Chronic Dietary PFOS Exposure on Heterogeneous Stock Rat Founder Strains

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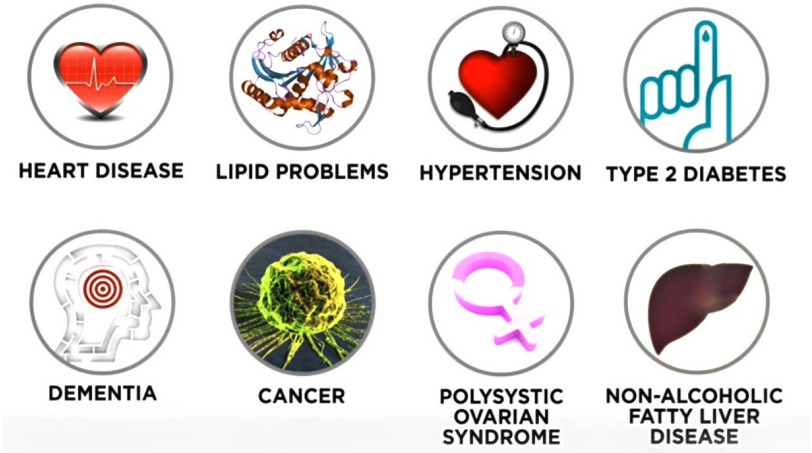
Metabolic Syndrome (MetS)

- Multifactorial conditions that together rise your risk of serious health complications such as:

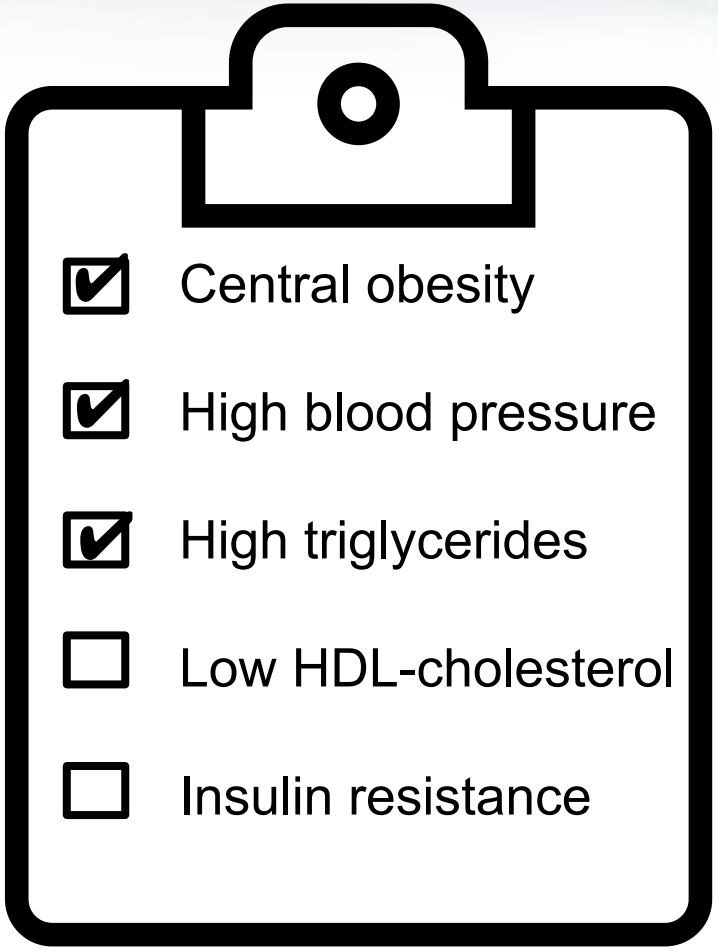


https://newhopefamilychiropractic.com/metabolic-syndrome/

- 1/3 of all US adults considered to have MetS

https://www.mayoclinic.org/diseases-conditions/metabolic-syndrome/symptoms-causes/syc-20351916

- **Complex syndrome with multiple factors, there is no simple answer to what causes it**

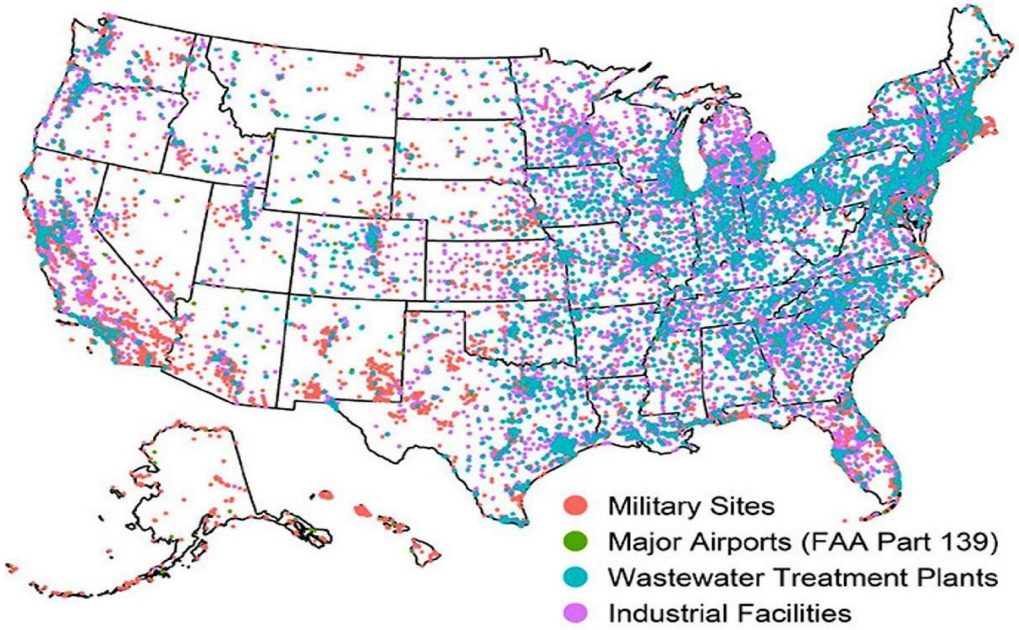


Endocrine Disrupting Chemicals: PFAS

- Artificially made “forever” chemical, resistant to water, oil, heat, or stains
- Half life ~2-5 years depending on the type of PFAS
- Over 15,000 types, only a few are studied

