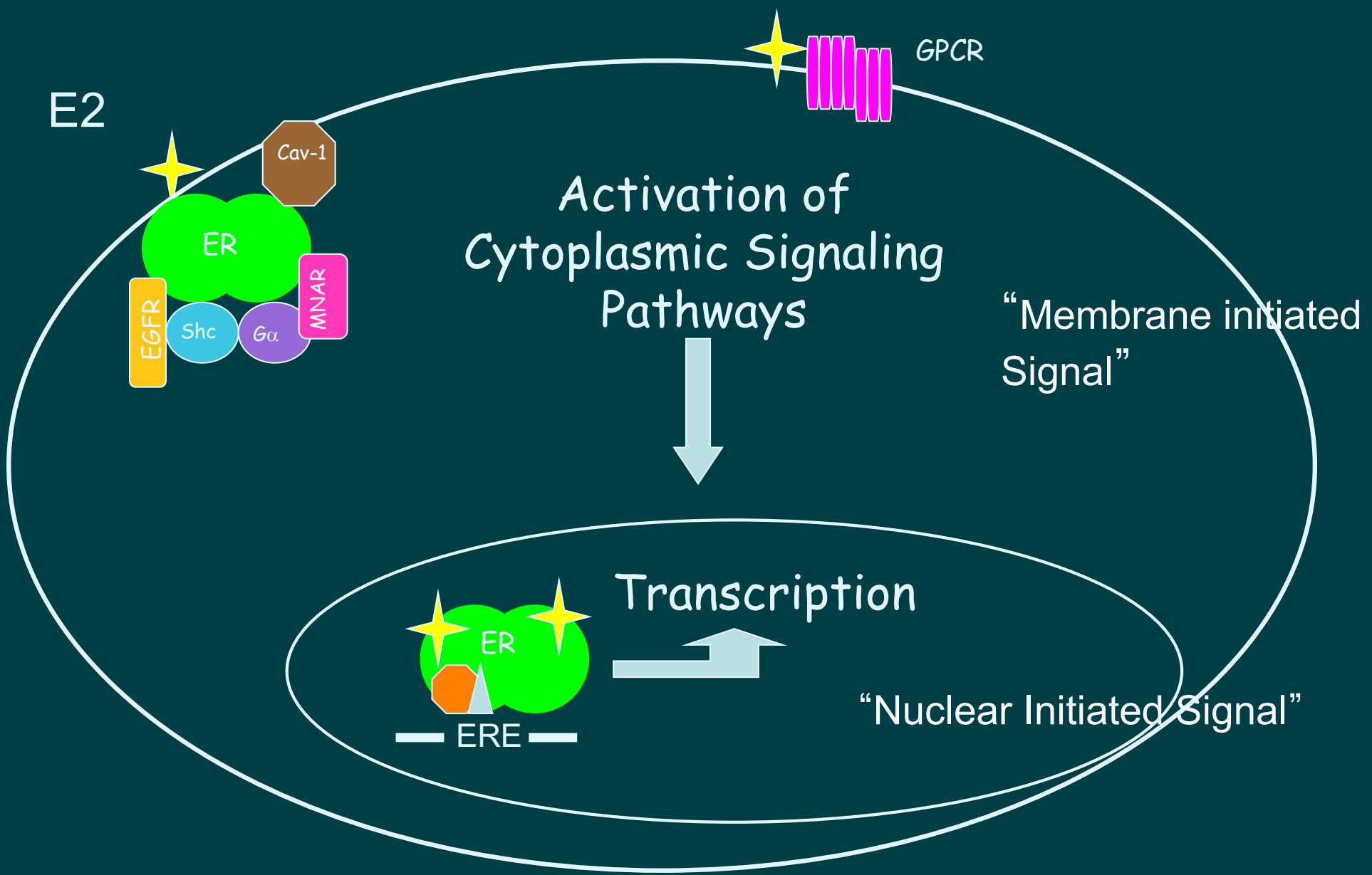
Biological Signaling

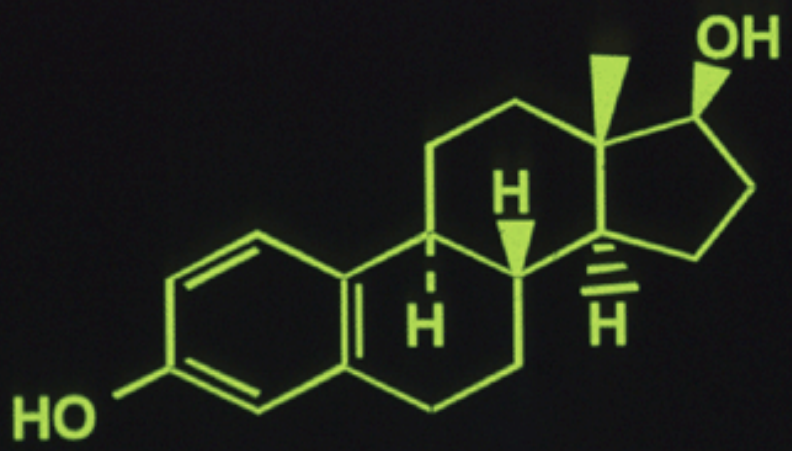
(Common to Most Vertebrates)

Hormones
Neurotransmitters
Other bio-molecules

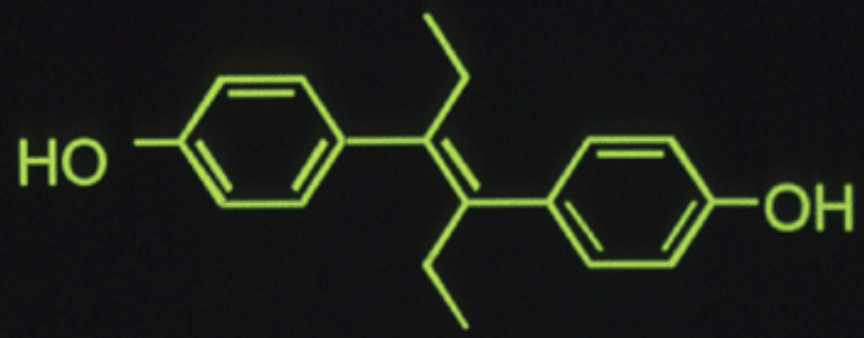


Mechanisms of E2 Action

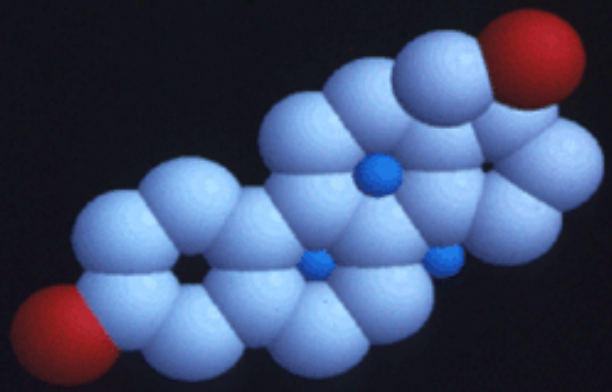




17 β-estradiol



Diethylstilbestrol



Estrogen is a Key Determinant in Women's Reproductive Health

Sexual development in utero

Attainment of puberty

Regulation of reproductive function

Absence results in menopause

Landmarks in Birth Defects Research

- 1956-1960 Chemicals toxic to the mother are also toxic to the fetus. The "placental barrier" falls and chemical "birth defects" arise (Mercury poisoning with severe neurological symptoms in Minamata, Japan).
- 1961 Chemicals with no maternal toxicity can induce birth defects in human fetus. The "privileged fetus" concept for humans changes. (Thalidomide is effective tranquilizer, but causes limb reduction defects).
- 1971 Chemicals taken during pregnancy for which there is no overt toxicity to mother or child can cause delayed "functional" effects in offspring. The transition from "birth defects" to "developmental basis of adult disease". (Diethylstilbestrol, DES, given to pregnant women causes vaginal cancer or infertility in daughters 14 to 42 years later).

A Paper that Changed the Way We Think

Diethylstilbestrol (DES) and Vaginal Cancer in Offspring

Adenocarcinoma of the Vagina — Association of Maternal Stilbestrol Therapy with Tumor Appearance in Young Women

Arthur L. Herbst, M.D., Howard Ulfelder, M.D., and David C. Poskanzer, M.D.

N Engl J Med 1971; 284:878-881 | April 22, 1971 | DOI: 10.1056/NEJM197104222841604

Animal Models demonstrate sensitivity to environmental estrogens across species

Diethylstilbestrol (DES) given to pregnant mice or women results in the following in offspring:

	Mice *	Human**
1. Vaginal Clear Cell Carcinoma	x	x
2. Malformed Fallopian Tubes	x	x
3. Ovarian Cysts	x	x
4. Uterine Fibroids	x	x
5. Infertility	x	x
6. Early Menopause	x	x
7. Second Generation Effects on Reproductive Health	x	x

- *Newbold, McLachlan et al
- **Various authors

Transgenerational Effects of Diethylstilbestrol

- DES administration during development alters the reproductive system in female offspring (daughters)
  - Functional, structural and cellular effects similar in mice and humans
  - Effects predicted by mouse experiments now seen in humans (for example, uterine fibroids, mammary cancer, early menopause
- Offspring's offspring (grand daughters) are effected
  - Signal lesion, vaginal adenocarcinoma, penetrates into second generation in mice
  - Subfertility and menstrual irregularities recently reported in humans (Int J Epi, August, 2006) and ovarian cancer (Epidemiology, March 2008)

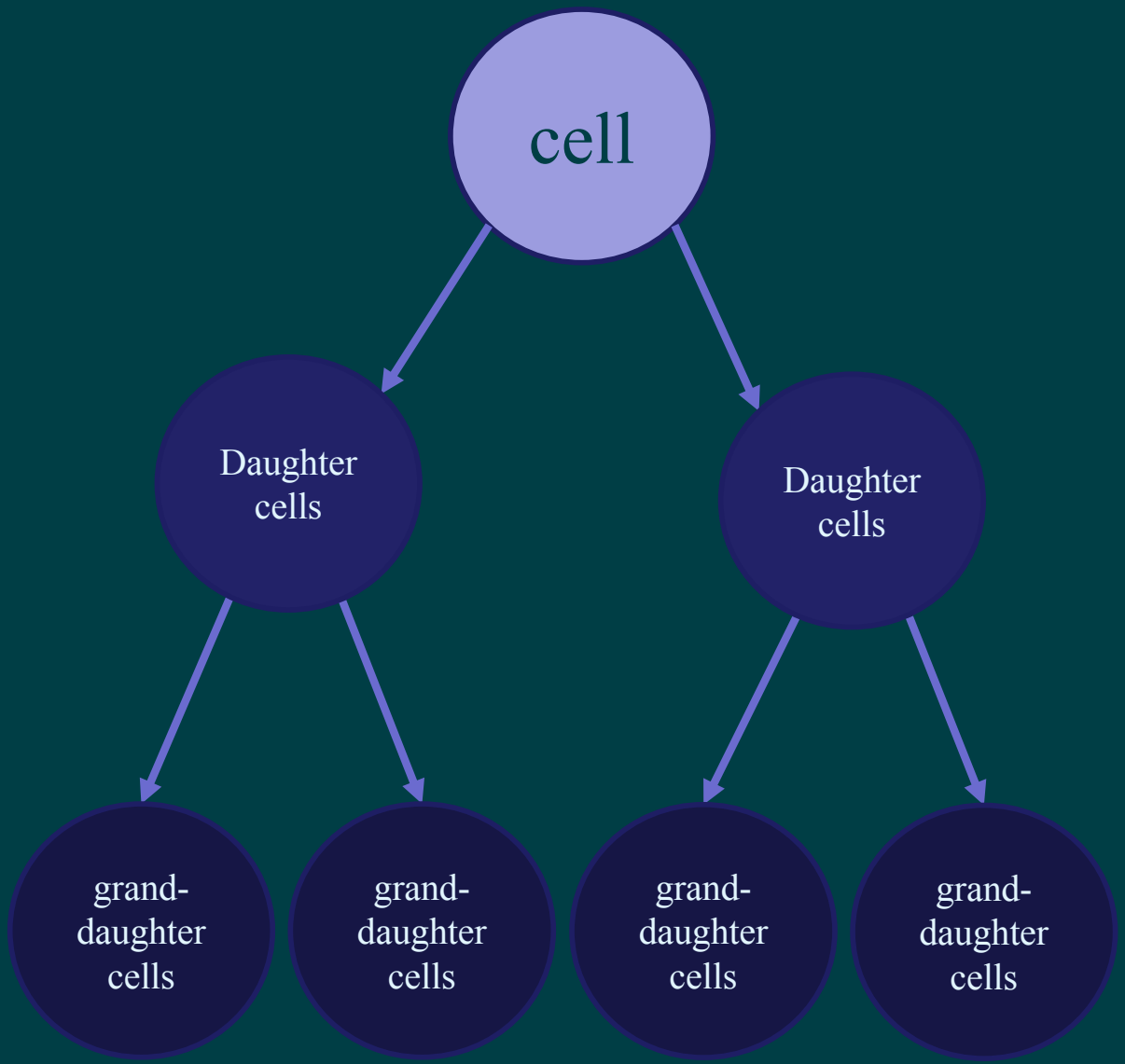
References contained in the following reviews,

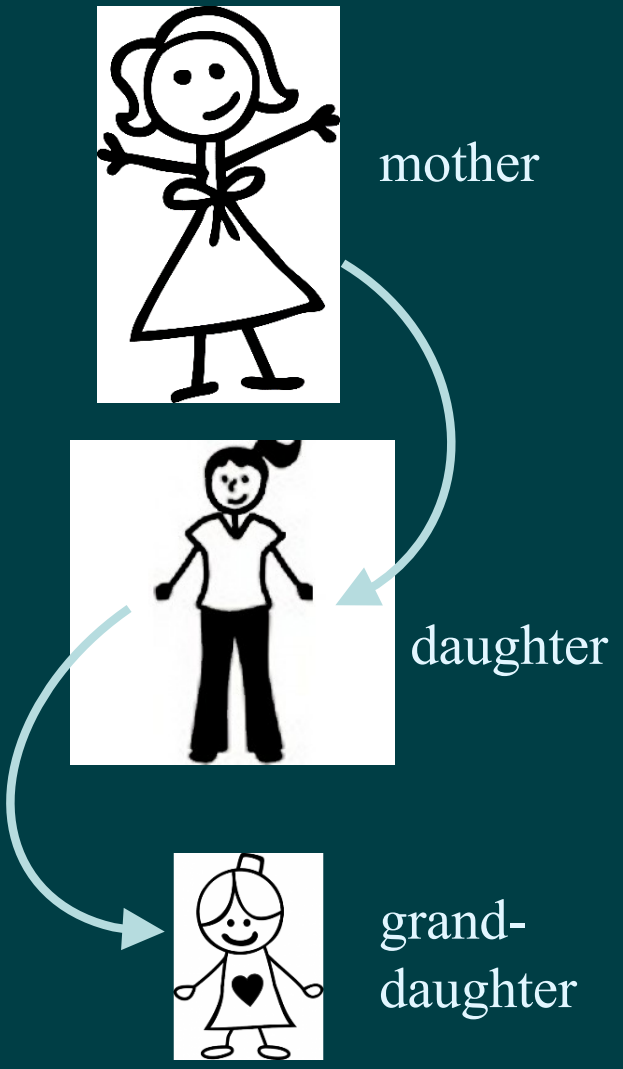
McLachlan. Endo Reviews 22: 319-341, 2001

Crews and McLachlan, Endocrinology 147: S4-10, 2006

McLachlan, Int J Epi 35: 868-869, 2006

GENERATIONAL EFFECTS OF ESTROGEN





DES exposure in utero changes the developmental program in tissues

Numerous studies have shown that DES works by epigenetic mechanisms to alter cell differentiation and tissue development hereditarily.

