Glyphosate, Epigenetics and Transgenerational Inheritance of Disease

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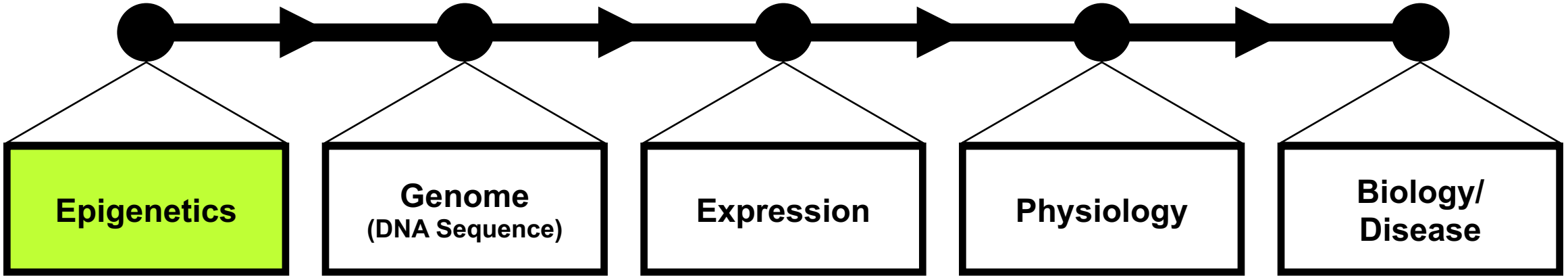
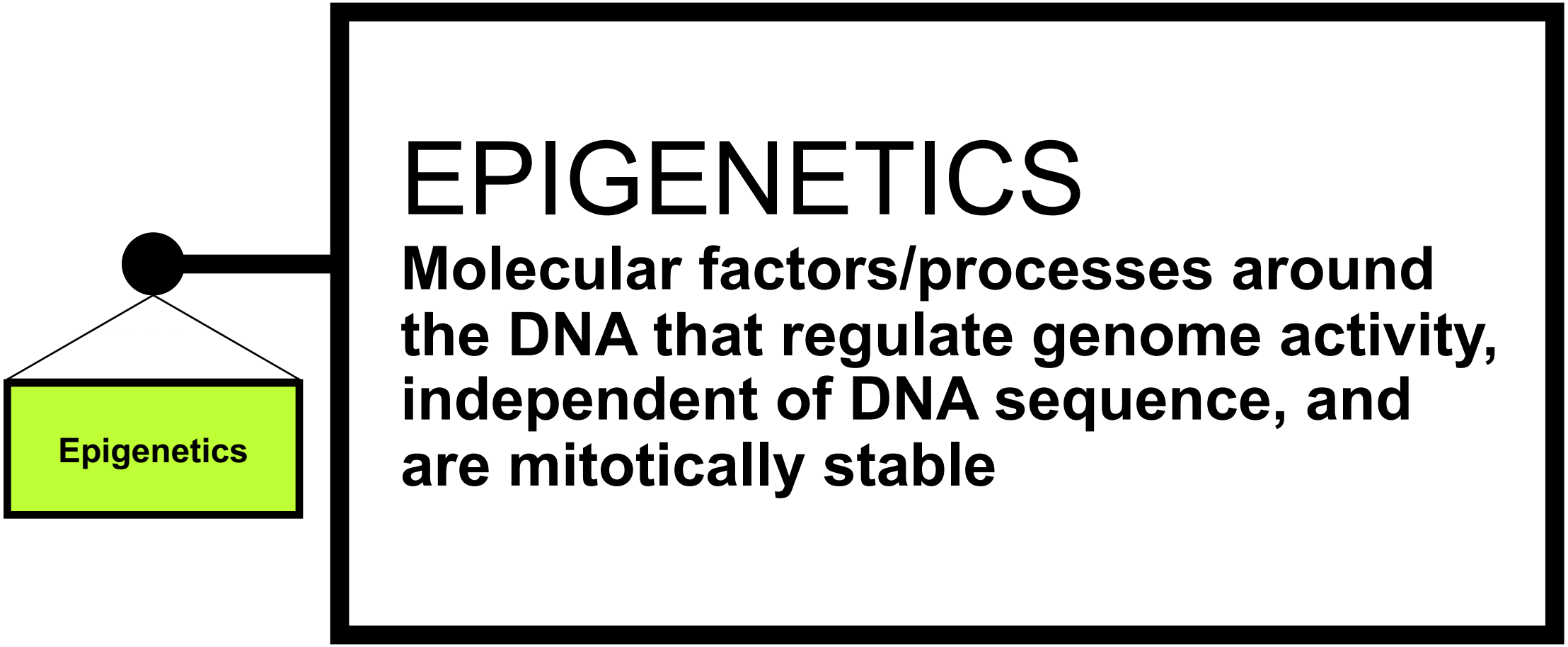
ENVIRONMENTAL IMPACT ON BIOLOGY

- **Regional Disease Frequencies**
- **Low Frequency of Genetic Component of Disease**
- **Increases In Disease Frequencies**
- **Identical Twins and Variable Disease Frequency**
- **Environmental Exposures and Disease**
- **Evolution and Rapid Induction**

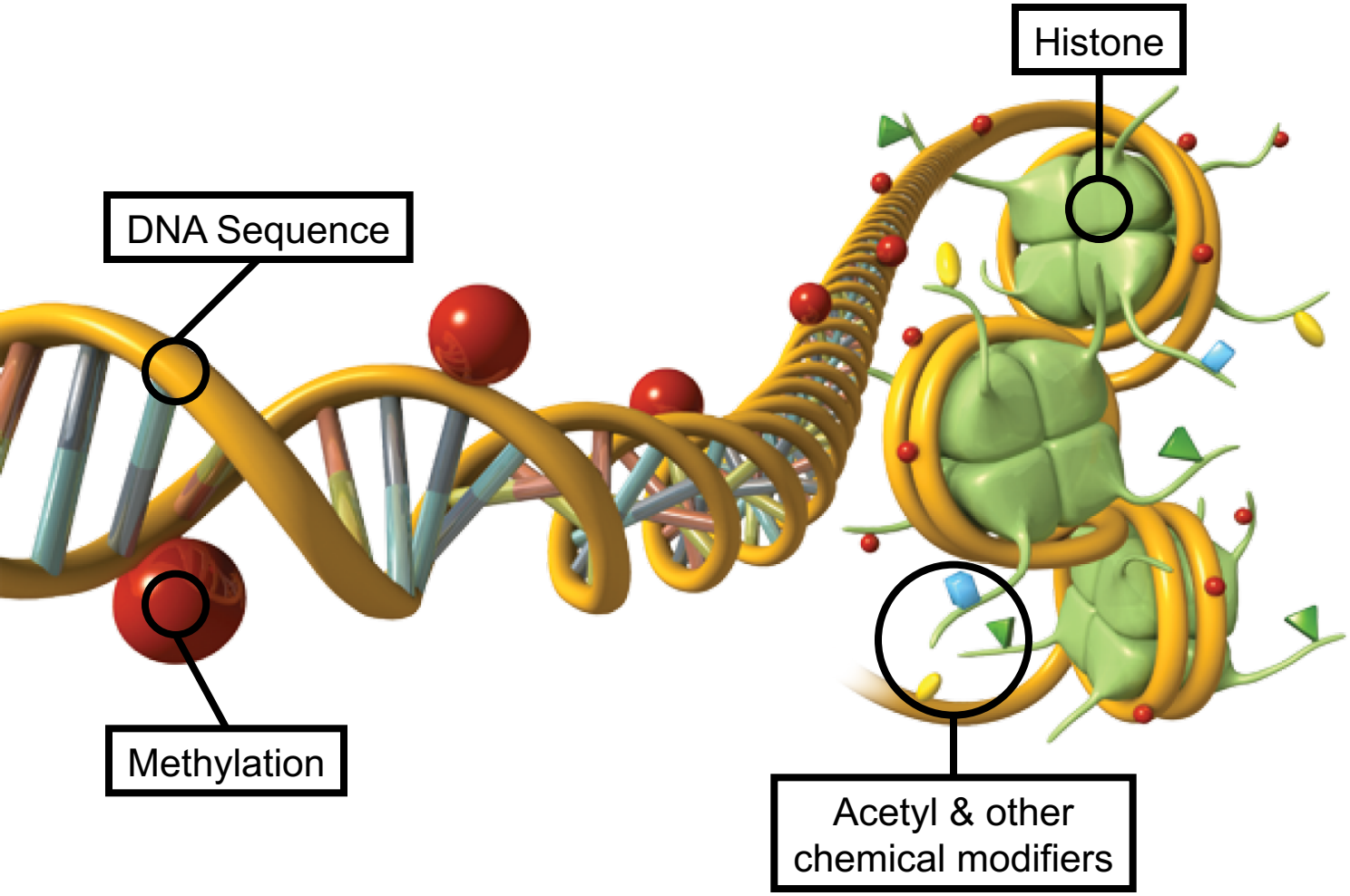
EPIGENETIC EXPLANATIONS FOR ENVIRONMENTAL IMPACTS





