

# Unconventional Oil and Gas Extraction and Endocrine Disruptors: Potential Implications for Human and Animal Health



Duke  
UNIVERSITY



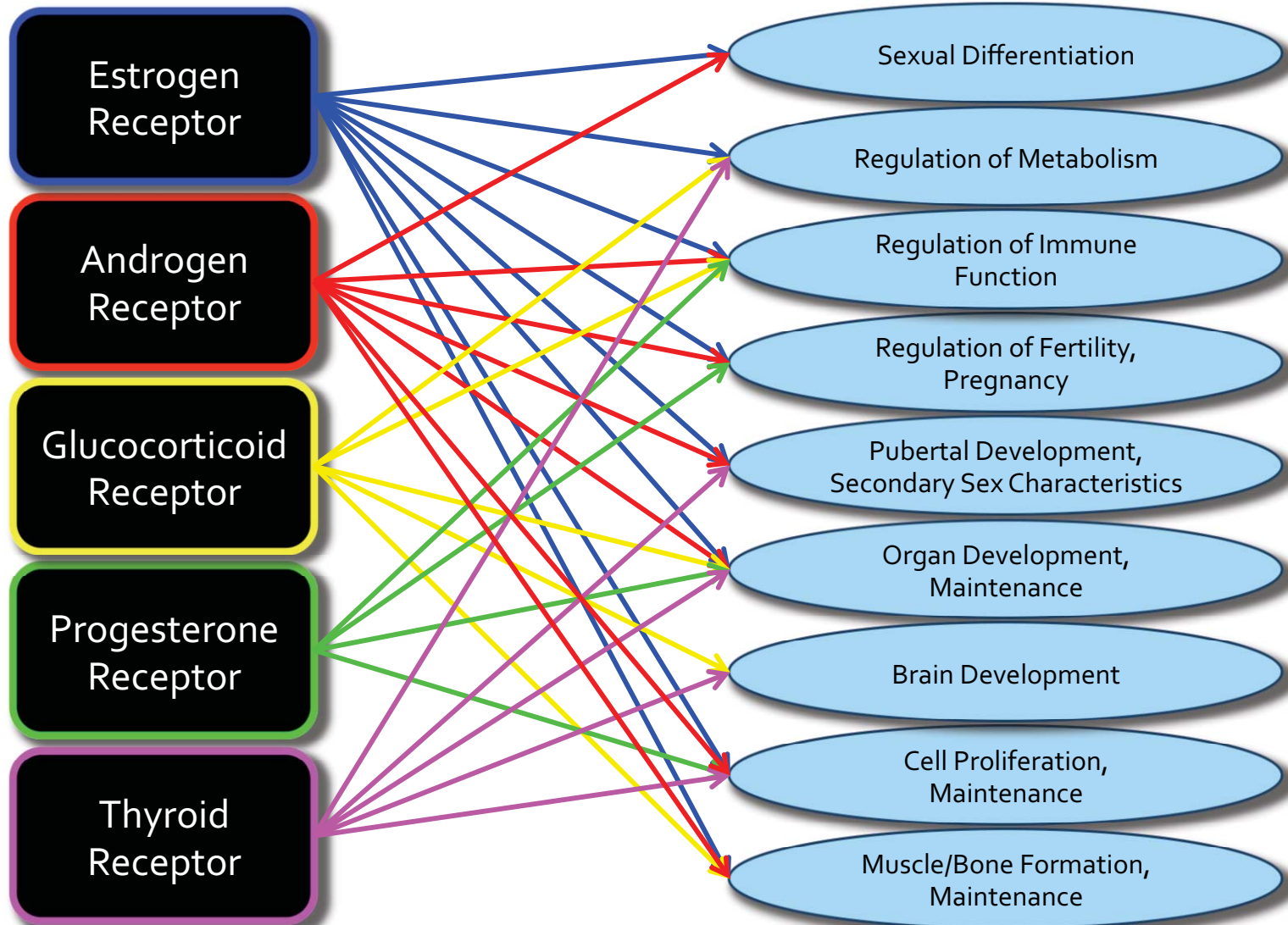
Chris Kassotis, PhD  
Postdoctoral Researcher  
Duke University  
 @cdkassotis

The Endocrine Disruption Exchange  
April 7, 2016

# Outline

- + Hormones and Endocrine Disrupting Chemicals (EDCs)
- + Hydraulic Fracturing
- + EDCs Associated with an Oil and Gas Wastewater Injection Operation
- + Gestational Exposure and Health Effects in Male and Female Mice

