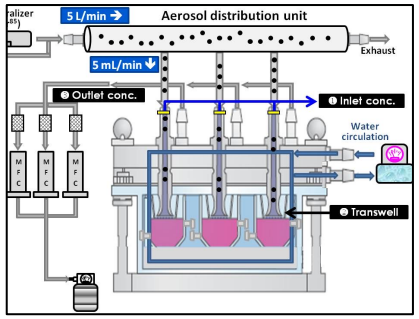


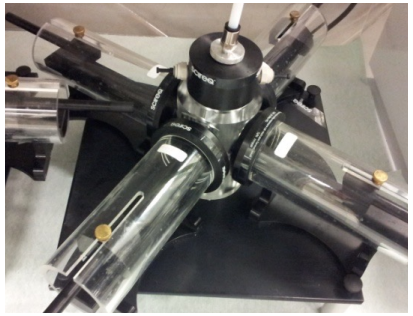
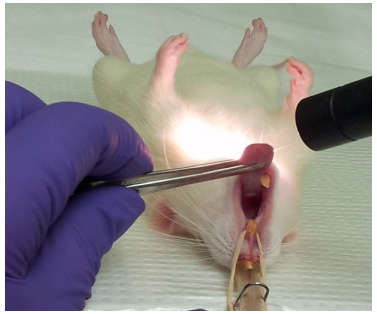
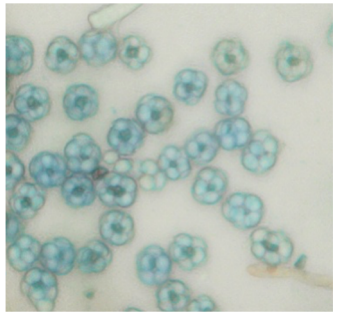
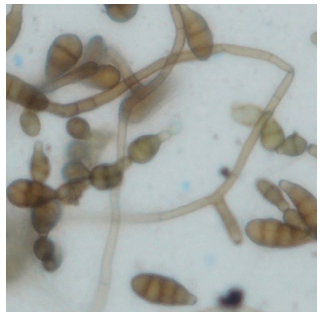
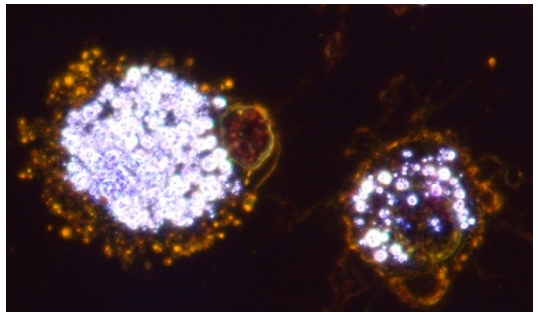
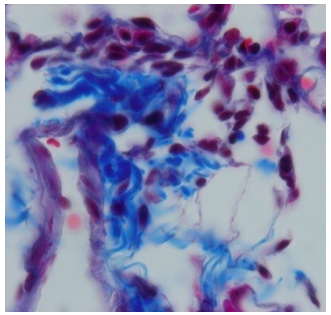

environmental health sciences research center

Pulmonary Toxicology Facility

Pulmonary Toxicology Facility

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ANDREA ADAMCAKOVA-DODD, PHD, RESEARCH SCIENTIST

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PTF Rationale

The human lung exposes a surface area of 75 m^2 to the environment, far more than our skin or GI tract.

Many exposures with adverse health effects are from breathing airborne PM, hazardous chemicals, bioaerosols, and smoke from wildfires.

Every year there are an estimated 6.5 million premature deaths globally associated with indoor and outdoor air pollutants, exclusive of bioaerosols and viruses.

In rural environments people suffer ill effects from both chemical and biological hazards: farm chemicals, welding fumes, endotoxins and fungal glucans.

EHSRC investigators have a critical need to design, perform and analyze *in vitro* to *in vivo* to epidemiology studies investigating relevant pulmonary exposures.

The PTF fulfills that need.