FUTURE RESEARCH

Find epigenetic marks in DES exposed humans as indications of risk and mechanism. Confirm relevance of animal models.

Developmental Exposure to Diethylstilbestrol Elicits Demethylation of Estrogen-responsive Lactoferrin Gene in Mouse Uterus

Shuanfang Li, Kimberly A. Washburn, Rick Moore, Tomohide Uno, Christina Teng, Retha R. Newbold, John A. McLachlan, and Masahiko Negishi[1]

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This Article

Cancer Res October 1, 1997 *57;* 4356

» Abstract
Full Text (PDF)
Classifications

Endocrinology. 2009 July; 150(7): 3376–3382. PMCID: PMC2703508
Published online 2009 March 19. doi: 10.1210/en.2009-0071

Hypermethylation of Homeobox A10 by *in Utero* Diethylstilbestrol Exposure: An Epigenetic Mechanism for Altered Developmental Programming

Jason G. Bromer,[a] Jie Wu,[a] Yuping Zhou, and Hugh S. Taylor

HORMONAL PARADOX
Heritable Change without DNA Damage

- THEN: Teratogenic and Carcinogenic Mechanisms Derived from Radiation Biology and Radiomimetic Chemical Research (Mutagenic Basis)
  - Led to the search for DNA adducts of estrogens

- NOW: Teratogenic and Carcinogenic Mechanisms Derive from Understanding the Role of Chemical Signals in Differentiation (Epigenetic Basis)
  - Led to search for persistent gene expression with estrogens

Differential Gene Expression

secret of cell differentiation and phenotypic stability (epigenetics)

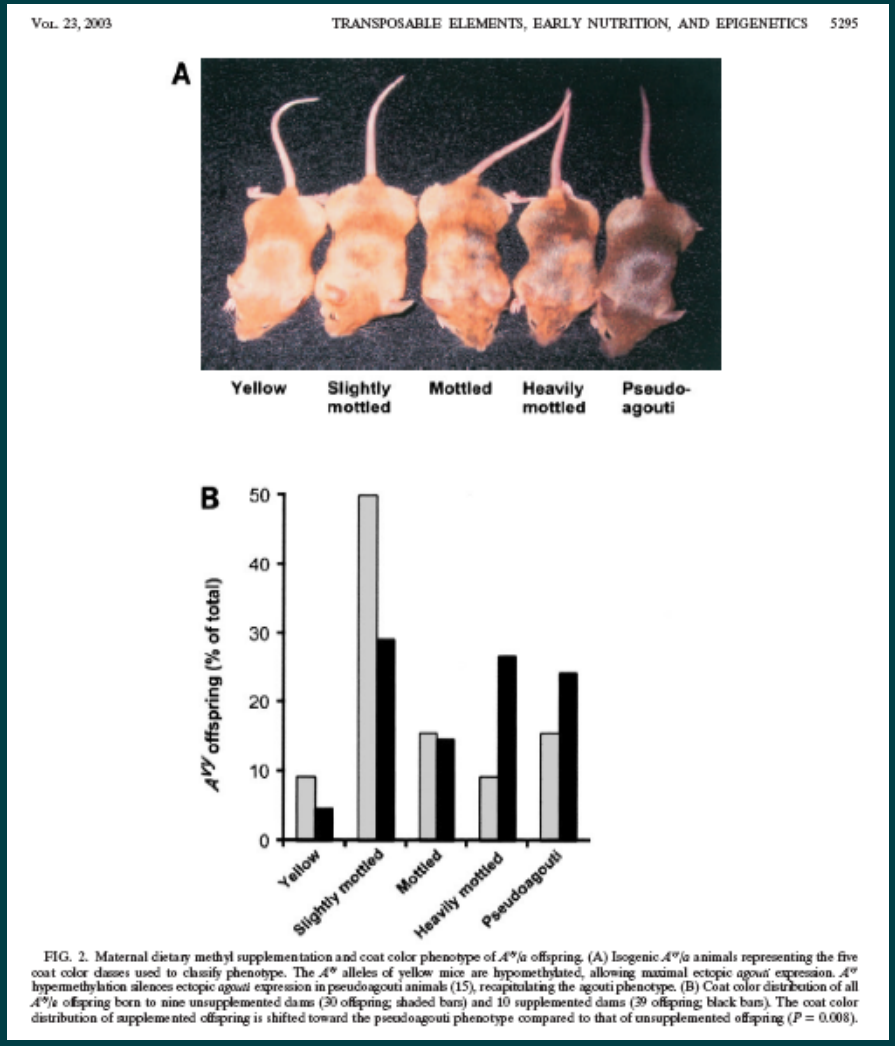
DNA sequence structure is same in eye and skin

eye genes on,
skin genes off

skin genes on,
eye genes off

Epigenetic Change in Cell Fate

- dietary supplement with folic acid during development results in permanent change in coat color via DNA methylation
- Waterland&Jirtle, 2003



DES: THE CHEMICAL THAT CHANGED THE WAY WE THINK

Rational synthesis (different structure same function)

Dodds, 1938 (Bisphenol A, 1936, same lab)

Use as endocrine support in pregnancy (4-8 million)

Smith and Smith, 1948 (efficacy refuted, Deickmann, 1951)

Vaginal cancer in offspring of treated pregnancies

Herbst et al, 1971

Growth promoting substance in cattle

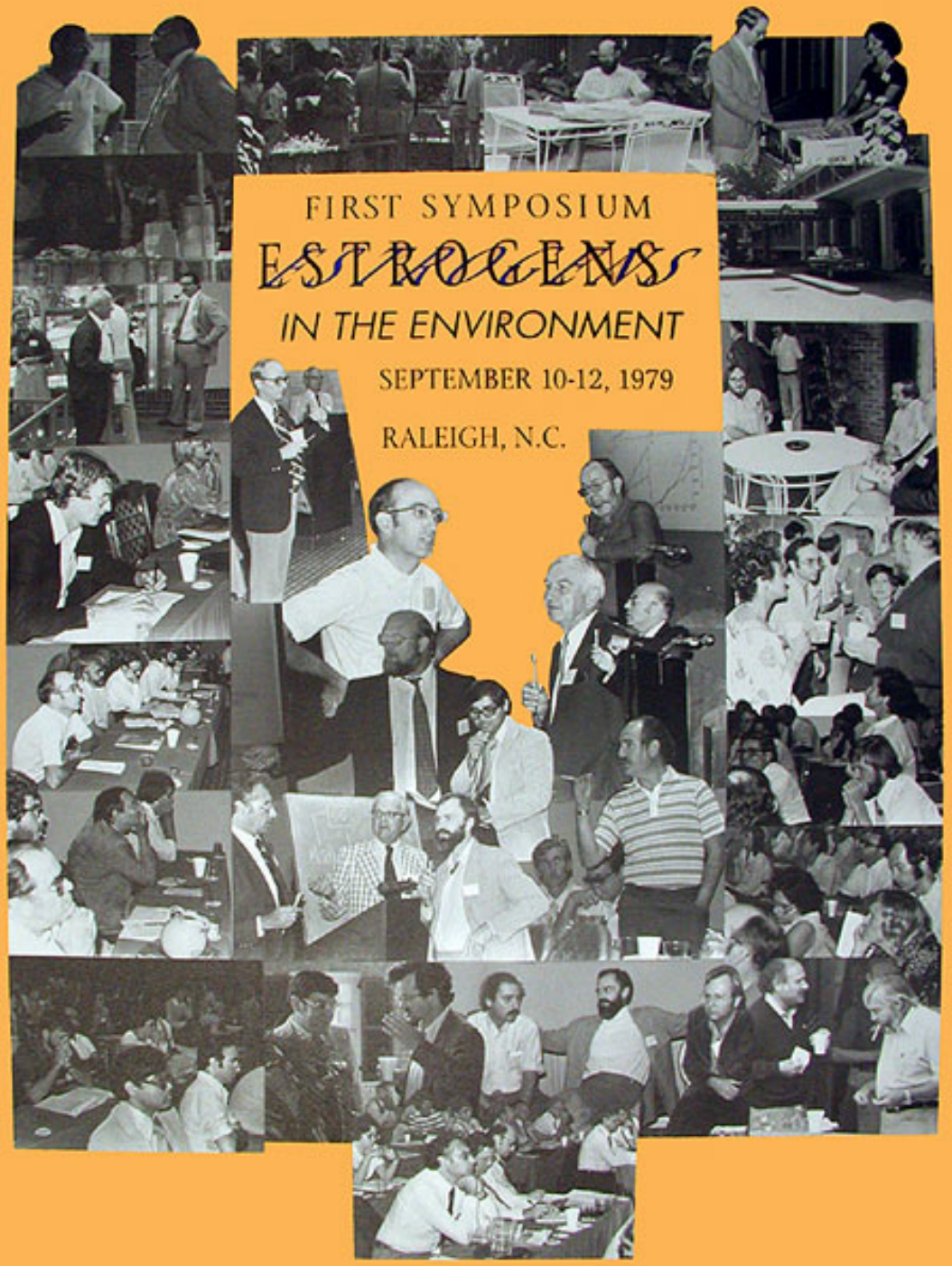
(approximately 13 tons/year) 1950's to 1976

DES

DDT

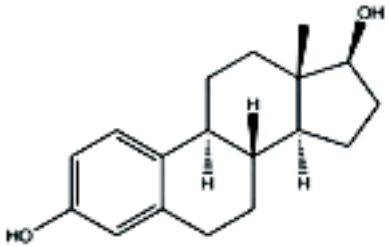
zearalenone

Kepone



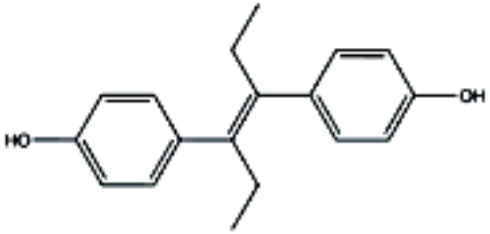
Chemicals Found in the Environment Reported to be Estrogenic

Steroids

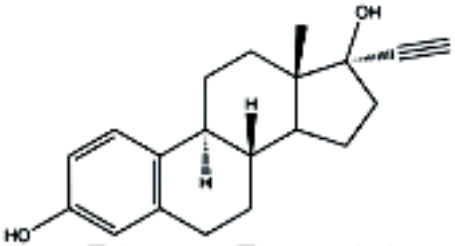


17β-Estradiol

Pharmaceuticals

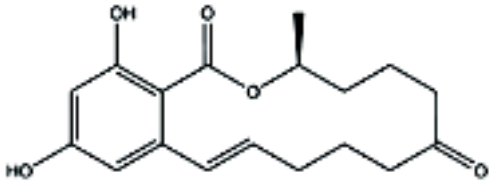


Diethylstilbestrol



Ethynyl Estradiol

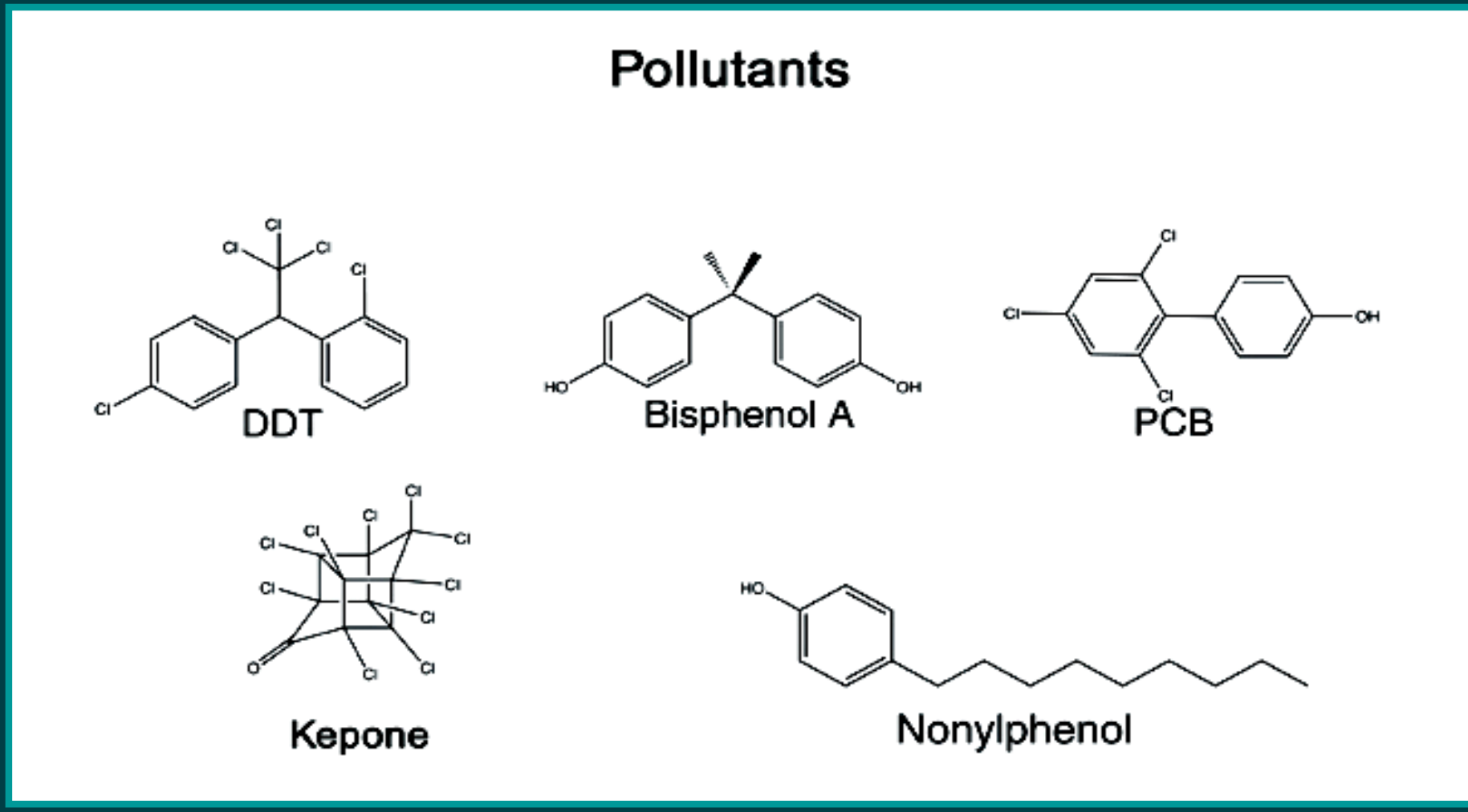
Fungal Products



Zearalenone

McLachlan, J.A. 2001 Environmental Signaling: What Embryos and Evolution Teach Us About Endocrine Disrupting Chemicals, Endocrine Reviews *22(3): 319-341.*

Chemicals Found in the Environment Reported to be Estrogenic



McLachlan, J.A. 2001 Environmental Signaling: What Embryos and Evolution Teach Us About Endocrine Disrupting Chemicals, Endocrine Reviews *22(3): 319-341.*

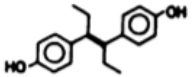
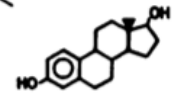
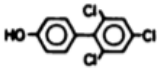
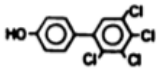
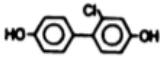
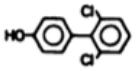
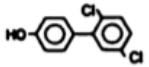
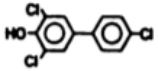
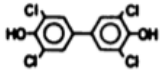
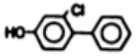
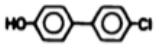
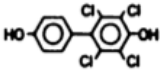
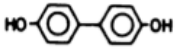
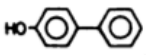
PCBs function as estrogens

Relative binding affinities to the estrogen receptor demonstrate capacity for estrogenic activity at the biochemical level.

