Cellular Inflammatory responses to Indoor-Source Particulate Matter

Air Resources Board Contract #05-302

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Significance of indoor air PM exposure

- Indoor environments: variable and potentially distinct sources of chemical exposure
- High concentrations
- Close to the source
- Time of exposure
- Small database

Sources of PM from Indoor Air

- Wood burning
- Candles
- Incense
- Cooking activities: Frying, Broiling, Oven etc.
- Flooring

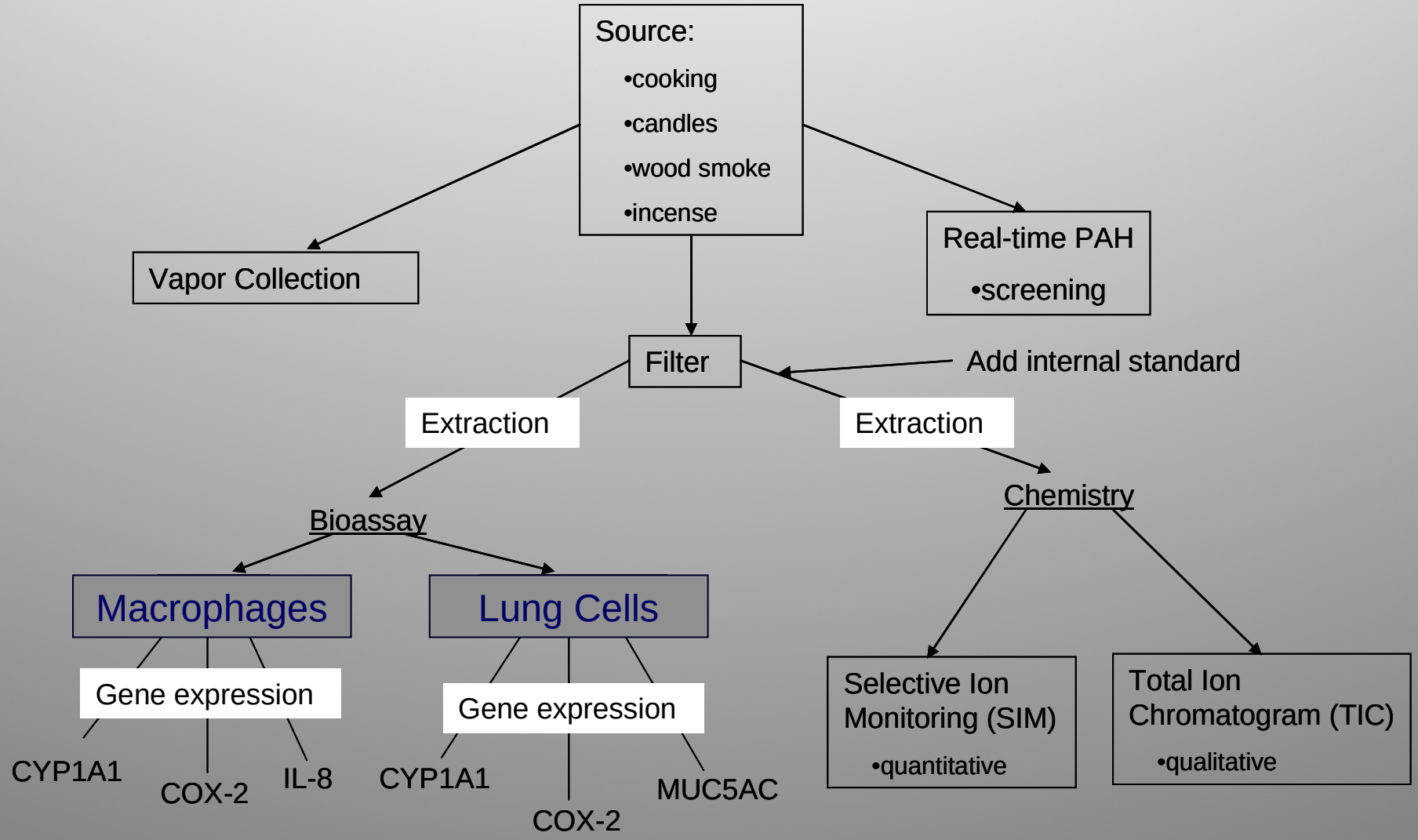
Indoor PM exposure
Possible Health Effects

