Endocrine disrupting activity associated with unconventional oil and natural gas operations

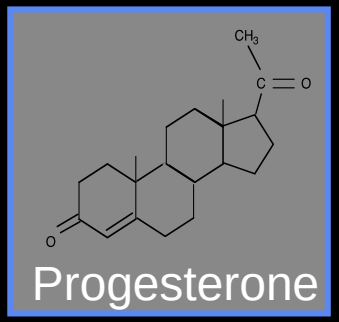
Susan C Nagel, PhD
Associate Professor
Obstetrics Gynecology and Women's Health
University of Missouri

1. Can chemicals used in oil and gas extraction disrupt normal endocrine signals?
2. Is endocrine disrupting activity in surface and ground water associated with oil and gas extraction?
3. What Health effects may be associated with exposure to chemicals?

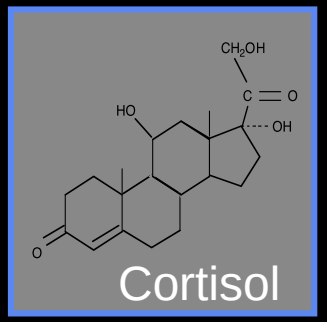
Steroid Hormones

Estradiol

Testosterone

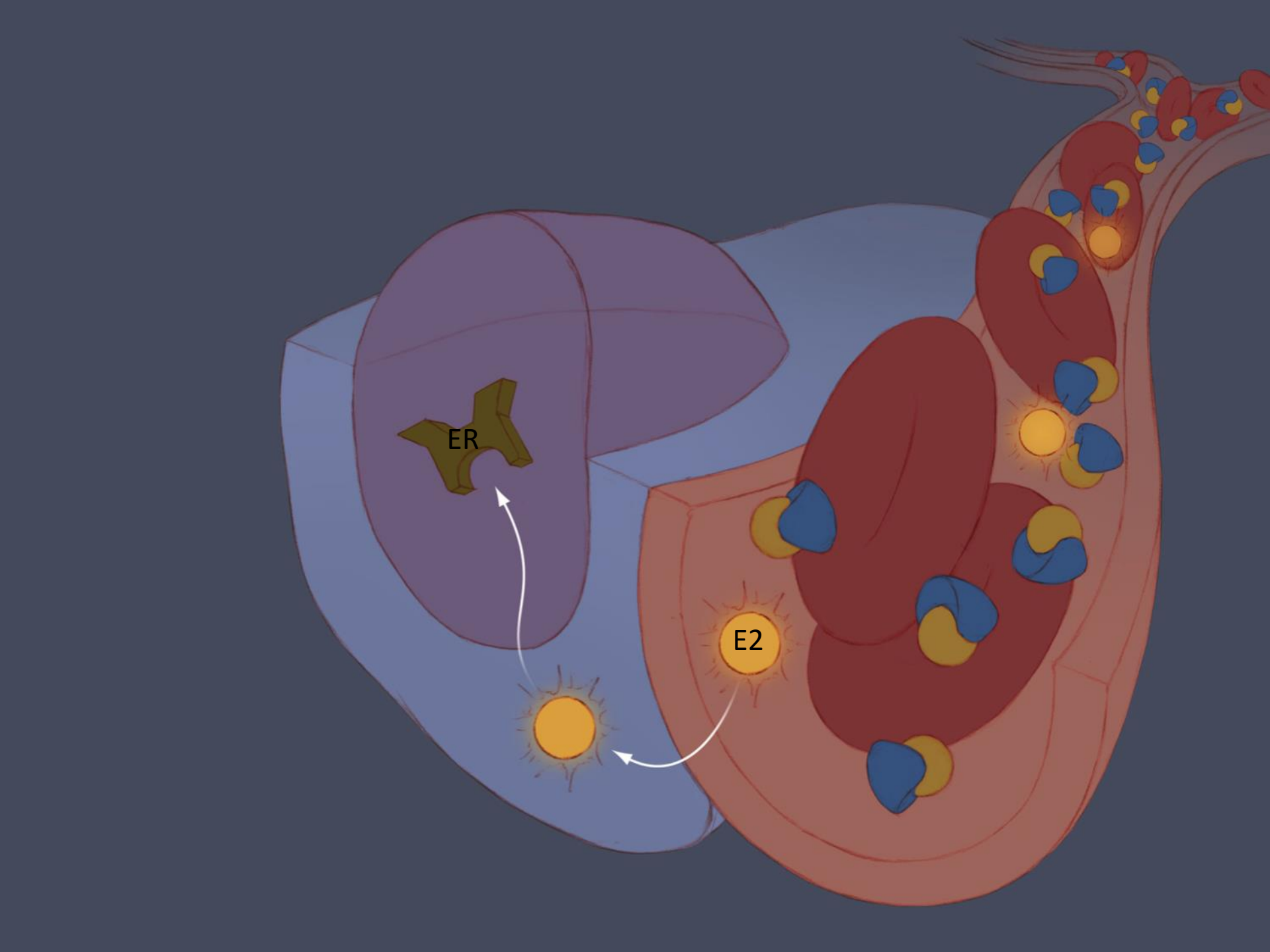


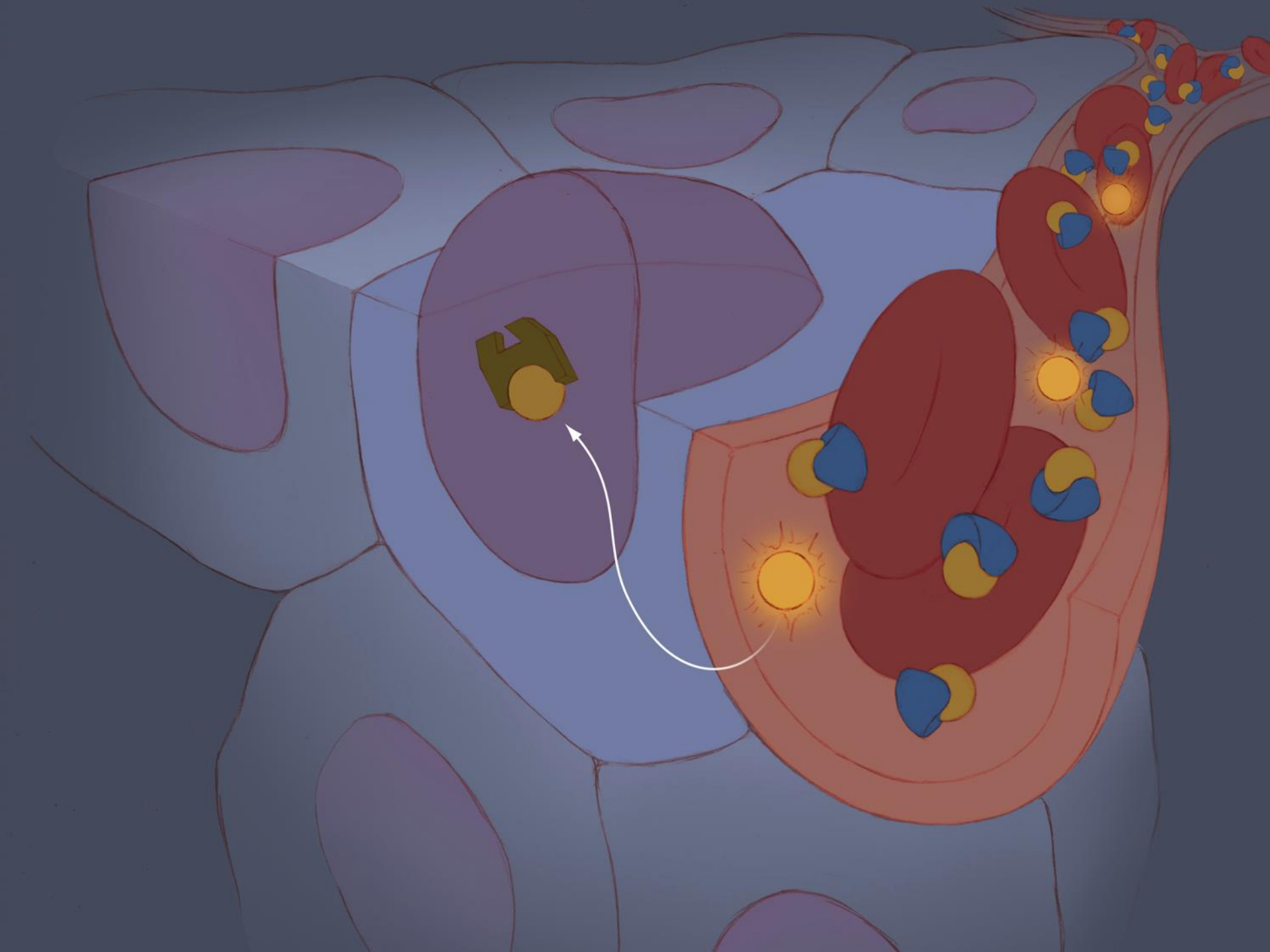
Progesterone



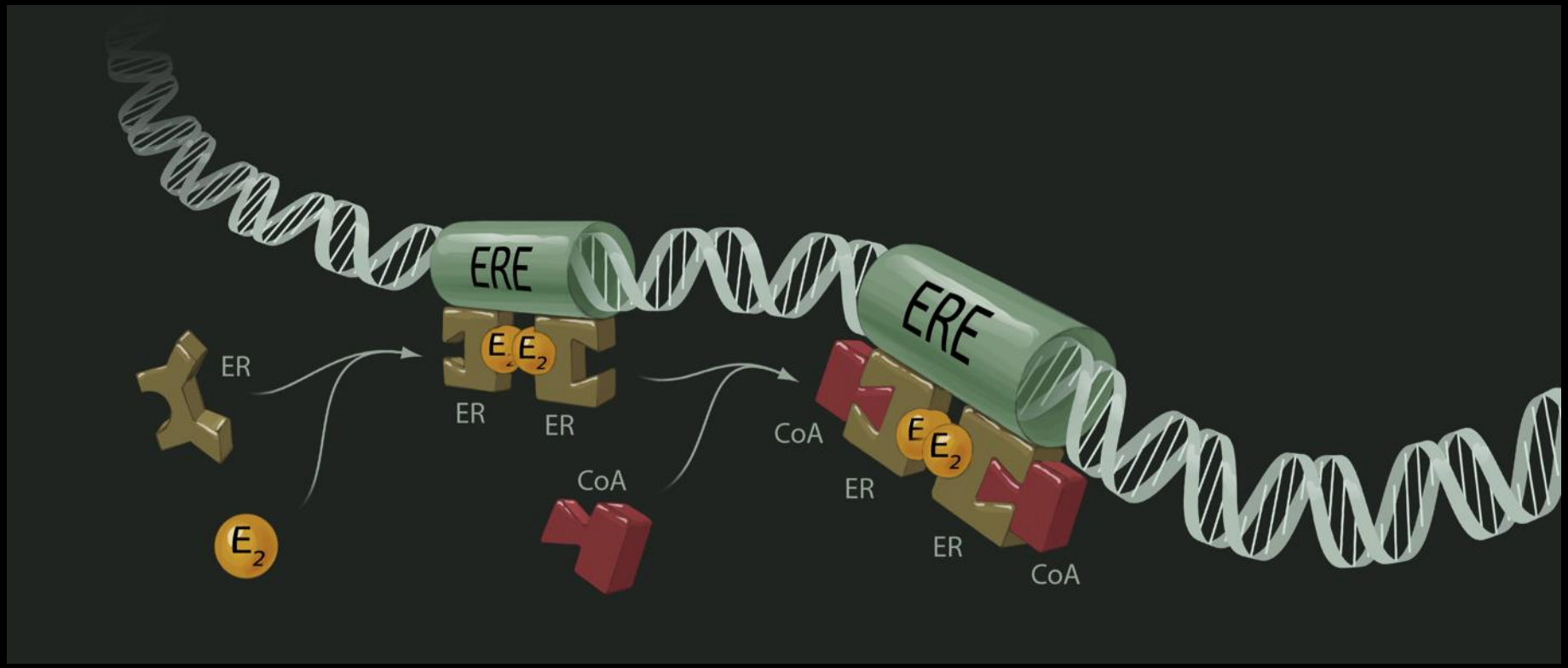
Cortisol

Aldosterone


ER
E2



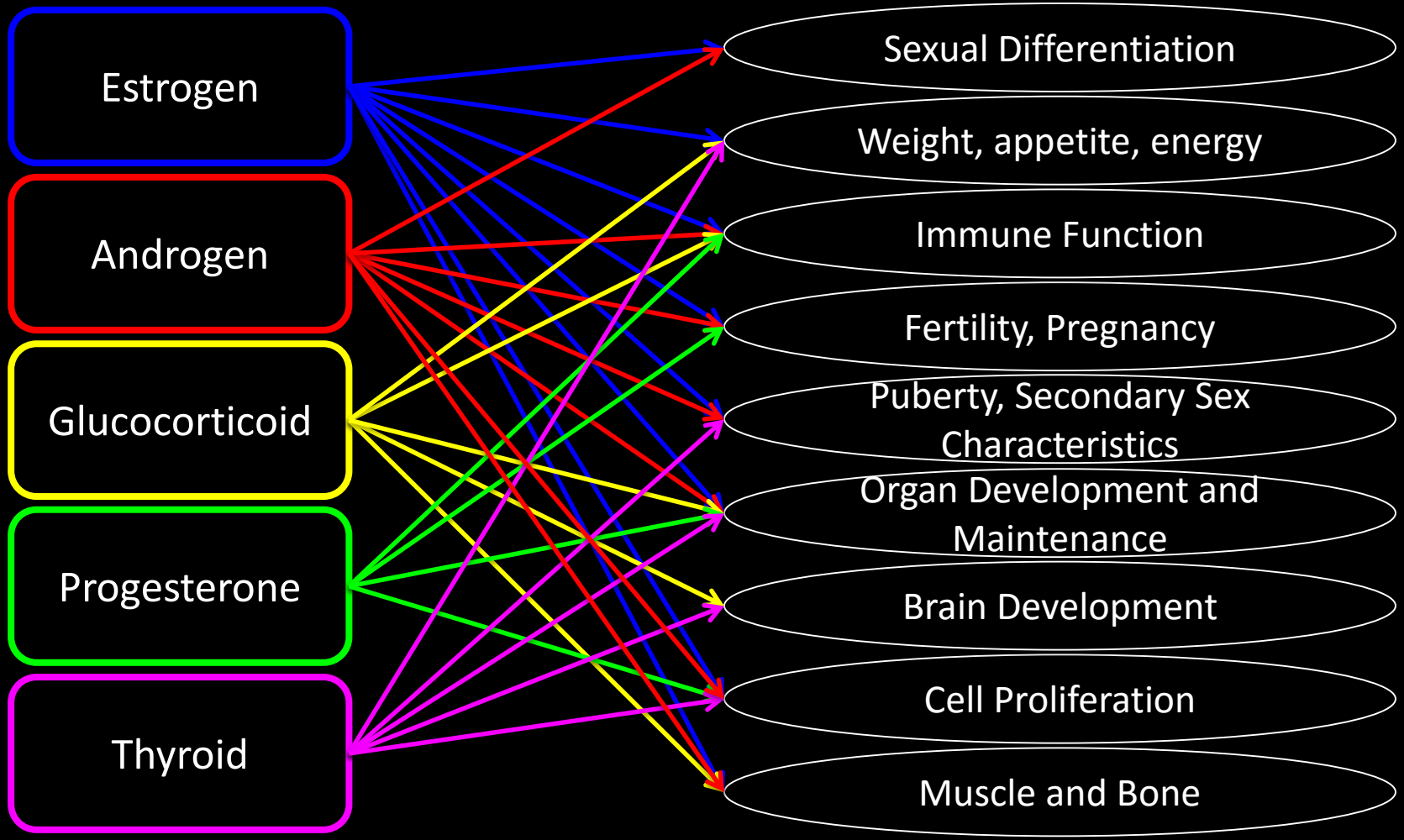
Estrogen receptor is a ligand activated transcription factor



Hormones can work at low concentrations

1 drop in olympic pool = 1 part per billion

Normal Function of 5 Hormones



Endocrine Disrupting Chemicals (EDC)

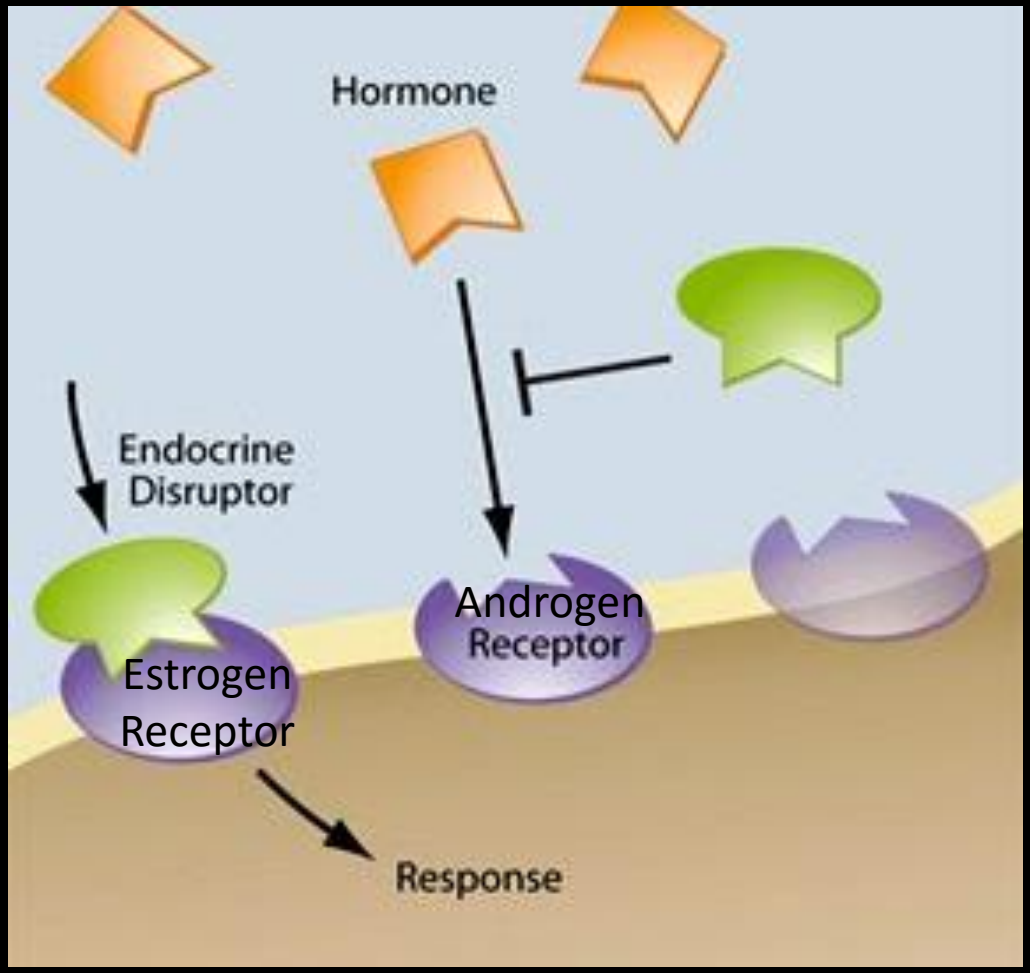
"A chemical, or mixture of chemicals, that interferes with any aspect of hormone action."