Korach et al, Mol Pharm 33: 120-126, 1988

Receptor binding activity of DES, estradiol, and PCBs

RECEPTOR BINDING ACTIVITY OF DES, ESTRADIOL AND POLYCHLORINATED BIPHENYL COMPOUNDS

	STRUCTURE	NAME	C_{50}
1.		DES	0.4
2.		ESTRADIOL	1.0
3.		4-hydroxy, 2',4',6'-trichloro biphenyl (4H2',4',6'TCB)	42
4.		4-hydroxy, 2',3',4',5'-tetrachloro biphenyl (4H2',3',4',5'TCB)	95
5.		4,4' dihydroxy 2'-chloro biphenyl (4,4'DH 2'CB)	90
6.		4-hydroxyl 2',6'-dichloro biphenyl (4H2',6'DCB)	388
7.		4-hydroxy 2',5' dichloro biphenyl (4H2',5'DCB)	506
8.		4-hydroxy 3,5,4'-trichloro biphenyl (4H3,5,4'TCB)	1000
9.		4,4'-dihydroxy 3,5,3',5'-tetrachloro biphenyl (4,4'DH3,5,3',5'TCB)	1354
10.		4-hydroxy 2-chloro biphenyl (4H2CB)	2500
11.		4-hydroxy 4'-chloro biphenyl (4H4'CB)	3900
12.		4,4'-dihydroxy 2',3',5',6'-tetrachloro biphenyl (4,4'DH2',3',5',6'TCB)	5000
13.		4,4'-dihydroxy biphenyl (4,4'DHB)	>5000
14.		4-hydroxy biphenyl (4HB)	>5000

Environmental Hormonal Activities

Hormonal Activity	Environmental Hormone	Environmental Anti-Hormone
Estrogen	Yes, Many*	Yes, Few*
Progestin	?	?
Androgen	Yes, Few[x]	Yes, Many[+]
Gluccocorticoid	?[●]	?
Mineralocorticoid	?	?
Retinoid	Yes, One	?
Thyroid	?[▲]	?

* See representative structures in figure 5

x Androstenedione, the product of bacterial metabolism of stigmasterol, see figure 3

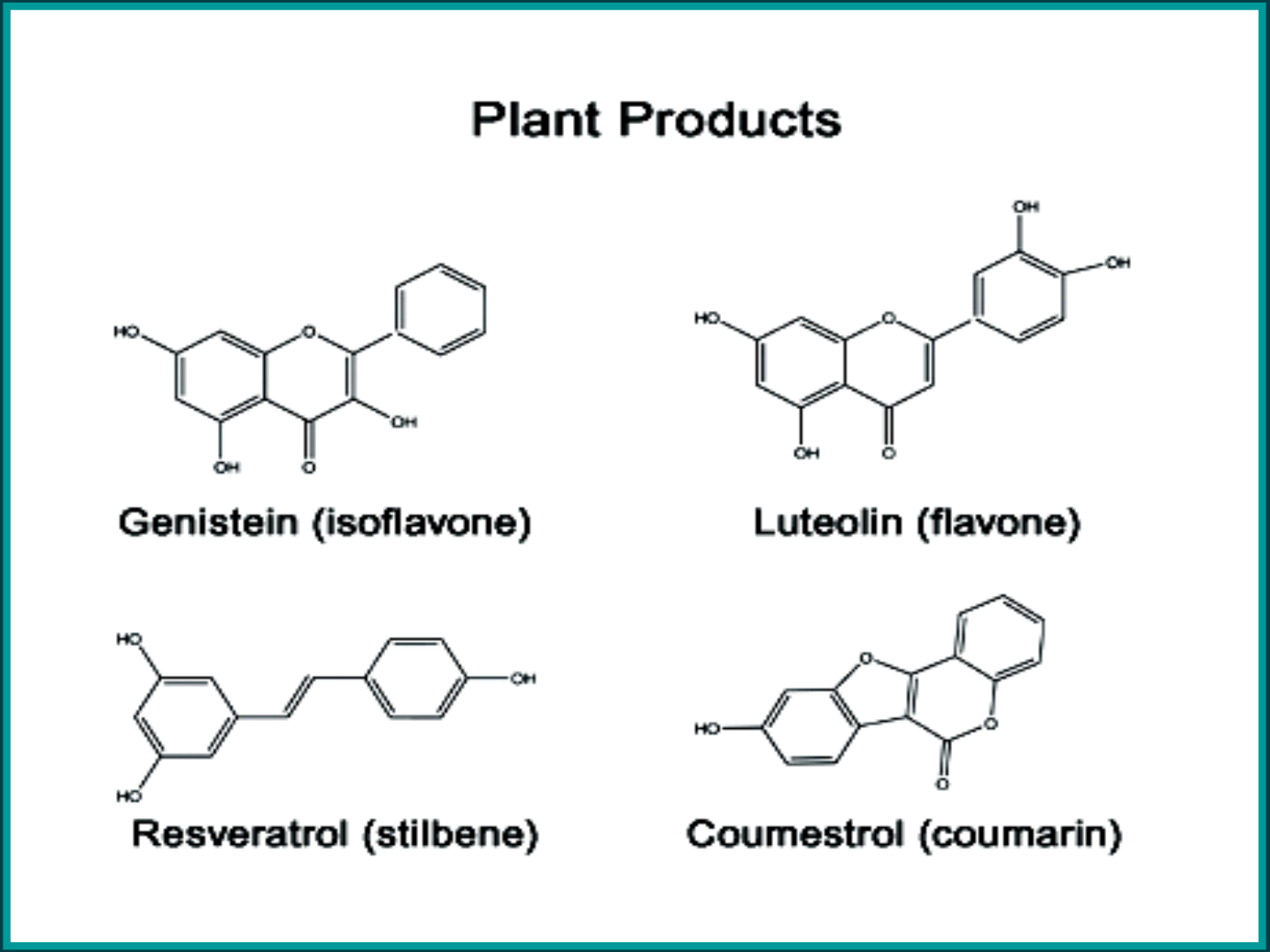
\+ See representative structures in figure 2

● Arsenic is reported to block the glucocorticoid receptor activation at the receptor binding level (35)

▲ PCB congeners elicit a thyroid hormone-like response, but no binding data for the thyroid Hormone receptor is available (22). One study that evaluated binding of chlorinated hydrocarbons to the thyroid hormone receptor and thyroid binding proteins did not demonstrate specific receptor binding, while binding to transthyretin was of the same affinity as thyroxin (23).

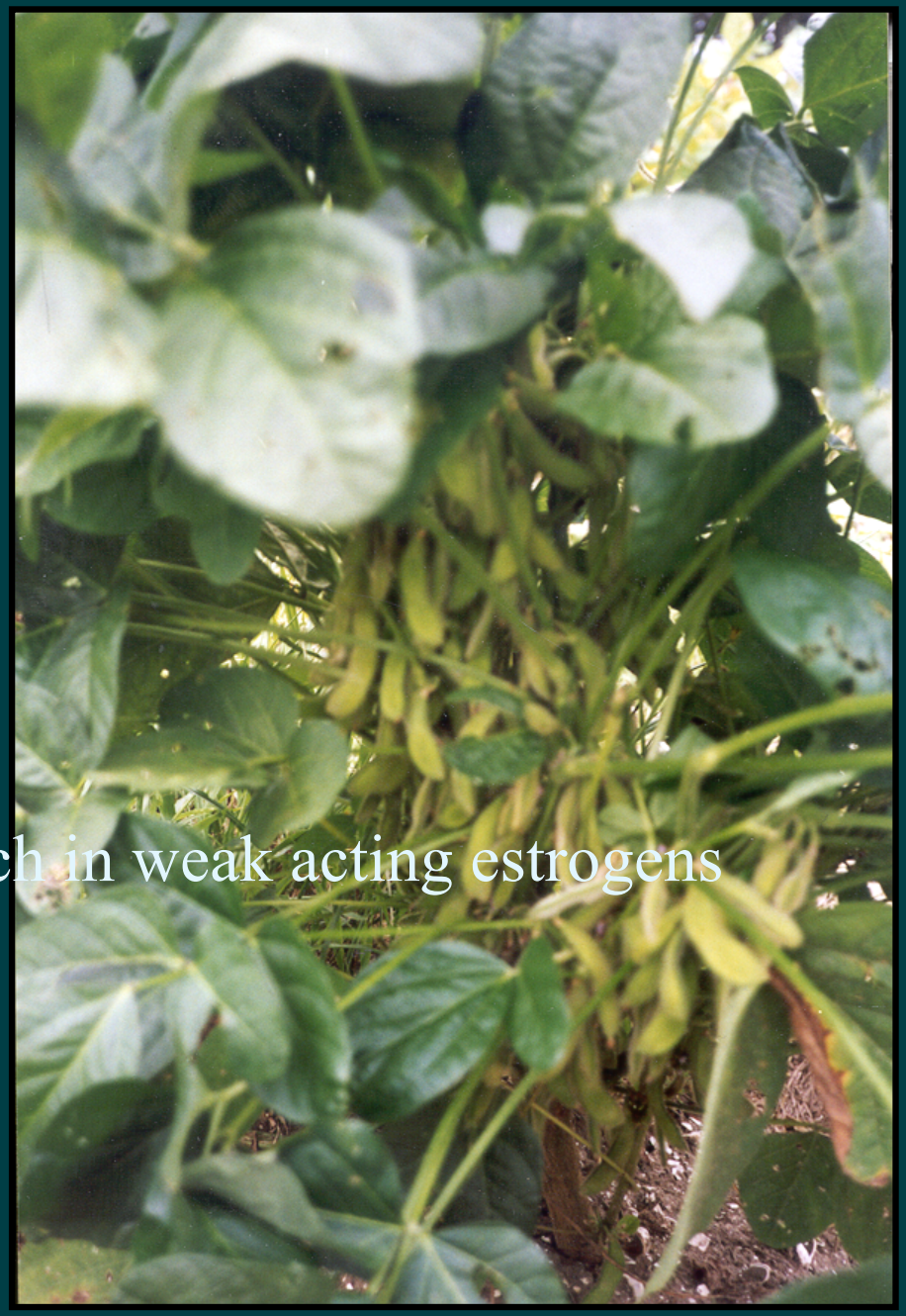
McLachlan, J.A. 2001 Environmental Signaling: What Embryos and Evolution Teach Us About Endocrine Disrupting Chemicals, Endocrine Reviews *22(3): 319-341.*

Chemicals Found in the Environment Reported to be Estrogenic



McLachlan, J.A. 2001 Environmental Signaling: What Embryos and Evolution Teach Us About Endocrine Disrupting Chemicals, Endocrine Reviews *22(3): 319-341.*

Soy beans rich in weak acting estrogens

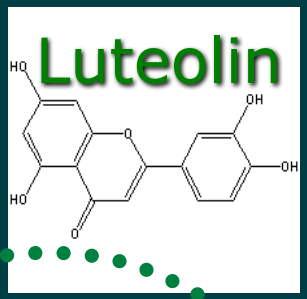


What types of signals control symbiotic N_2-fixation?