- Airway Symptoms and Allergy
- Cardiovascular diseases (CVD) like atherosclerosis
- Endocrine disrupting effects
- Immunotoxic effects
- Chronic inflammatory response as a main cause for adverse health effects

In vitro Cell Model

- Critical sensors for smoke, stress, and PM exposure
- Arylhydrocarbon-Receptor (AhR): Ligand-activated through numerous planar aromatic hydrocarbons as well as stress
- Toll-like receptors (TLR): Pathogen recognition and activation of innate immunity
- Nuclear factor-kappa B (NF-κB): Sensor for smoke and stress

Study Objective

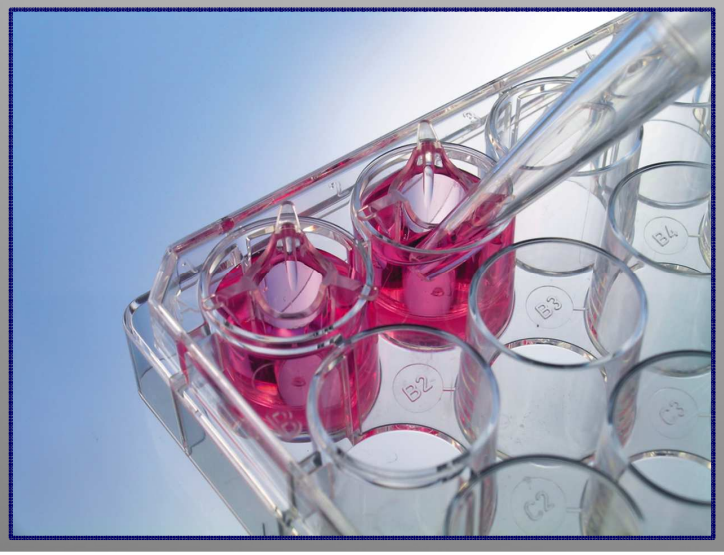


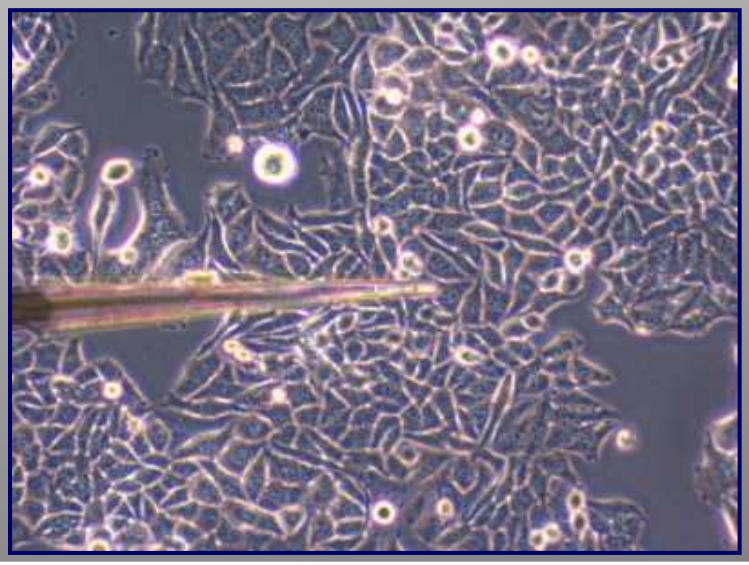
Study Design

- Two main target cell types

a) Phagocytotic cell types as first line of defense, human macrophages (U937)

b) Lung Clara cells from pulmonary epithelium (NCI H441)