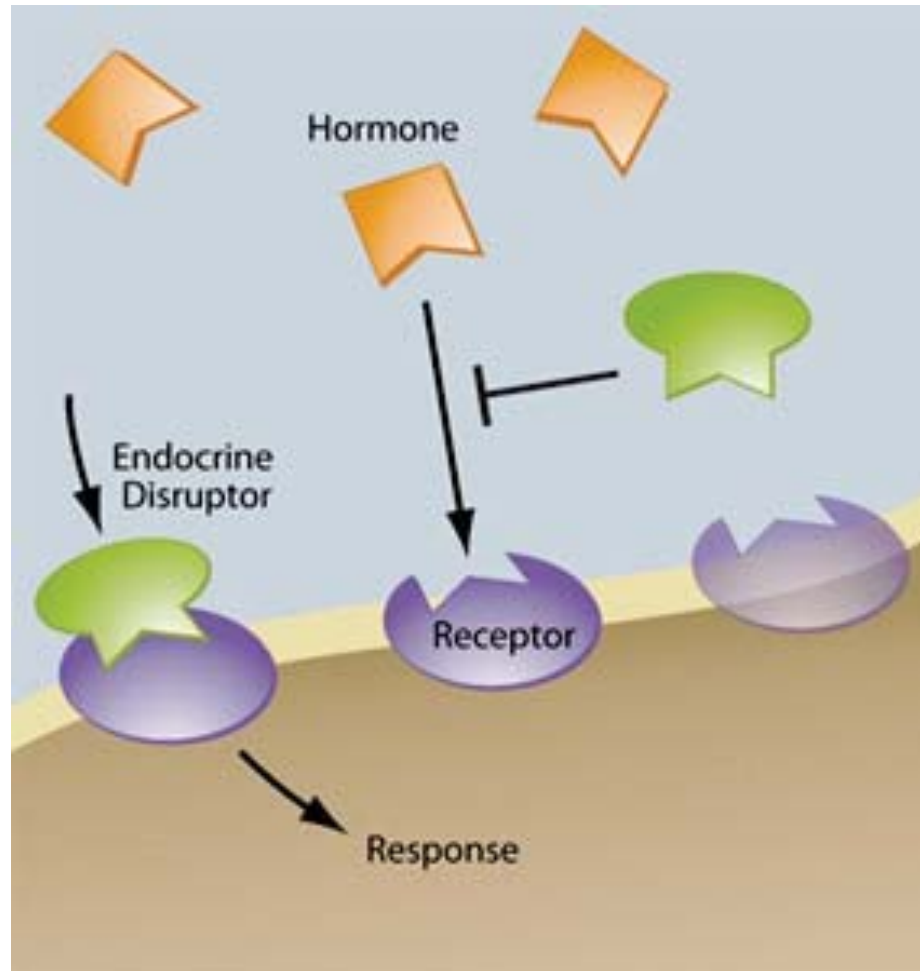
# Normal Hormonal Function



# Hormone/EDDC Action

## 1) Direct Interactions

Receptor  
Agonists  
Antagonists

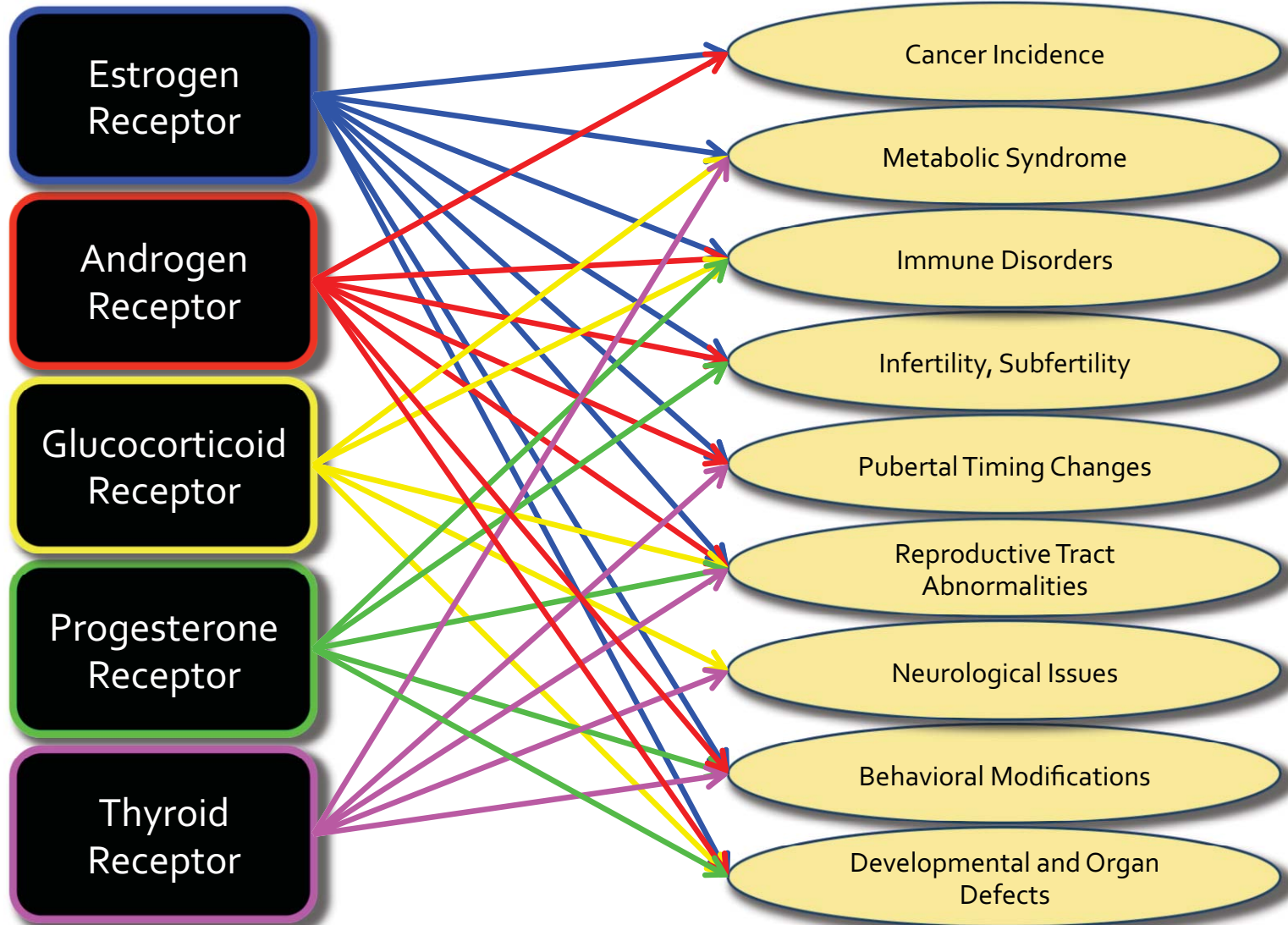


## 2) Indirect Interactions

Receptor Expression  
Hormone Levels  
Receptor Response

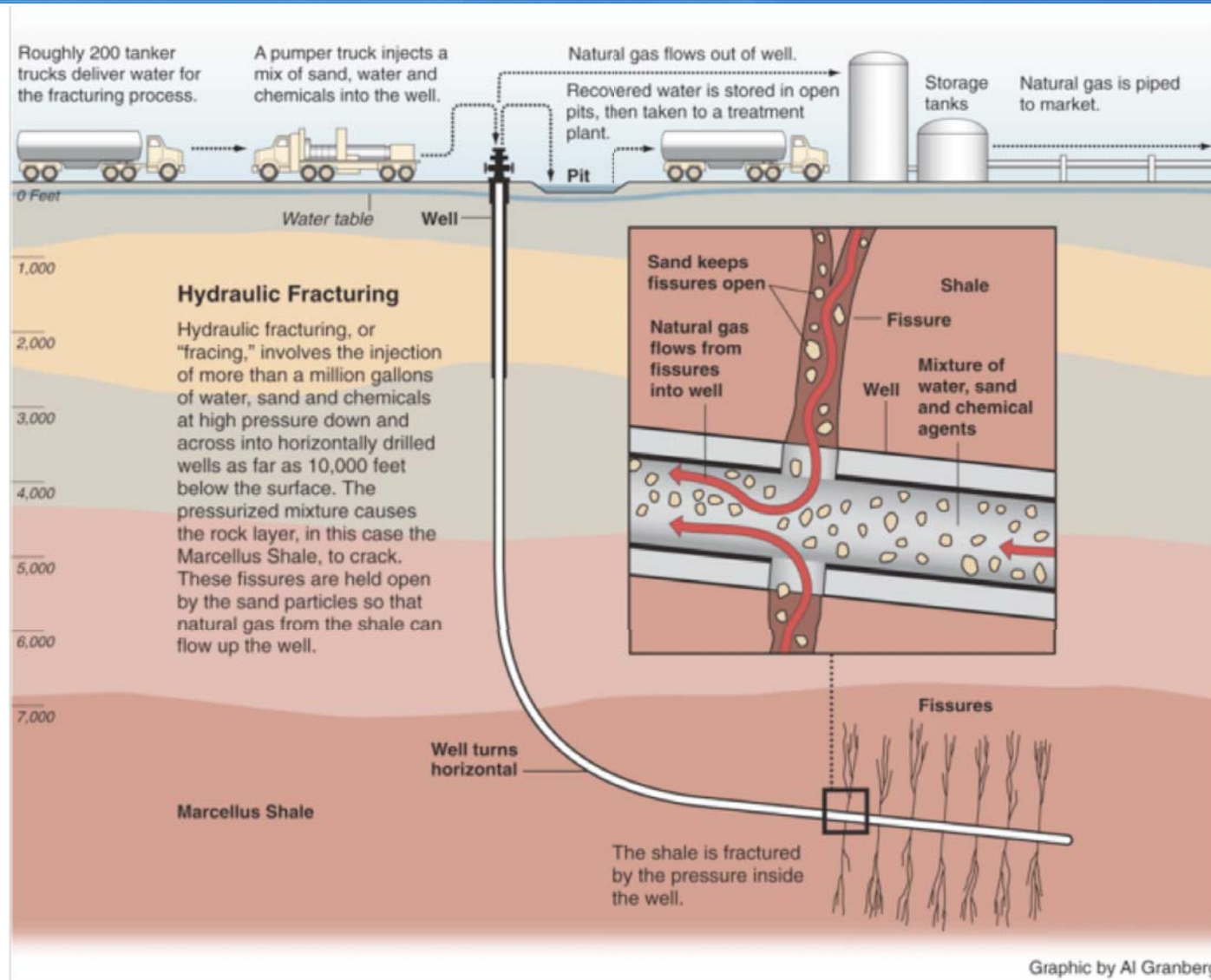
An endocrine disruptor is “a chemical or mixture of chemicals in the environment that interferes with any aspect of hormone action.” – The Endocrine Society, 2012.