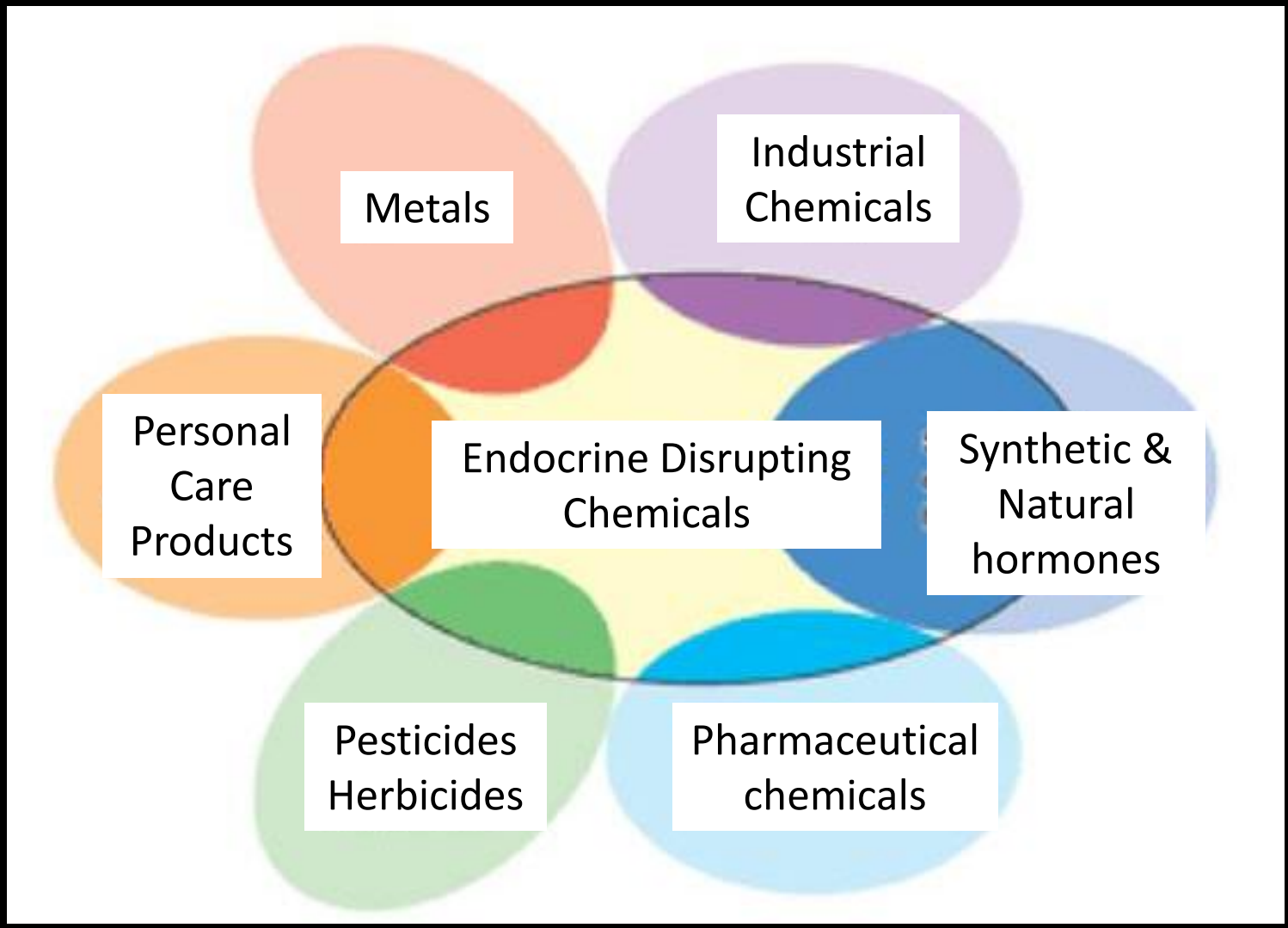


The Endocrine Society Statement on endocrine disrupting chemicals. Endocrinology 2012

EDCs can disrupt hormone receptors



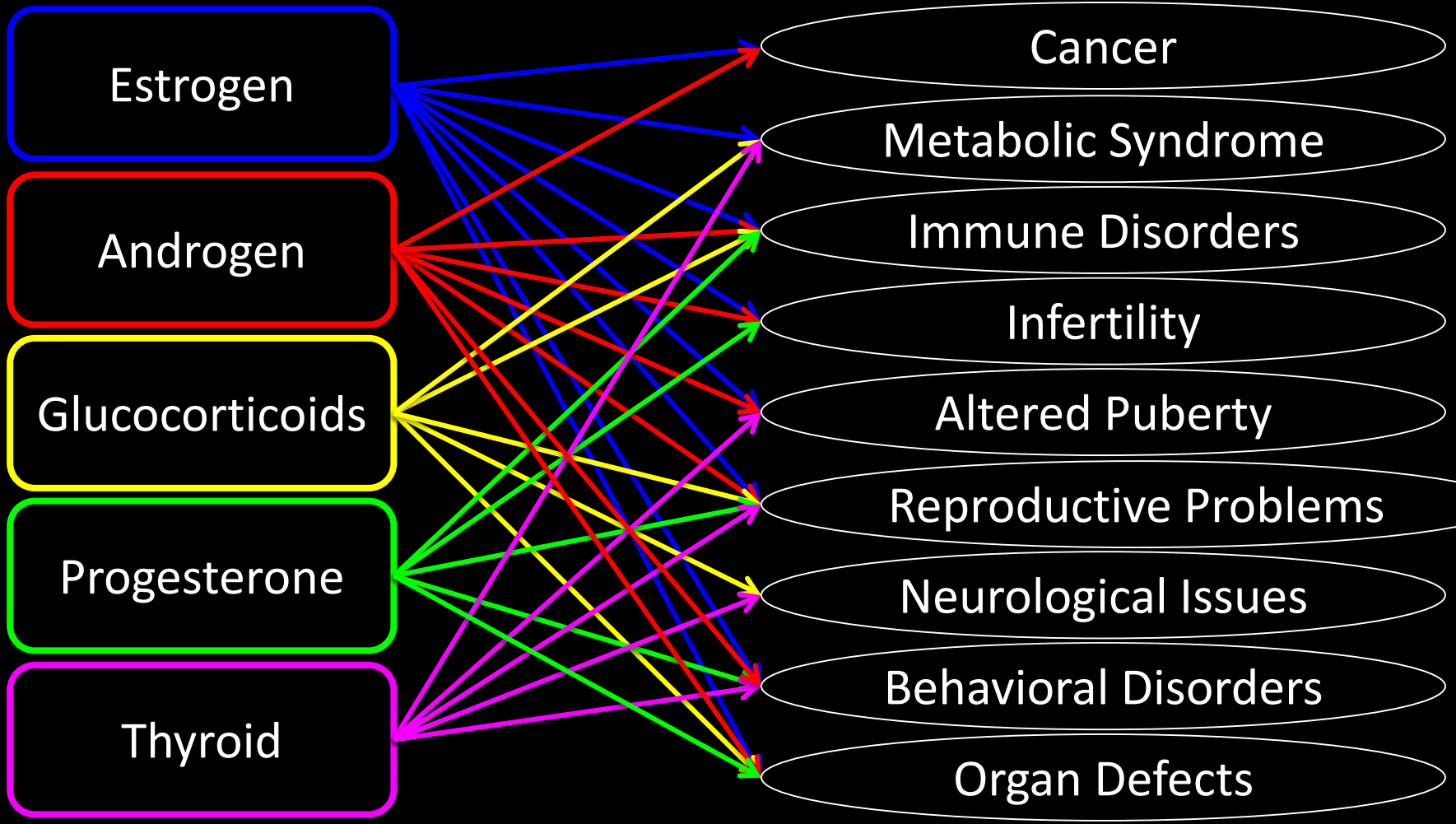
EDCs are found in many products



Why is endocrine disruption important to human health and disease?

- Hormones and EDCs can act at low concentrations
- Human exposure can be within the range of bioactivity
- Developmental exposure can alter adult health & disease