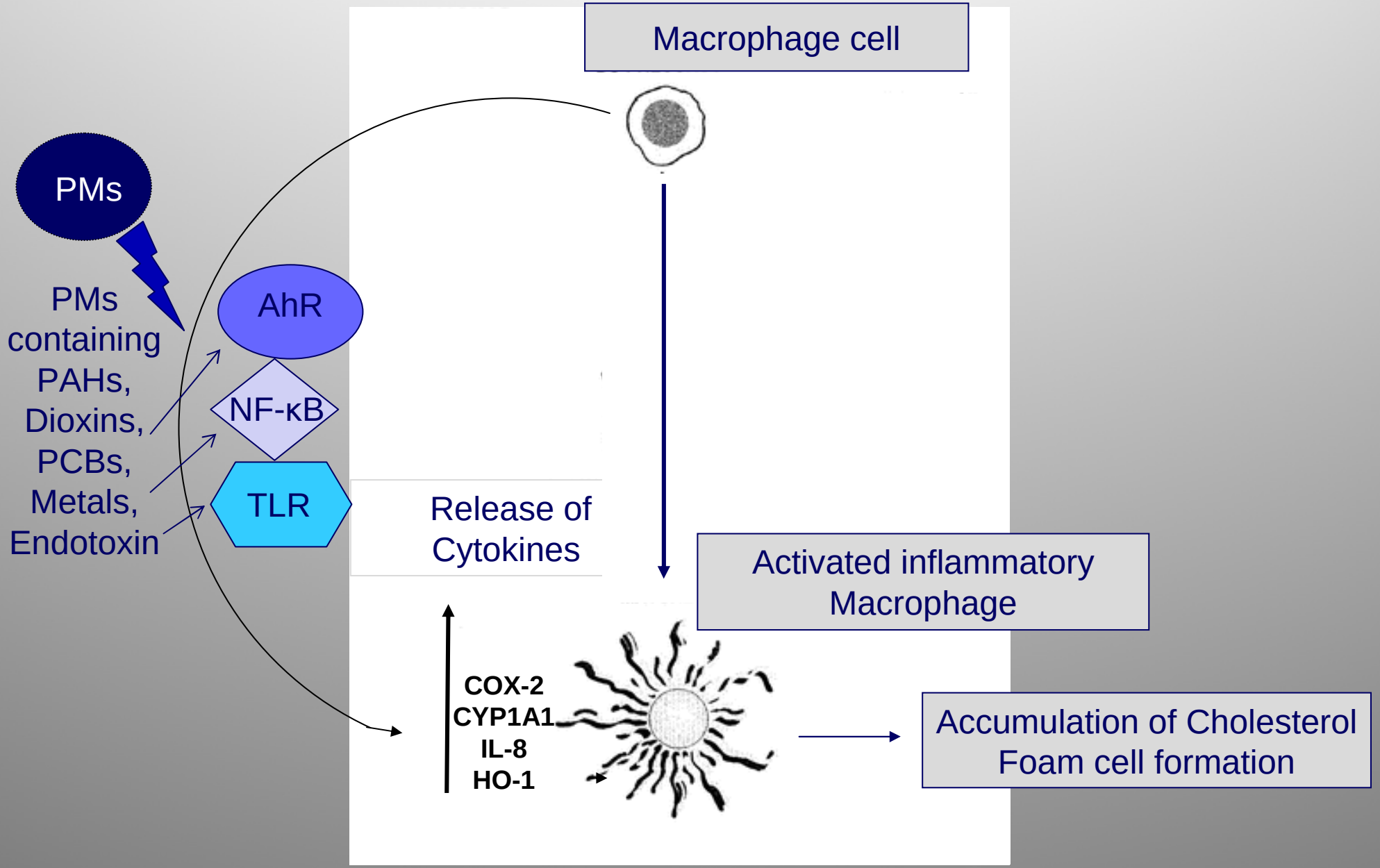




Biomarkers of PM exposure

- CYP1A1: Cytochrome P450 monooxygenase, xenobiotic metabolizing enzyme, bioactivation, Ah-Receptor regulated
- COX-2: Cyclooxygenase, key enzyme for production of prostaglandins involved in inflammation, upregulated in cancer cells
- IL-8: Interleukin 8, chemoattractant peptide for neutrophils, major mediator of inflammatory response
- HO-1: Hemeoxygenase 1, essential enzyme in heme catabolism, protect cells against oxidative injury. HO-1 is a stress-responsive protein and induced by exposure to various forms of oxidative stress