# Disruption of Hormone Receptors and Adverse Health Outcomes

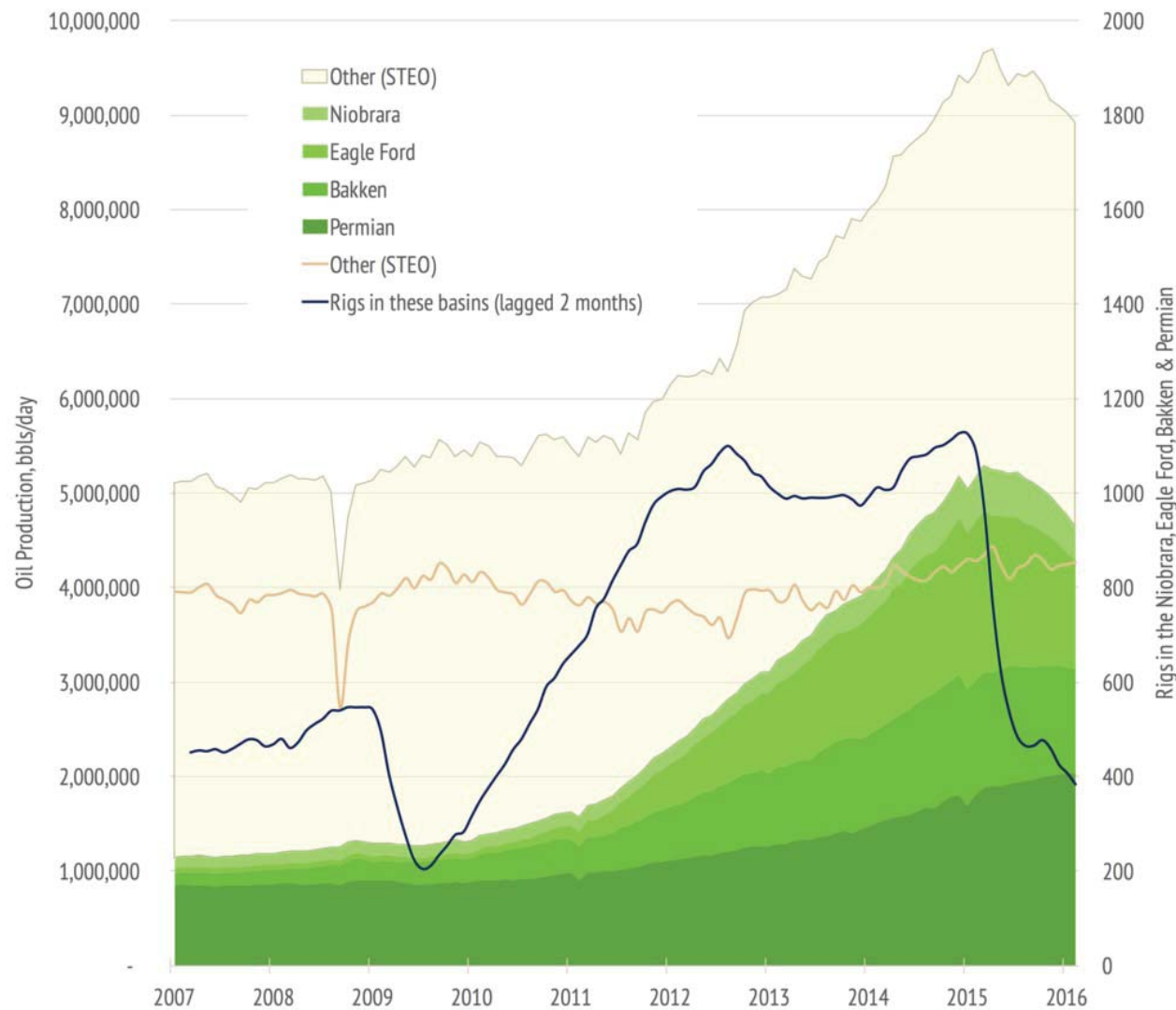




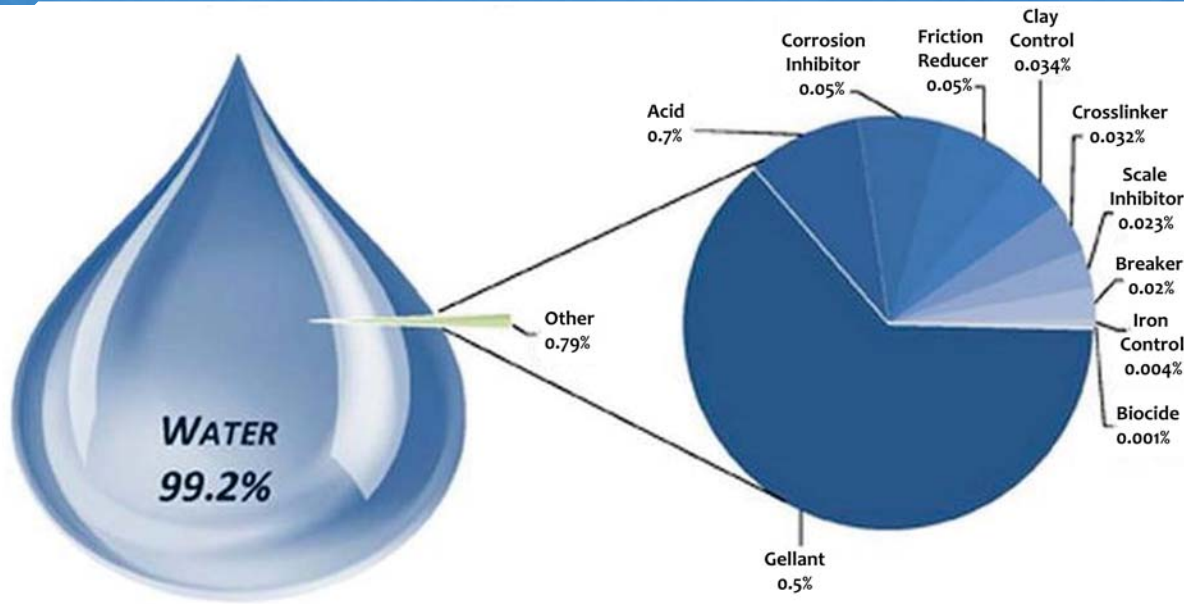
# The Hydraulic Fracturing Process



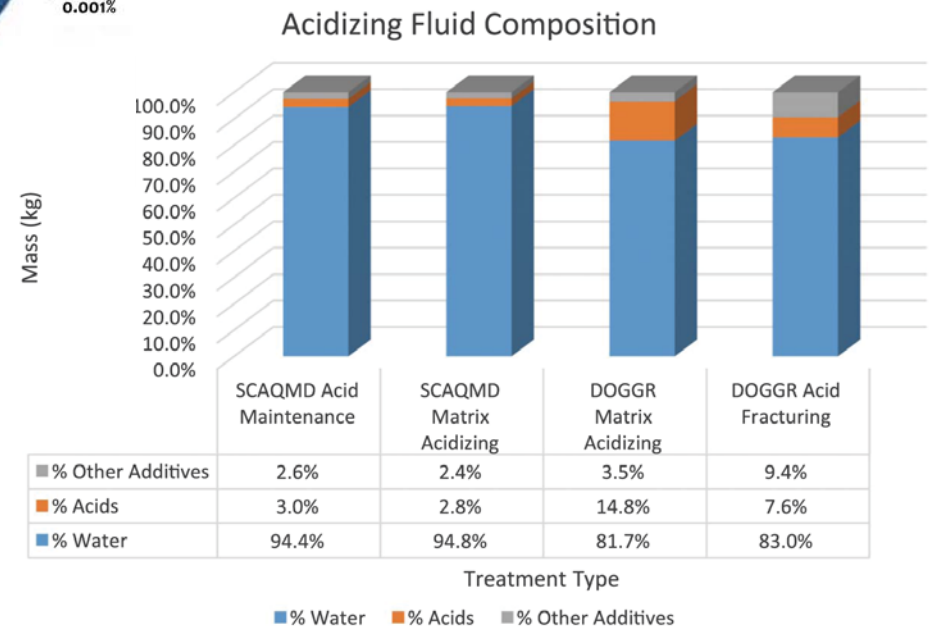
# US Oil Production Boom and Bust



# Fracturing Fluid Composition

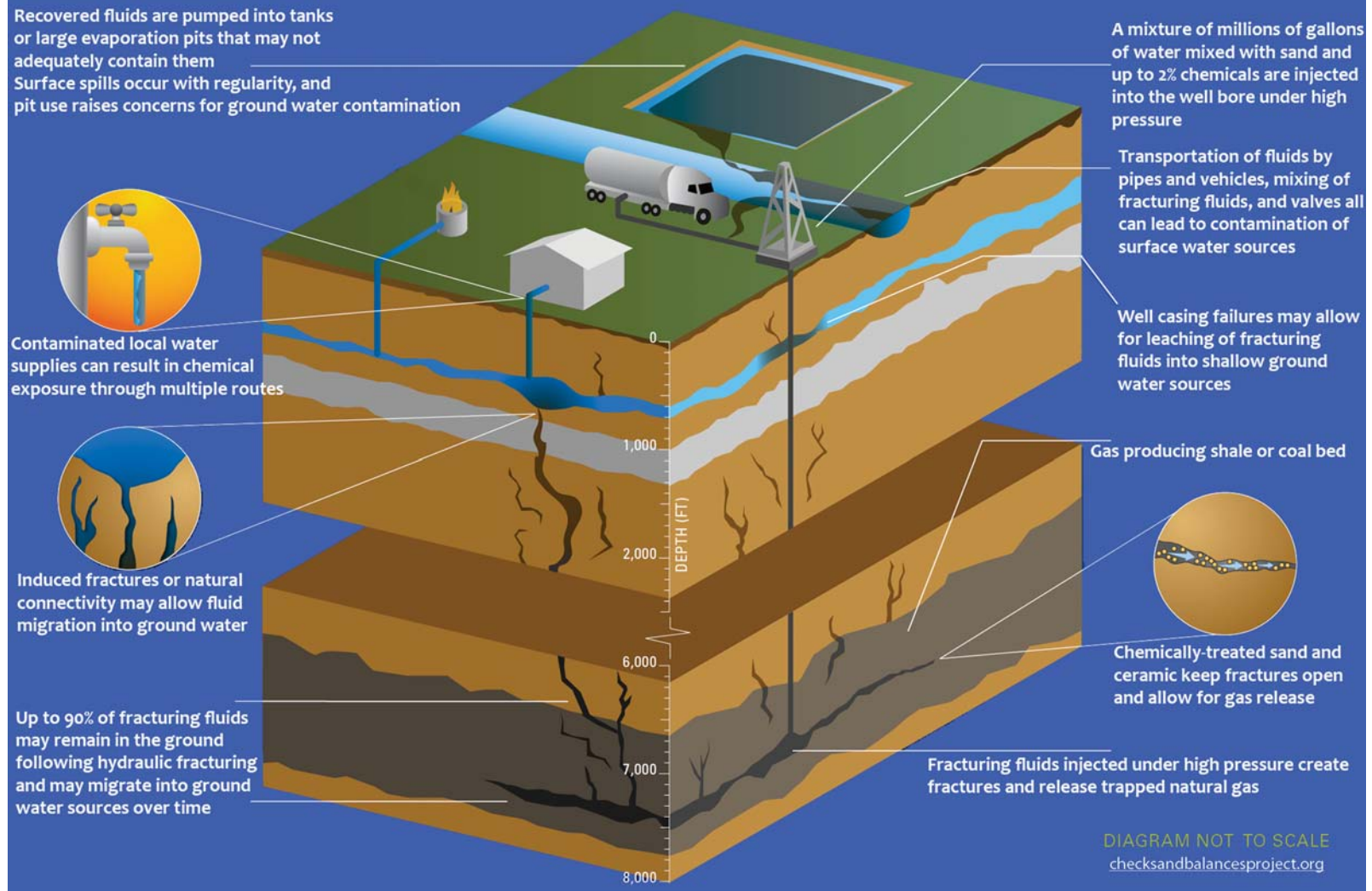


<http://fracfocus.org>



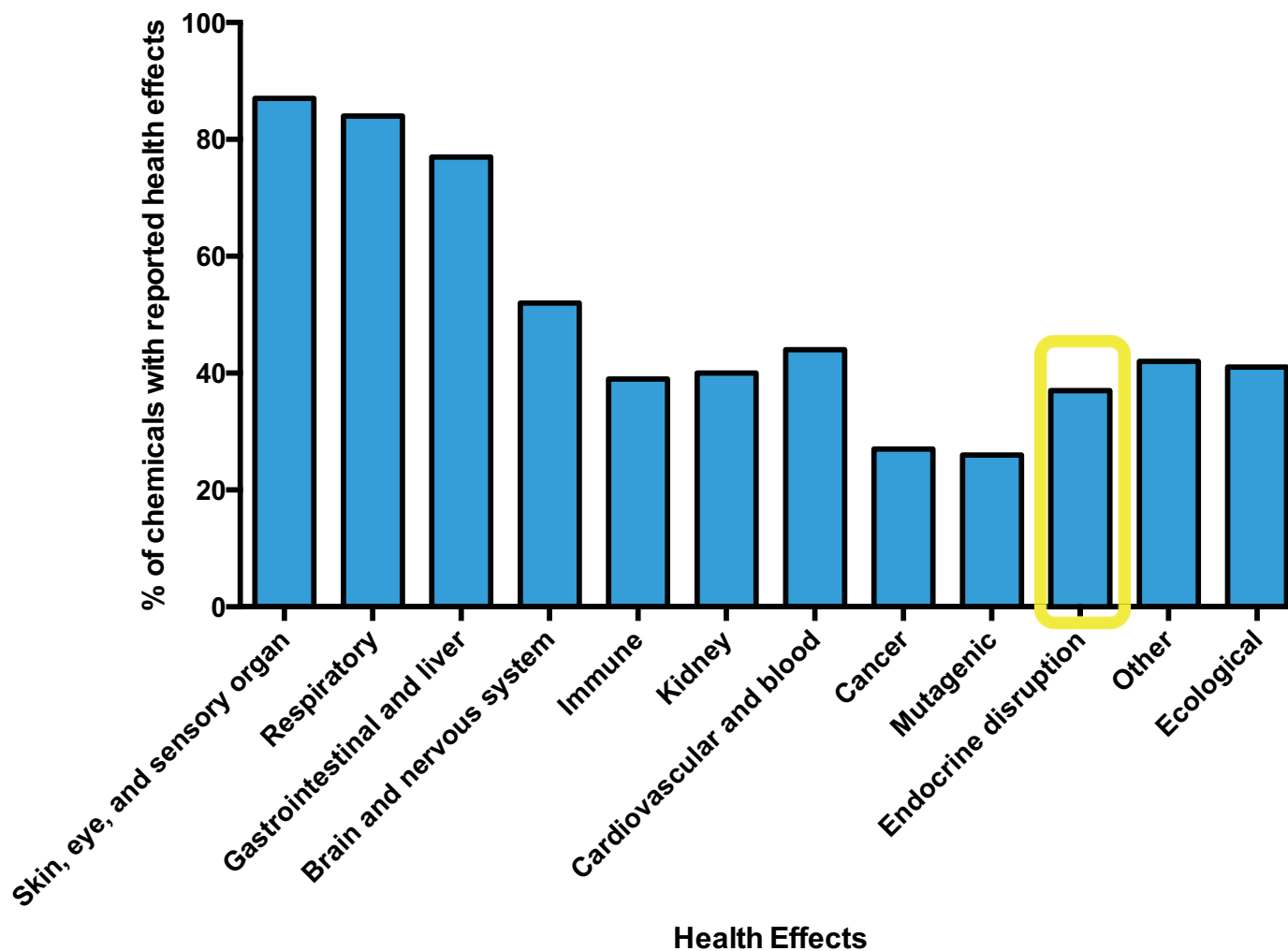


# Potential Routes of Water Contamination



# EDCs Used in Unconventional Oil and Gas Operations

10

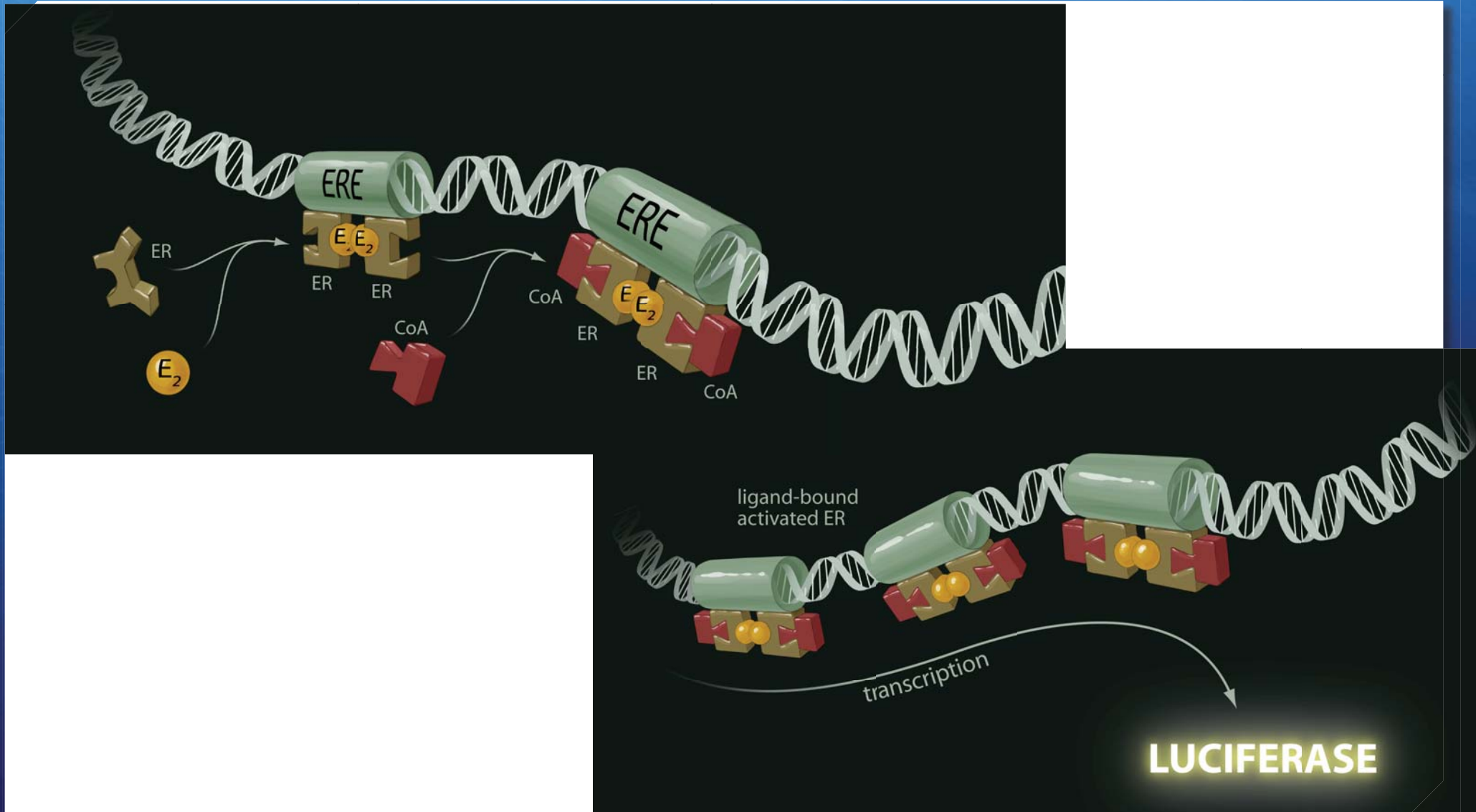


Theo Colborn

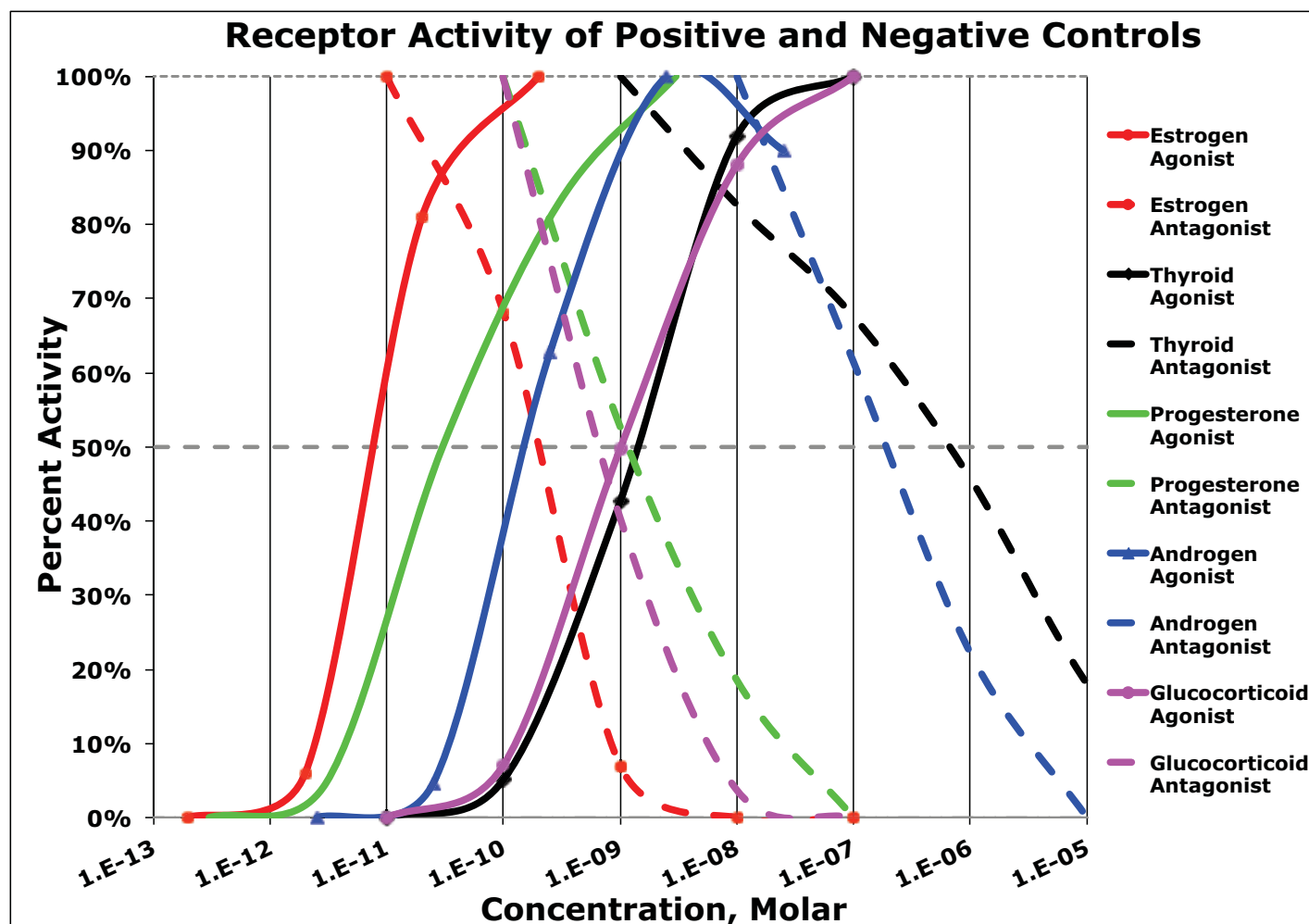
# Previous Work in our Lab

- + Detected greater estrogenic, anti-estrogenic and anti-androgenic activities in surface and groundwater near drilling-dense sites with history of fracking fluid spills (Kassotis et al. 2014).
- + Reported that 23 of 24 commonly-used hydraulic fracturing chemicals act as agonists and/or antagonists for five nuclear receptors (Kassotis et al. 2015).
- + Have begun to report chemicals and concentrations of oil/gas production chemicals in wastewater with Dr. Chung-Ho Lin (Kassotis et al. 2015).
- + Reported adverse health effects in male C57 mice exposed prenatally to likely environmentally relevant concentrations of a fracking chemical mixture (Kassotis et al. 2015).