- Plant chemicals activate NodD signaling
- Bacterial chemicals inactivate plant's defense system

Alfalfa (*Medicago sativa*)

Luteolin



Sinorhizobium meliloti
soil bacteria

NodD receptor

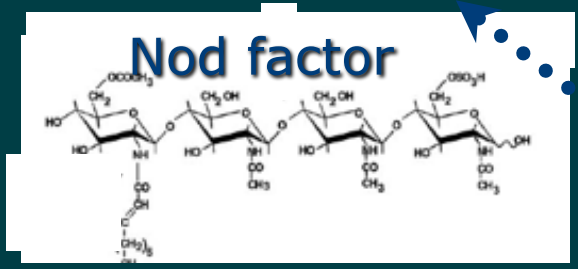
NodD NodD

Activates responsive genes

nod box

nod genes

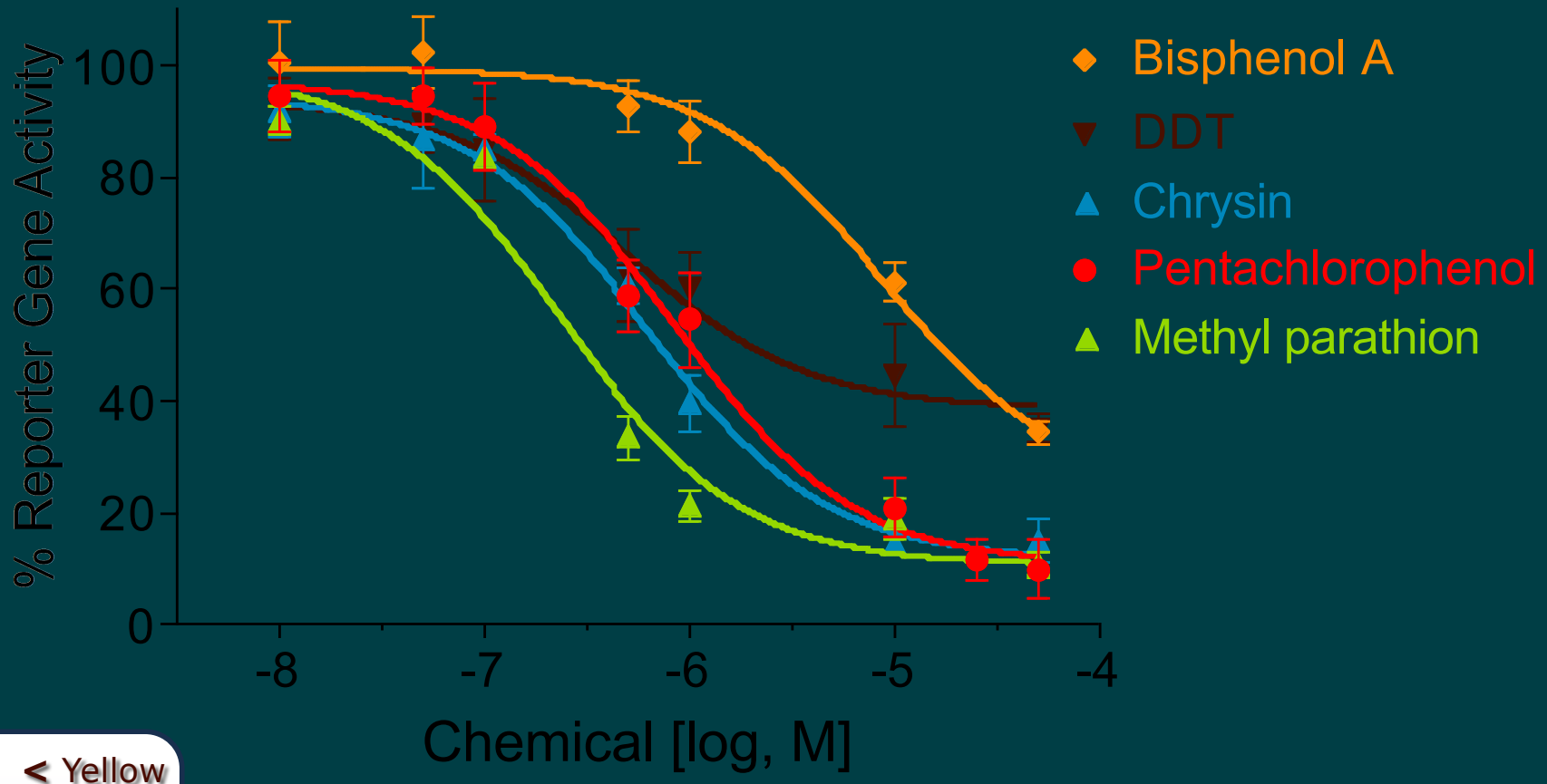
Nod factor



Function=produce Nod factor to signal host plant

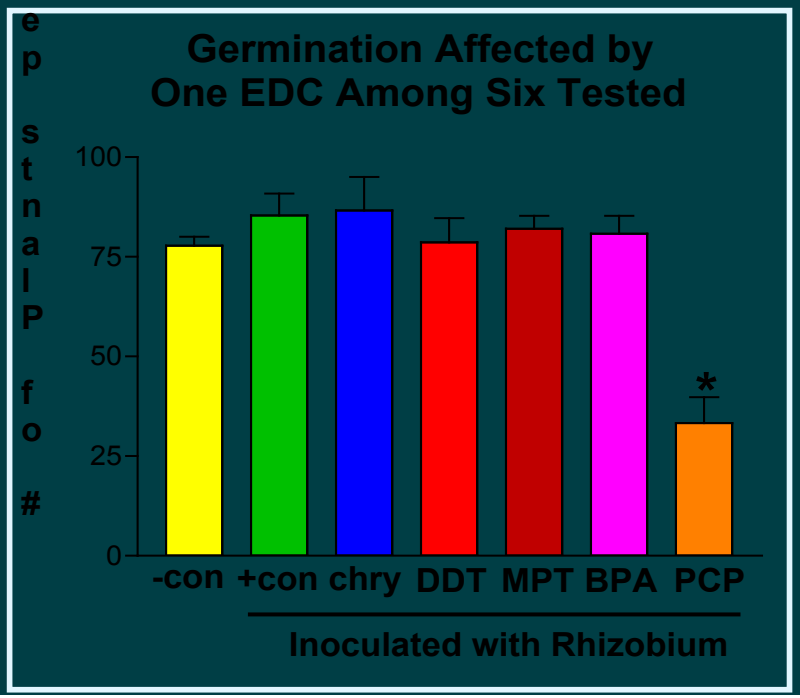
Do synthetic environmental chemicals inhibit the symbiotic gene network?

- **Yes**, a wide variety of endocrine-disrupting chemicals inhibit symbiotic signaling



Fox et al., *Nature* 413: 128-129 (2001).

+ *Rhiz* - *Rhiz*



+ PCP + *Rhiz* + *Rhiz*

Fox et al, PNAS 104: 10282 (2007)

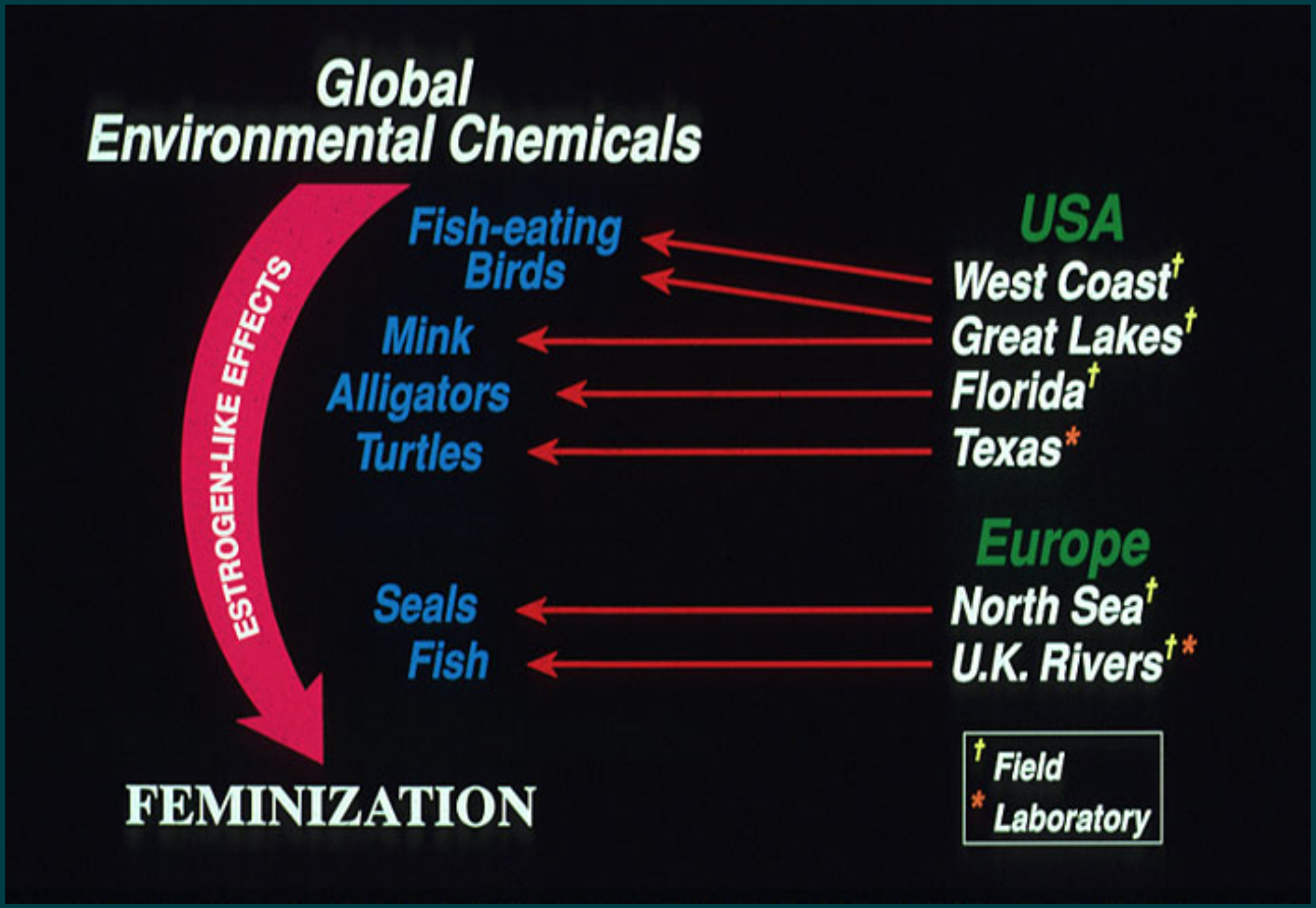
Endocrine Disruption Studied through...

Epidemiology…effects on humans
rodent models

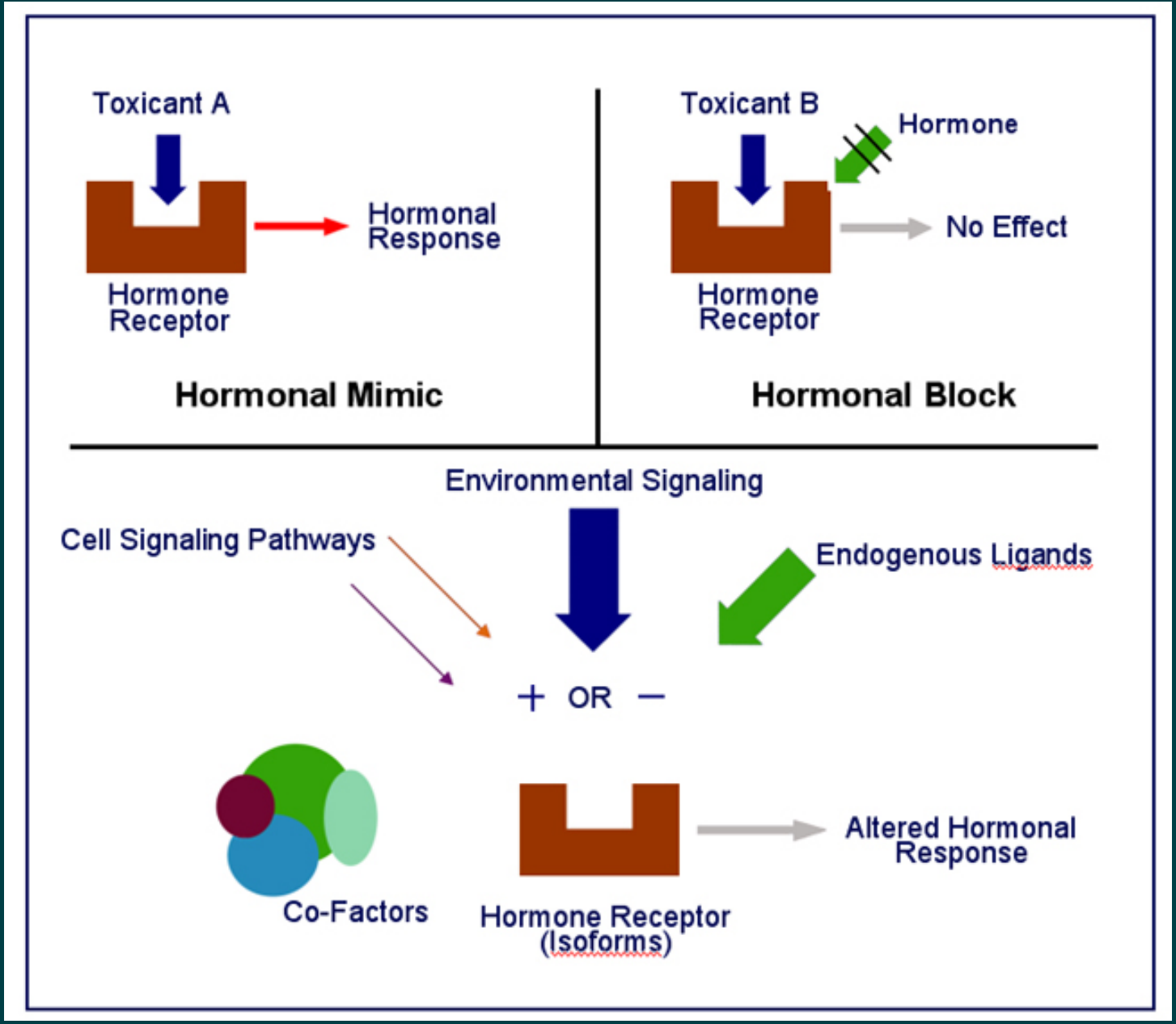
Wildlife effects
panthers
gulls
songbirds
alligators
frogs
fish
snails
barnacles
Daphnia

Coral Reefs??

Rhizobium


Global
Environmental Chemicals
ESTROGEN-LIKE EFFECTS
Fish-eating Birds
Mink
Alligators
Turtles
Seals
Fish
USA
West Coast†
Great Lakes†
Florida†
Texas*
Europe
North Sea†
U.K. Rivers†*
† Field
* Laboratory
FEMINIZATION

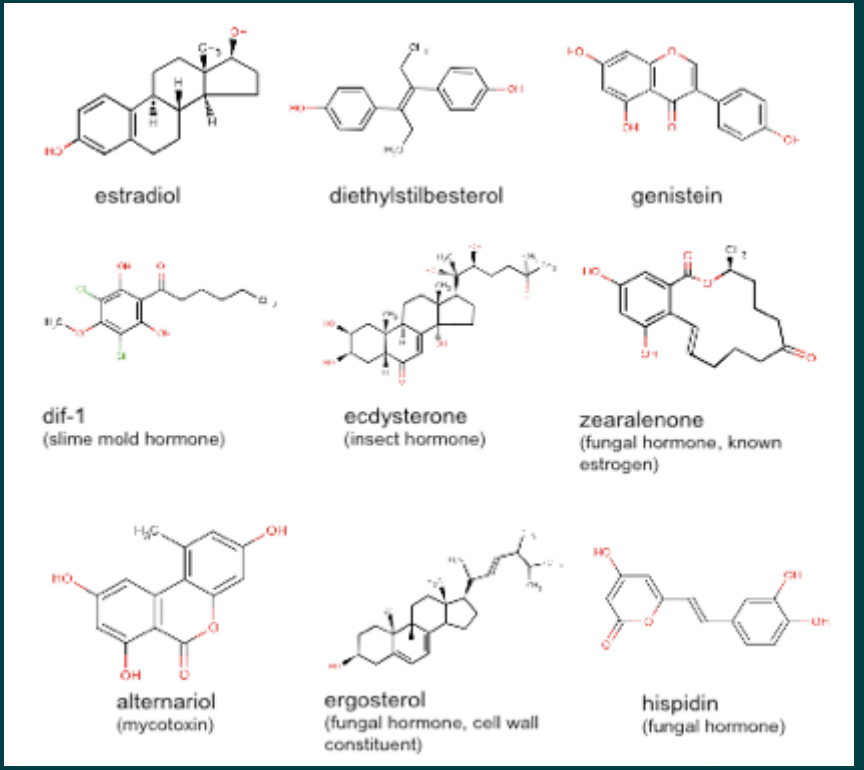
Functional or Receptor-Based Toxicology



McLachlan, J.A. 2001 Environmental Signaling: What Embryos and Evolution Teach Us About Endocrine Disrupting Chemicals, Endocrine Reviews *22(3): 319-341.*

MOLDS SECRETE BIOACTIVE SUBSTANCES

- Zearalenone, produced by Fusarium, is the best known fungal signal with potent estrogenic activity in swine (*moldy corn syndrome* includes vulvular prolapse, mammary hyperplasia, uterine growth, lactation suppression).
- In mold, zearalenone stimulates formation of perithecia
- Other compounds less well studied



Ergot and Witches

- In 1976 Linnda Caporael offered the first evidence that the Salem witch trials followed an outbreak of rye ergot. Ergot is a fungus blight that forms hallucinogenic drugs in bread. Its victims can appear bewitched when they're actually stoned.