Specific Aims

- **Provide expertise and facilities for the use of animal models** to elucidate adverse outcome pathways of xenobiotics or to test novel inhalation therapies;
- **Design and perform inhalation exposure studies** to groups of laboratory animals under rigidly controlled exposure conditions;
- **Assess biomarkers and sensitive physiologic endpoints** to identify biological response profiles, low-dose functional changes, and susceptibility factors;
- **Provide high-content *in vitro* studies** using tri-cultured lung cells exposed at the air-liquid interface;
- **Perform exposure assessment** of endotoxins, glucans, allergens, and metagenomics of microbial communities **in support of epidemiologic studies of environmental lung diseases;**
- **Facilitate pre-doctoral, post-doctoral and EHSRC member training.**

PTF AOP Framework

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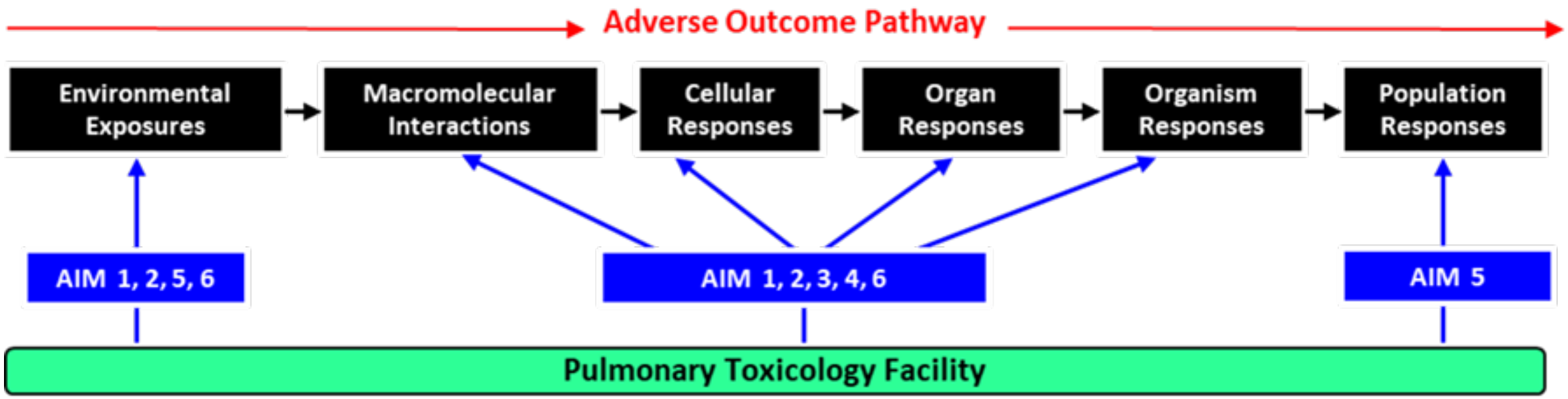
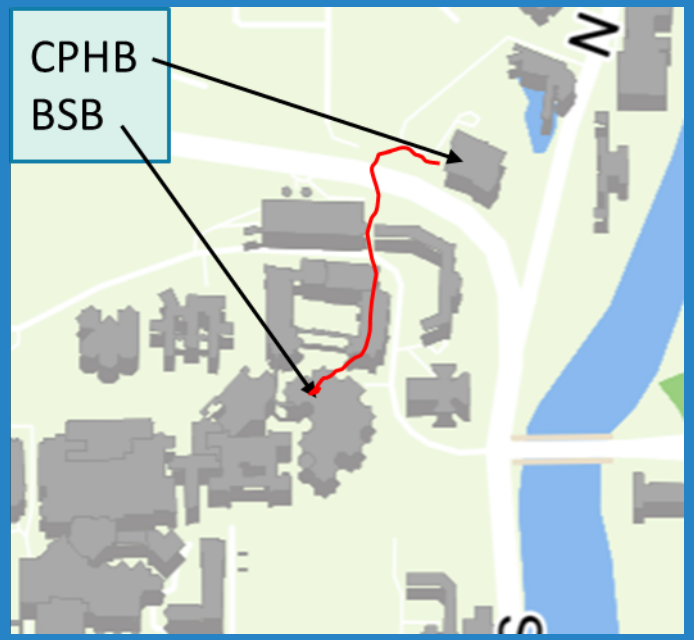
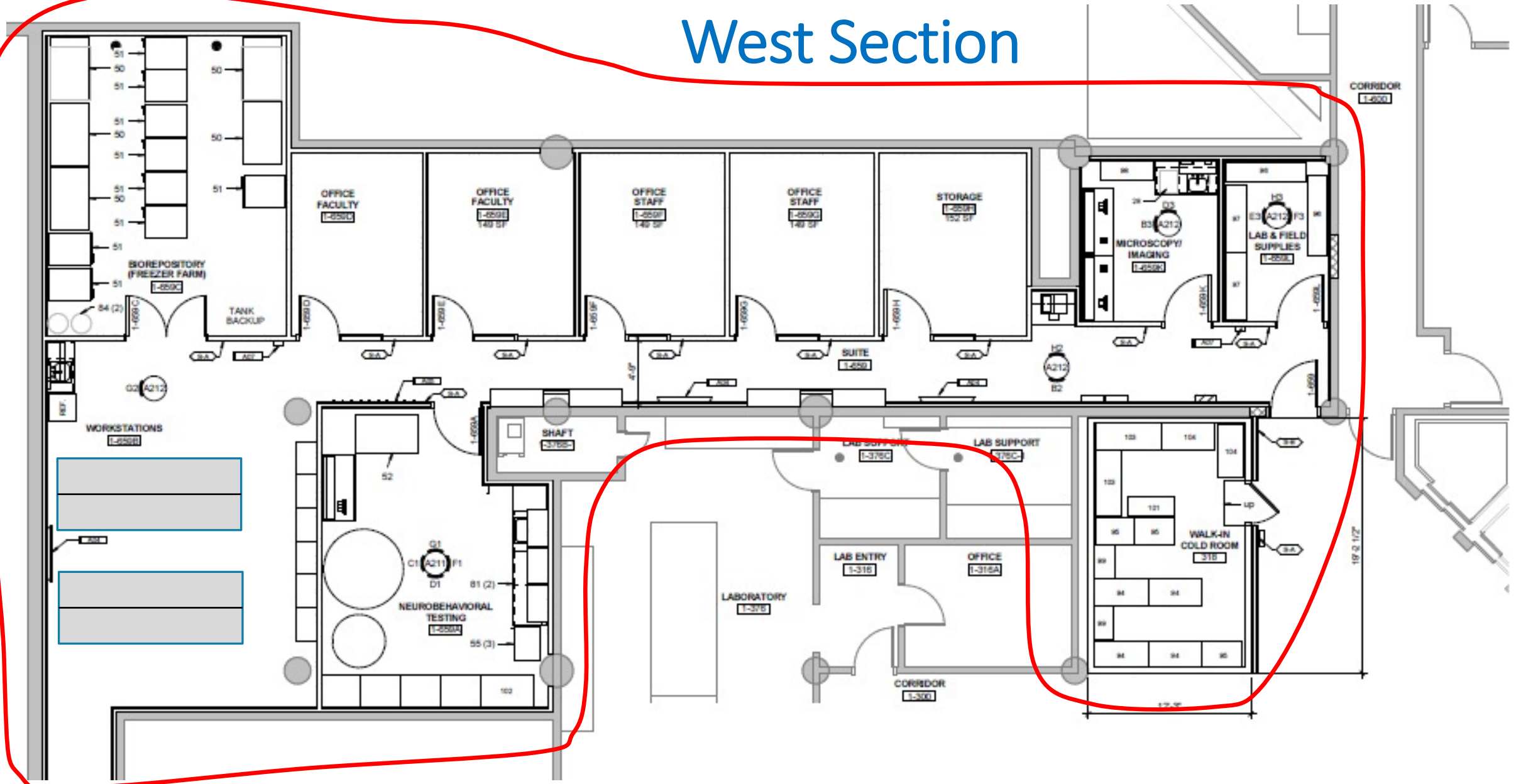