EPIGENETICS

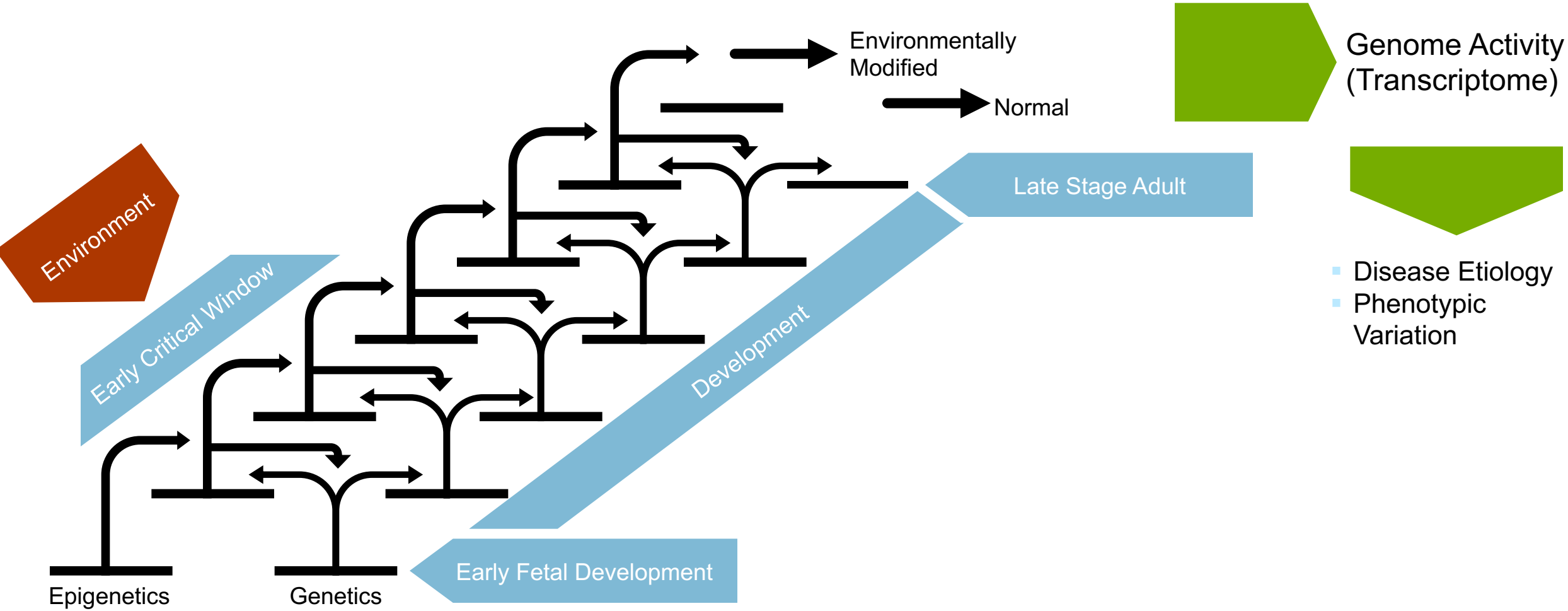
Molecular factors/processes around the DNA that regulate genome activity, independent of DNA sequence, and are mitotically stable