The victims of ergot might suffer paranoia and hallucinations, twitches and spasms, cardiovascular trouble, and stillborn children. Ergot also seriously weakens the immune system.

The Witches , painted byWalter McEwan, 1892

Source: John H. Lienhard,MD *The Engines of Our Ingenuity*

“Indirect” environmental estrogens via environmental signaling

- What if environmental chemicals changed production of endogenous estrogen?
- What if non-chemical environmental factors like light or trauma changed estrogen levels or had estrogen like effects?

Atrazine feminizes male frogs

Atrazine is widely used in US agriculture

It has been shown to result in multiple female gonadal structures and female sexual behavior in male frogs (Tyrone Hayes lab)

Atrazine estrogenizes the organism, but is not, per se, an estrogen

Testosterone is converted to estradiol by the enzyme, aromatase

Research

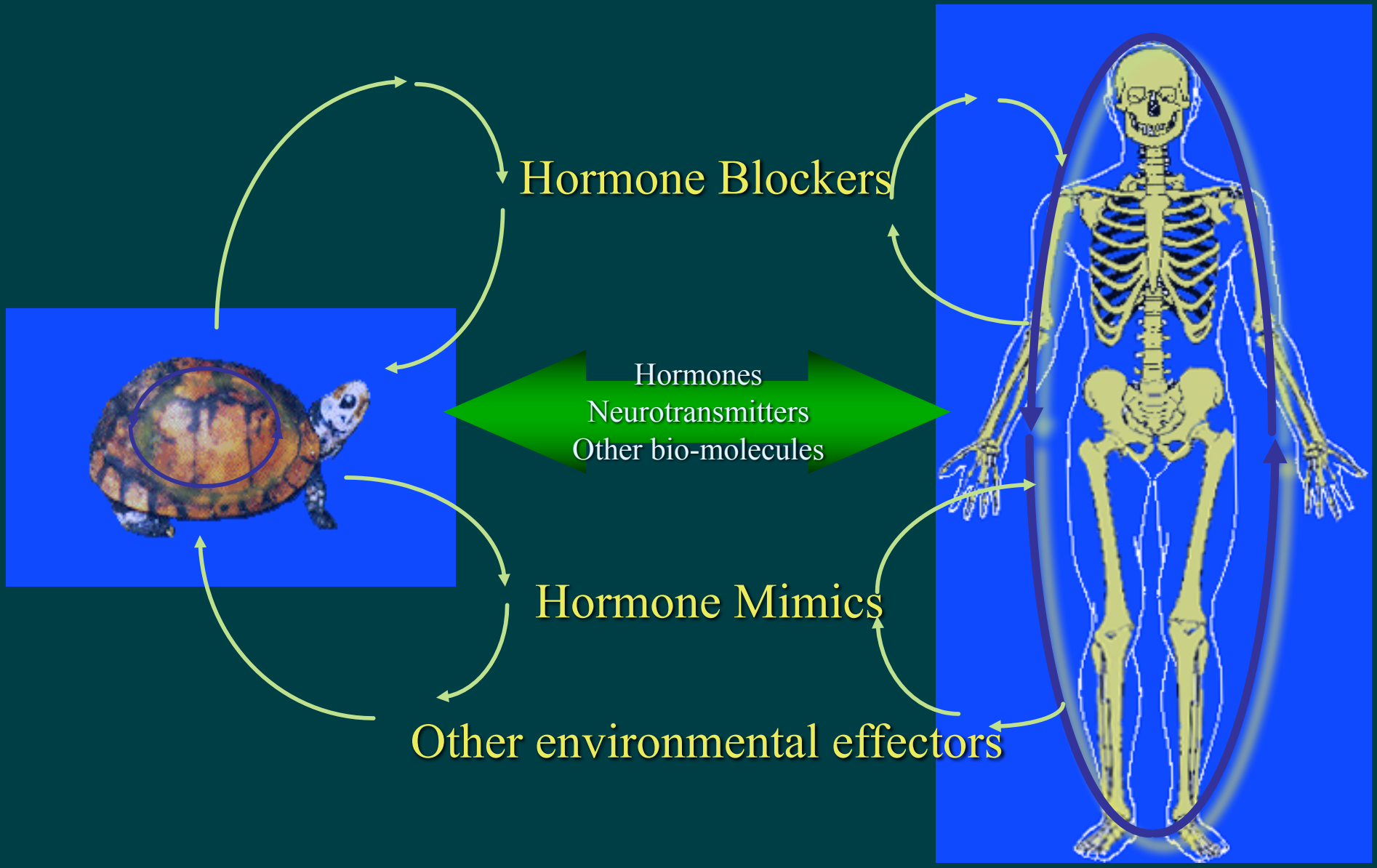
Atrazine-Induced Aromatase Expression Is SF-1 Dependent: Implications for Endocrine Disruption in Wildlife and Reproductive Cancers in Humans

WuQiang Fan,[1] Toshihiko Yanase,[1] Hidetaka Morinaga,[1] Shigeki Gondo,[1] Taijiro Okabe,[1] Masatoshi Nomura,[1] Tomoko Komatsu,[2] Ken-Ichirou Morohashi,[2] Tyrone B. Hayes,[3] Ryoichi Takayanagi,[1] and Hajime Nawata[4]

[1]Department of Medicine and Bioregulatory Science, Graduate School of Medical Science, Kyushu University, Fukuoka, Japan; [2]Department of Developmental Biology, National Institute for Basic Biology, Okazaki, Japan; [3]Laboratory for Integrative Studies in Amphibian Biology, Group in Endocrinology, Museum of Vertebrate Zoology, Energy and Resources Group, and Department of Integrative Biology, University of California, Berkeley, California, USA; [4]Graduate School of Medical Science, Kyushu University, Fukuoka, Japan

Environmental Health Perspectives 115: 720, 2007

Environmental Signaling



Endocrinology in Action!

"The annual output of cocoa in Ghana couldn't help you".

ESTROGENS IN THE ENVIRONMENT

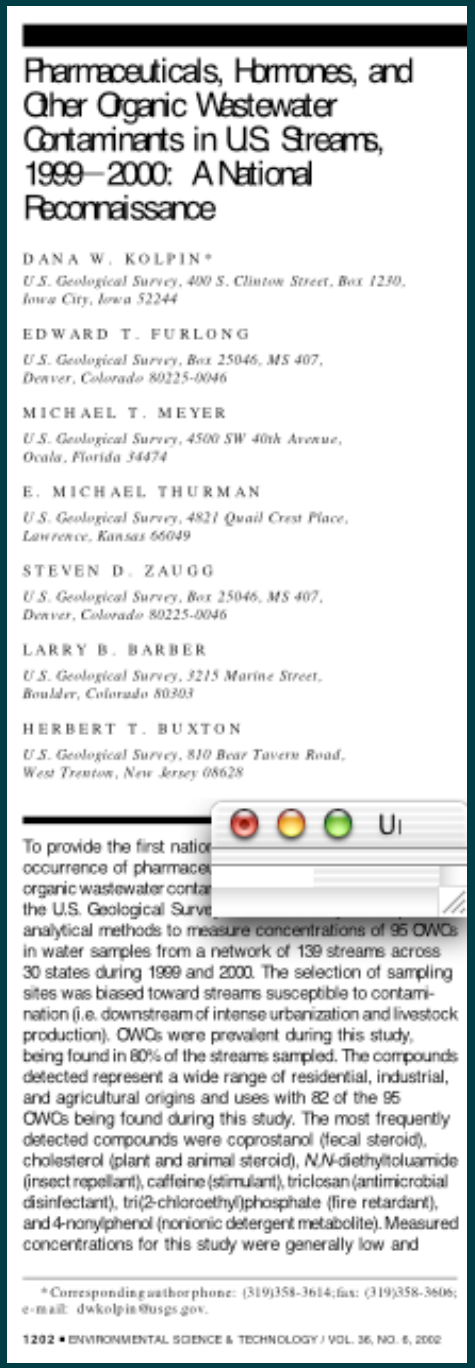
- *Pharmaceutical* compounds as environmental estrogens
- Primarily components of oral contraceptives or hormone replacement therapies
- For example, *NuvaRing* - vaginal ring containing 2.4 mg of estrogen at disposal (Joakim Larsson, Goteborg, quoted in *Science News* 163: 62, January 25, 2003)
  - One ring contains the equivalent of six times the estrogen in a month's supply of OC pills
  - That is enough estrogen to reach biologically active levels for fish in twenty four million liters of water

CAFFEINE EXCRETION

in humans,

One cup of coffee contains approximately 100 mg of caffeine

- 6mg/kg body weight ingestion enough for urine effect (60 kg of body weight)
- Leads to excretion of 360 mg (almost one to one/ingestion to excretion)
  - (Barone and Roberts, Food Chem Tox 134:119-129, 1996)
- One coffee break for three people adds about one gram of caffeine to the waste water system
- For three million people, about one thousand kilos



Pharmaceuticals, Hormones, and Other Organic Wastewater Contaminants in U.S. Streams, 1999–2000: A National Reconnaissance

DANA W. KOLPIN*

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To provide the first natio
occurrence of pharmace
organic wastewater conta
the U.S. Geological Surve
analytical methods to measure concentrations of 95 OWCs in water samples from a network of 139 streams across 30 states during 1999 and 2000. The selection of sampling sites was biased toward streams susceptible to contamination (i.e. downstream of intense urbanization and livestock production). OWCs were prevalent during this study, being found in 80% of the streams sampled. The compounds detected represent a wide range of residential, industrial, and agricultural origins and uses with 82 of the 95 OWCs being found during this study. The most frequently detected compounds were coprostanol (fecal steroid), cholesterol (plant and animal steroid), *N,N*-diethyltoluamide (insect repellant), caffeine (stimulant), triclosan (antimicrobial disinfectant), tri(2-chloroethyl)phosphate (fire retardant), and 4-nonylphenol (nonionic detergent metabolite). Measured concentrations for this study were generally low and

* Corresponding author phone: (319)358-3614; fax: (319)358-3606; e-mail: dwkolpin@usgs.gov.

First systematic analysis of pharmaceuticals and personal care products in American streams

139 streams sampled for 95 contaminants by the United States Geological Survey

Kolpin et al, Environmental Science and Technology 36: 1202-1211, 2002


TRUE STORY*—THE ESTROGEN, STEROIDS, PROZAC AND OTHER DRUGS WE TAKE...
PAXIL
ZOLOFT
...ARE NOT BEING FILTERED OUT OF OUR WASTE BY SEWAGE TREATMENT PLANTS OR SEPTIC SYSTEMS
AND THEY'RE TURNING UP IN INCREASING CONCENTRATIONS IN RIVERS AND LAKES, ...AND IN THE FISH THAT INHABIT THEM.
*11|14|03 CNN.COM
THAT WAS DELICIOUS TROUT! SUDDENLY, I FEEL LESS DEPRESSED ABOUT MY ERECTILE DYSFUNCTION
SINGER

MEDICAL INTELLIGENCE

THE MORTICIAN'S MYSTERY

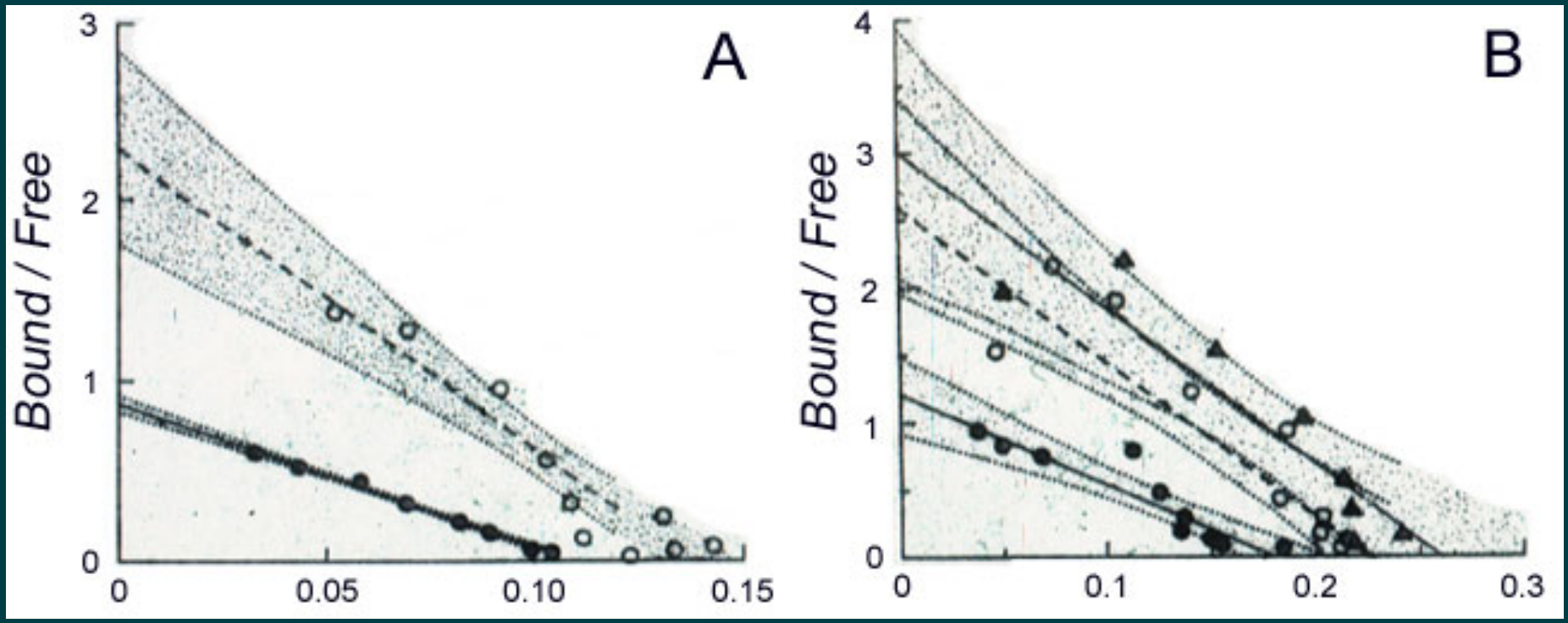
Gynecomastia and Reversible Hypogonadotropic Hypogonadism in an Embalmer

JOEL S. FINKELSTEIN, M.D.,
WILLIAM F. MCCULLY, B.A.,
DAVID T. MACLAUGHLIN, PH.D.,
JOHN E. GODINE, M.D., PH.D.,
AND WILLIAM F. CROWLEY, JR., M.D.