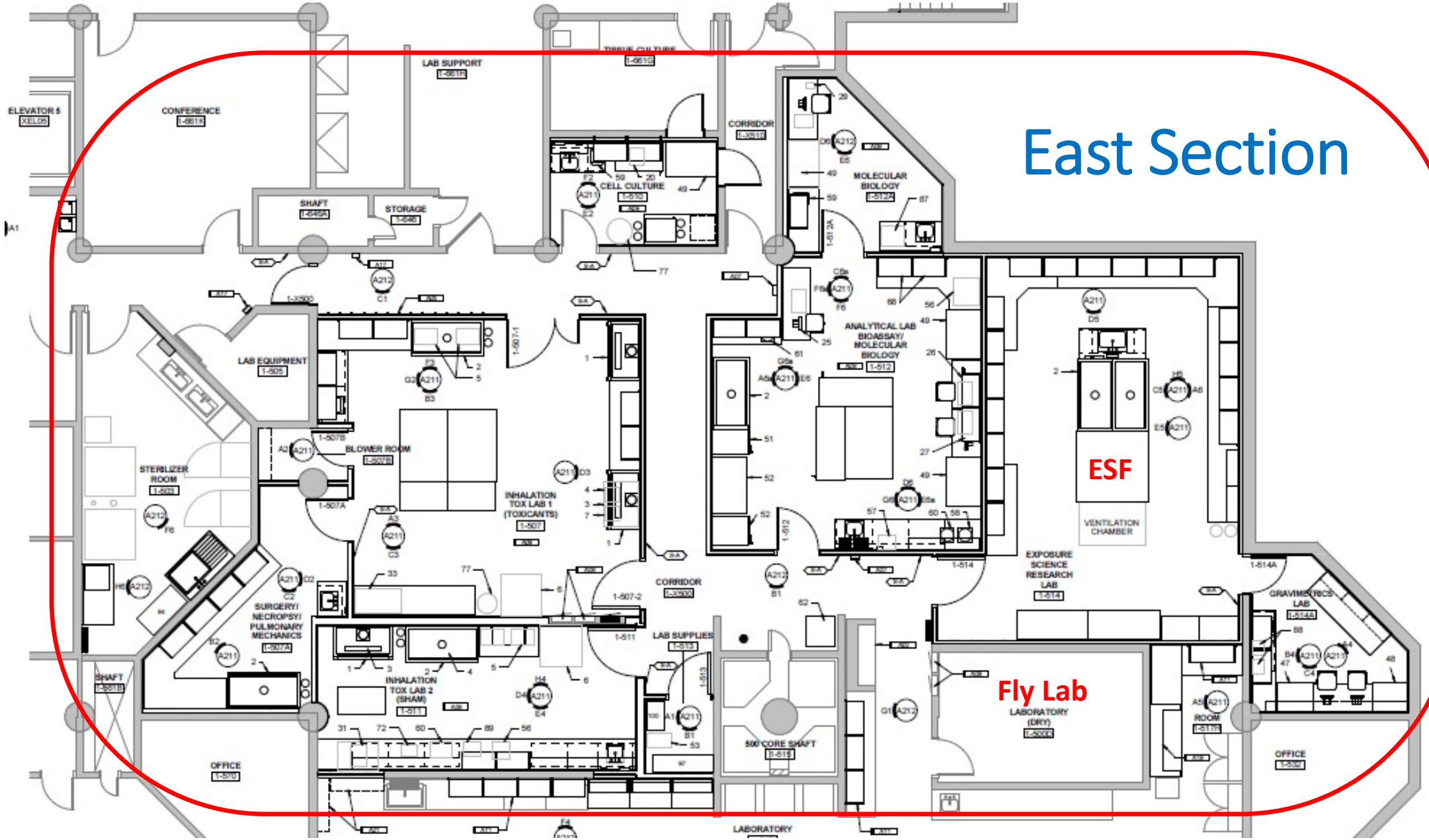
New PTF Laboratories



- Since 2019 the PTF and ESF are co-located in the Human Toxicology and Exposomics Laboratory (HTEL)
- 6,500 sq ft (604 m^2) in Bowen Science Building
- $4,300,000 total gut and rebuild completed December 2018
- $500,000 new equipment (thanks to the Roy G. Carver Charitable Trust)

West Section




East Section
ESF
Fly Lab
ELEVATOR 5
CONFERENCE
LAB SUPPORT
SHAFT
STORAGE
CELL CULTURE
CORRIDOR
MOLECULAR BIOLOGY
ANALYTICAL LAB BIOASSAY/ MOLECULAR BIOLOGY
LAB EQUIPMENT
BLOWER ROOM
STERILIZER ROOM
INHALATION TOX LAB 1 (TOXICANTS)
SURGERY/ NECROPSY/ PULMONARY MECHANICS
INHALATION TOX LAB 2 (SHAM)
LAB SUPPLIES
500 CORE SHAFT
LABORATORY
OFFICE
VENTILATION CHAMBER
EXPOSURE SCIENCE RESEARCH LAB
LABORATORY (DRY)
GRAVIMETRICS LAB
ROOM
OFFICE