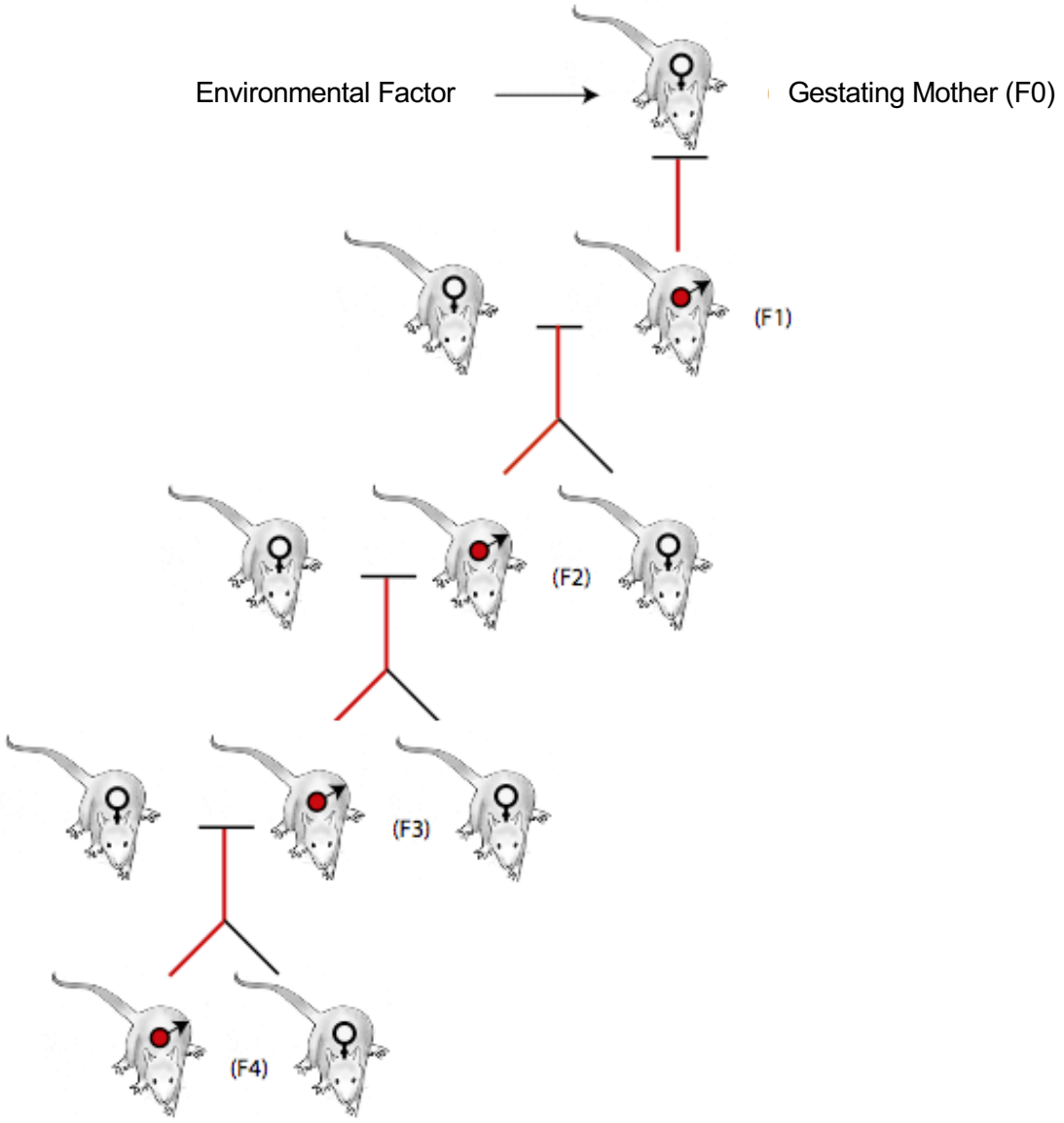
EPIGENETIC MECHANISMS AND MARKS

- **DNA Methylation**
- **Histone Modifications**
- **Chromatin Structure**
- **Non-coding RNA**
- **RNA methylation**

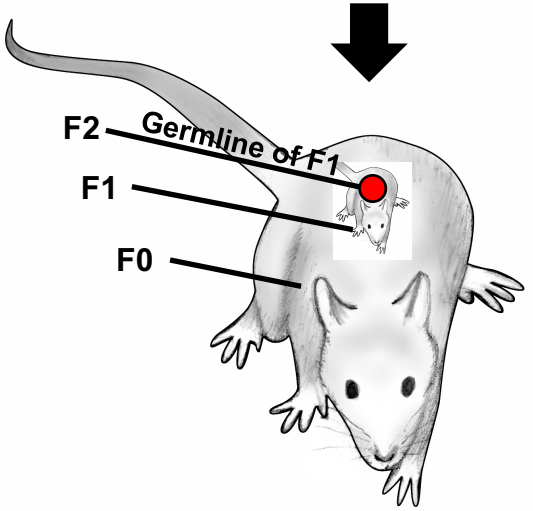
EPIGENETIC AND GENETIC CASCADE OF EVENTS INVOLVED IN DEVELOPMENT



Transgenerational Inheritance of Disease



Gestating Female
Environmental Exposure



Multigenerational Exposures

Transgenerational Inheritance

F3 Generation
First Unexposed

Environmental Compound Specificity

(Exposure Groups)	F1	F3
A. Vinclozolin [agricultural fungicide]	Yes	Yes
B. Flutamide [anti-androgenic pharmaceutical]	Yes	No
C. TCDD/Dioxin (industrial pollutant)	Yes	Yes
D. Plastics Compounds [Bisphenol-A BPA, Phthalate-DEHP & DBP]	Yes	Yes
E. Jet Fuel [JP8] (Hydrocarbon Mixture)	Yes	Yes
F. Pesticide & Insect Repellent [Permethrin & DEET]	No	Yes
G. DDT (pesticide)	Yes	Yes
H. Methoxychlor (pesticide, replace DDT)	Yes	Yes
I. Mercury (Industrial pollutant)	Yes	Yes
J. Atrazine (agricultural herbicide)	No	Yes

ENVIRONMENTALLY INDUCED EPIGENETIC TRANSGENERATIONAL INHERITANCE

Environmental Toxicants

Vinclozolin (Agricultural Fungicide)

Methoxychlor (Agricultural Pesticide)

Dioxin/TCDD (Industrial Contaminant)

Plastic Compounds (BPA & Phthalates)

Permethrin & DEET (Insect Repellants)

DDT (Pesticide)

Tributyltin (Industrial Toxicant & Biocide)

Hydrocarbons (Jet Fuel)

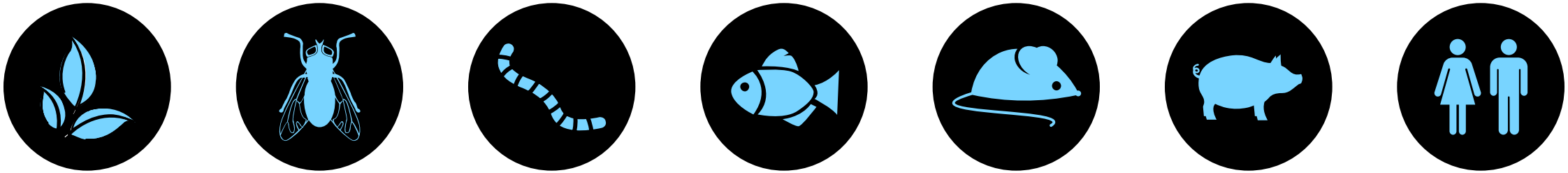
Other Types Exposures

Nutrition (High Fat or Caloric Restriction)

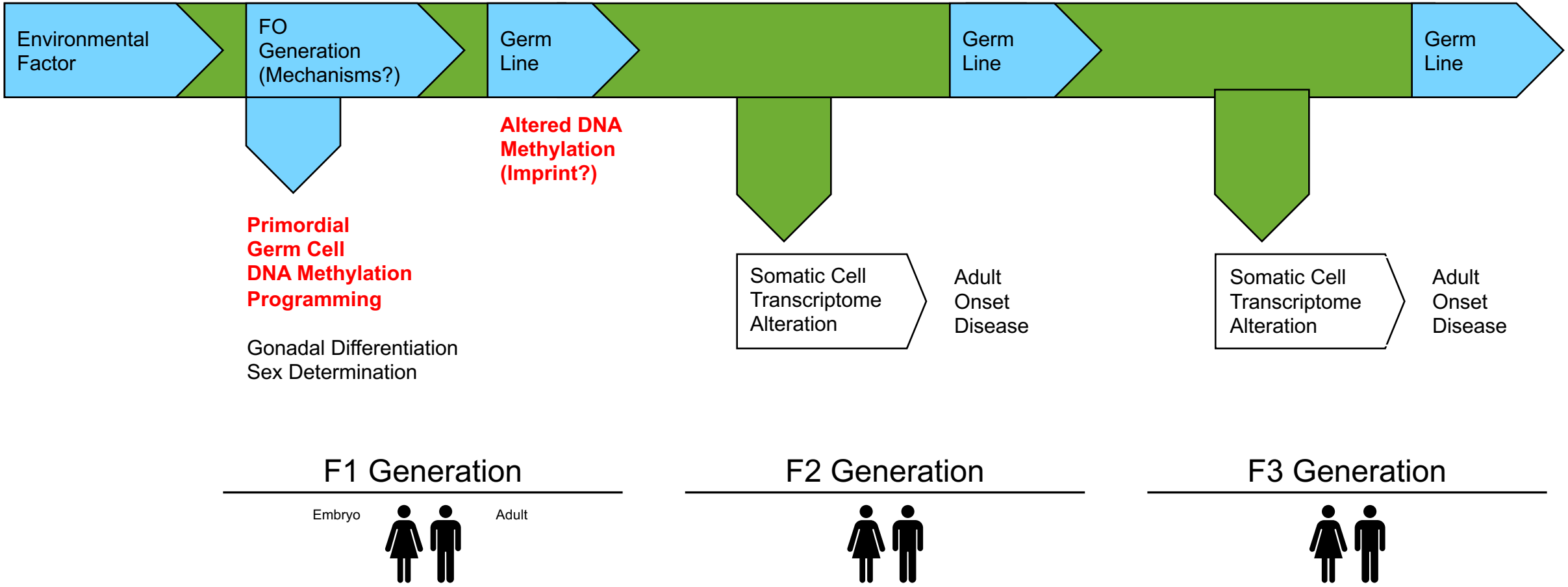
Temperature & Drought (Plant Health & Flowering)