Table 1. Hormone Concentrations in a Mortician with Gynecomastia and Hypogonadotropic Hypogonadism.

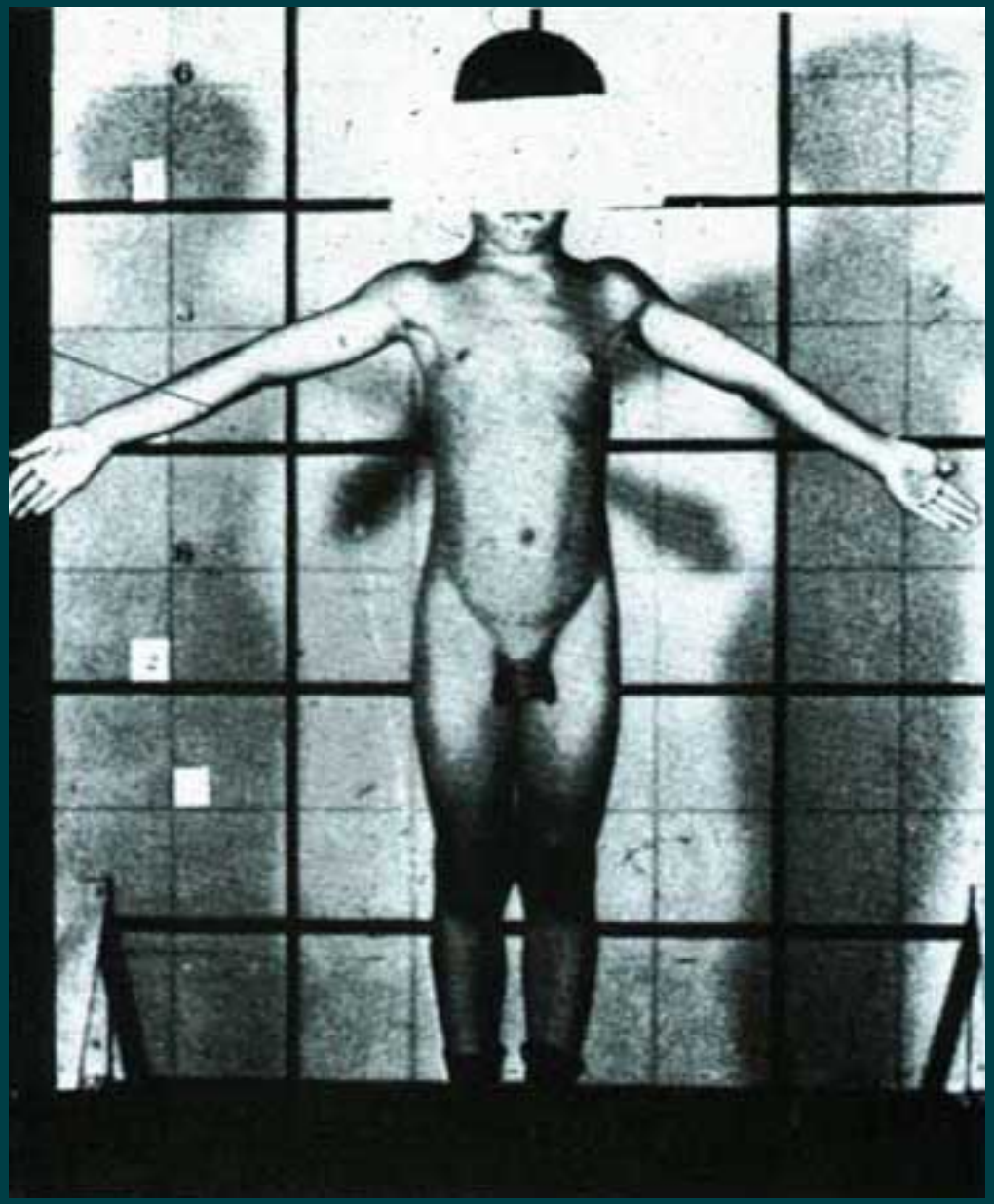
HORMONE	PATIENT	NORMAL RANGE
Testosterone	2.7 nmol/liter (0.8 ng/ml)	10.4 - 34.7 (3 - 10)
Estradiol	Undetectable	37 - 213 pmol/liter
Estriol	Undetectable	Undetectable
Estrone	79 pmol/liter (21 pg/ml)	37 - 259 (10 - 70)
Luteinizing hormone	2.3 mlU/ml	3 - 19
Follicle-stimulating hormone	1.8 mlU/ml	3 - 19
Thyroxine	172 nmol/liter (13.4 μg/ml)	51 - 154 (4 - 12)
Free thyroxine index	41 pmol/liter (3.2 ng/dl)	13 - 51 (1 - 4)
Triiodothyronine resin uptake	24%	25 - 35

From Finkelstein el al. NEJM 318:961 (1988)



[H] Estradiol Bound (nM)

[H] Estradiol Bound (nM)



7 year old boy with breast enlargement.

from Hertz, Estrogens in the Environment (1979)


OCTOBER 30, 2000 $3.50
www.time.com AOL Keyword: TIME
TIME
Is it hormones? Is it fat? Is it something in the water? How parents and kids are coping
EARLY PUBERTY
WHY GIRLS ARE GROWING UP FASTER

Number of Children Reported with Precocious Breast Development Attributed to Potential or Certain Estrogen Intoxication

Before Puerto Rico Report (1952 - 1982)

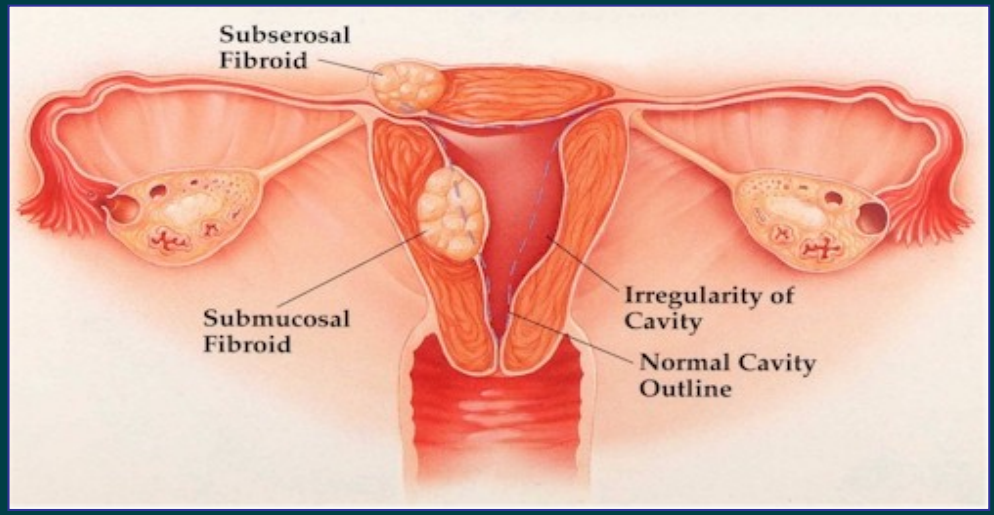
Boys	Girls	
94	70	Includes epidemics in Bahrain, Chile, Rome, and Milan, Italy [2-11, 13, 14, 18, 24, 25]

Puerto Rico Experience

Saenz et al, 1982	322 cases (256 between 1978-81) [15, 16, 21]
Comas, 1982	272 cases of precocious puberty, 121 precocious thelarche only (70 cases between 1978-82) [17]
Frazer et al, 1983	100 cases of precocious thelarche in 1982 [20]

from New, Estrogens in the Environment II (1985)

Uterine Fibroid Disease



- One-third of all women are symptomatic
- Benign, monoclonal, myometrial origin
- Initiation event unclear
- *Increased rates of proliferation*
- Estrogen plays central role

Altered Gene Expression and DNA Methylation Persists through Four Generations following Prenatal Exposure to EDC

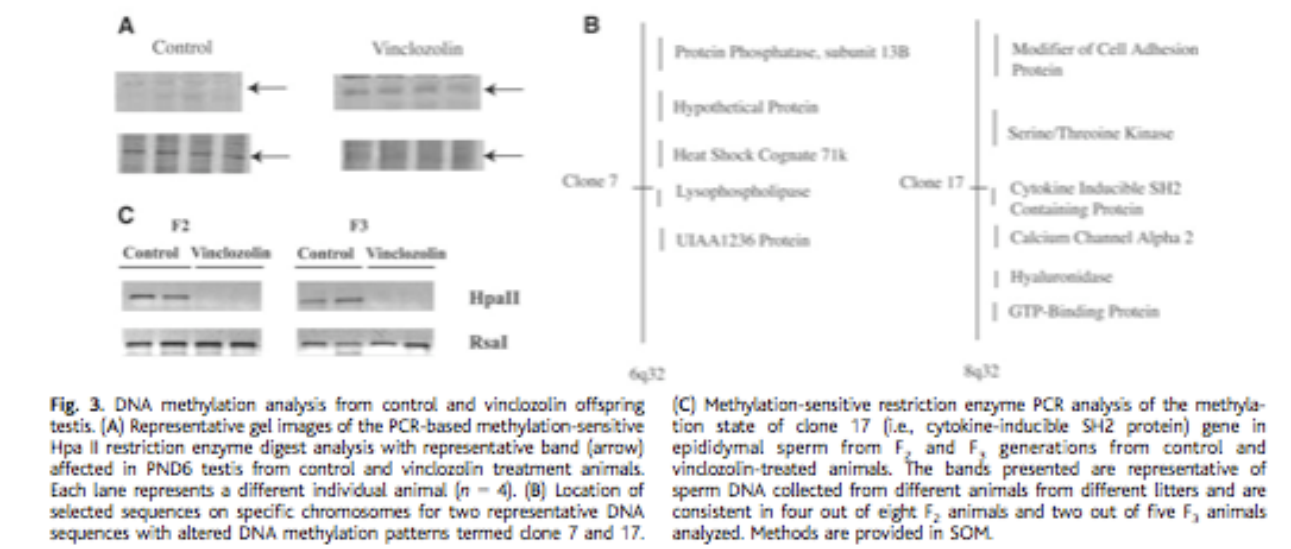


Fig. 3. DNA methylation analysis from control and vinclozolin offspring testis. (A) Representative gel images of the PCR-based methylation-sensitive Hpa II restriction enzyme digest analysis with representative band (arrow) affected in PND6 testis from control and vinclozolin treatment animals. Each lane represents a different individual animal ($n = 4$). (B) Location of selected sequences on specific chromosomes for two representative DNA sequences with altered DNA methylation patterns termed clone 7 and 17. (C) Methylation-sensitive restriction enzyme PCR analysis of the methylation state of clone 17 (i.e., cytokine-inducible SH2 protein) gene in epididymal sperm from F_2 and F_3 generations from control and vinclozolin-treated animals. The bands presented are representative of sperm DNA collected from different animals from different litters and are consistent in four out of eight F_2 animals and two out of five F_3 animals analyzed. Methods are provided in SOM.

Taken from Anway et al, Science 308:1466, 2005.

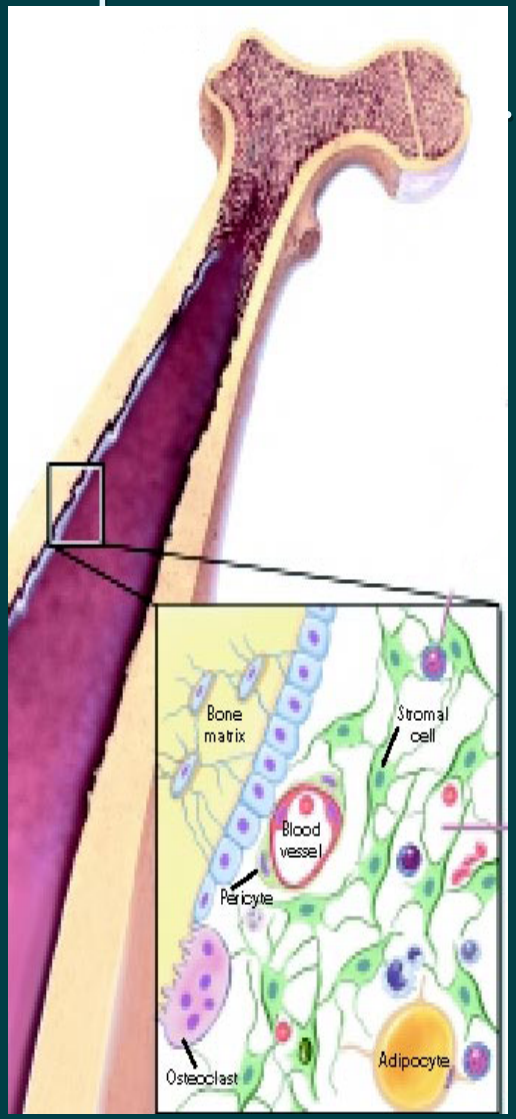
- Male rats treated prenatally with the endocrine disrupters, methoxychlor or vinclozolin are subfertile
- This fertility defect is transmitted through the male germ line for at least four generations
- DNA methylation changes apparently are associated with the defect