PTF Laboratories & Rooms

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Lab Name	Size	Room #	Lab Name	Size	Room #
Inhalation Tox/Aerosols Lab I	620 ft^2	1-507	Biorepository (Freezer Farm)	407 ft^2	1-659C
Inhalation Tox/Aerosols Lab II	320 ft^2	1-511	Gravimetrics Lab	100 ft^2	1-514A
Molecular Biology Lab	138 ft^2	1-512A	Centrifuge Room	240 ft^2	1-504
Analytical/Bioassay Lab	518 ft^2	1-512	Sterilizer/Dish Washing Room	313 ft^2	1-503
Neurobehavioral Testing Lab	354 ft^2	1-659A	Cold Room, 4°C	210 ft^2	1-318
Exposure Science Lab (ESF)	705 ft^2	1-514	Supply Storage Room	95 ft^2	1-659L
Tissue Culture Lab	120 ft^2	1-510	Large Equipment Storage	400 ft^2	LL WL
Surgery/Necropsy Lab	198 ft^2	1-507A	Conference Room	475 ft^2	1-659B
Microscopy/Imaging Lab	125 ft^2	1-659K	Suite of 5 Offices	732 ft^2	1-659 D-H

Types of Research Supported

- Pulmonary Toxicology or Inhalation Therapeutics Projects
- Environmental Epidemiology Projects
- Exposure Assessment of Biological Agents for Epidemiology

Research Supported

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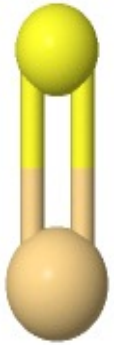
- Pulmonary Toxicology Models
  - In vitro:
    - submerged cell culture systems
    - air liquid interface exposures - single or multiple cell systems
  - In vivo:
    - Mice, rats, guinea pigs, ferrets, pigs
    - Inhalation, insufflation, instillation
    - Whole-body or nose-only exposures
    - Exposures in whole-body plethysmographs with monitored breathing
    - Acute, subacute, subchronic, chronic exposure models
  - Exposures:
    - Gases, vapors, droplets, particulate matter, nanoparticles, therapeutic agents
- Extensive capabilities to generate, characterize, and monitor stable exposures
- Flexivent and plethysmograph systems for measuring pulmonary mechanics
- Neurobehavioral testing facilities

Example:

Engineered Nanomaterials Inhalation Toxicology Assessment

NIEHS FUNDED STUDY



Cadmium Sulfide Inhalation Studies in Mice

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Acute – 4 hr, 1 day, 3.6 mg/m^3

Sub-acute – 4 hr, 10 days, 3.6 mg/m^3, necropsy at 0 and 3 wks post

Timecourse – 4 hr, 14 days, 3.6 mg/m^3, necropsy at 0, 4, 5, 8, 13 wks post

Perinatal – 4 hr, 17 (+ 22) days, 3.6 mg/m^3, Dams and Pups

Nose-Only Inhalation Exposure System

Separate Systems for ENM-exposed and Sham-exposed

SciReq InExpose System

ENM Particle Generation and Characterization

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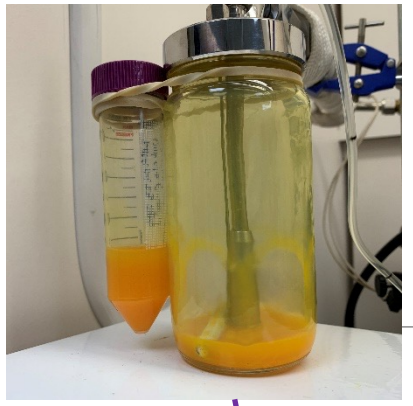
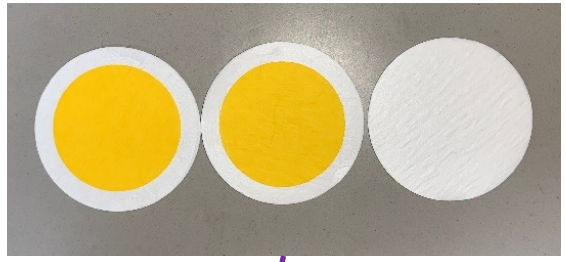
Generation: Collison Nebulizer