Smoking & Alcohol

Stress (Behavioral)



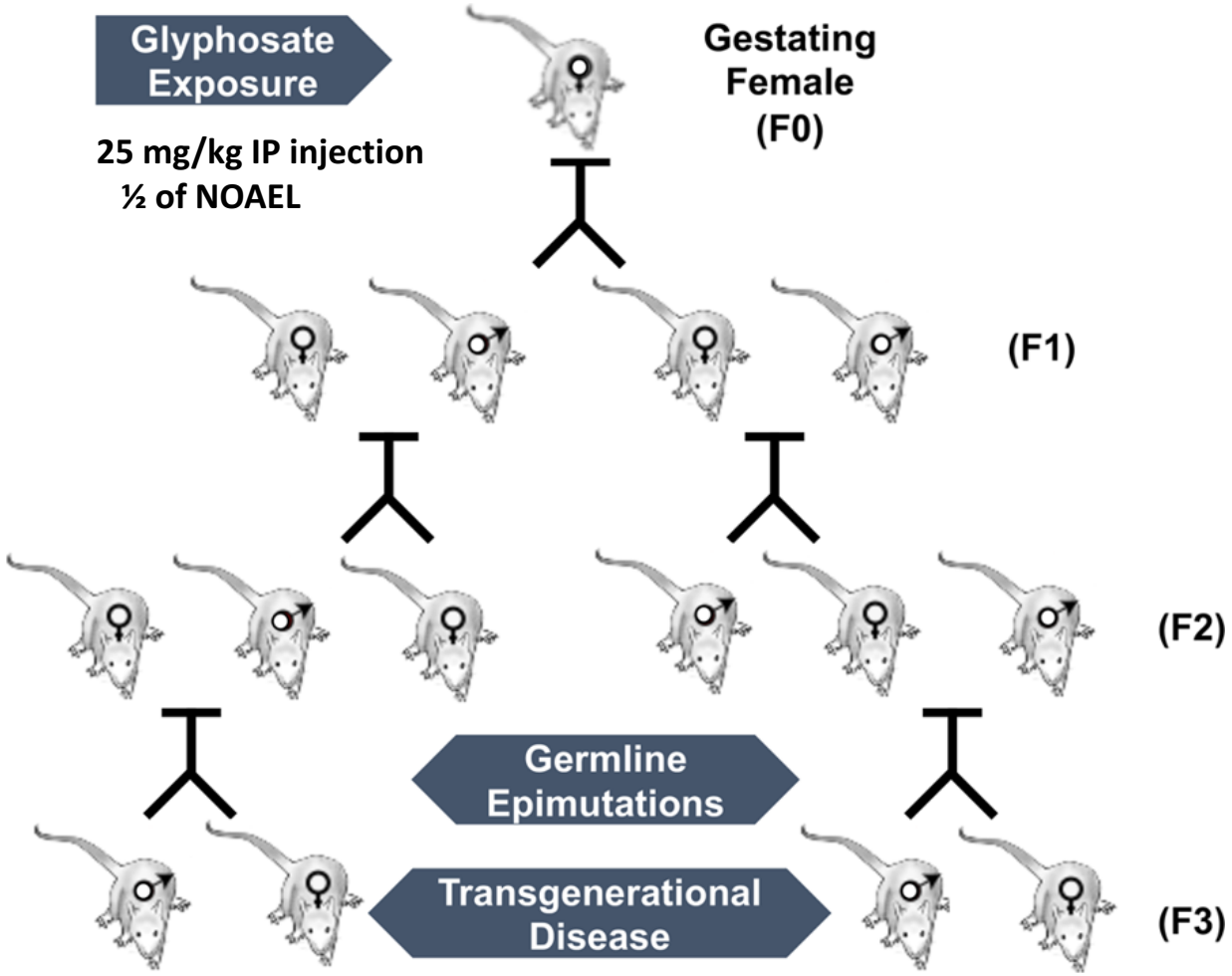
ROLE OF GERM LINE IN EPIGENETIC TRANS-GENERATIONAL INHERITANCE



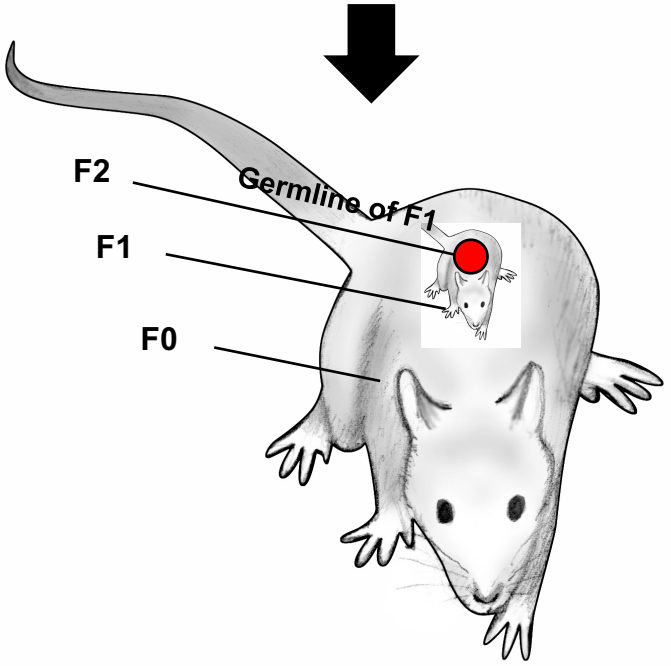
Assessment of Glyphosate Induced Epigenetic Transgenerational Inheritance of Pathologies and Sperm Epimutations: Generational Toxicology