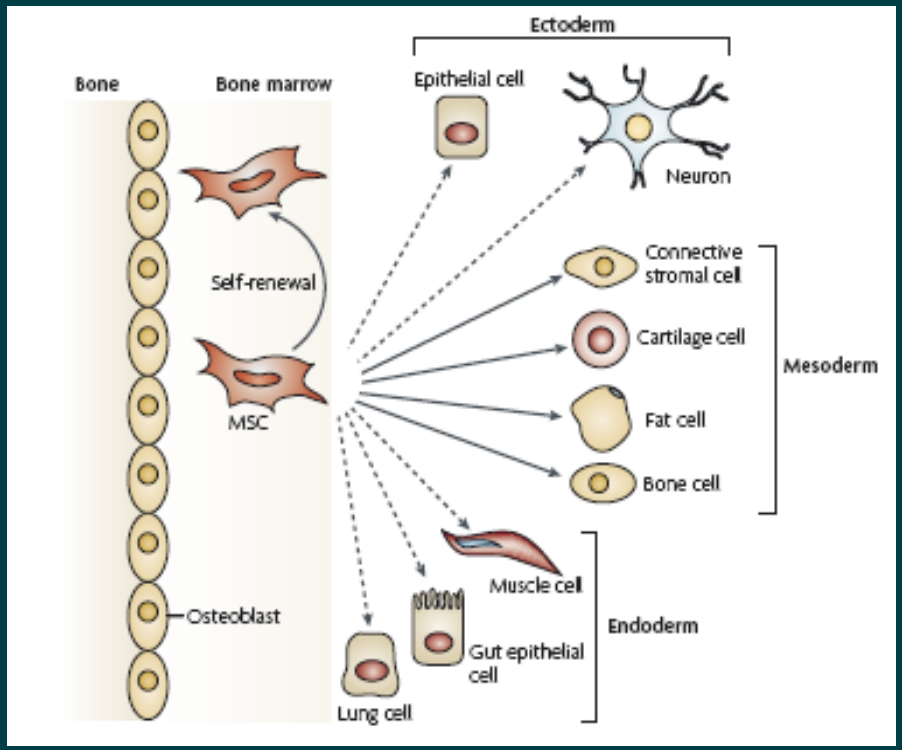
Signals and Sensors

- Environmental factors, including chemicals, can generate functional signals
- Some signals may result in persistent change
- Signaling networks (nuclear, membrane, intercellular, inter-organ?) may adopt cellular differentiation systems based on epigenetic mechanisms

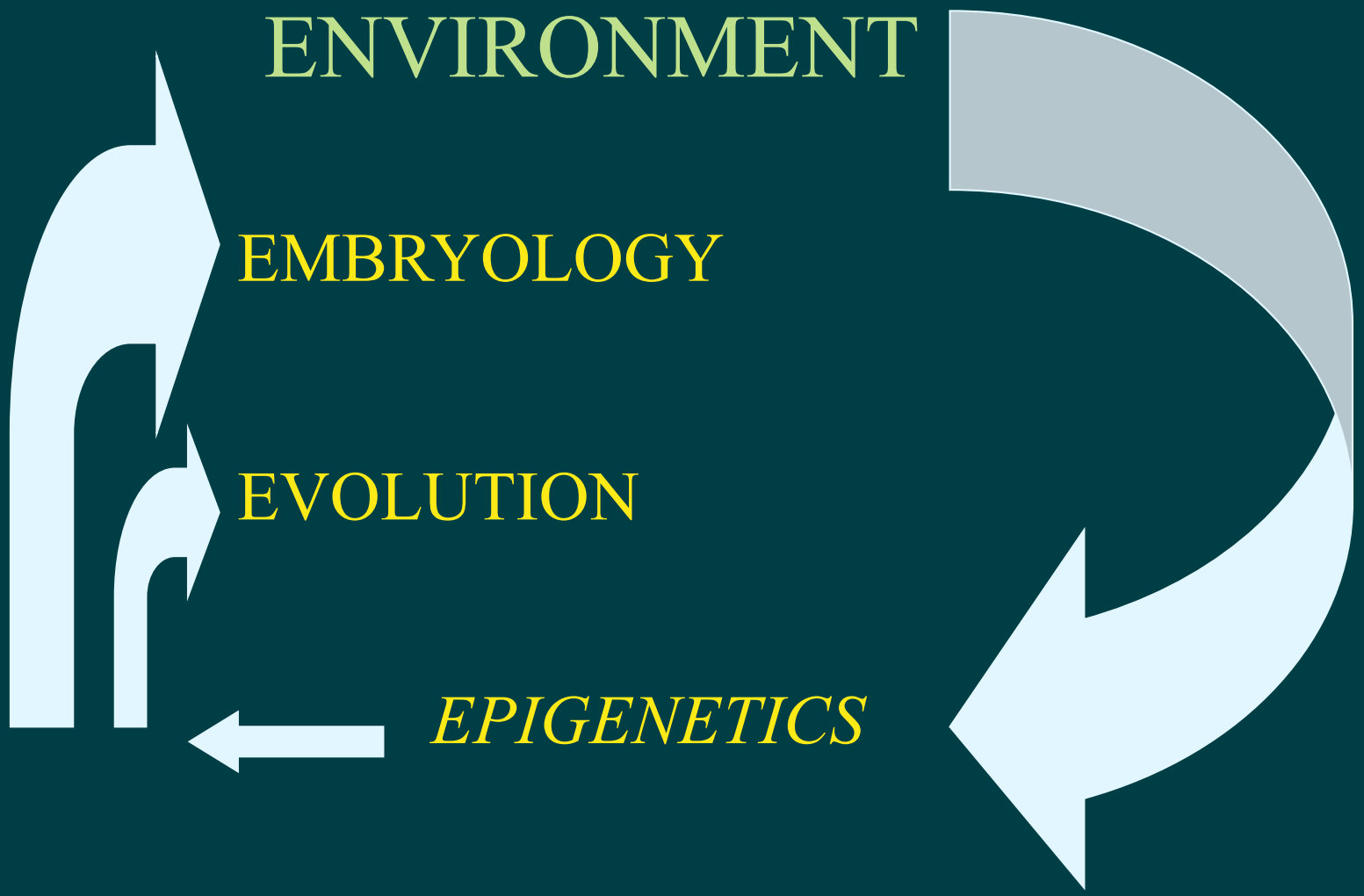
Human Mesenchymal Stem Cells

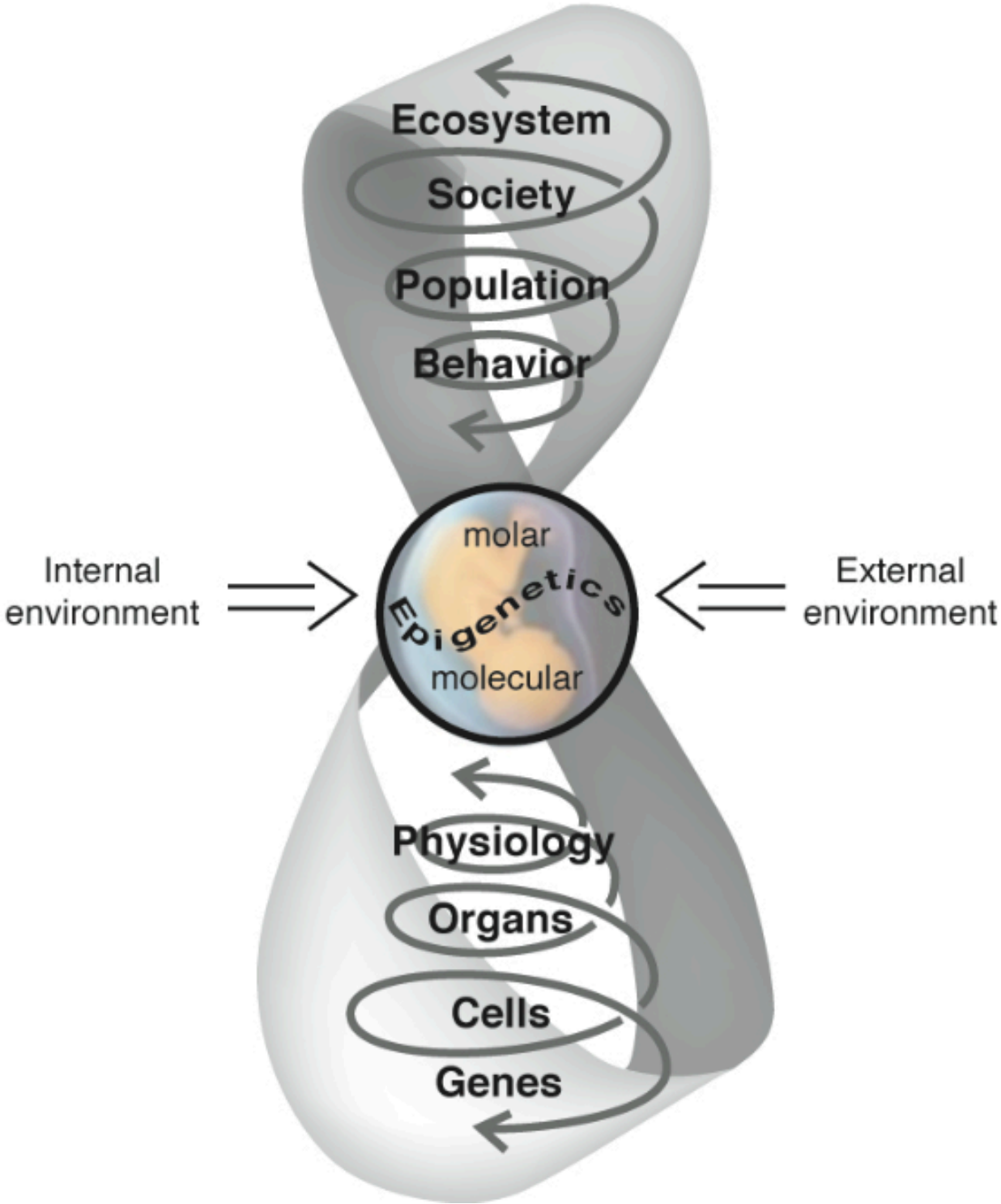
Impact and mechanisms of phytochemicals and





Dr. Bruce Bunnell – Center for Regenerative Medicine -Tulane University


ENVIRONMENT
EMBRYOLOGY
EVOLUTION
EPIGENETICS



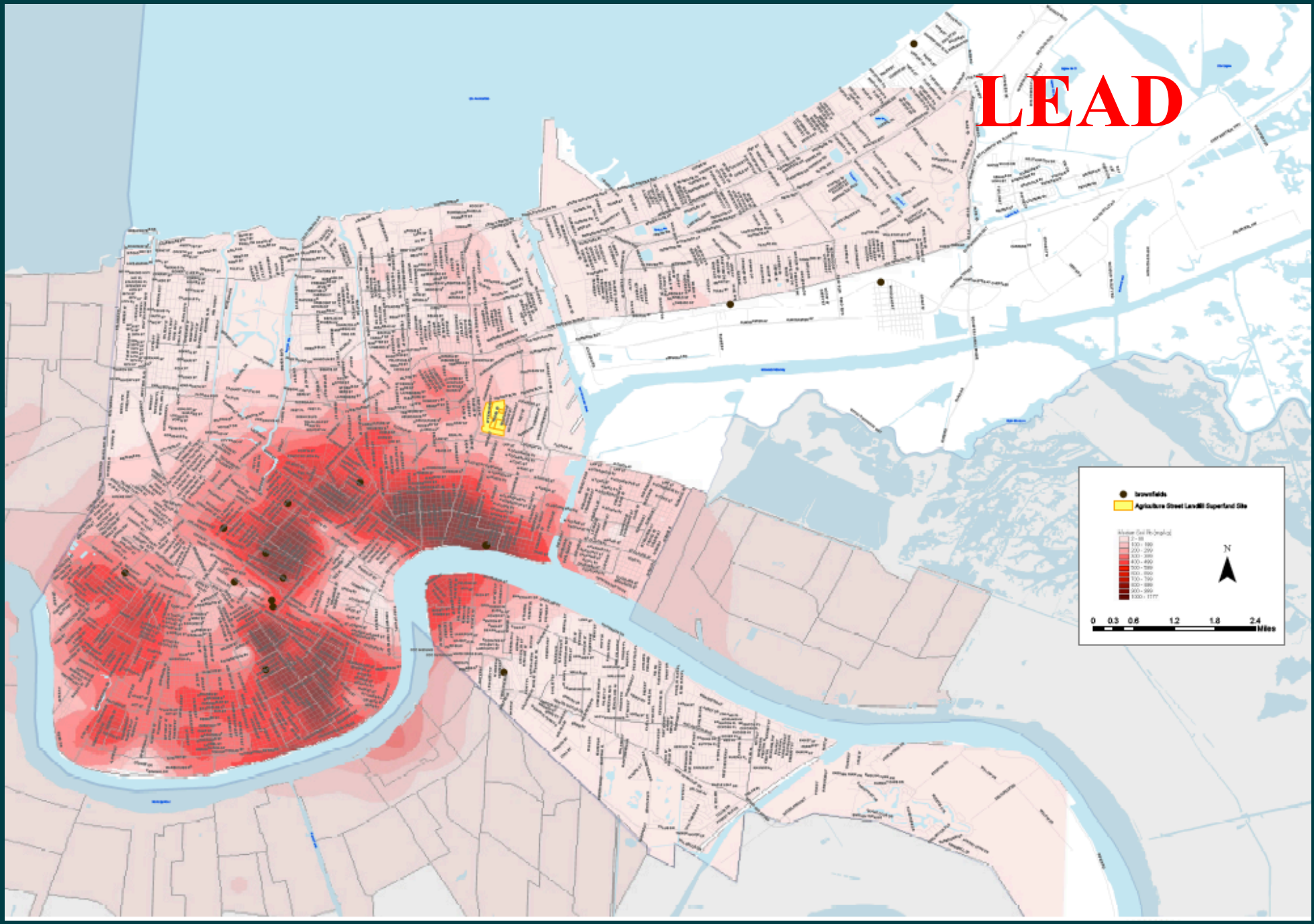
Epigenetics, Evolution, Endocrine Disruption, Health, and Disease

Crews and McLachlan
Endocrinology, 2006

Contributions of Environmental Endocrine Disruption Science to Reproductive Biology