# Reporter Gene Assay System

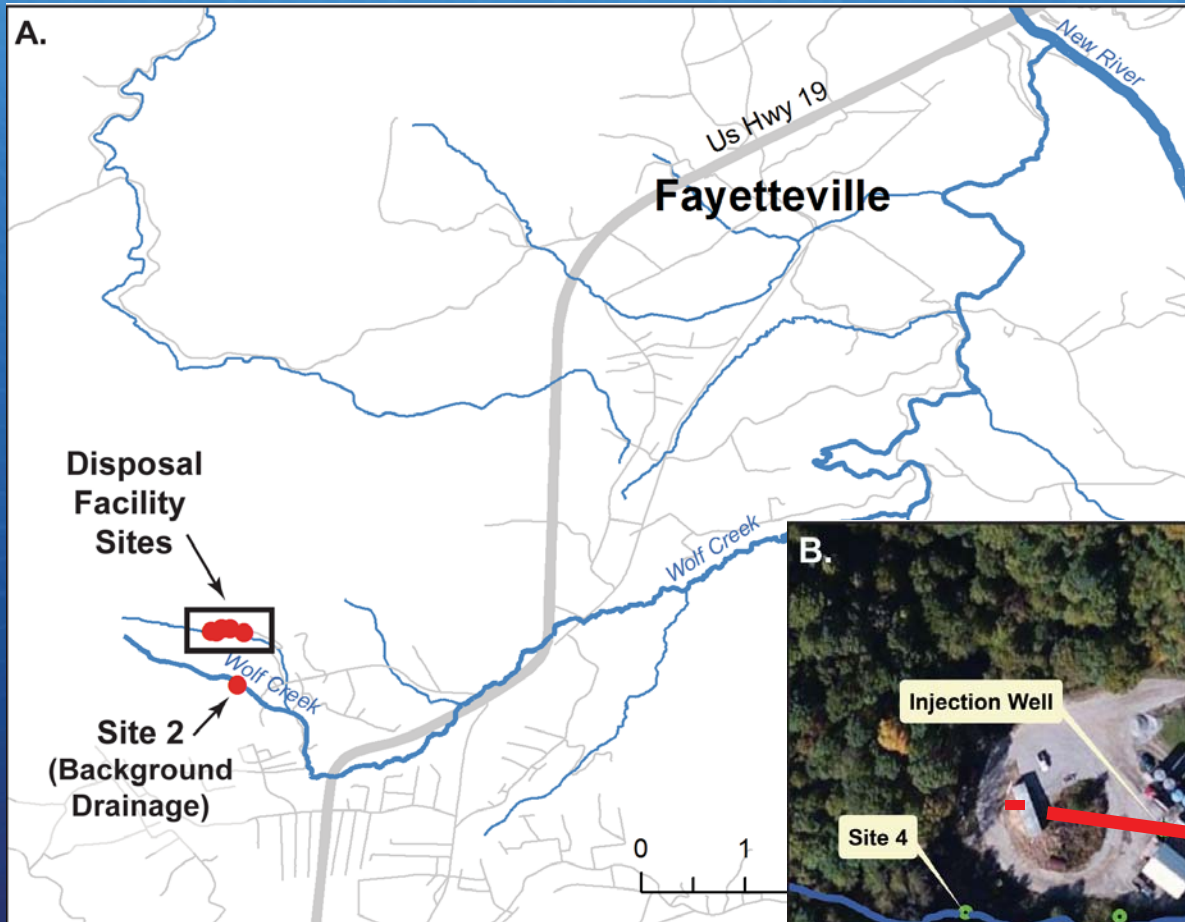


# Reporter Gene Bioassay Activities

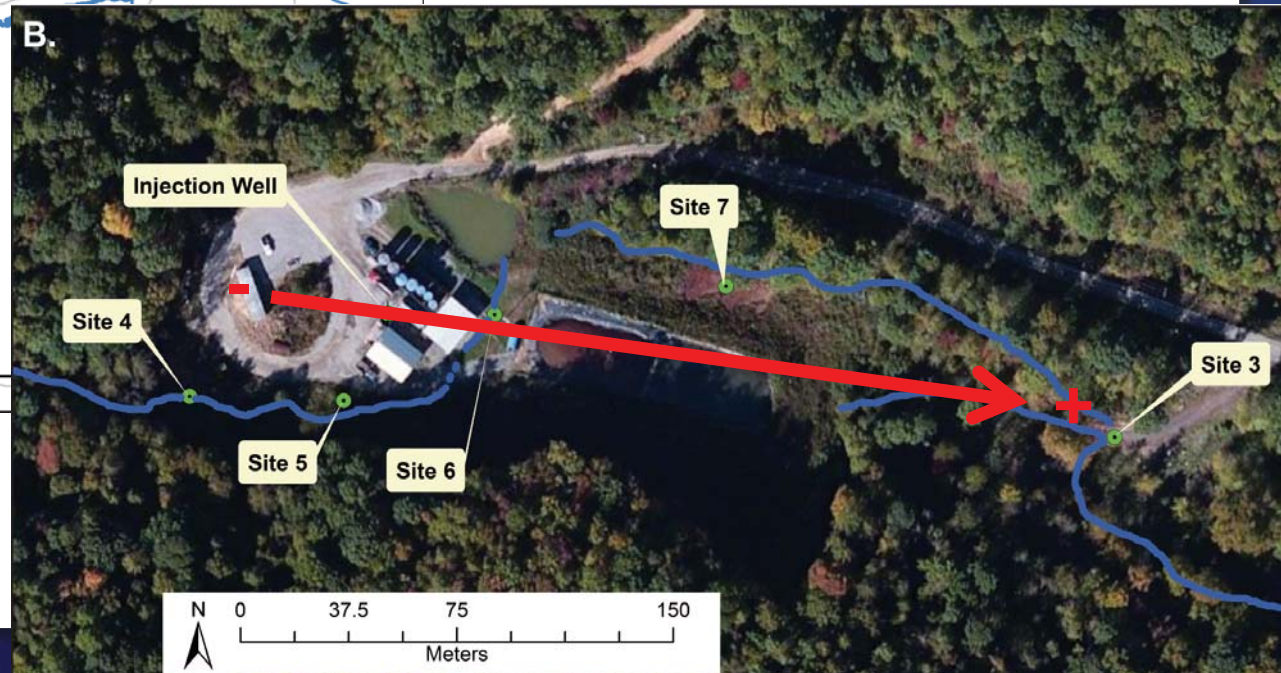




# West Virginia Wastewater Disposal Well

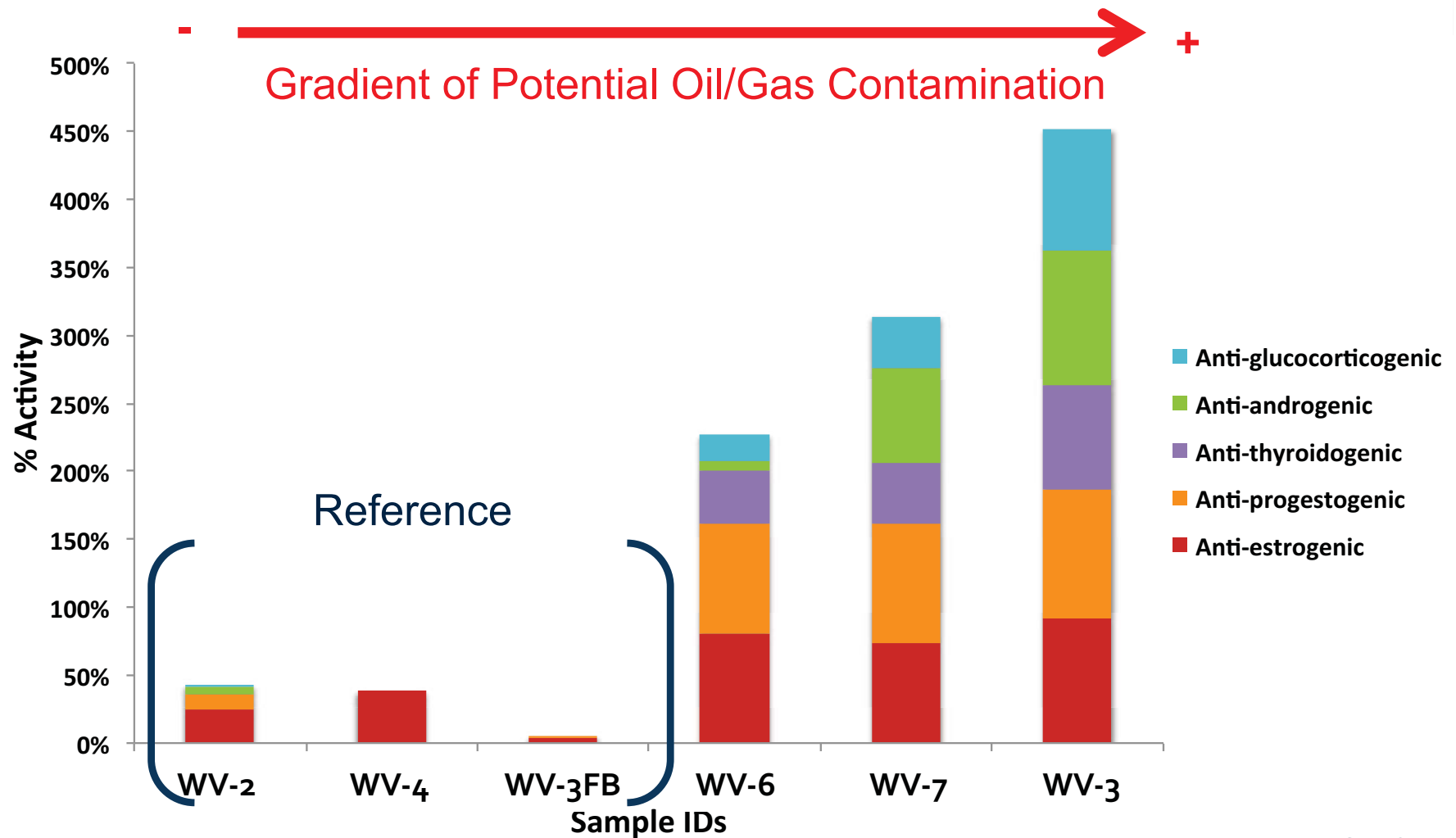


**Gradient of Potential Oil/Gas Contamination**

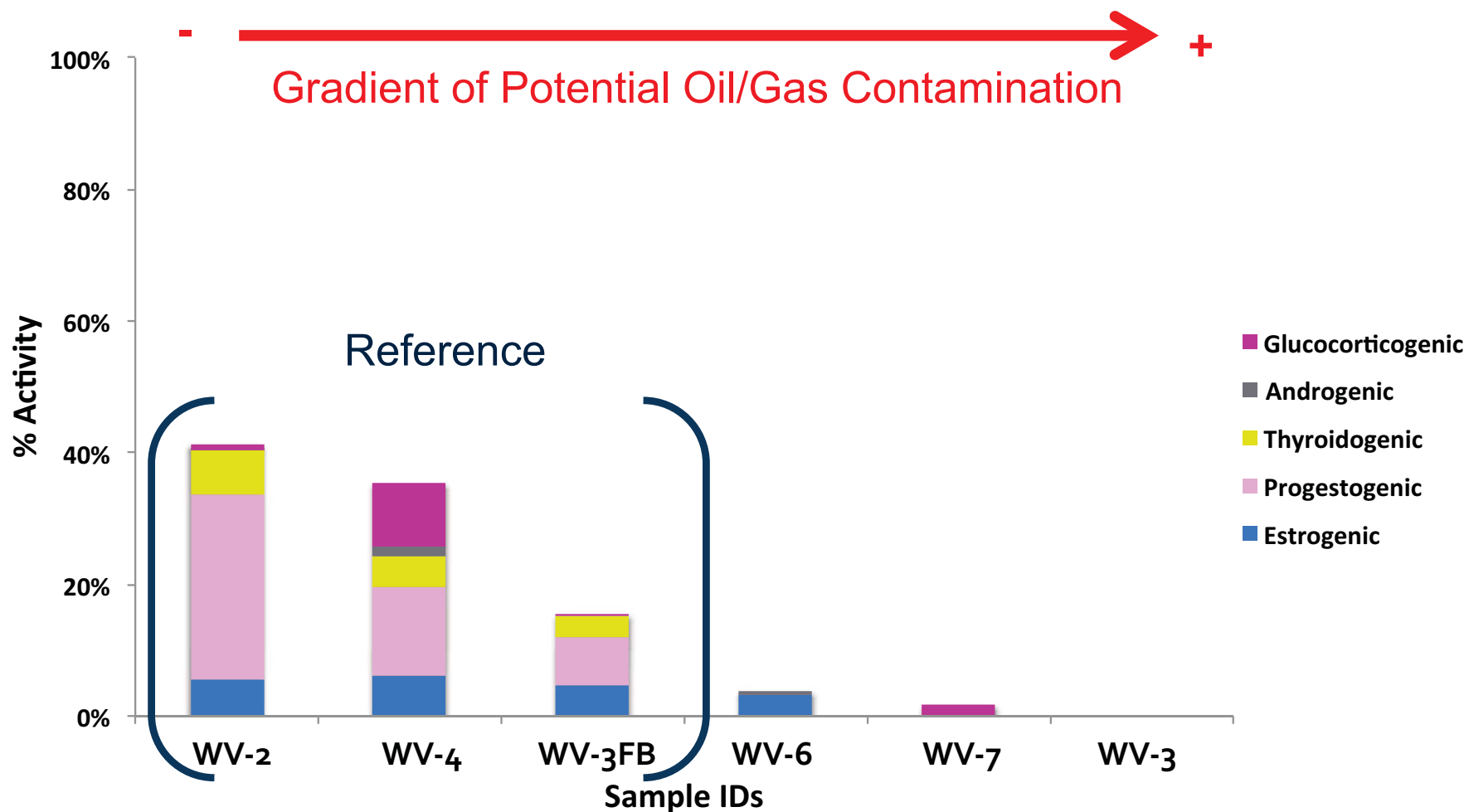


*Kassotis et al 2016a, STOTEN*

# Combined Surface Water Antagonist Activities WV Injection Well Site



# Combined Surface Water Agonist Activities WV