Disruption of hormones can result in adverse health uutcomes



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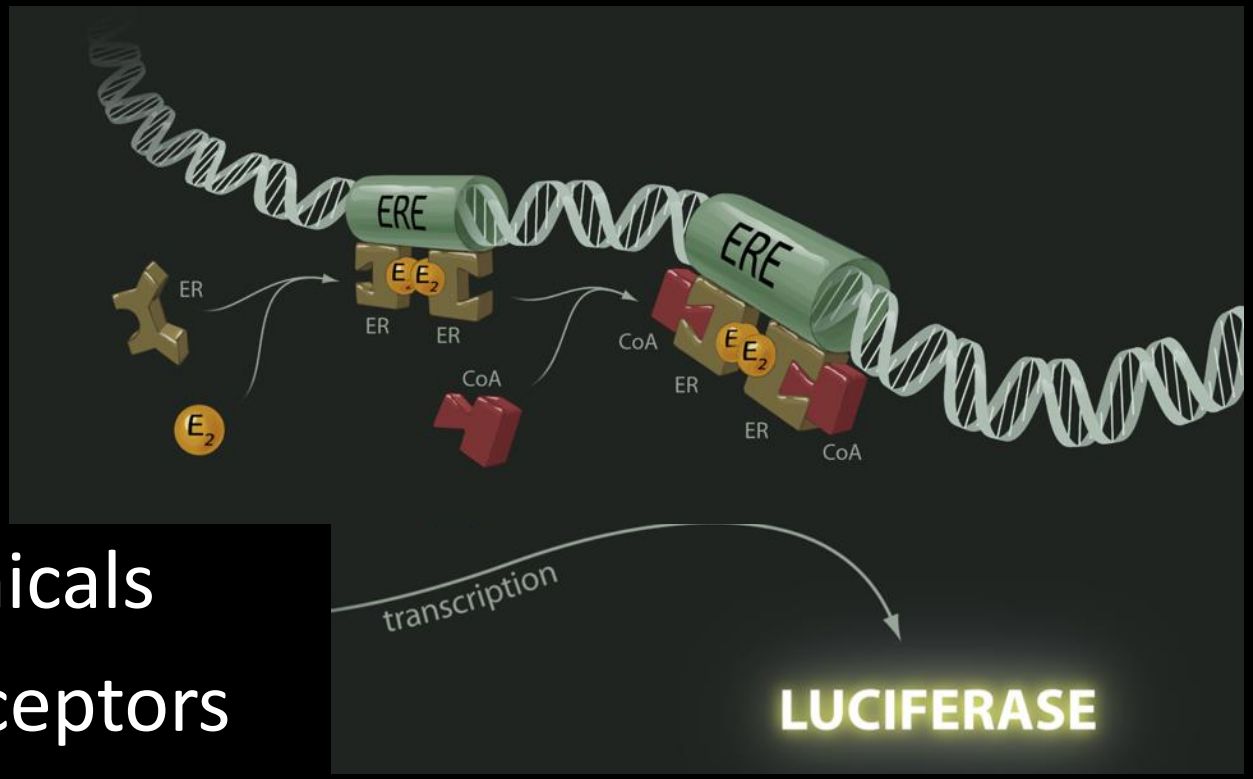
Our hypothesis: Chemicals used in hydraulic fracturing will disrupt hormone receptors

- Estrogen
- Androgen
- Glucocorticoid
- Progesterone
- Thyroid

Chris Kassotis, PhD

EDC activity measured with nuclear receptor reporter gene asssy



- Tested 24 chemicals
- Five nuclear receptors
- Measured receptor activation
- Measured receptor inhibition

Oil and Gas Chemicals Tested

Chemical Name	CAS #	Oil and Gas Operation Use
1,2,4-trimethylbenzene	95-63-6	Surfactant
2-(2-methoxyethoxy) ethanol	111-77-3	Biocide, Surfactant
2-ethylhexanol	104-76-7	Defoamer, Breaker
Acrylamide	79-06-1	Scale Control, Friction Reducer
Benzene	71-43-2	Paraffin Inhibitor, Surfactant
Bronopol	52-51-7	Biocide
Cumene (Isopropylbenzene)	98-82-8	Paraffin Inhibitor
Diethanolamine	111-42-2	Friction Reducer, Corrosion Inhibitor
Dimethylformamide	68-12-2	Corrosion Inhibitor
Ethoxylated nonylphenol	9016-45-9	Surfactant, Corrosion Inhibitor
Ethoxylated octylphenol	9036-19-5	Surfactant, Corrosion Inhibitor
Ethylbenzene	100-41-4	Non-emulsifier, paraffin inhibitor
Ethylene glycol	107-21-1	Crosslinker, Friction reducer
Ethylene glycol monobutyl ether (2-BE)	111-76-2	Surfactant, Foamer
Methyl-4-isothiazolin	2682-20-4	Biocide
Naphthalene	91-20-3	Surfactant, Acid Inhibitor
Phenol	108-95-2	Resin-coating for proppants
Propylene glycol	57-55-6	Gellant, Breaker
Sodium tetraborate decahydrate	1303-96-4	Crosslinker
Styrene	100-42-5	Proppant
Toluene	108-88-3	Non-emulsifier, paraffin inhibitor
Triethylene glycol	112-27-6	Biocide, Dehydration
Xylenes	1330-20-7	Non-emulsifier, Breaker

EDC Activity of 24 Fracking Chemicals

Receptor	Activation	Inhibition
Estrogen	1	21
Androgen	0	21
Progesterone	1	12
Glucocorticoid	0	10
Thyroid	2	7

Kassotis, et al, 2014 and 2015

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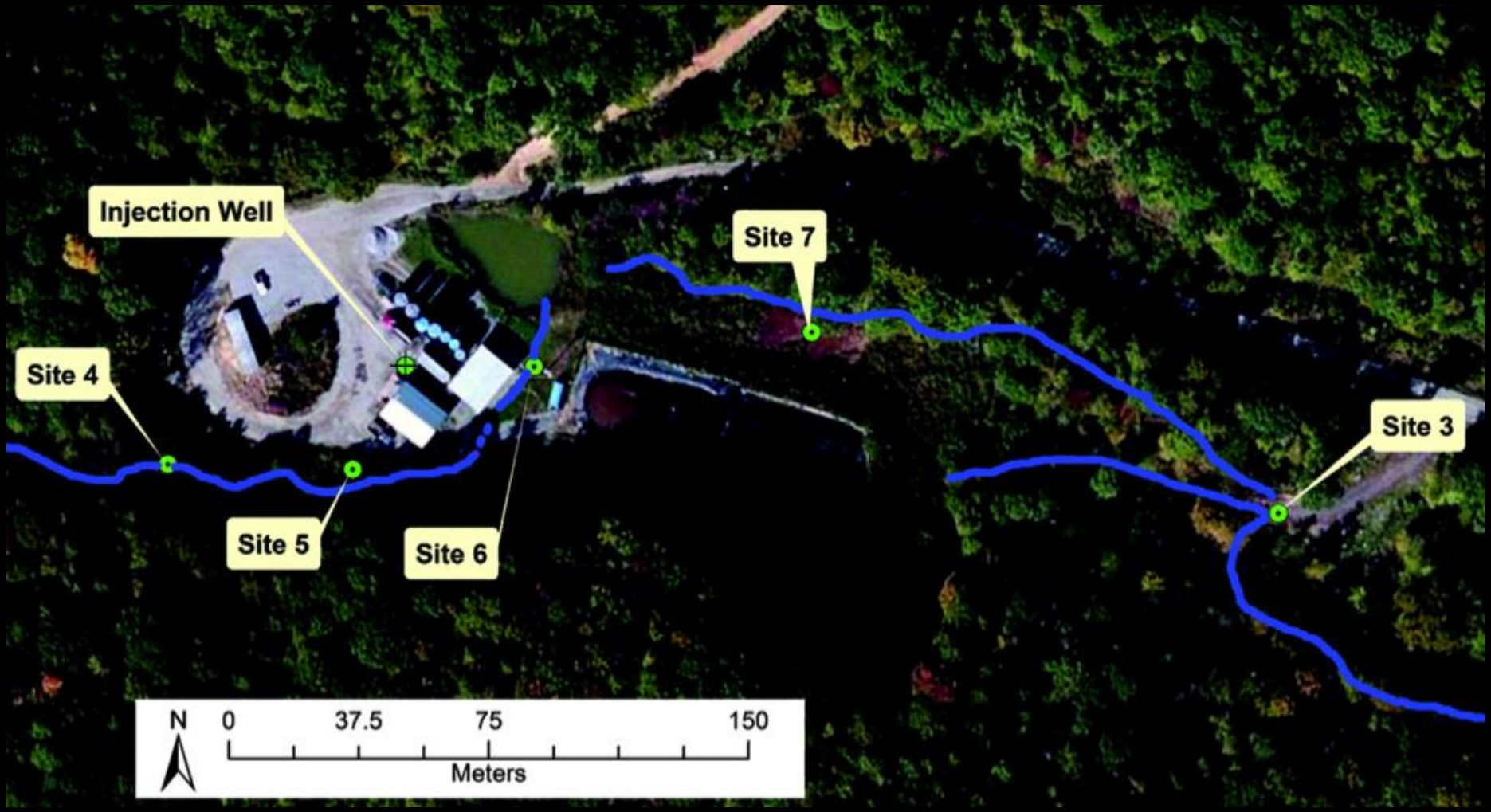
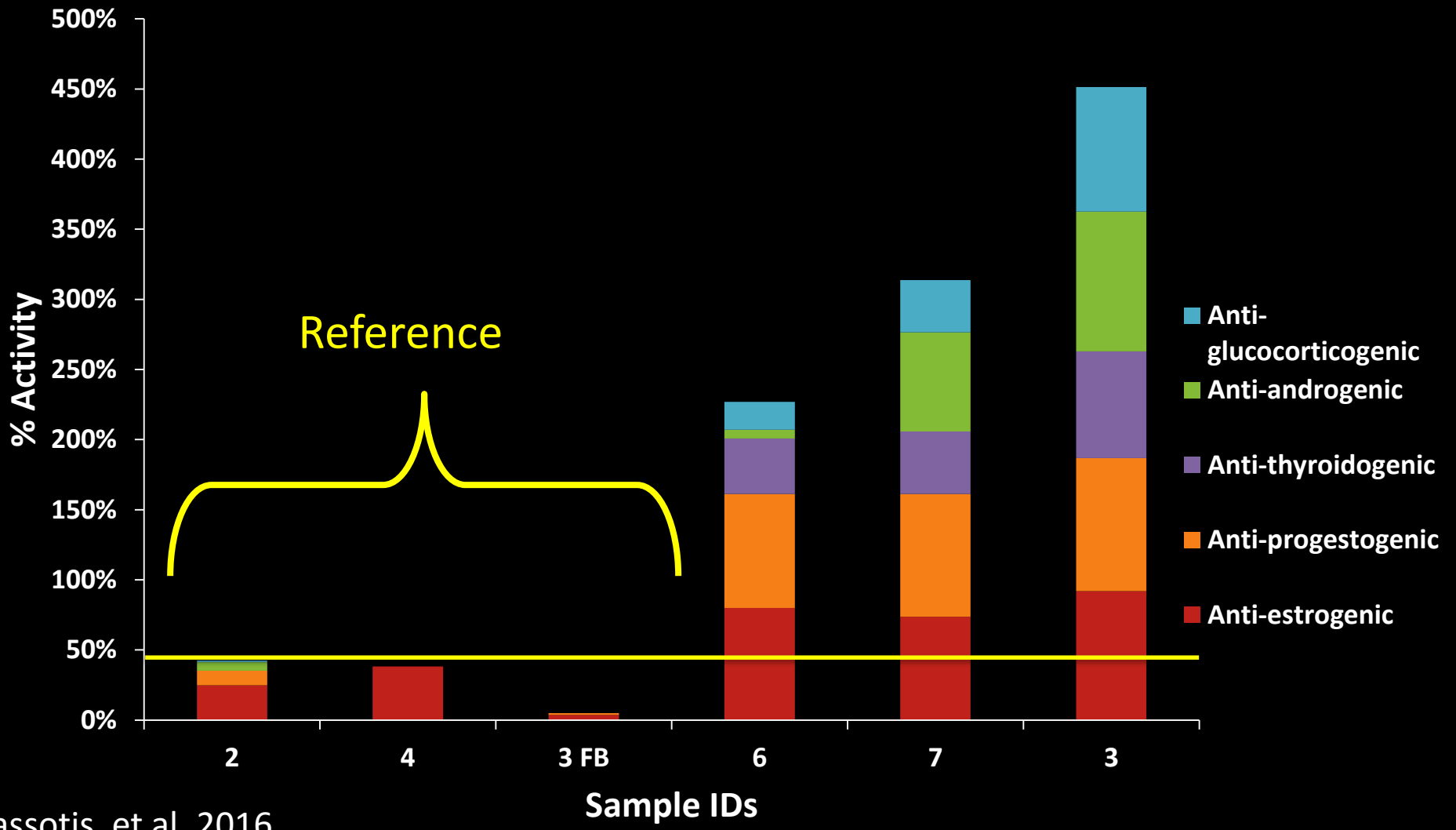
Oil and Gas Waste Water Injection Disposal Facility in West Virginia