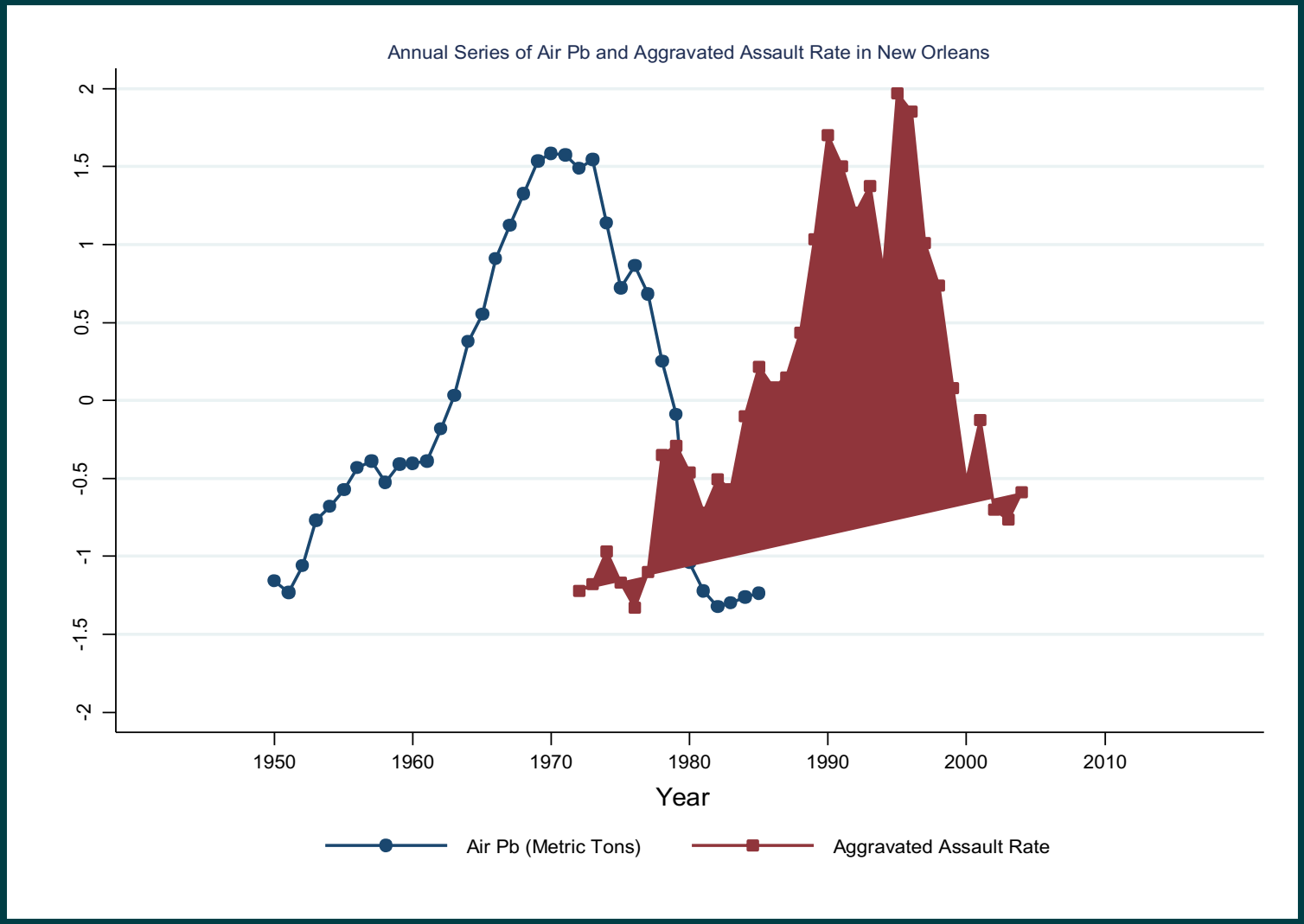
- Highlighted diverse structures and sources of hormonally active chemicals (environmental *SERMs*)
- Reinforced importance of comparative biology (epigenetic memories of frogs)
- Demonstrated the conservation of biological signaling strategies (bacteria to humans)
- Provided insights into the bases for environmental disease in humans, domestic animals and wildlife (*germ theory of the environment*)

Soil Lead Levels in New Orleans (Howard Mielke and team)



Lead and Violence

(Zahran and Mielke, Env Sci, 2012)



SCIENTIFIC REPORTS

OPEN

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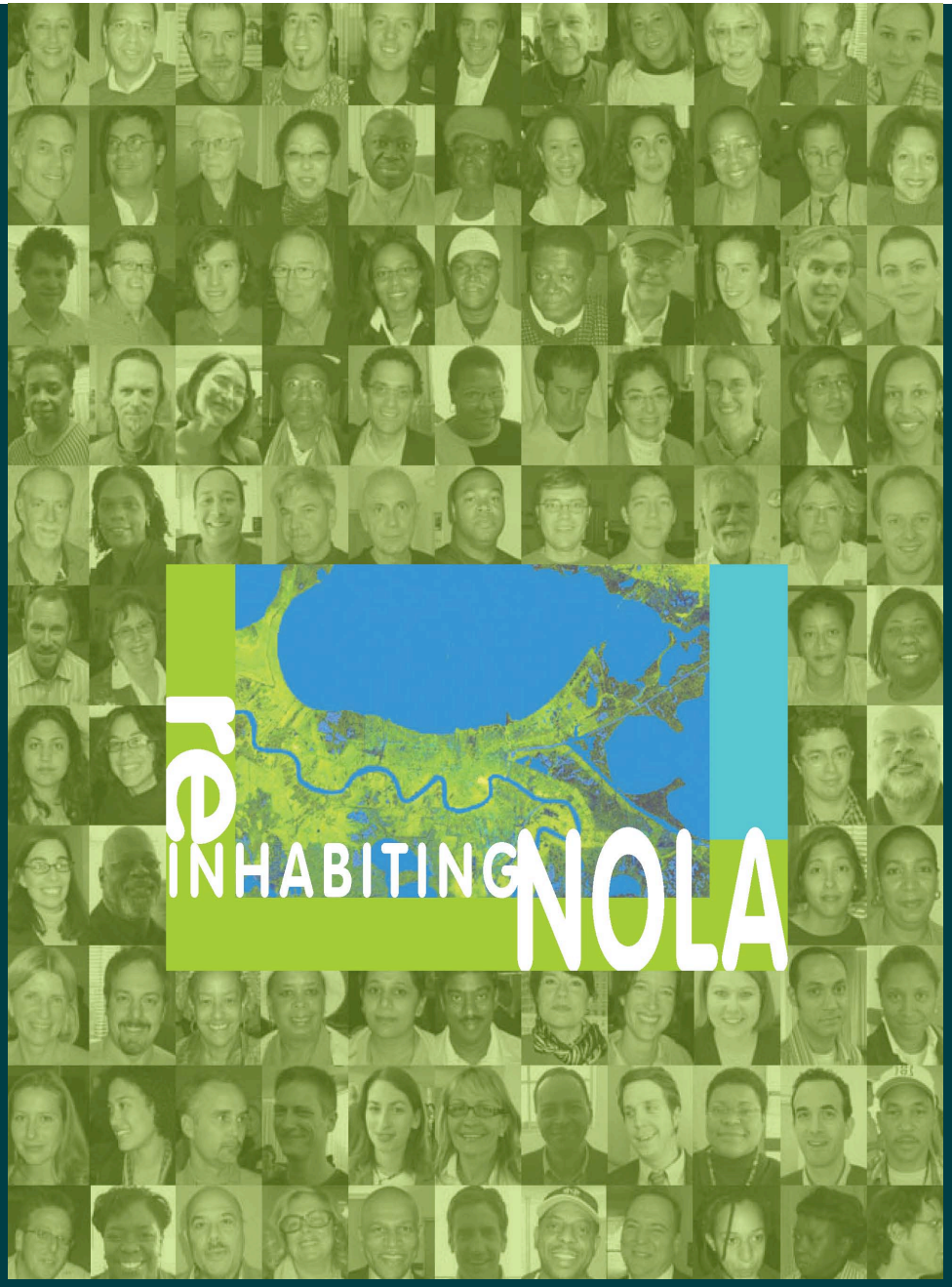
Multigenerational epigenetic inheritance in humans: DNA methylation changes associated with maternal exposure to lead can be transmitted to the grandchildren

Arko Sen[1,2], Nicole Heredia[1], Marie-Claude Senut[1], Susan Land[3,4], Kurt Hollocher[5], Xiangyi Lu[1], Mary O. Dereski[6] & Douglas M. Ruden[1,3,4]

Light at Night

- “Shift work” was judged a “probable carcinogen” by IARC (2007)
- Increase in breast cancer in women who work night shifts
- Risk greatest in women four years before their first pregnancy
- Hypotheses involve changes in melatonin levels in response to light and subsequent changes in estrogen (or direct action of melatonin).



What residents care about:

1. Natural Systems
2. Buildings & Infrastructure
3. Public Health
4. Social & Political

For report and other info:
http://www.kerrn.org

A Tulane Community Workshop Held in New Orleans, November 2005

Reconsidering the "New Normal:" The Impact of *Trauma* on Urban Ecological and Social Diversity

- Part of the Resilient Urban Ecosystem Project
- Funded by NSF in 2009
- Co-Pis – Social Scientist and Biologist
- Faculty expertise includes geology, biology, ecology, sociology, law, mathematics, informatics, modeling and mapping

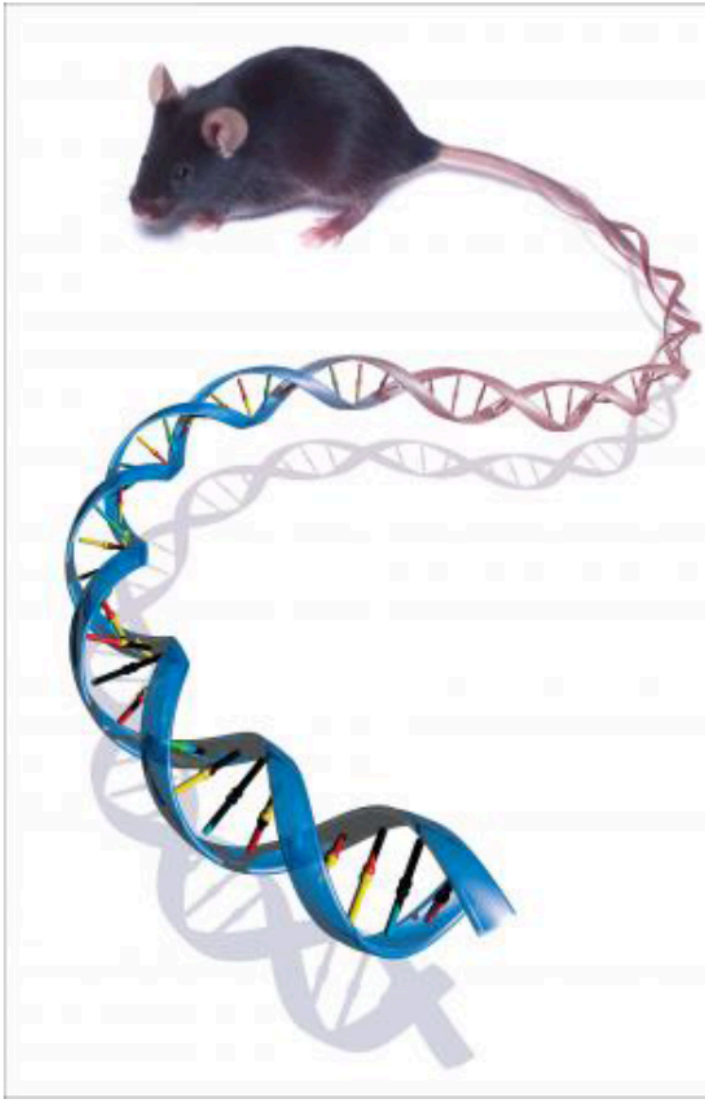
TRAUMA

- Following two disasters, the federal floods of Katrina and the BP oil gusher – common medical finding and complaint was mental health related
- Is Trauma itself and environmental factor?!

Trauma is an epigenetic signal

Young mice subjected to maternal separation stress developed behavioral symptoms that were passed on for three generations.

Franklin et al, Biol Psychiatry. 2010 Sep 1;68(5):408-15

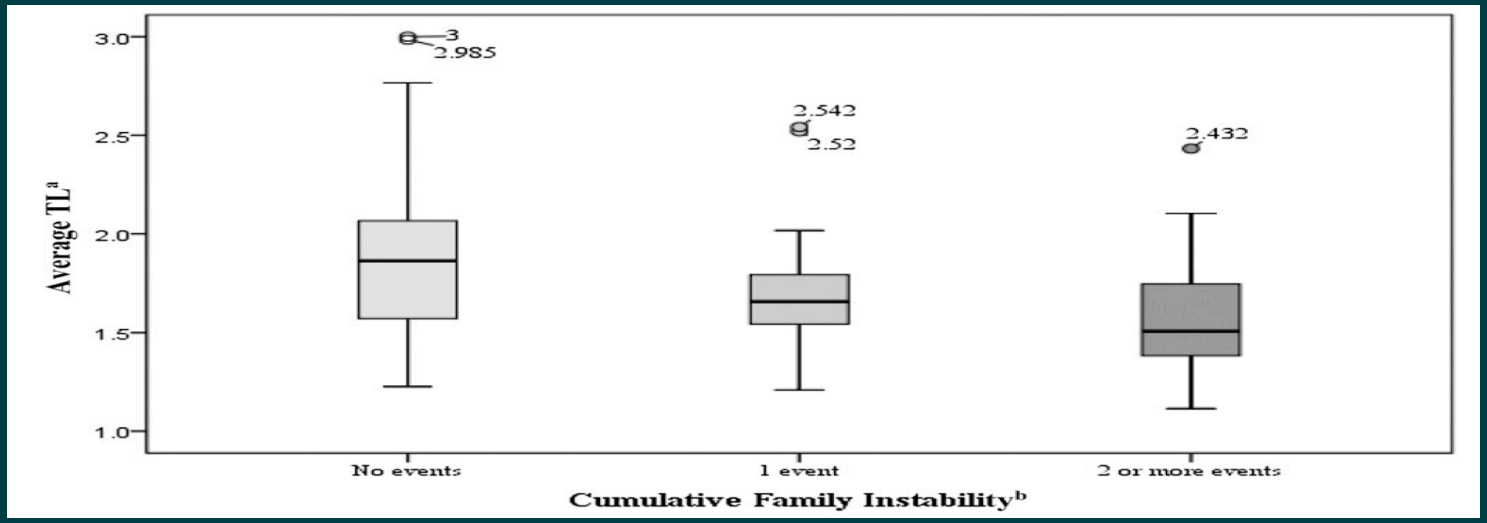


Traumatic stress experienced by mice early in life has epigenetic repercussions that reverberate across multiple generations. Source: NIH

Trauma and Epigenetics in Humans

- Rachel Yehuda (Mt Sinai Medical School) working on Holocaust victims, pregnant women who survived 9/11 and veterans with PTSD
- *On Being* , https://onbeing.org/programs/rachel-yehuda-how-trauma-and-resilience-cross-generations-nov2017/

Novel link from environment to the genome



Stacy Drury Katherine Theall Tulane Schools of Medicine and Public Health

The Association of Telomere Length With Family Violence and Disruption
Pediatrics (published on line June 2014) Drury, SS et al.

A Comprehensive View of Environmental Signaling