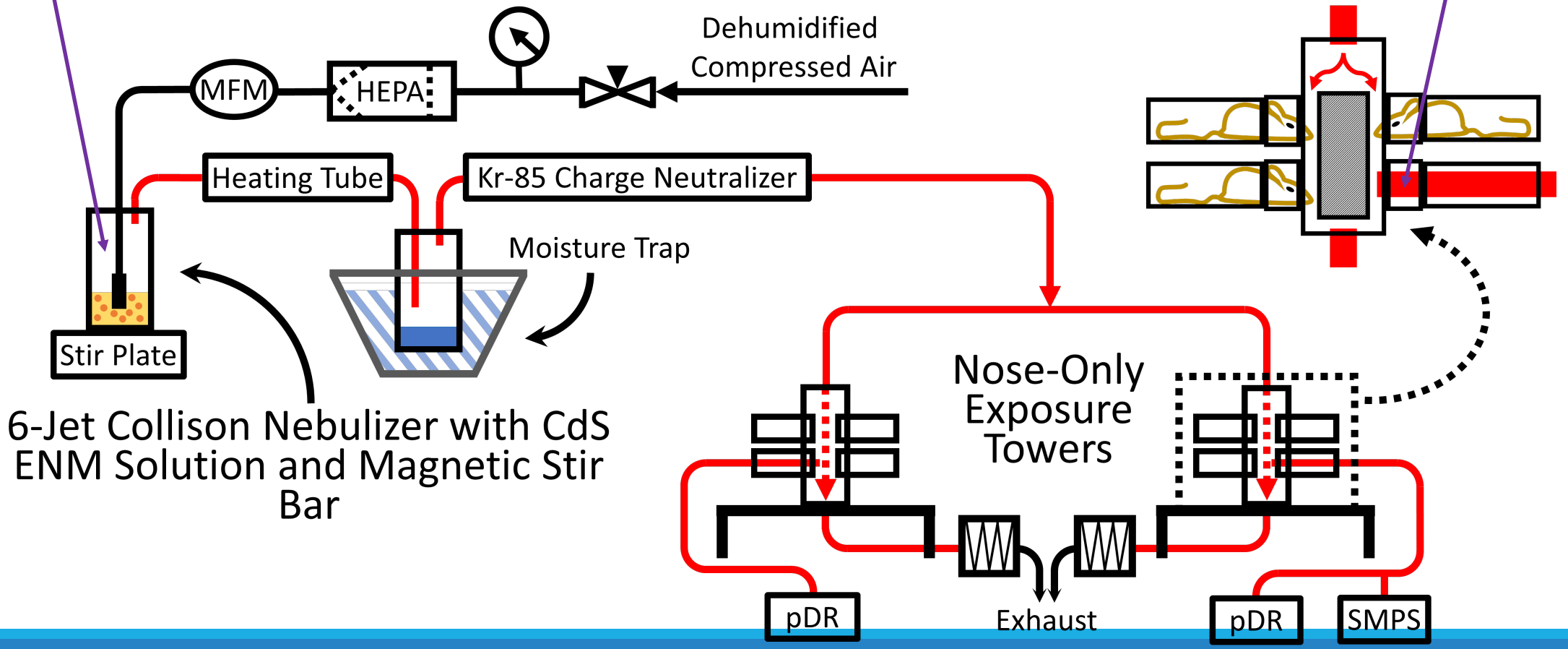
Characterization:

- Aerosol size distribution and concentration: SMPS, APS
- Primary size and aggregation: TEM, SEM-EDX
- Mass concentration: Chamber air sampling and gravimetric analysis