Injection Well Site



# Water Quality Take-Homes

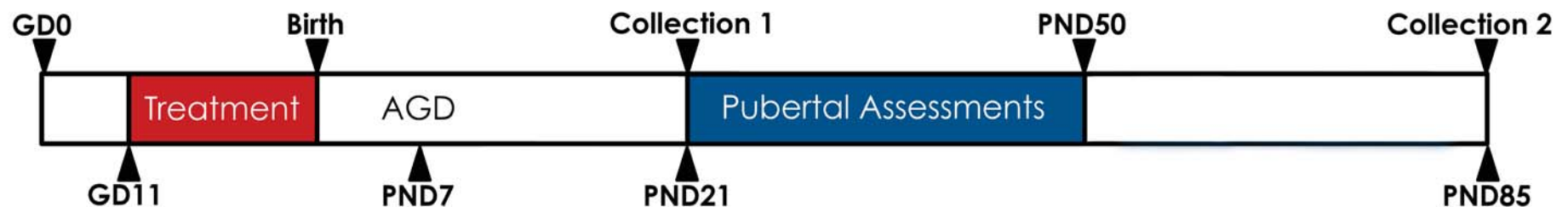
- + Elevated antagonist activities present in surface water downstream from oil and gas wastewater disposal operation.
- + Geochemical and organic chemical analyses (Akob et al. and Orem et al.) demonstrate unconventional oil and gas wastewater influence on stream quality.
- + Antagonist equivalent concentrations at levels known to result in adverse health effects in aquatic organisms.