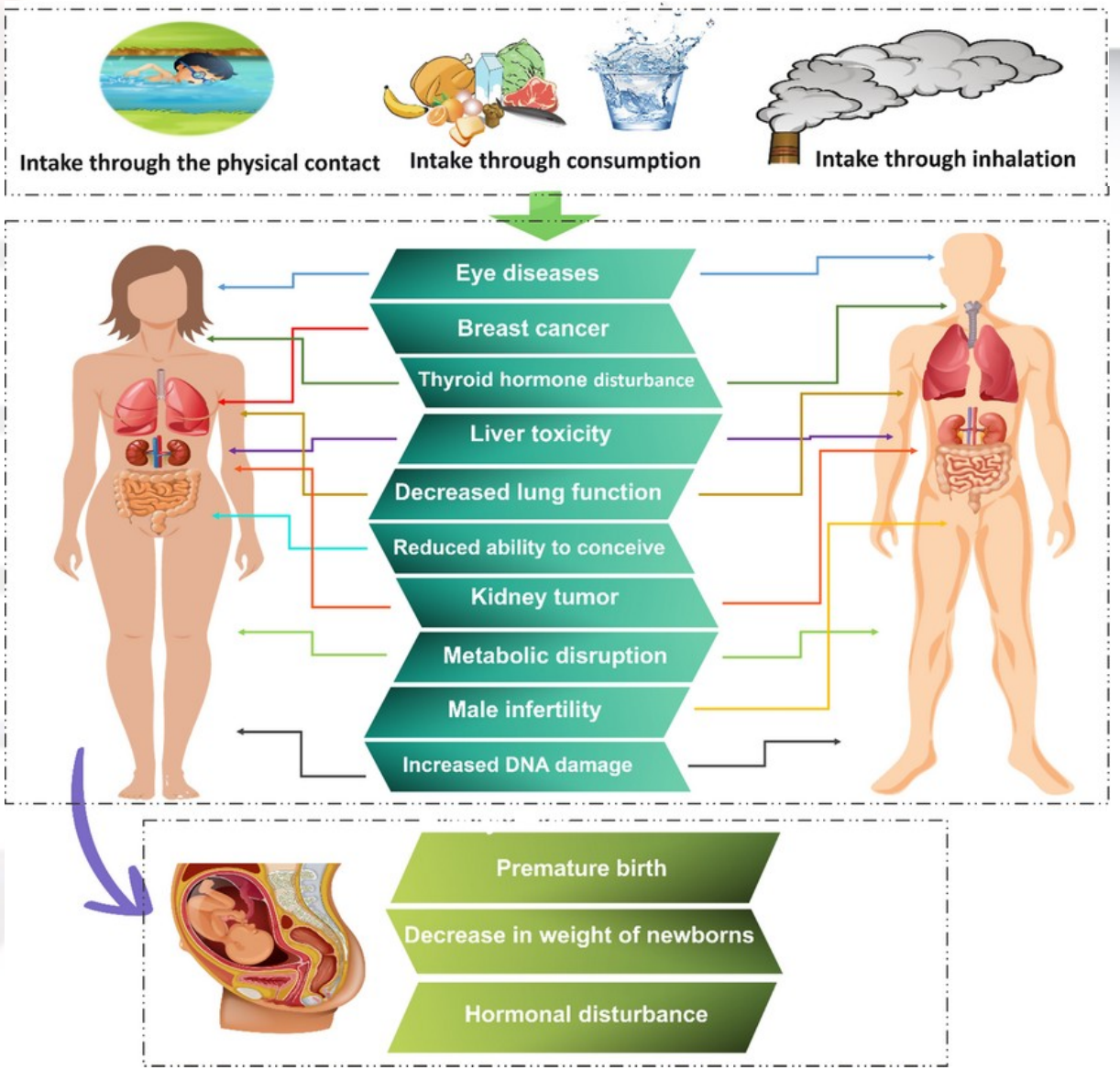
https://www.westernvawater.org/water/water-quality/learn-about-pfas

2022 98% of Americans have PFAS in their blood



https://coastalreview.org/2022/11/pfas-contamination-is-likely-at-58000-sites-in-us-study/

PFAS Dangers and Exposure



https://www.researchgate.net/figure/A-number-of-negative-effects-of-PFAS-on-human-health_fig3_355393062

European Food Safety Authority Tolerable Daily Intake (TDI)

0.63ng/kg BW/Day
150lb person = 43ng/day

57ng in ONE meal

Environmental Research and Education Foundation estimates exposure of 146-600ng/day from food and dust

Gene x Environment

OXFORD
SOT | Society of Toxicology
academic.oup.com/toxsci

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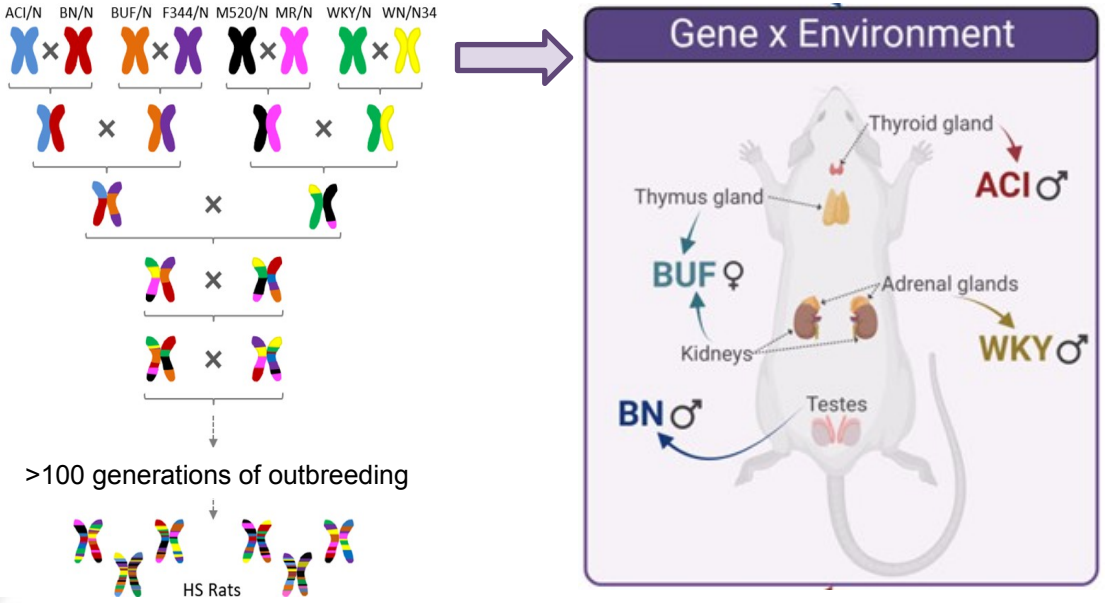
Research article

Genetic background in the rat affects endocrine and metabolic outcomes of bisphenol F exposure