Kubsad D, Nilsson EE, King SE, Sadler-Riggleman I, Beck D, Skinner MK

Scientific Reports 23;9(1):6372

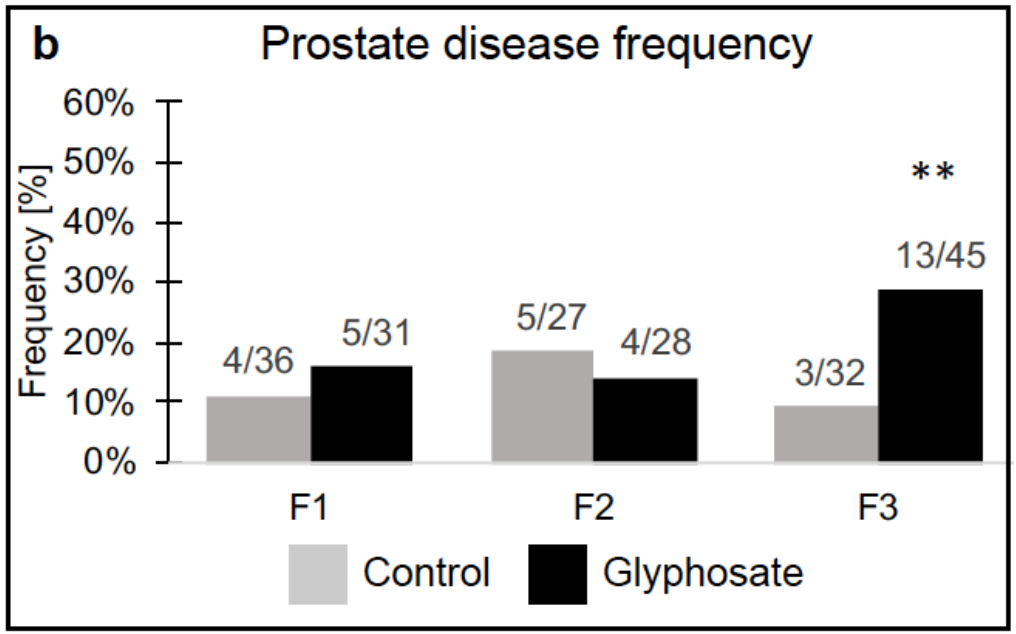


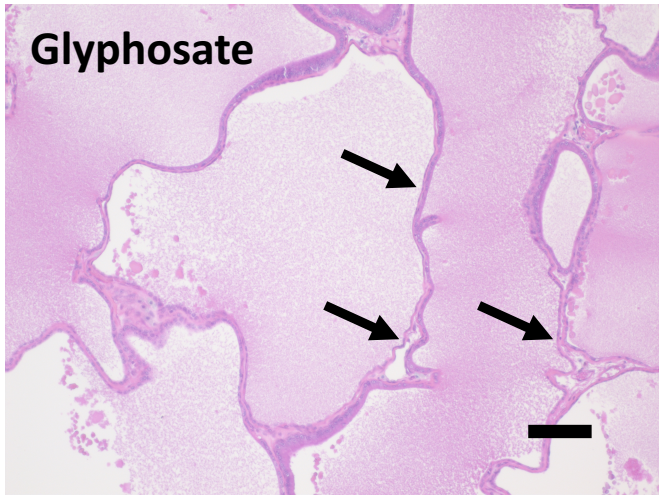
Gestating Female Glyphosate Exposure

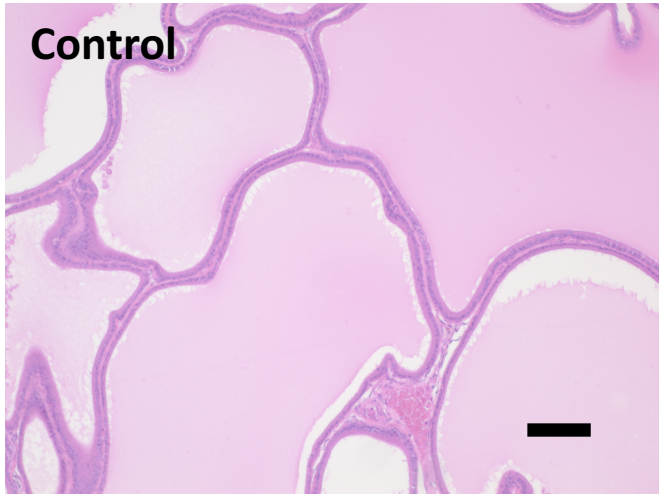


Note: not a risk assessment study.

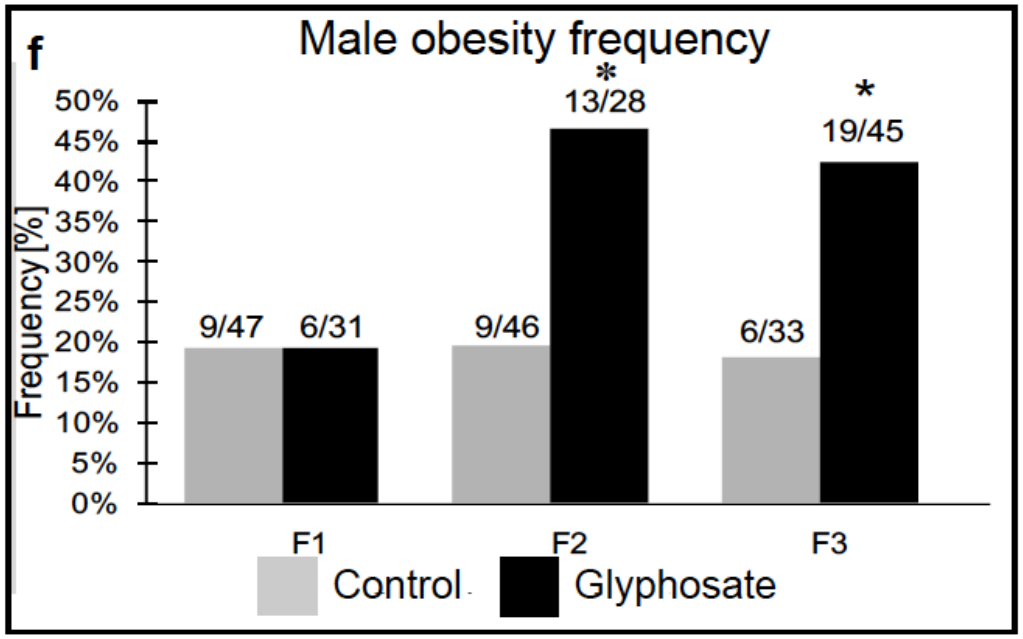
Glyphosate Study: Transgenerational Increase in Disease in Males