# Growing Understanding of Adverse Human and Animal Health Outcomes

- + General adverse health
  - + Increased reported health symptoms in humans (Rabinowitz et al. 2014) and dogs (Slizovskiy et al. 2015)
  - + Increased inpatient hospital utilization rates (Jemielita et al. 2015)
  - + Respiratory, GI, immune, reproductive, other issues for humans, companion and food animals, wildlife, etc. (Bamberger & Oswald)
  - + Symptom abatement for families, animals that left drilling areas (Bamberger & Oswald 2015)
  
- + Reproductive/developmental effects
  - + Increased rate of congenital heart defects (McKenzie et al. 2014)
  - + Increased rates of preterm birth, high risk pregnancies (Casey et al. 2015)
  - + Increased rates of low birth weight and SGA babies with greater density (Stacy et al. 2015)



# Gestational Exposure in C<sub>57</sub>BL/6J Mice



- **Concentrations in drinking water (each of 23 chemicals; 23-mix):**

0.01, 0.1, 1.0, 10 mg/L or

3, 30, 300, 3,000 µg/kg/day

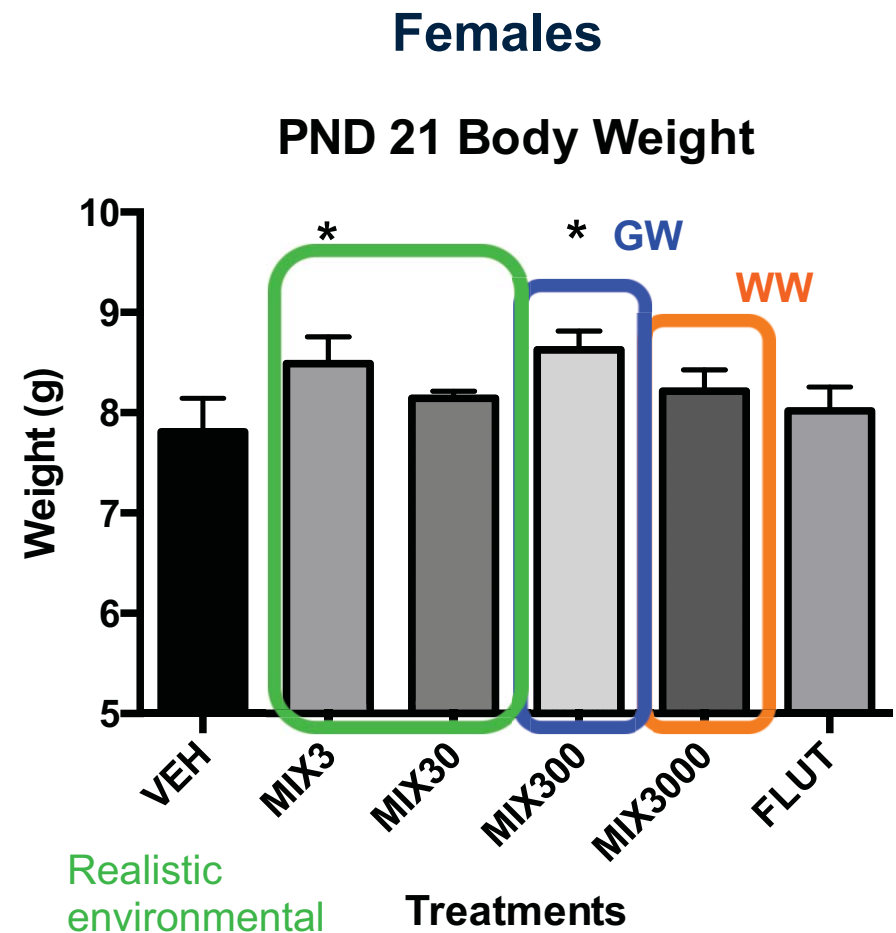
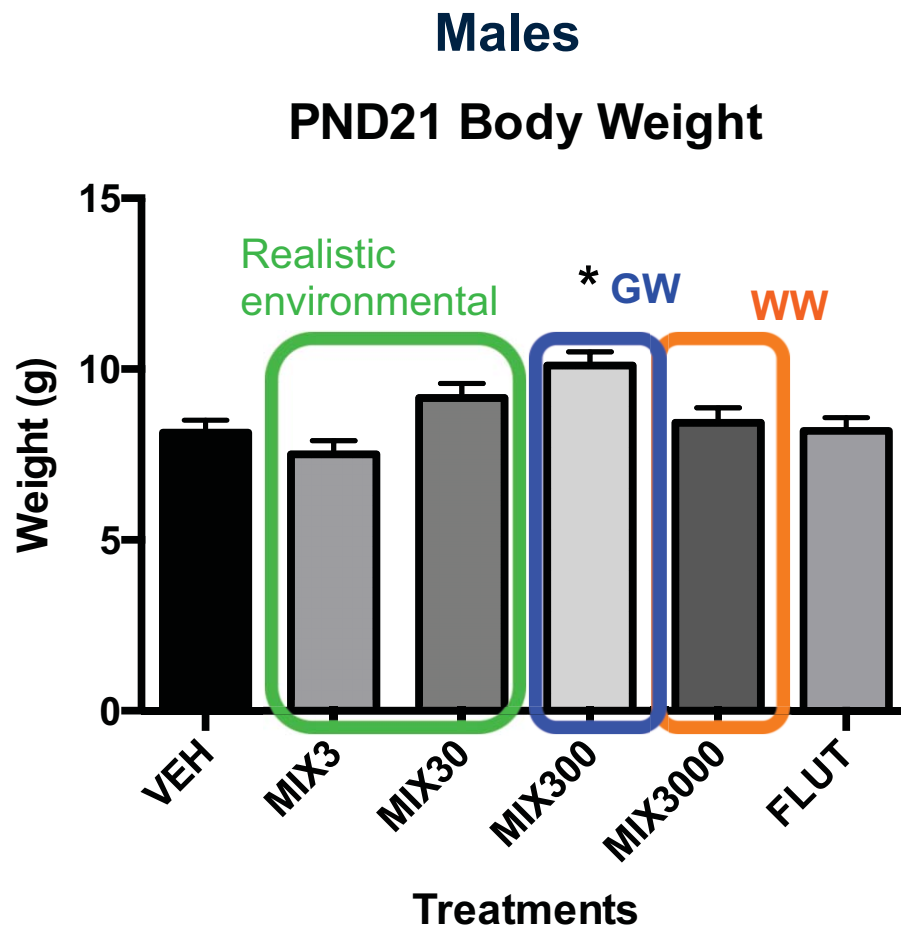
in 0.2% ethanol vehicle (~500 mg/kg/day),

& 50 mg/kg/day flutamide (AR antagonist) control

# Oil & Gas Operation Chemicals in 23-mix

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

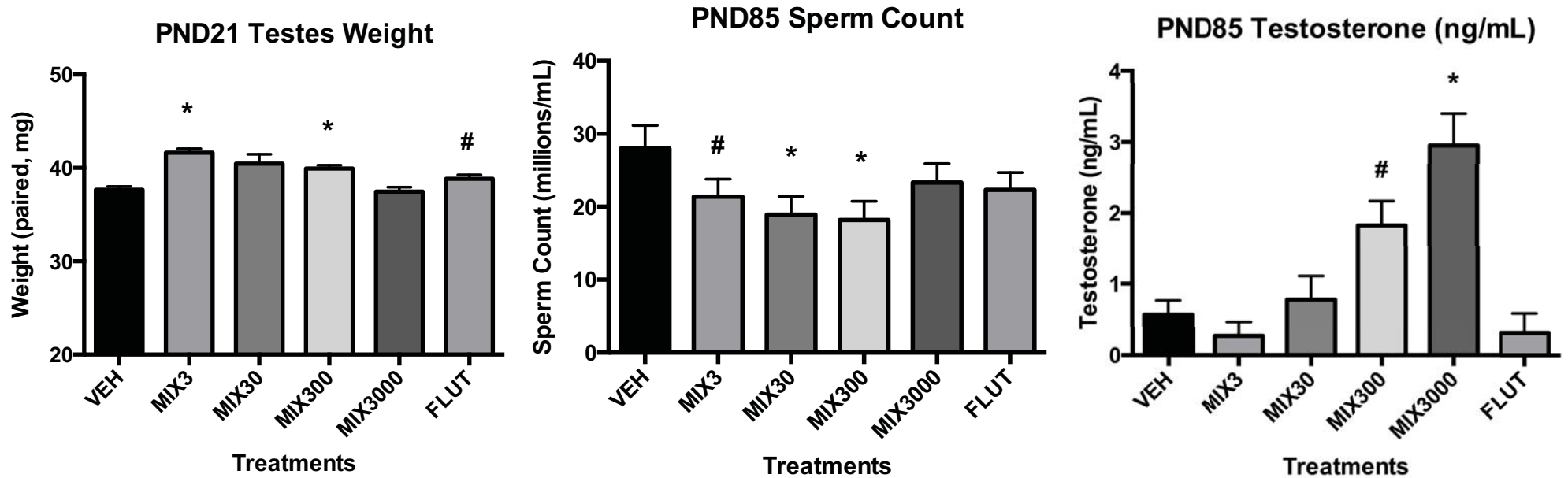
# Altered Body and Organ Weights in Developmentally Exposed Mice