Valerie A. Wagner,[1] Katie L. Holl,[1] Karen C. Clark,[2,3] John J. Reho,[1,4] Melinda R. Dwinell,[1,2,5] Hans-Joachim Lehmler,[6] Hershel Raff,[1,2,3,7] Justin L. Grobe,[1,2,4,8] Anne E. Kwitek[1,2,5,8,*]



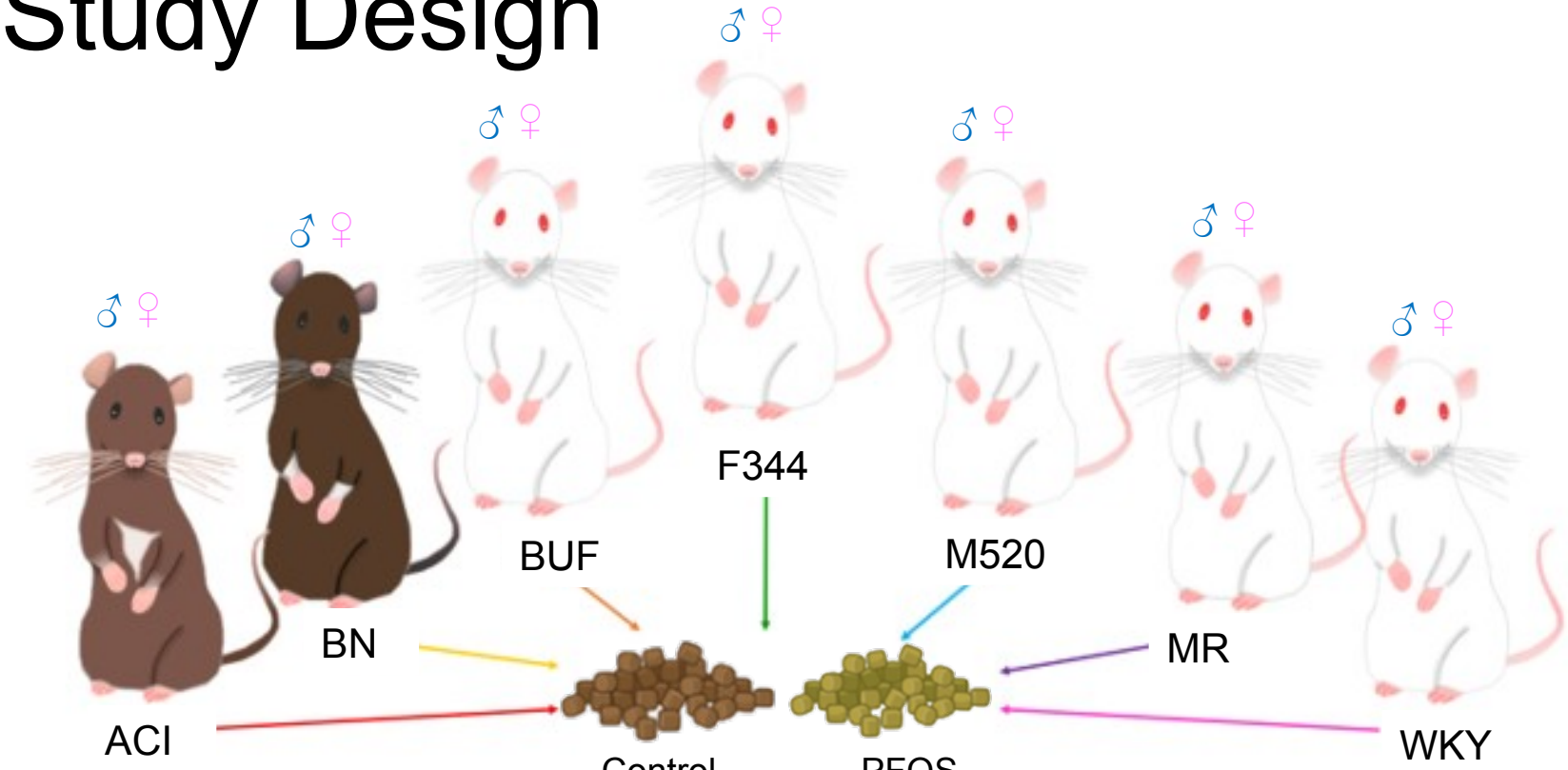
Adapted from PMID:201045

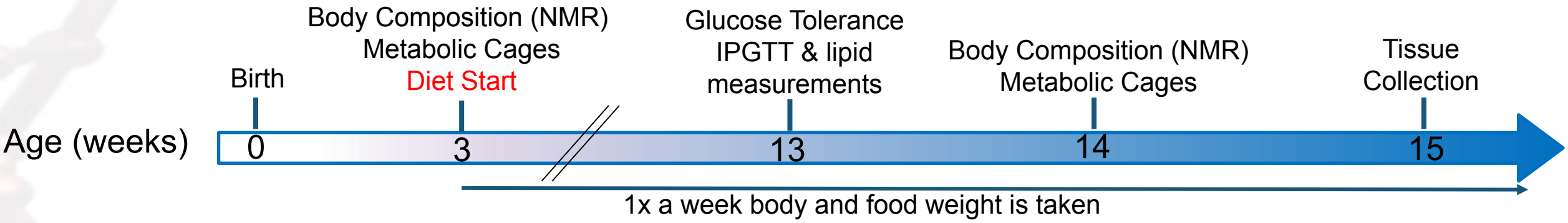
Wagner VA, et al. 2023; Toxicol Sci; PMID: 37191987

Hypothesis

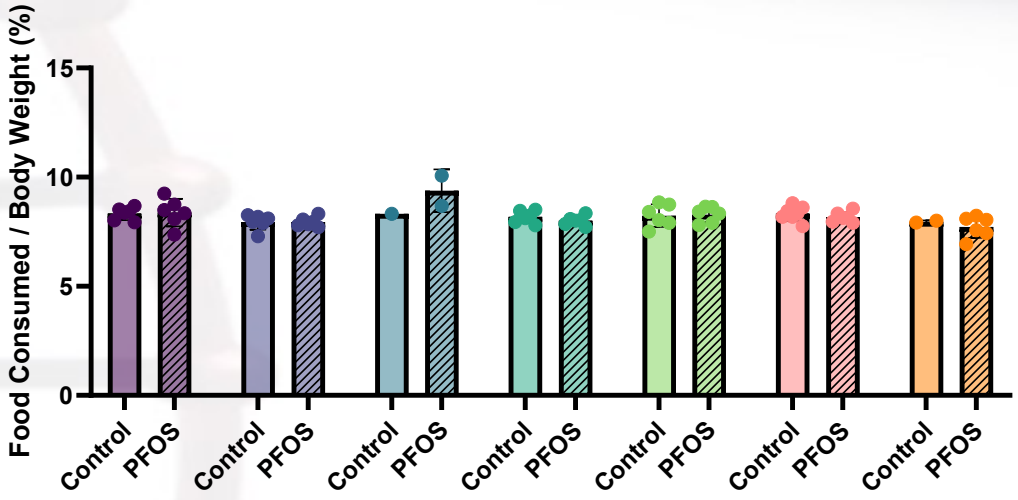
Chronic PFOS exposure will have strain specific effects towards metabolic disease and endocrine disruption