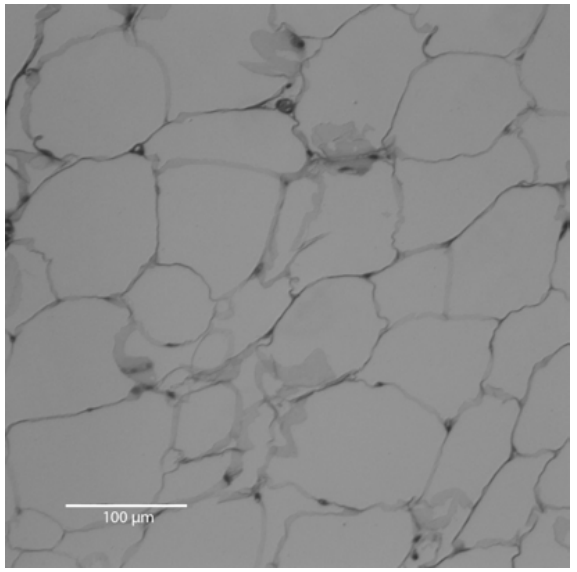




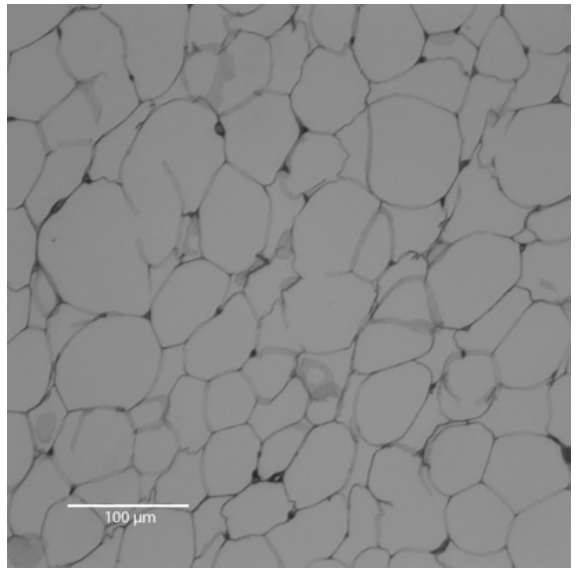
Glyphosate Study: Transgenerational Increase in Disease in Males



Glyphosate

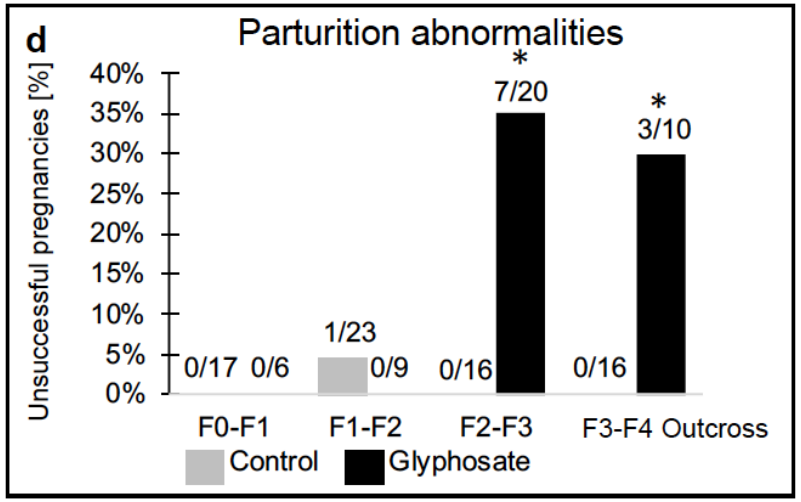


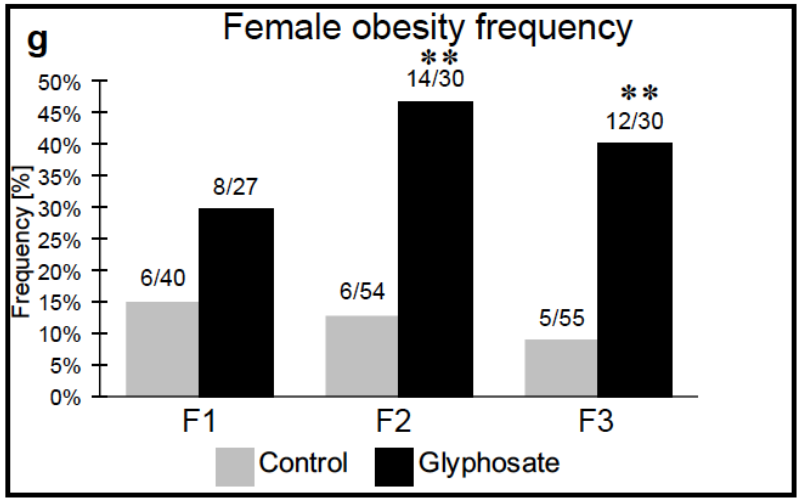
Control



Adipocyte (fat cell) size – Correlates with weight/fat mass

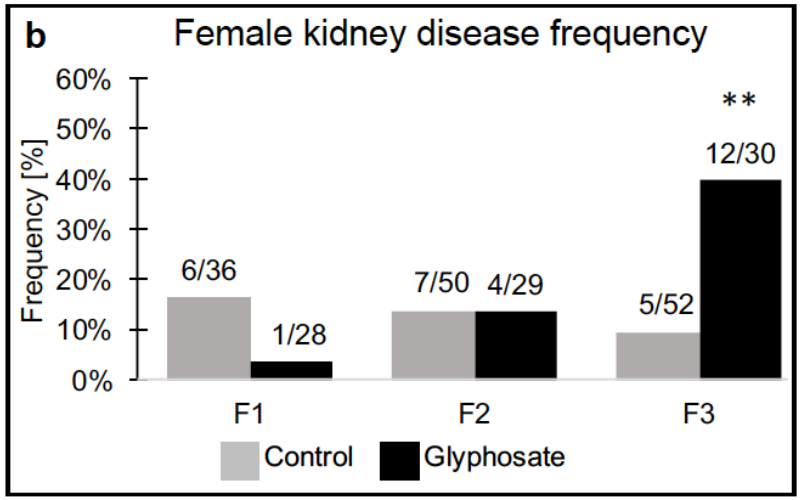
Glyphosate Study: Transgenerational Increase in Disease in Females