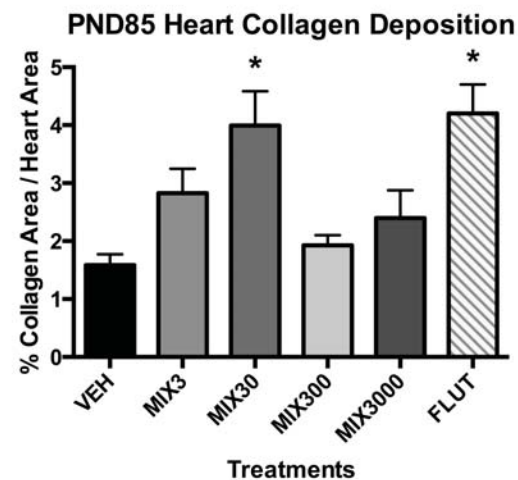
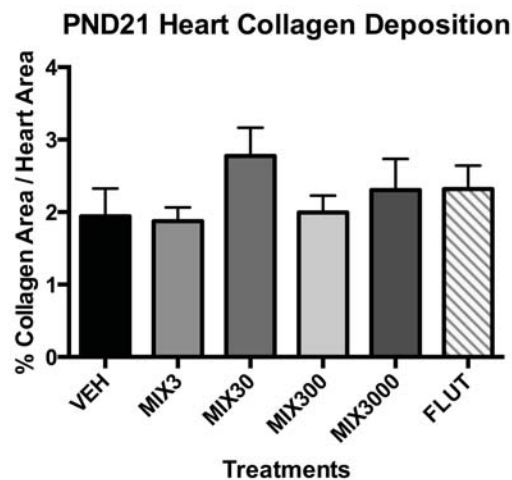
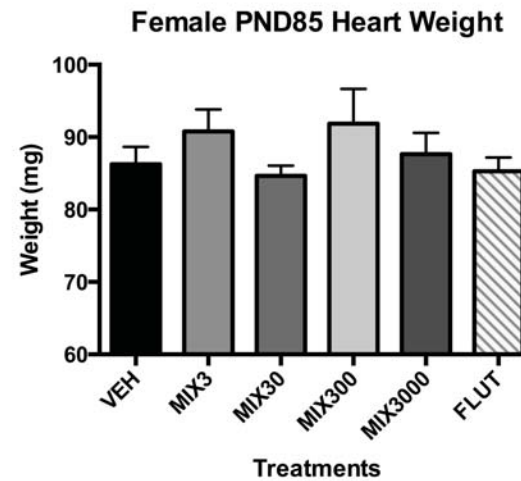
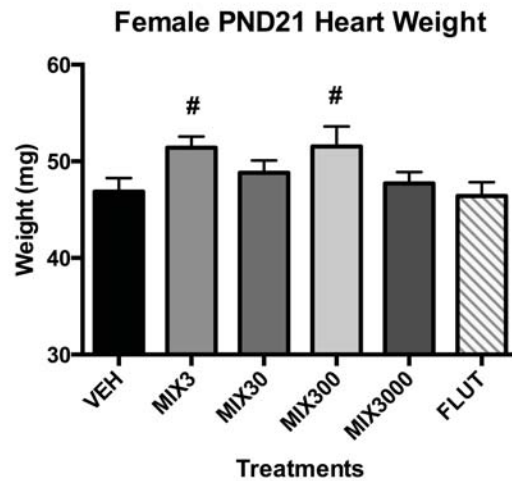
Ground water directly below surface spills, *Gross et al*  
Kassotis et al 2015, *Endocrinology*

Kassotis et al 2016b, *in prep*

# Adverse Reproductive Health Outcomes in Developmentally Exposed Male Mice

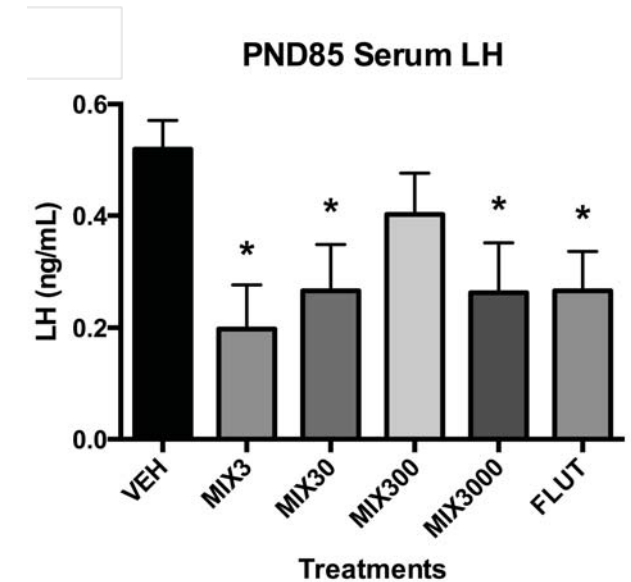
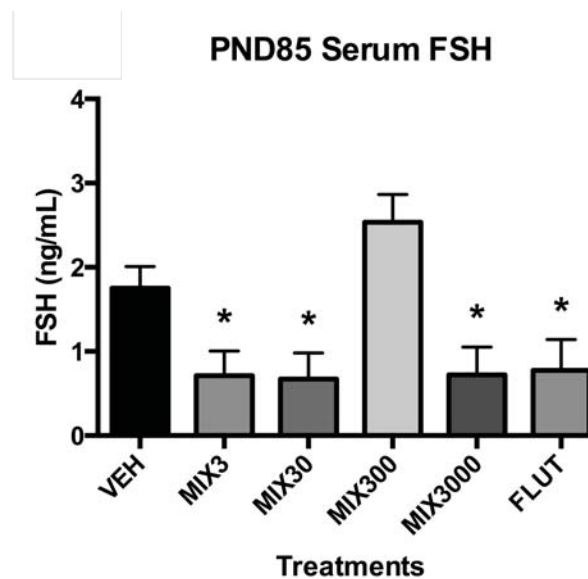
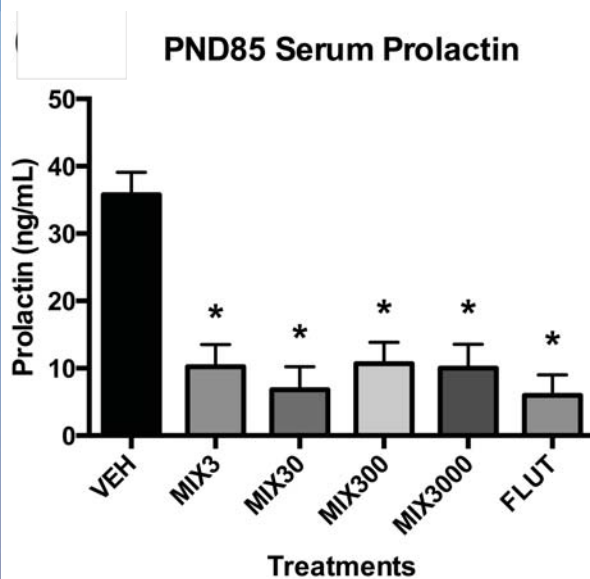


# Disrupted Heart Development in Developmentally Exposed Female Mice

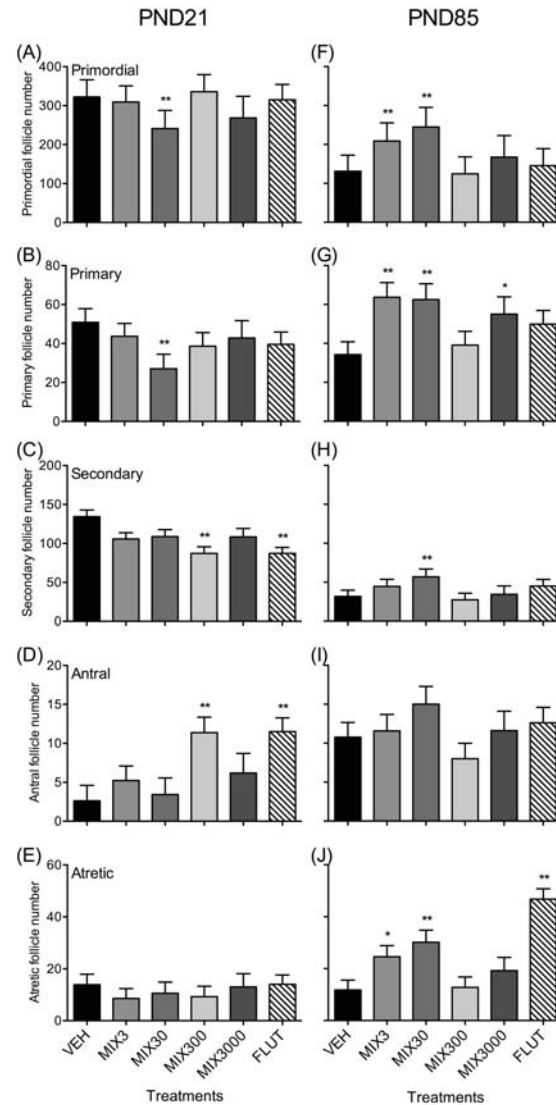




# Suppressed Pituitary Hormones in Developmentally Exposed Female Mice



# Disrupted Folliculogenesis in Developmentally Exposed Female Mice



# Overall Take-Homes

- + Some chemicals used in and/or produced by oil and natural gas operations can act as nuclear receptor agonists and antagonists.
- + Humans and animals are likely exposed to these chemicals via multiple routes in drilling-dense areas
  - + Drinking water, inhalation, and dermal absorption.
- + Injection sites may represent another route through which oil and gas operations may influence EDC contributions to surface/groundwater.
- + Gestational exposure to a mixture of oil and gas operation chemicals at likely environmentally-relevant concentrations resulted in adverse health outcomes in C57 mice.
  - + Increased body weights, reduced sperm counts in males.
  - + Increased body weights, suppressed pituitary hormones, altered folliculogenesis in females.

# Acknowledgements

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Nagel & vom Saal Labs – June 2012



Nagel Lab – May 2013