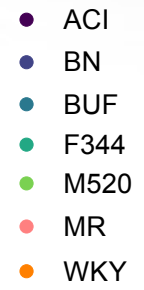
PFOS Study Design

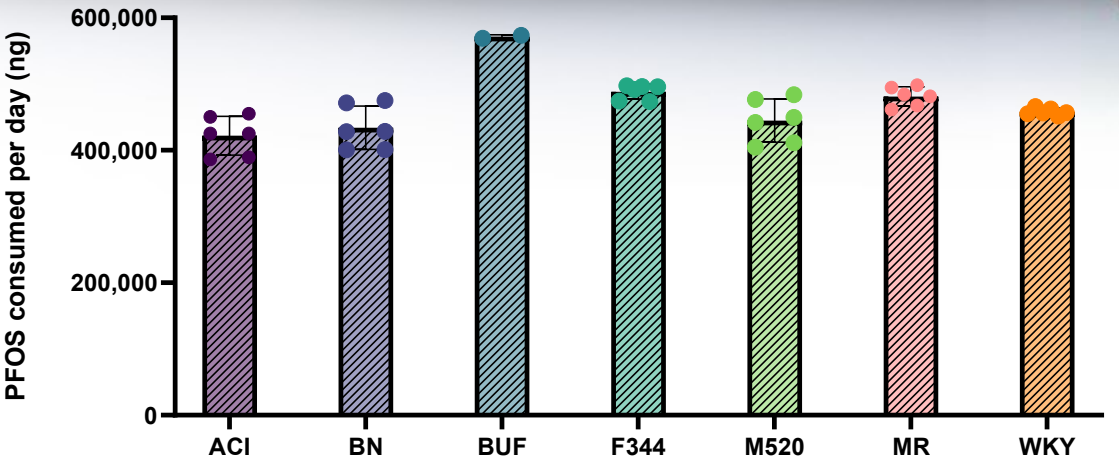


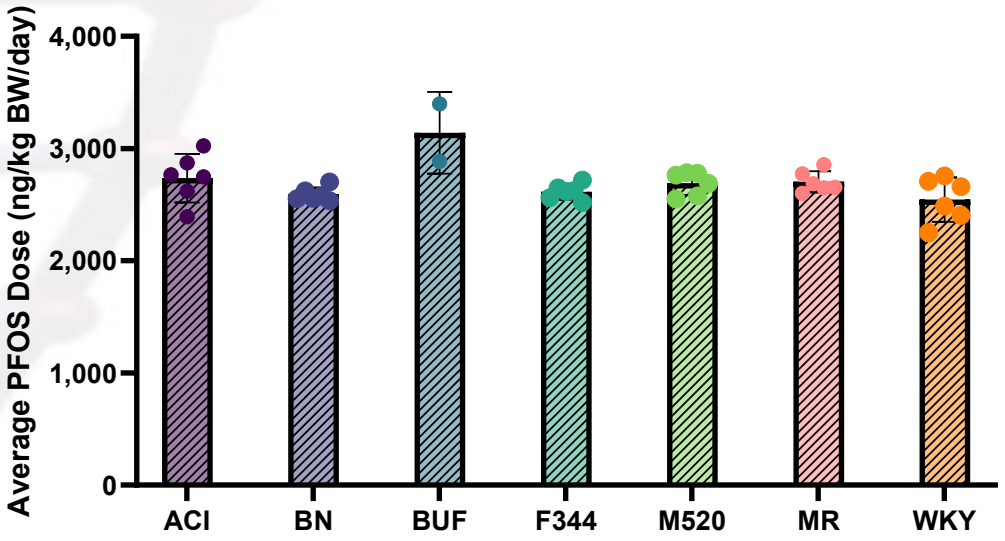


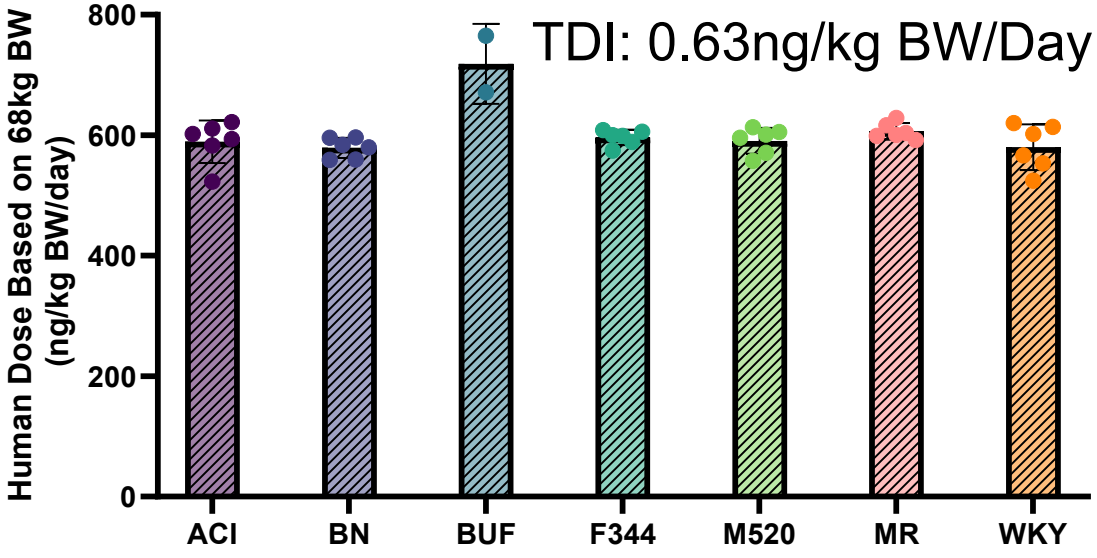
No food bias:


Food Consumed / Body Weight (%)
15
10
5
0
Control
PFOS

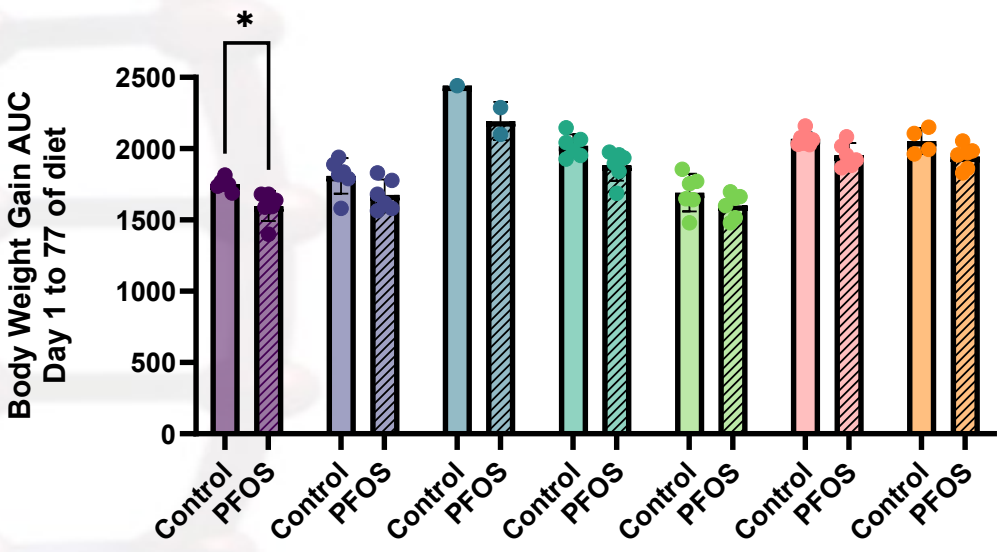

ACI
BN
BUF
F344
M520
MR
WKY

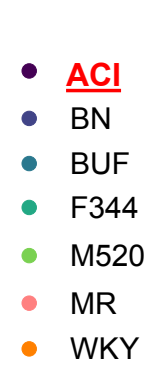

PFOS consumed per day (ng)
600,000
400,000
200,000
0
ACI
BN
BUF
F344
M520
MR
WKY

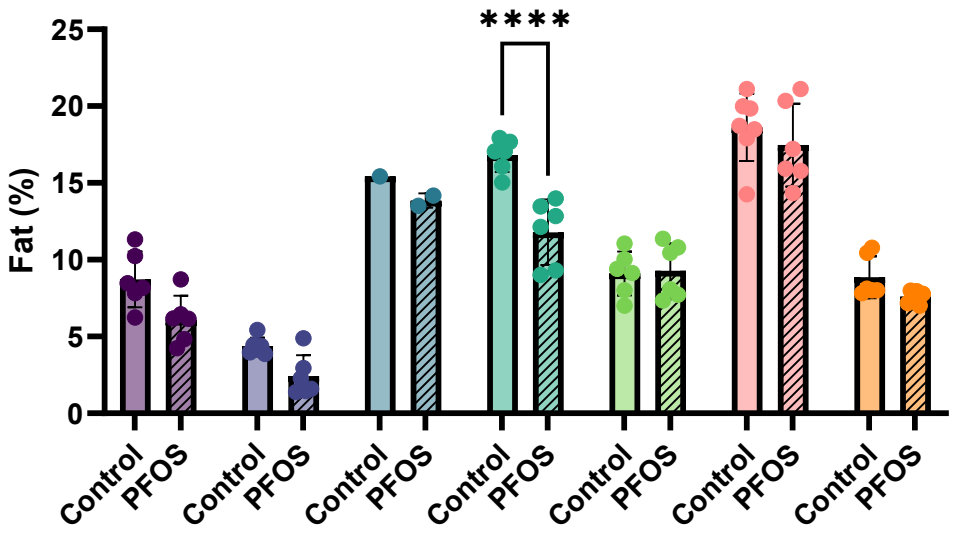

Average PFOS Dose (ng/kg BW/day)
4,000
3,000
2,000
1,000
0
ACI
BN
BUF
F344
M520
MR
WKY

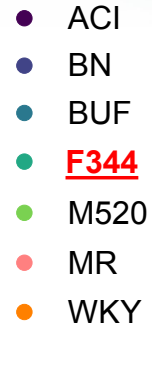

Human Dose Based on 68kg BW (ng/kg BW/day)
800
600
400
200
0
ACI
BN
BUF
F344
M520
MR
WKY
TDI: 0.63ng/kg BW/Day

Body morphology-lower weight gain:



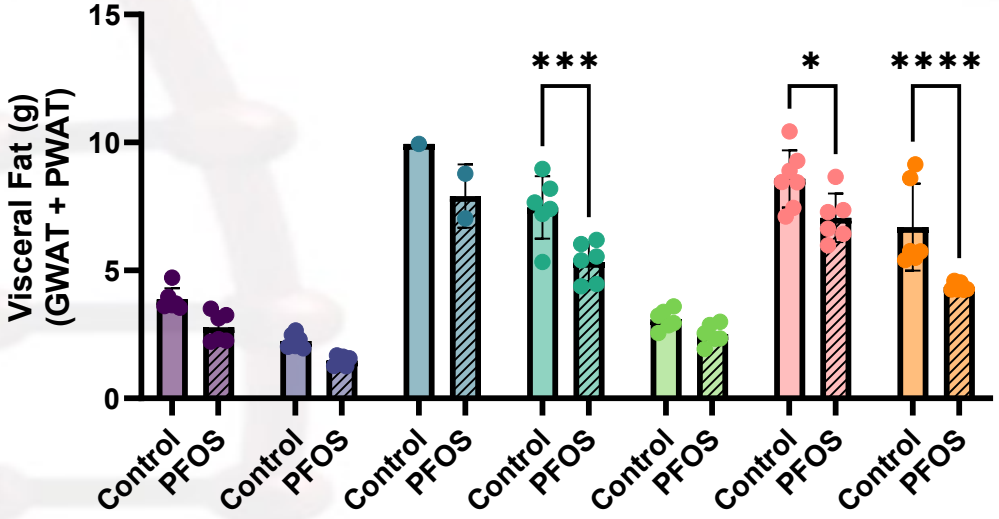


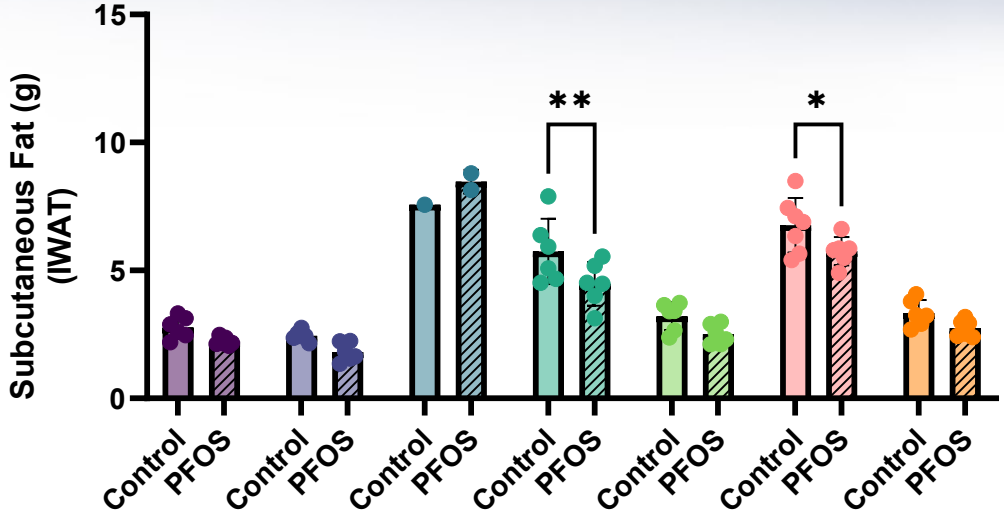


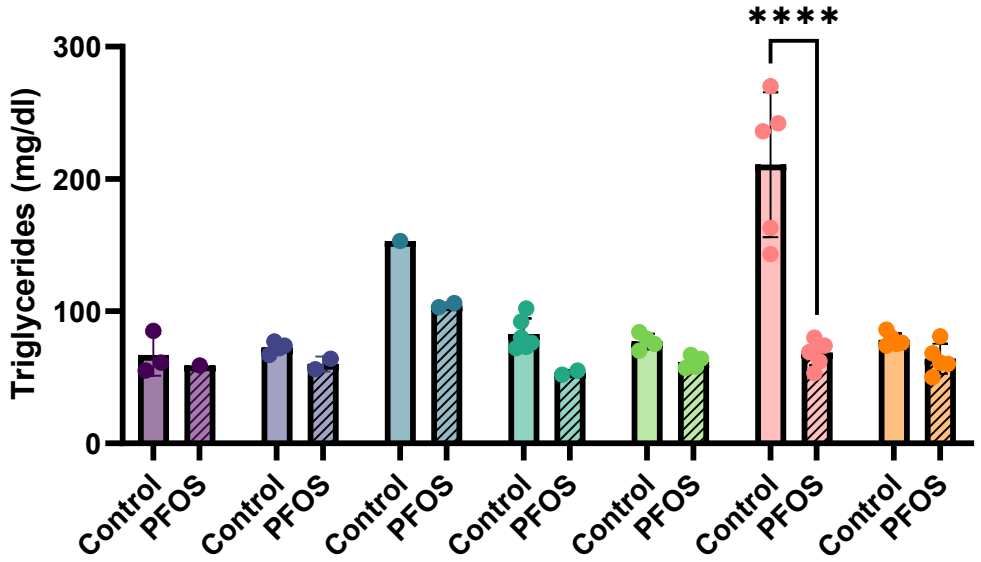


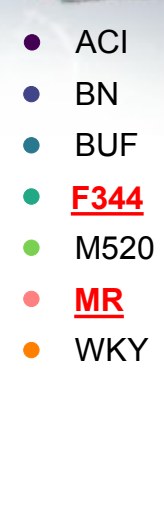
Two-way ANOVA, * p<0.05, ****p<0.00005

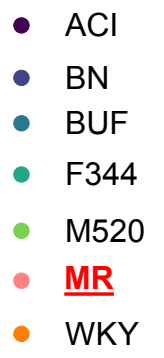
Lower adiposity and plasma lipid:





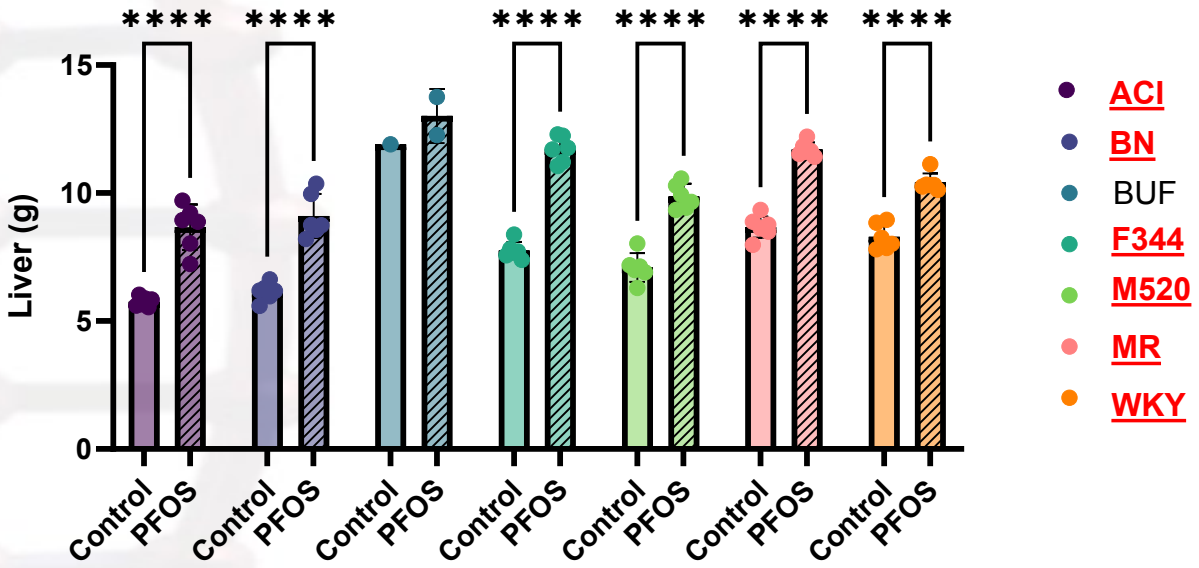


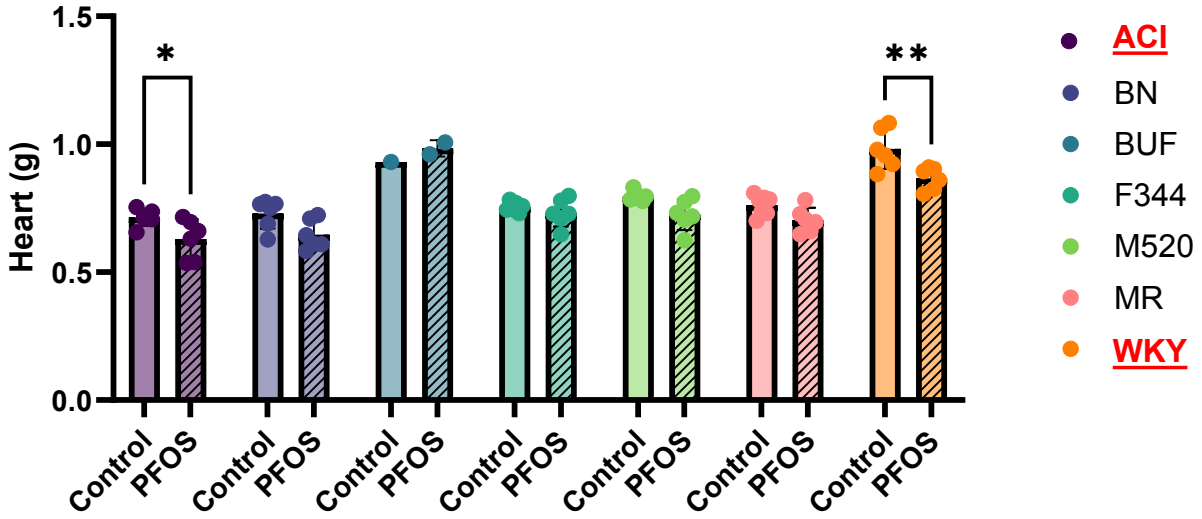




Two-way ANOVA, * p<0.05,**p<0.005,***p<0.0005, ****p<0.00005

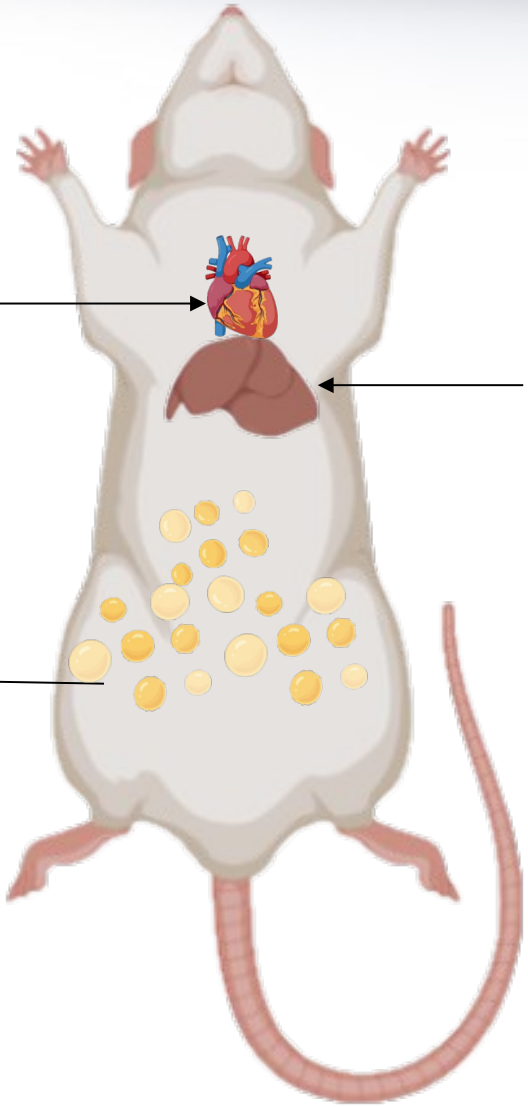
PFOS-induced liver and heart size:





Two-way ANOVA, * p<0.05,**p<0.005,****p<0.00005

Strain specific effects from PFOS exposure:



Decreased Heart
ACI
WKY

Increased Liver
ACI
BN
F344
M520
MR
WKY

Decreased Fat
F344
MR
WKY

Decreased Body Weight Gain
ACI

Biorender.com

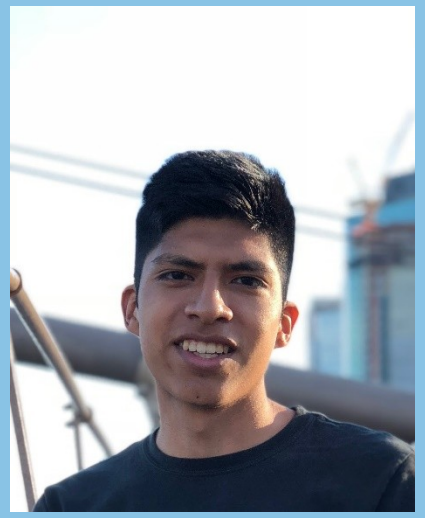
Future directions:

- Nonalcoholic fatty liver disease
  - Liver lipids
  - Liver enzymes
  - Histology-Fibrosis and lipid accumulation
- RNA extraction and qPCR on genes associated with fatty acid metabolism and liver injury
- Serum cholesterol
- Hormone effects; thyroid T3 & T4
- Blood pressure to measure cardiovascular differences
- Repeat using HS Rats - GWAS to identify genetic risk

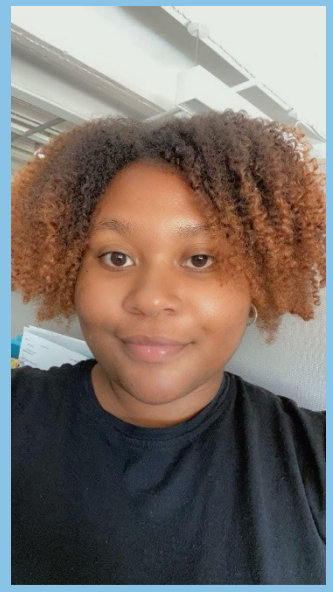
Acknowledgements:

Kwitek Lab

Dr. Anne Kwitek, PhD



Samuel Hernandez, BA
Medical Scientist Training Program (MSTP)



Doriann Pina, BS
ASPIRE/SPUR

- Dr. John Reho ~ Manager, Comprehensive Rodent Metabolic Phenotyping Core (CRMPC) MCW
- Dr. Melinda Dwinell ~ Hybrid Rat Diversity Panel (HRDP)
- Lynn Malloy ~ Research Technologist III, Dr. Mindy Dwinell Lab MCW