Surface Water Antagonist Activities



Kassotis, et al, 2016

Contents lists available at ScienceDirect

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Endocrine disrupting activities of surface water associated with a West Virginia oil and gas industry wastewater disposal site

Christopher D. Kassotis [a,*], Luke R. Iwanowicz [b], Denise M. Akob [c], Isabelle M. Cozzarelli [c], Adam C. Mumford [c], William H. Orem [d], Susan C. Nagel [e,**]

Chris Kassotis, PhD

Denise Akob, PhD

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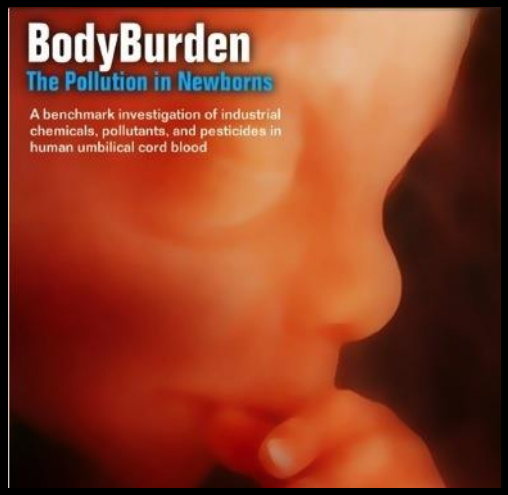
Fetal and early life exposure to EDCs is associated with adult disease

Pollutants

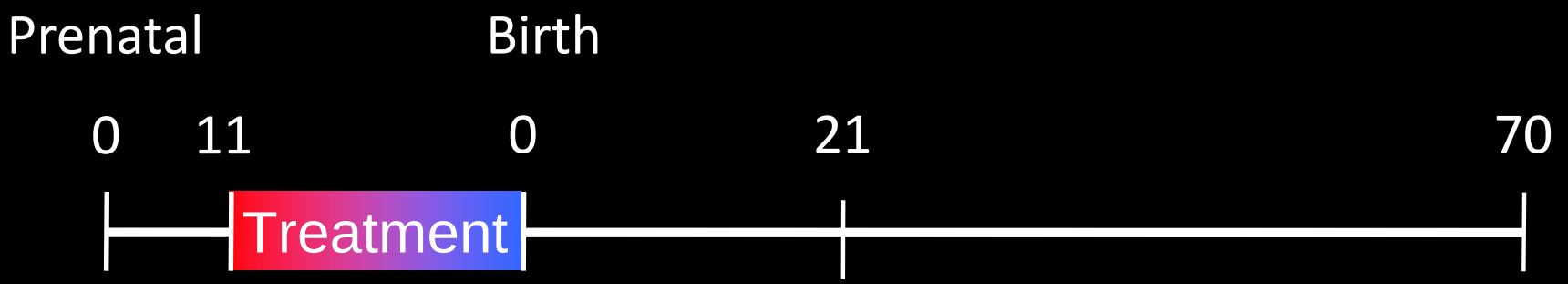
Nutrition

Maternal Health and Disease



Infertility
Obesity
Heart Disease
Diabetes
Hypertension
Hyperactivity
Bone Health
Endometriosis
Breast Cancer
Testicular Cancer

Developmental exposure to a mixture of 23 UOG chemicals via drinking water

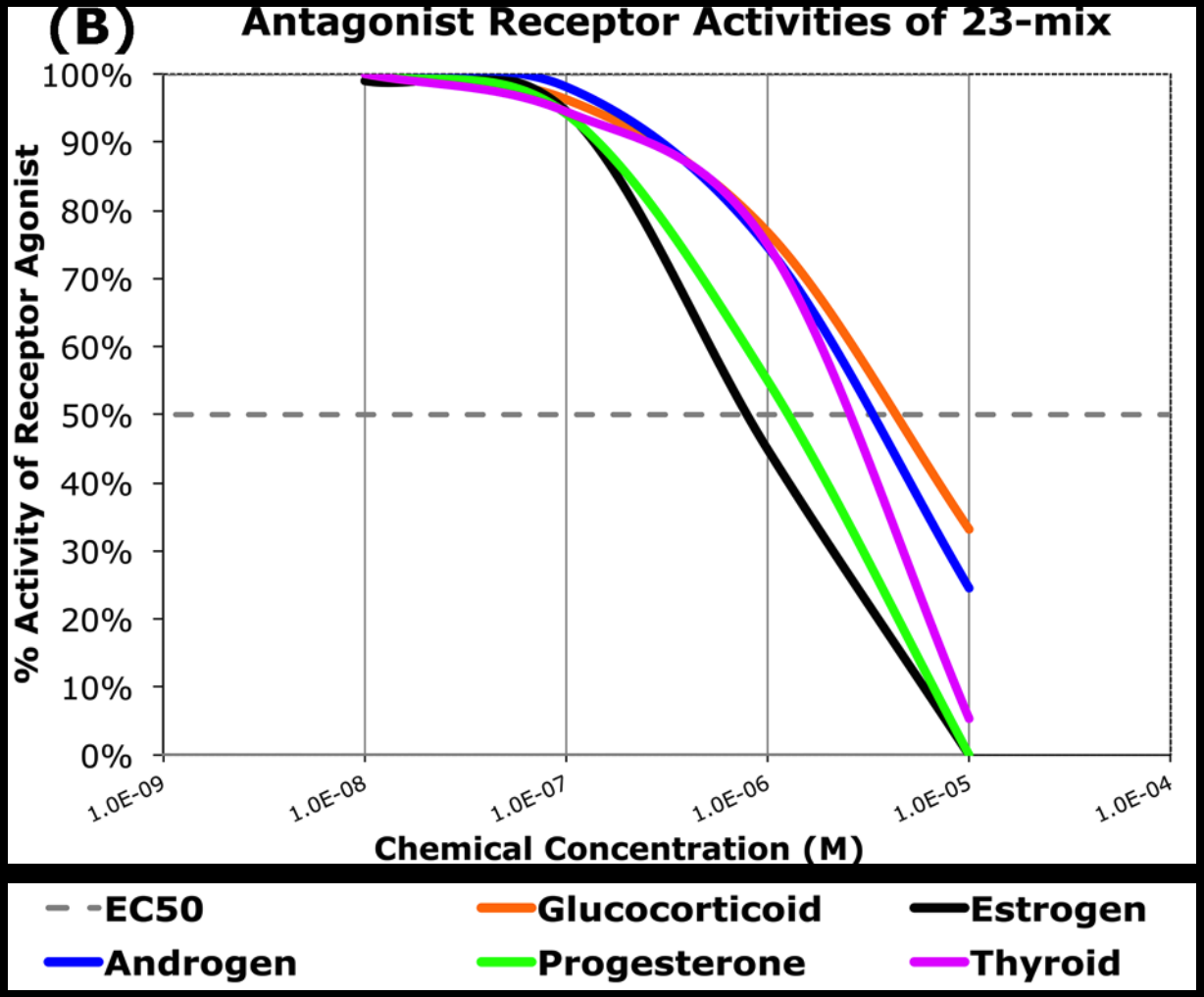


Vehicle	0.2% ethanol
Mix 1	3000 µg/kg
Mix 2	300 µg/kg
Mix 3	30 µg/kg
Mix 4	3 µg/kg