CdS Inhalation Studies







CdS Inhalation Exposures

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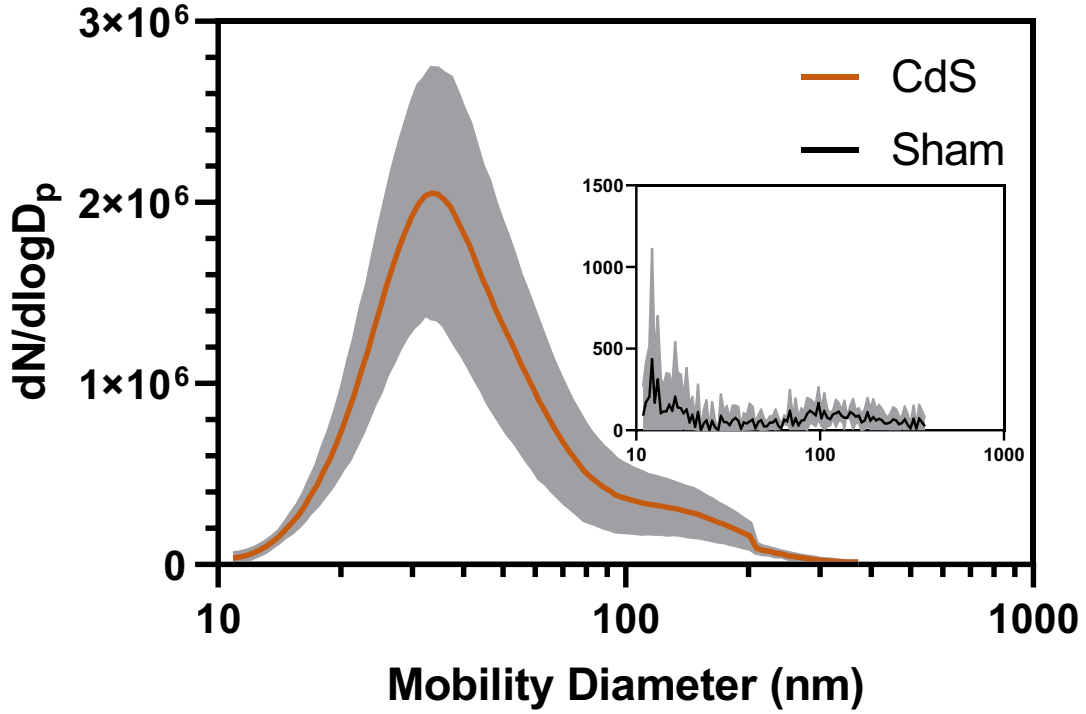
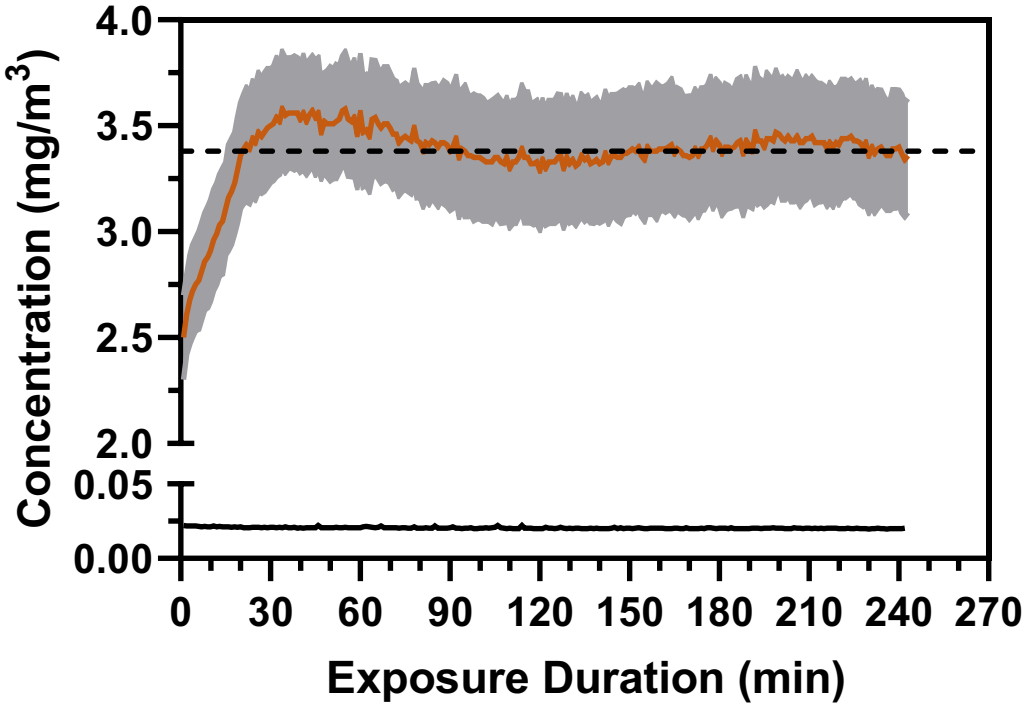
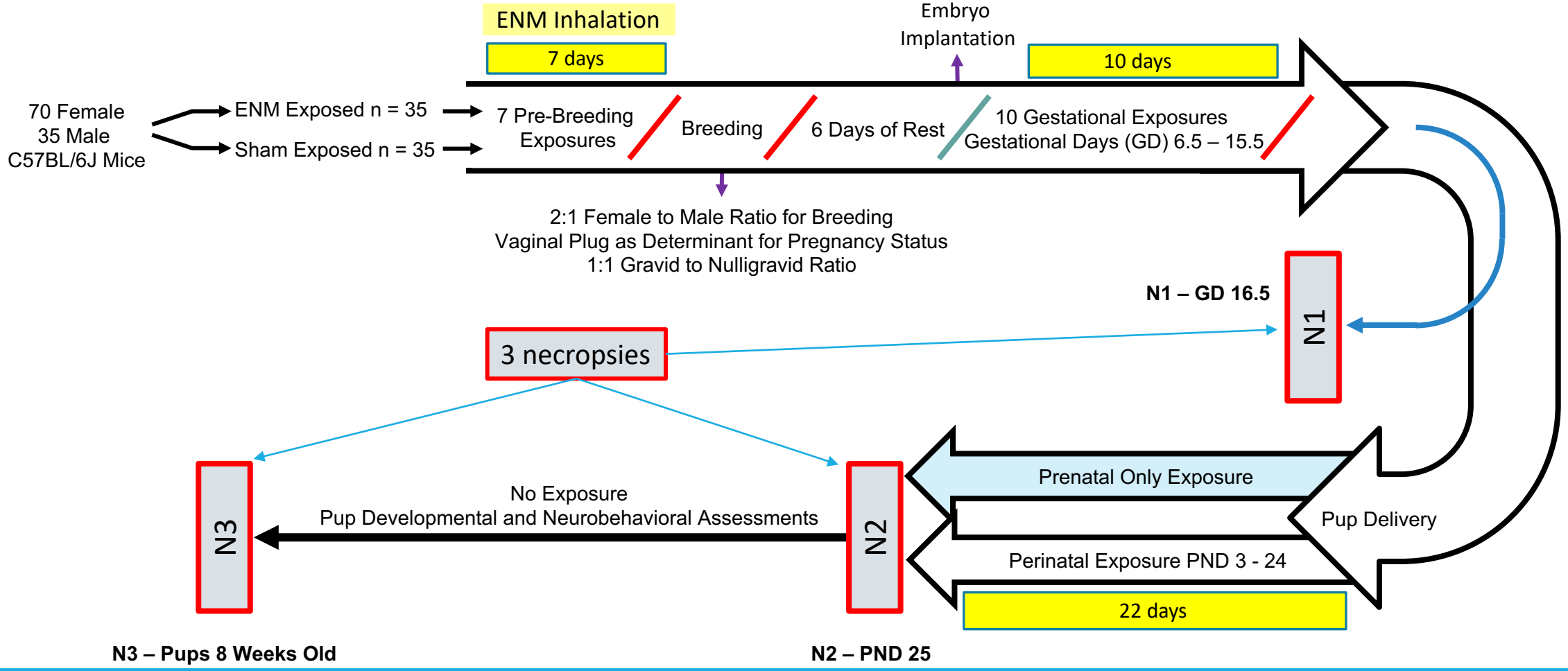
Protocol: Inhalation Exposure 5 days/wk, 4 hr/day at 3.5 mg/m^3





CdS Perinatal Exposure Protocol



Examples of Current Studies

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- Chlorine gas exposures for medical countermeasures research – Salem, Thorne, Adamcakova-Dodd
- Mouse models of vaping-induced lung disease and EVALI – Ng, Adamcakova-Dodd, Thorne
- Inhalation delivery of CRISPR ribonucleoproteins, antisense oligos, and novel peptides for gene therapy – McCray
- Trachea-on-a-Chip characterization of lung clearance - Xie
- Inhalation studies of PCB 52 – ISRP Lehmler, Klingelhutz
- PK/PD modeling of PCBs - ^{14C}PCB 11, 28, 52 – Adamu, Thorne, Adamcakova-Dodd
- Development of sensors to monitor GHG emissions in distributed networks - Toor
- Assessment of exposures to cyanobacterial toxins (microcystins, anatoxins, saxitoxins, cylindrospermopsin) – Metwali, Thorne
- Biological agents exposure assessment in U.S. households - NHANES 2022-2024 – Zeldin, Salo (NIEHS)
- Exposures to endotoxin allergens and glucans in intervention studies of asthma and COPD
  - SICAS 2, SICAS 3, PARK, EASY, IDEA, AERO-BPD, Smart-Phone


Questions?