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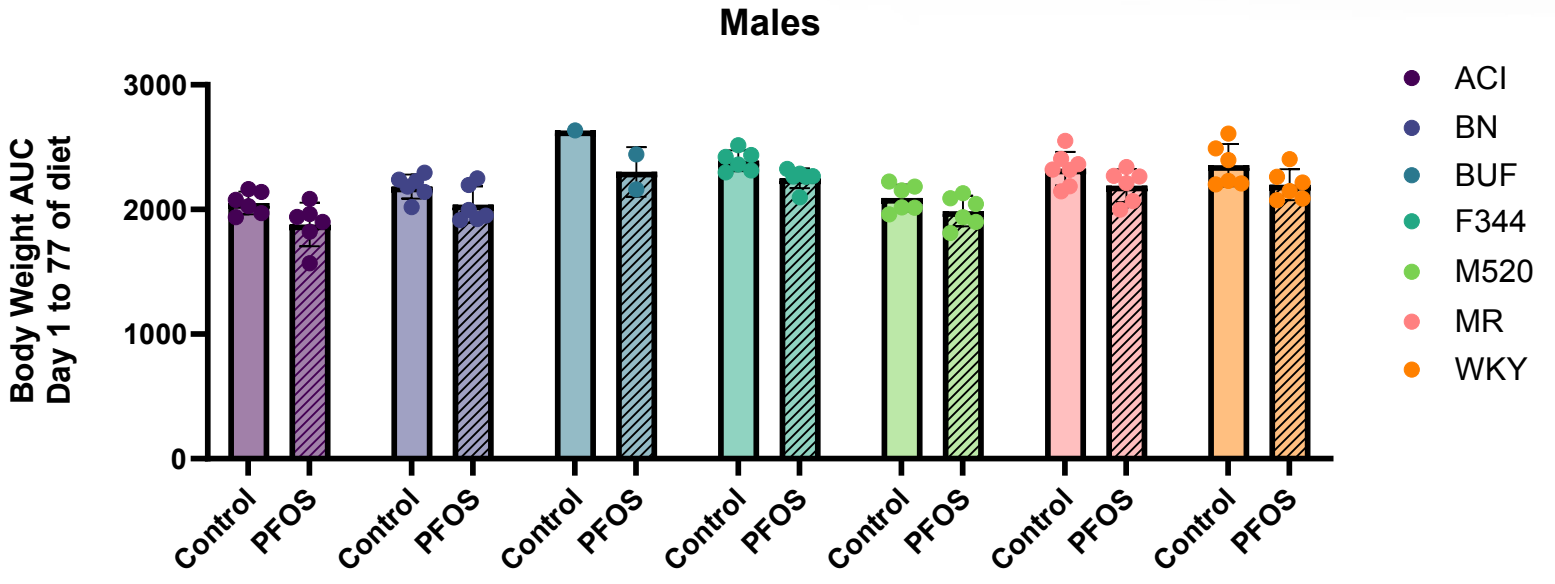
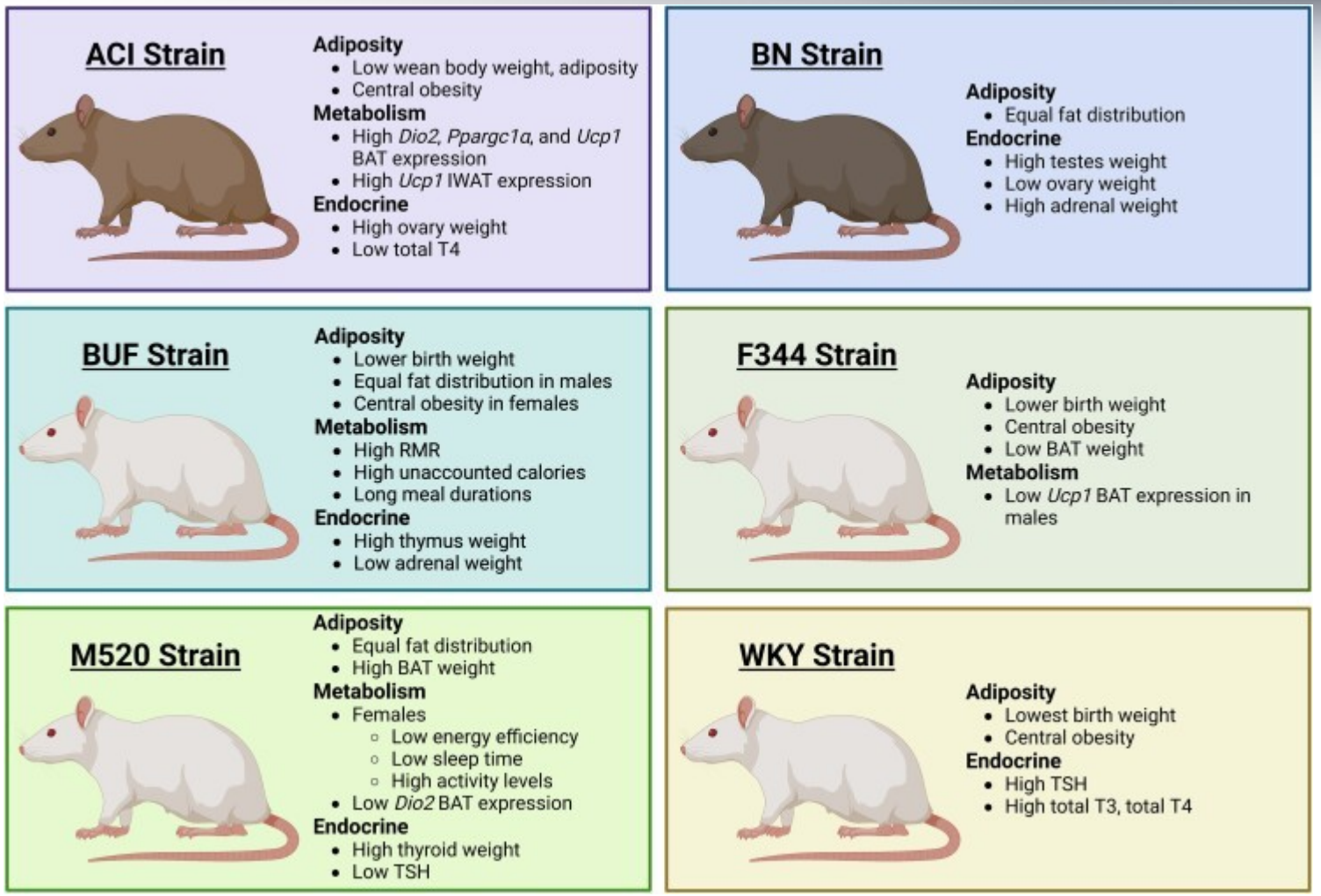
Hybrid Rat Diversity Program (grant 5R24OD024617 from the NIH Office of the Director)

No difference in body weight:



Adiposity, metabolism, and endocrine health:

Decreased Body Weight Gain
Decreased Heart



Decreased Visceral Fat
Decreased SubQ Fat

Decreased Visceral Fat
Decreased Heart

Wagner VA, et al. 2023; Endocrinology; PMID: 37882530

Female PFOS Overview:

Strain	Body Weight AUC	Body Weight Gain AUC	Feeding Efficiency	Energy Efficiency	Triglycerides	Liver	Heart	Kidney	Visceral Fat
ACI		↓				↓			
BN		↓	↓	↓		↓	↓		
BUF	↓				↓			↓	
F344						↓			↓
M520						↓			
MR						↓			
WKY		↓				↓	↓		↓