Erma Drobnis

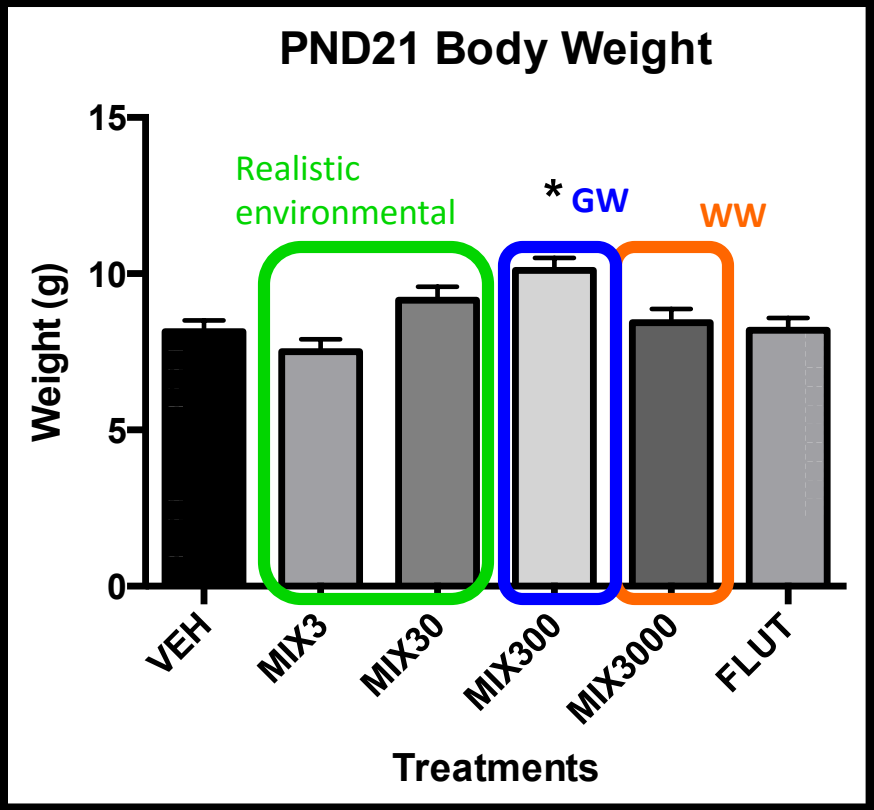
Chris Kassotis, PhD

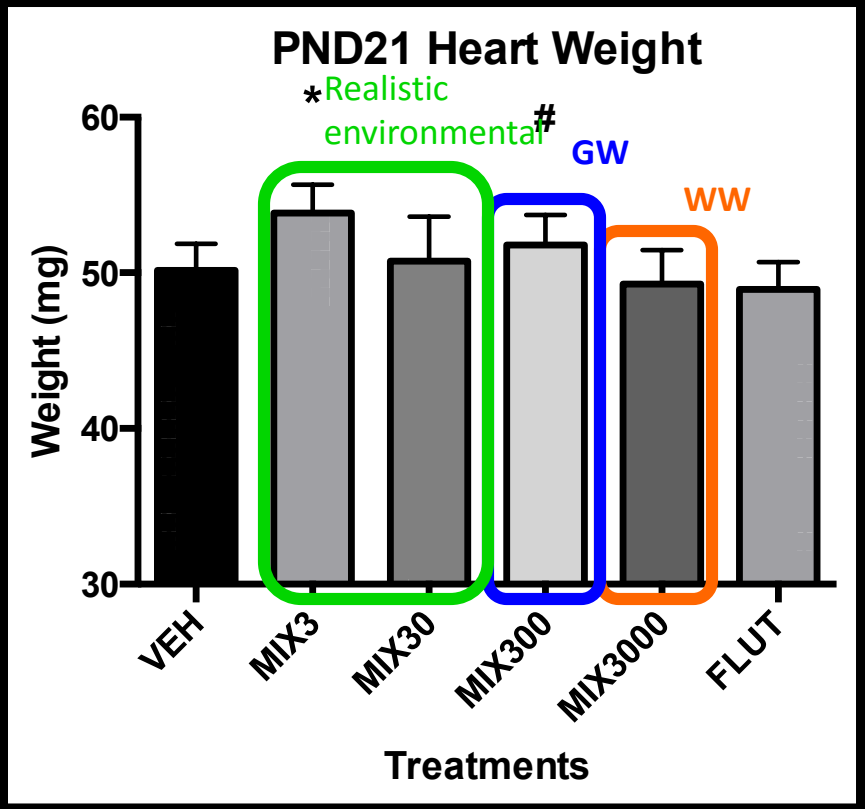
Activity of Chemical Mixture



Kassotis, et al, 2015

Prenatal exposure to UOG mixture increased altered body and organ weights in adult male mice