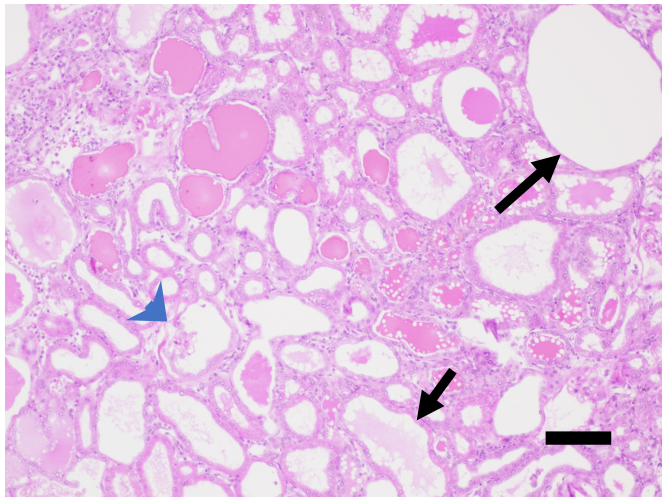


- Death of mother at birth
- Death of pups at birth
- Dystocia

Glyphosate Study: Transgenerational Increase in Disease in Females



Glyphosate



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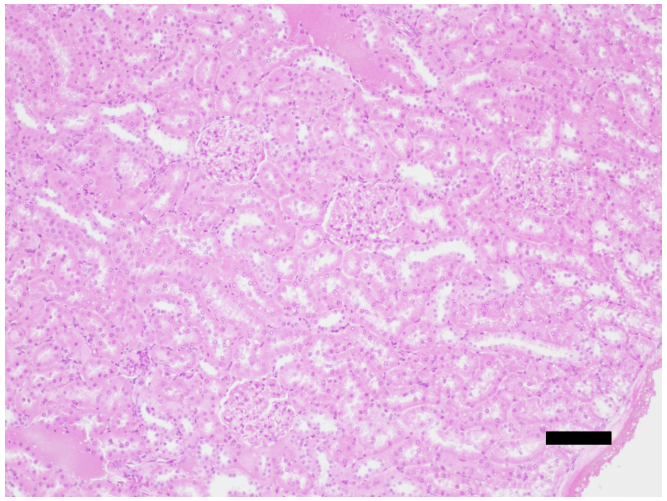
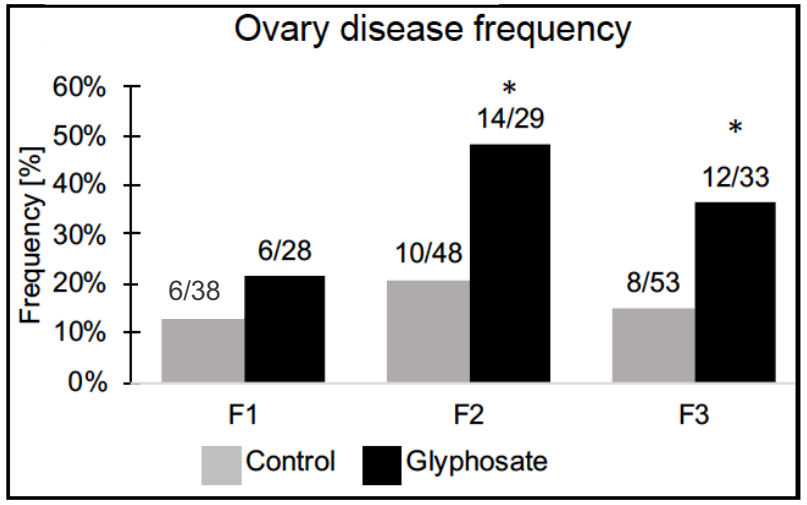
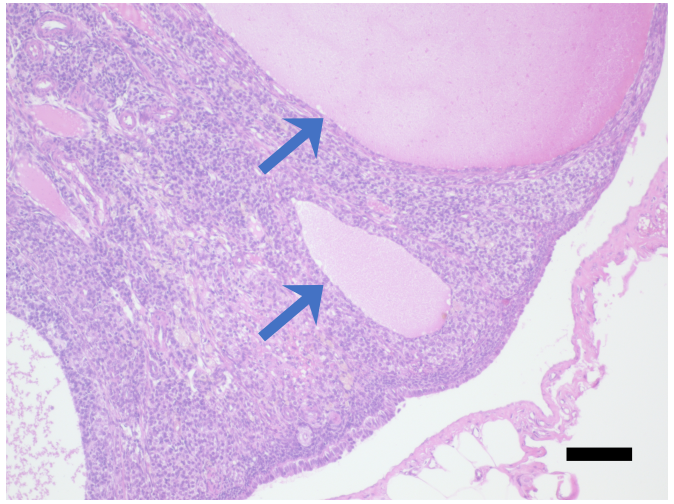


- Glomerulosclerosis
- Thickened Bowman's capsules
- Renal cysts

Glyphosate Study: Transgenerational Increase in Disease in Females



Glyphosate



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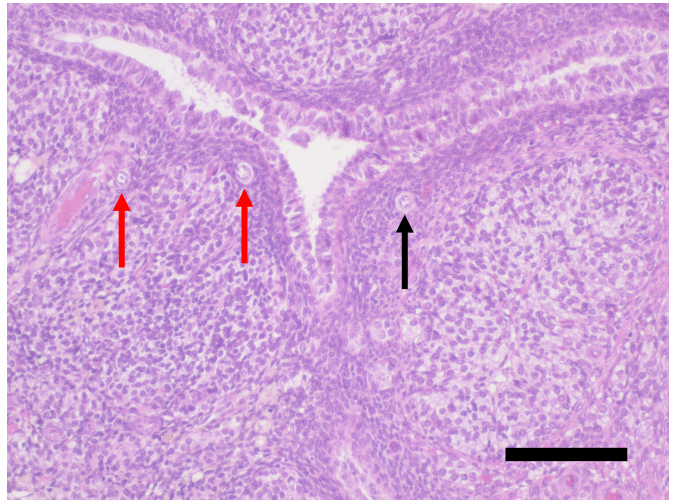


- Ovarian cysts
- Decreased oocytes (eggs)

Glyphosate Study: Other parameters measured

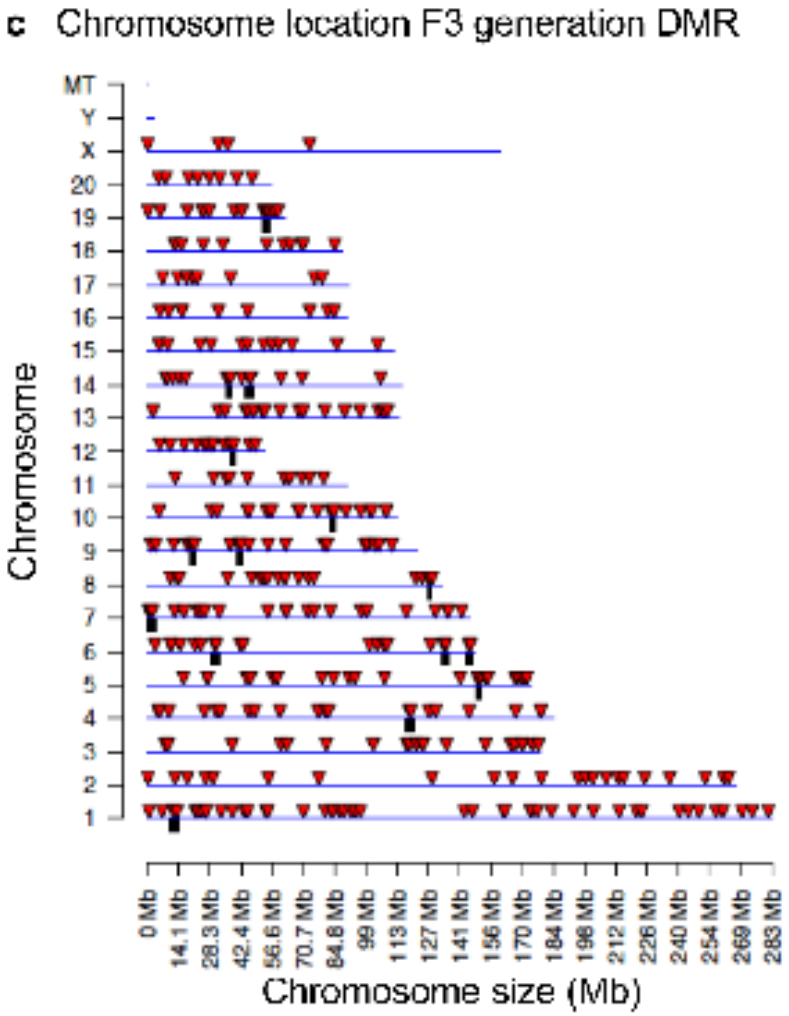
F3 generation difference seen:

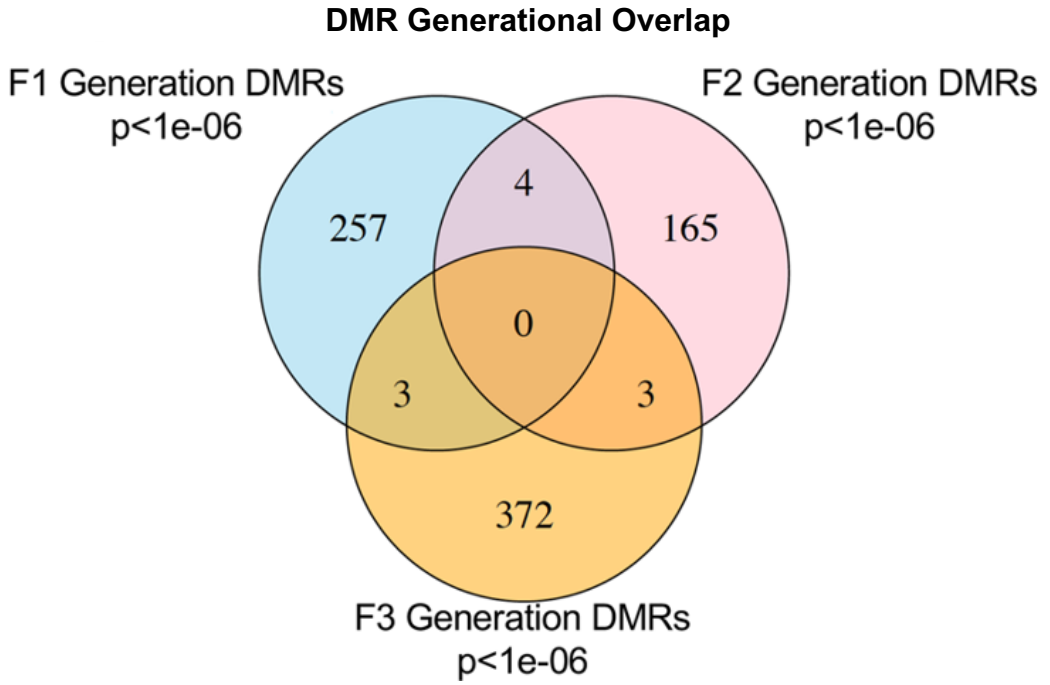
- Average weaning weight in males.
- Increased frequency of multiple diseases in females.

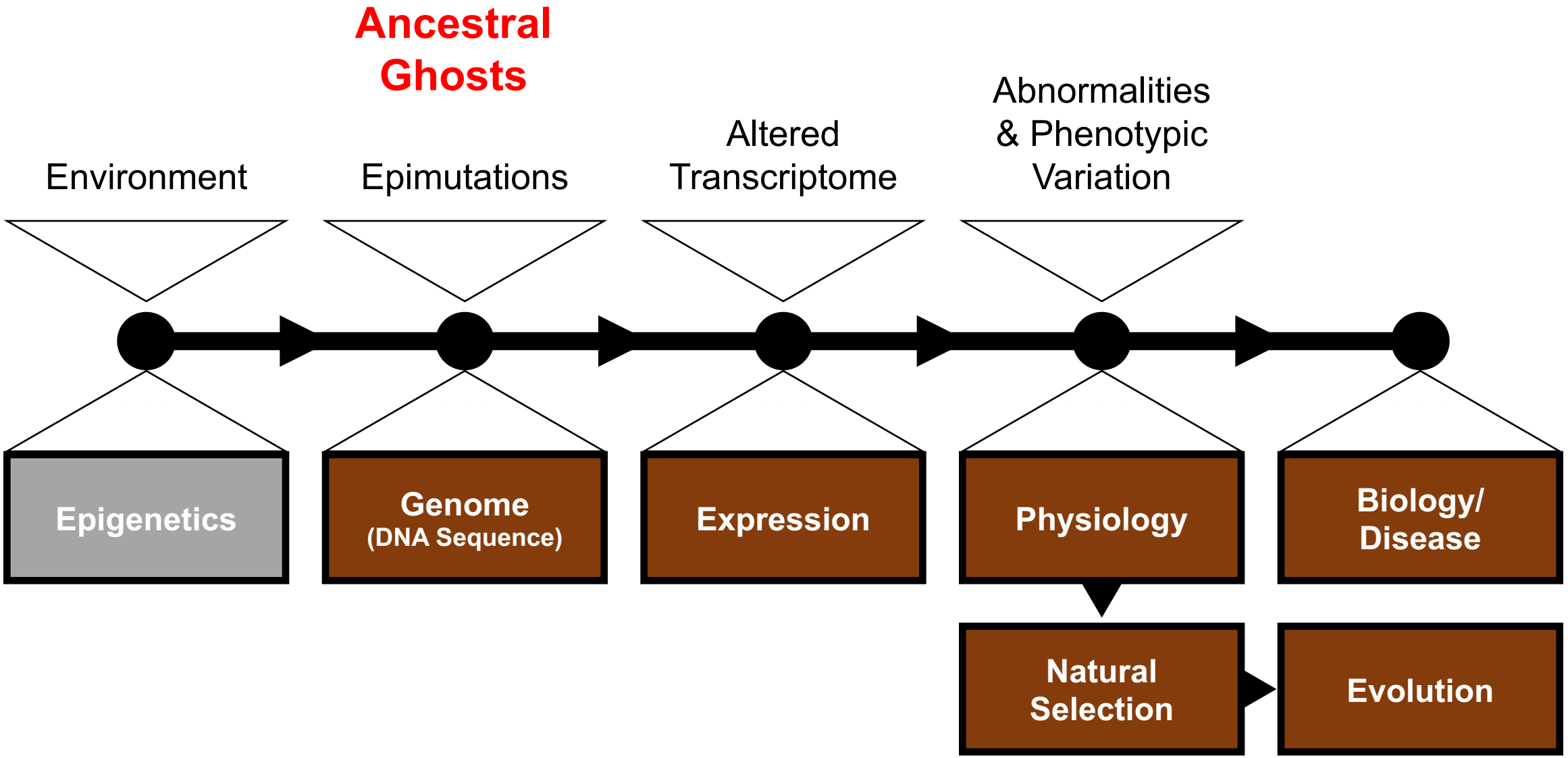
F3 generation difference not seen:

- Testis disease.
- Male kidney disease.
- Age of puberty.
- Weaning weight.
- Tumor frequency.
- Litter size.
- Gestation length.

Glyphosate Study: Transgenerational Epigenetic Changes in Sperm






Ancestral Ghosts
Environment
Epimutations
Altered Transcriptome
Abnormalities & Phenotypic Variation
Epigenetics
Genome (DNA Sequence)
Expression
Physiology
Biology/ Disease
Natural Selection
Evolution

EPIGENETIC TRANSGENERATIONAL INHERITANCE