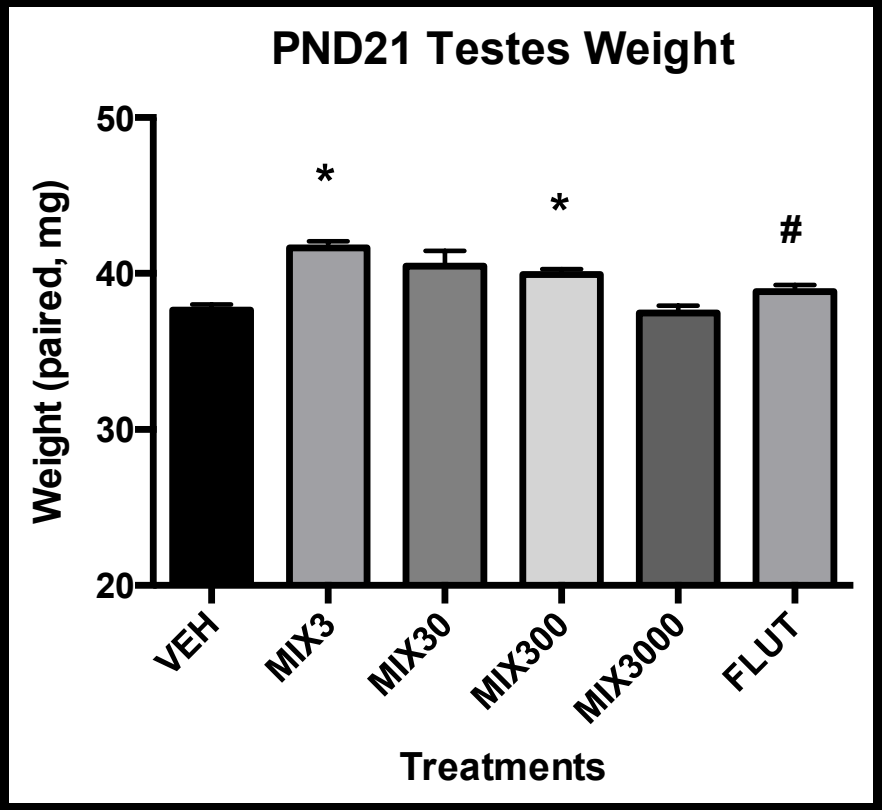


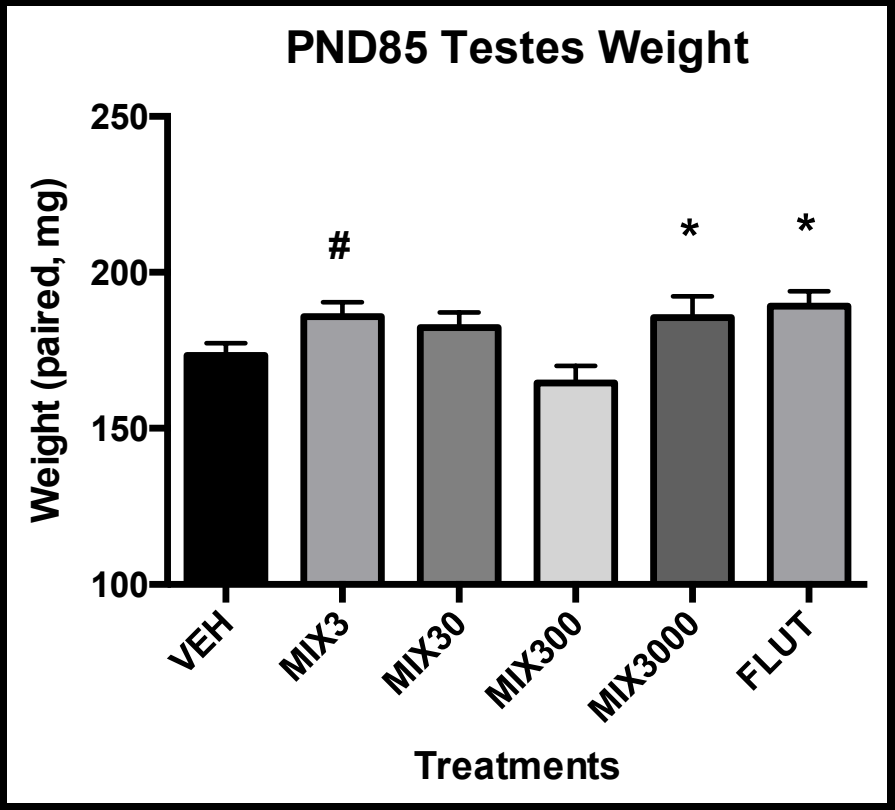


Ground water directly below surface spills, *Gross et al*

Kassotis et al 2015, Endocrinology

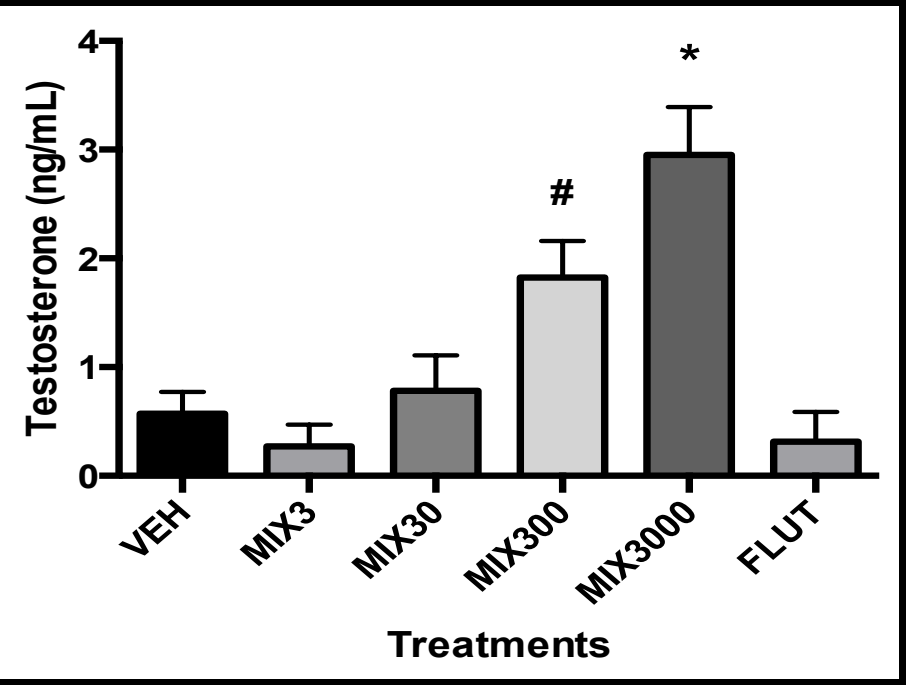
Prenatal exposure to UOG mixture increased testis weight

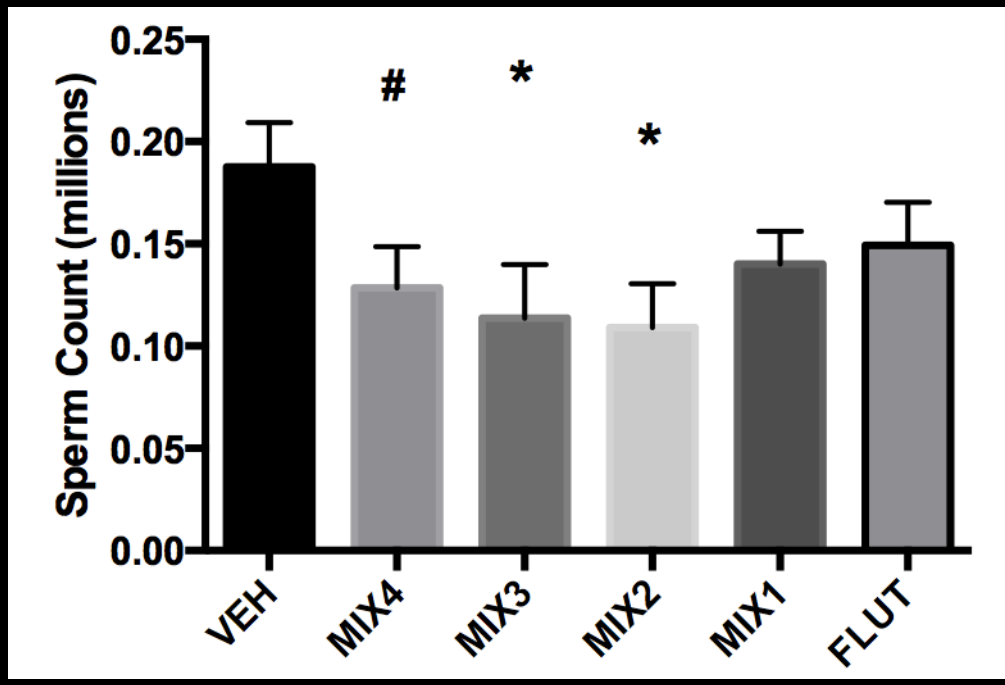




Kassotis et al 2015, Endocrinology

Prenatal exposure to UOG mixture increased adult testosterone and decreased sperm counts





Kassotis et al 2015, Endocrinology

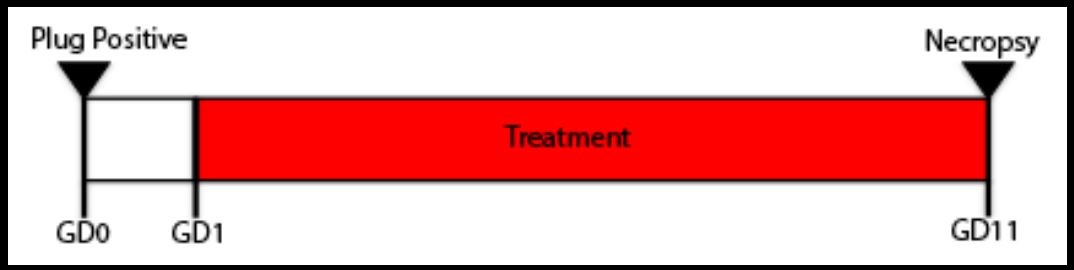
Prenatal Exposure: Prolactin and FSH Levels in Females

Kassotis et al 2016 Submitted

Prenatal Exposure: LH and Increases GH in females

Kassotis et al 2016 Submitted

Does maternal exposure alter embryo development



Jenn Green

Tori Balise

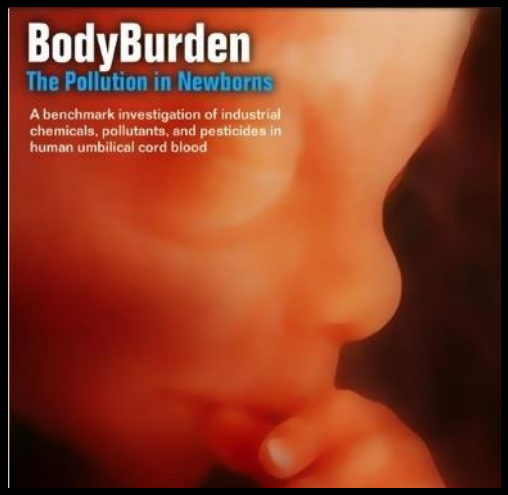
Maternal exposure to mixture and embryo abnormalities

Fetal and early life exposure to EDCs is associated with adult disease

Pollutants

Nutrition

Maternal Health and Disease



Infertility
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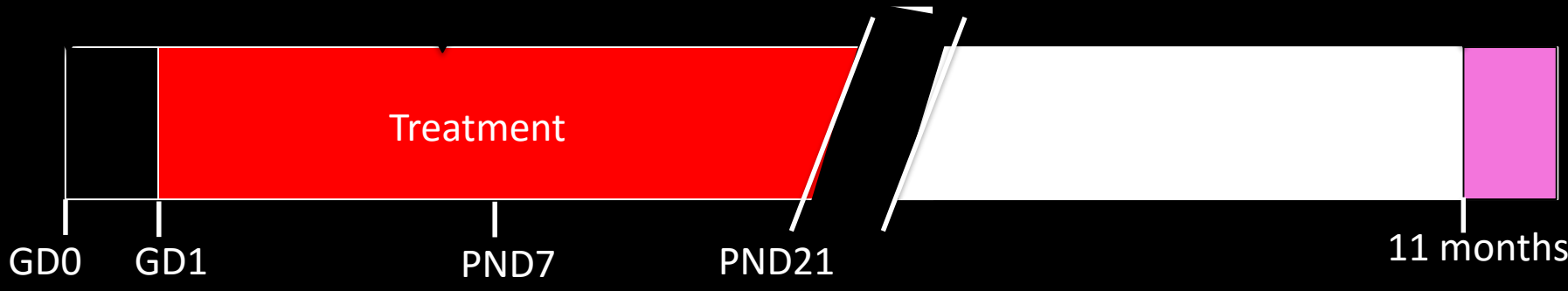
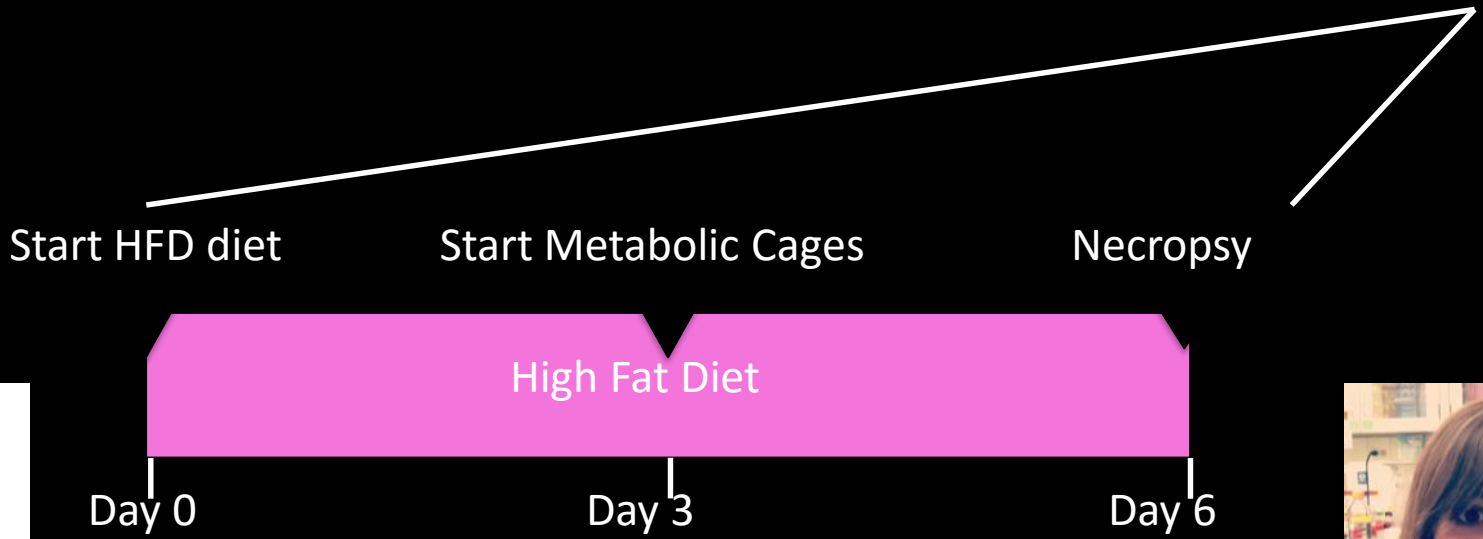
Bone Health
Endometriosis
Breast Cancer
Testicular Cancer

Exposure





John Thyfault

Tori Balise

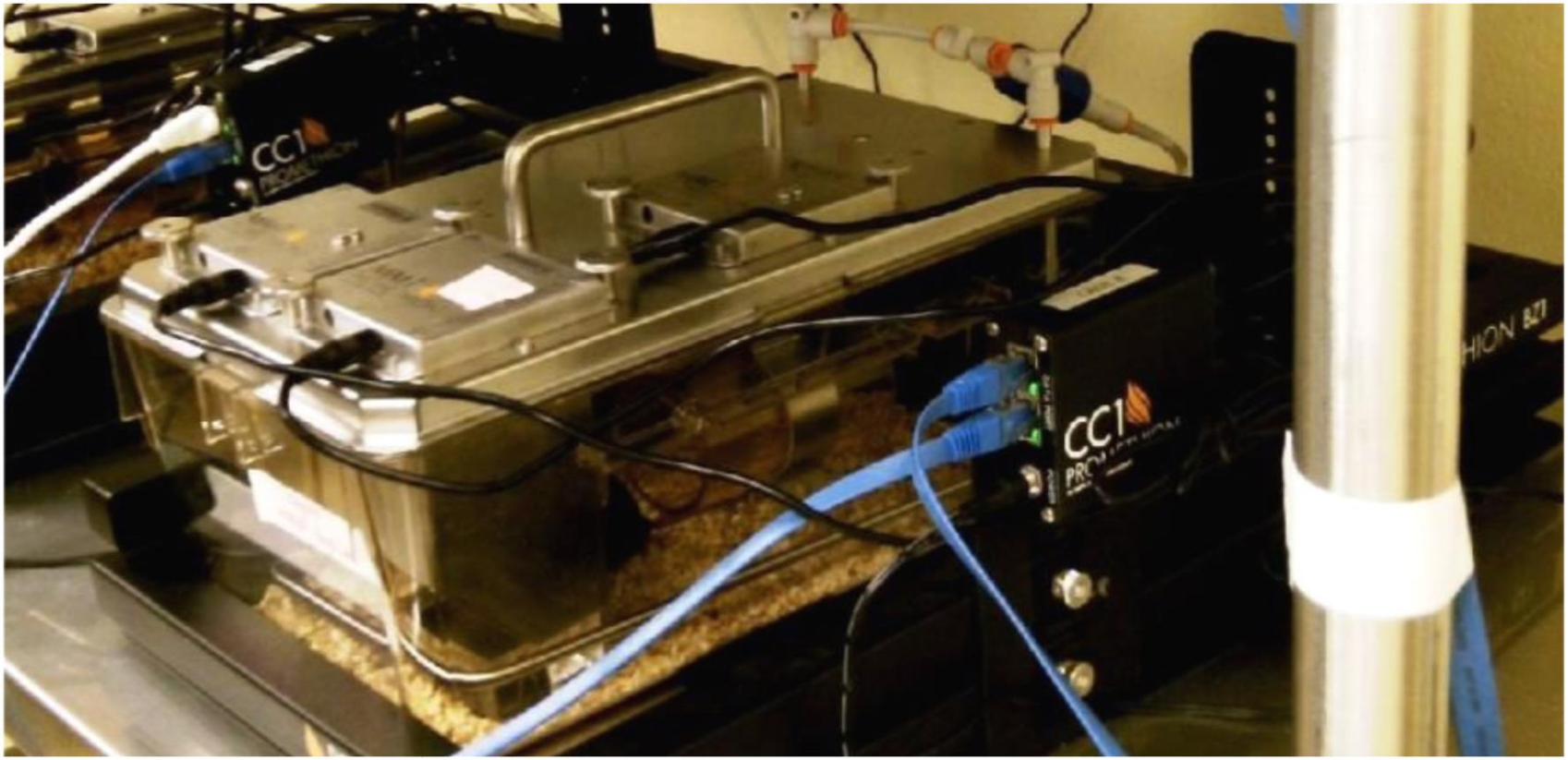
Exposure

C57Bl6 were exposed to either a vehicle or 1 of 4 different concentrations of equimolar mixture of 23 chemicals.

Treatments:

- Vehicle
- 1.5 ug/kg/day
- 15 ug/kg/day
- 150 ug/kg/day
- 1500 ug/kg/day

Sable Systems Metabolic Cages



Perinatal exposure: energy expenditure in adulthood

Light Cycle

* P<.05 ** P<.0125

Perinatal exposure: activity in adulthood

Spontaneous Activity

Meters Travelled

* P<.05 ** P<.0125

Adiposity

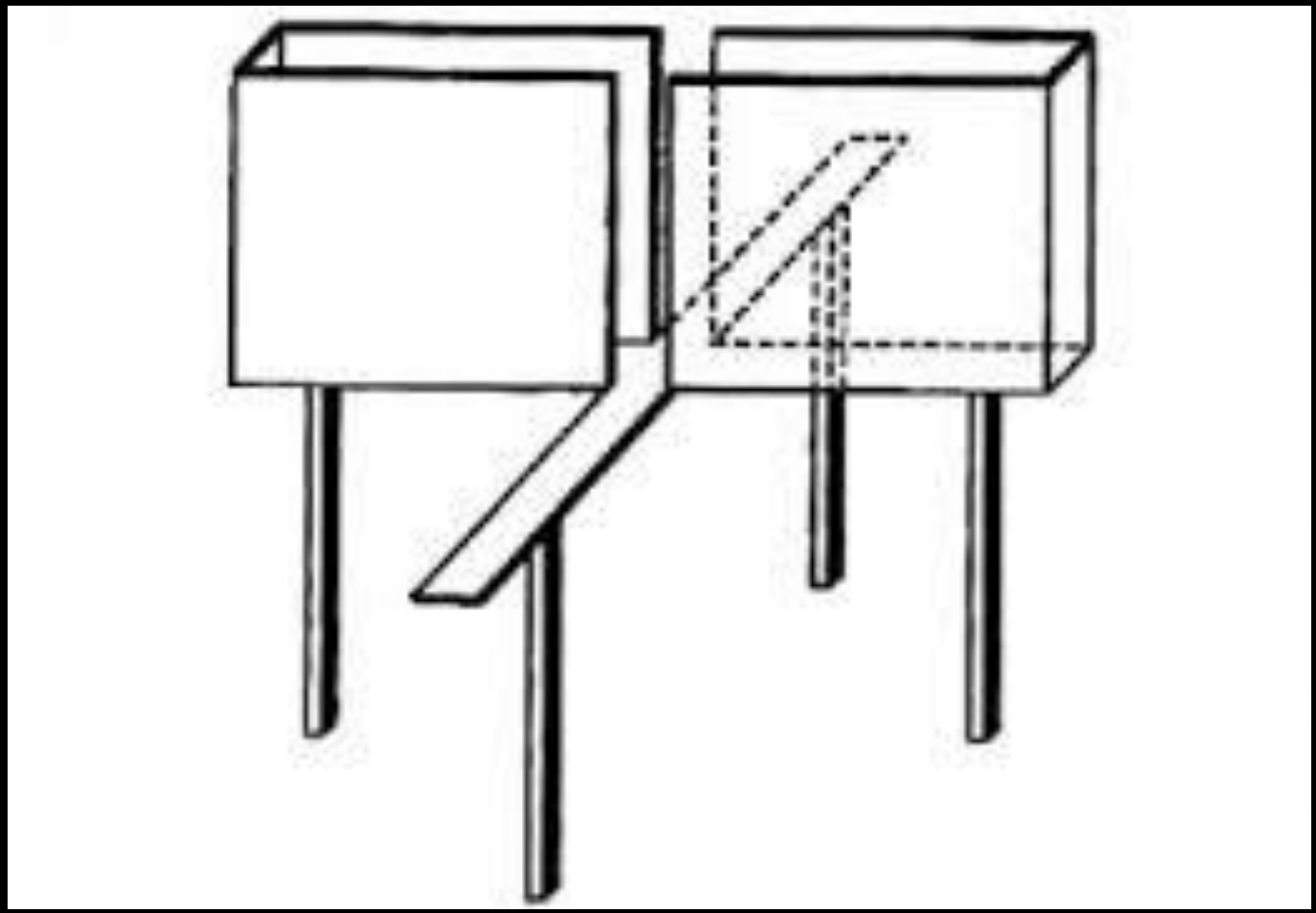
Perirenal fat pad

Periuterine fat pad

* P<.05 ** P<.0125

Perinatal exposure: recovery after glucose challenge

Elevated Plus Maze



Paola Palanza

http://www.nature.com/scitable/knowledge/library/rapid-effects-of-steroid-hormones-on-animal-15104619

Perinatal Exposure: Exploratory Behavior

Conclusions

- Oil and gas activities use and produce EDCs
- EDC activity in surface and ground water is associated with oil and gas activities
- Laboratory studies suggest a potential for negative impacts on health from exposure to these chemicals





Balise

Kassotis





Lin

Tillit

Vengosh

McElroy

Akob

Funding: The Passport Foundation, University of Missouri, EPA STAR Fellowship to Kassotis, NIH NIEHS R21