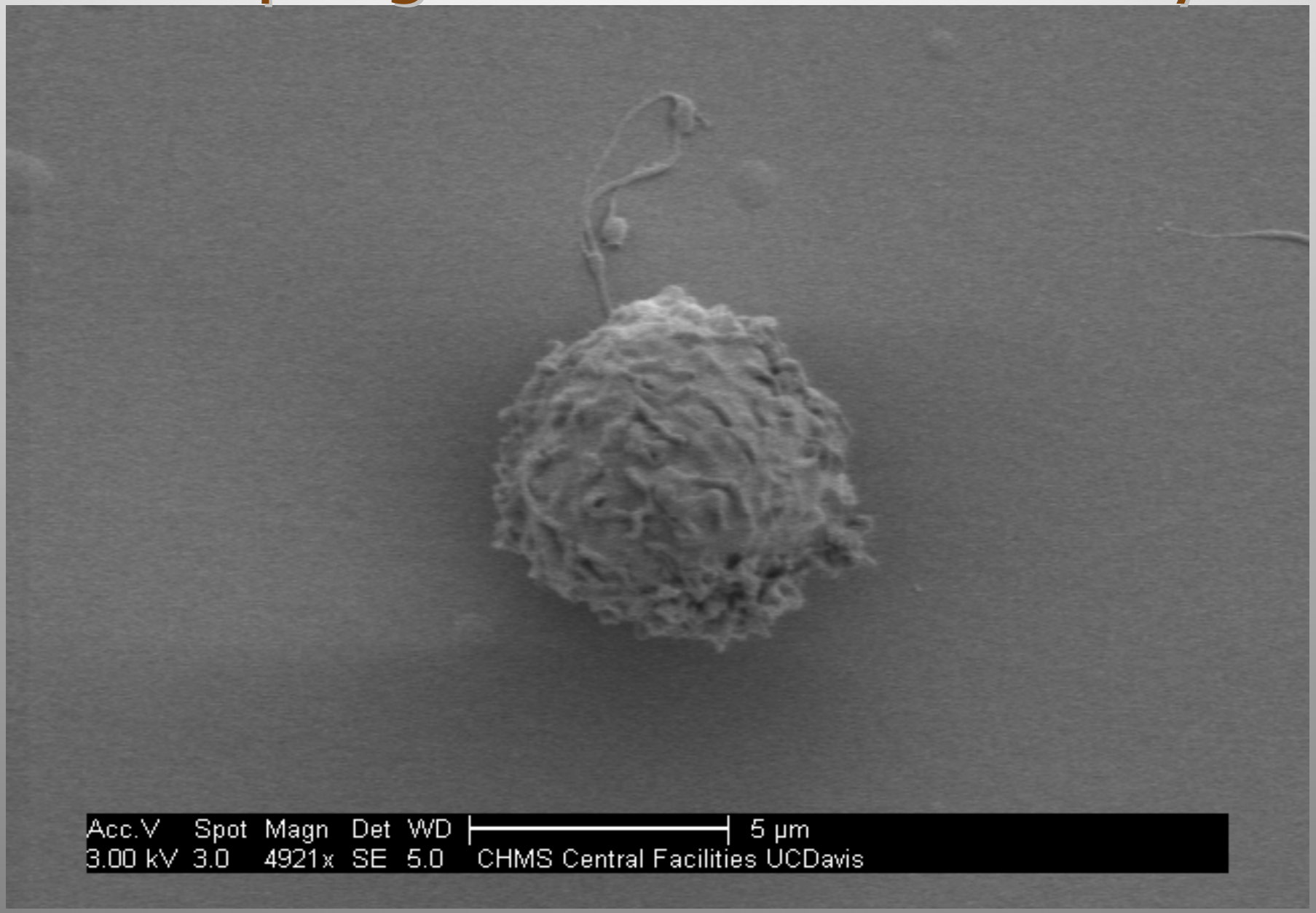
Macrophage Model



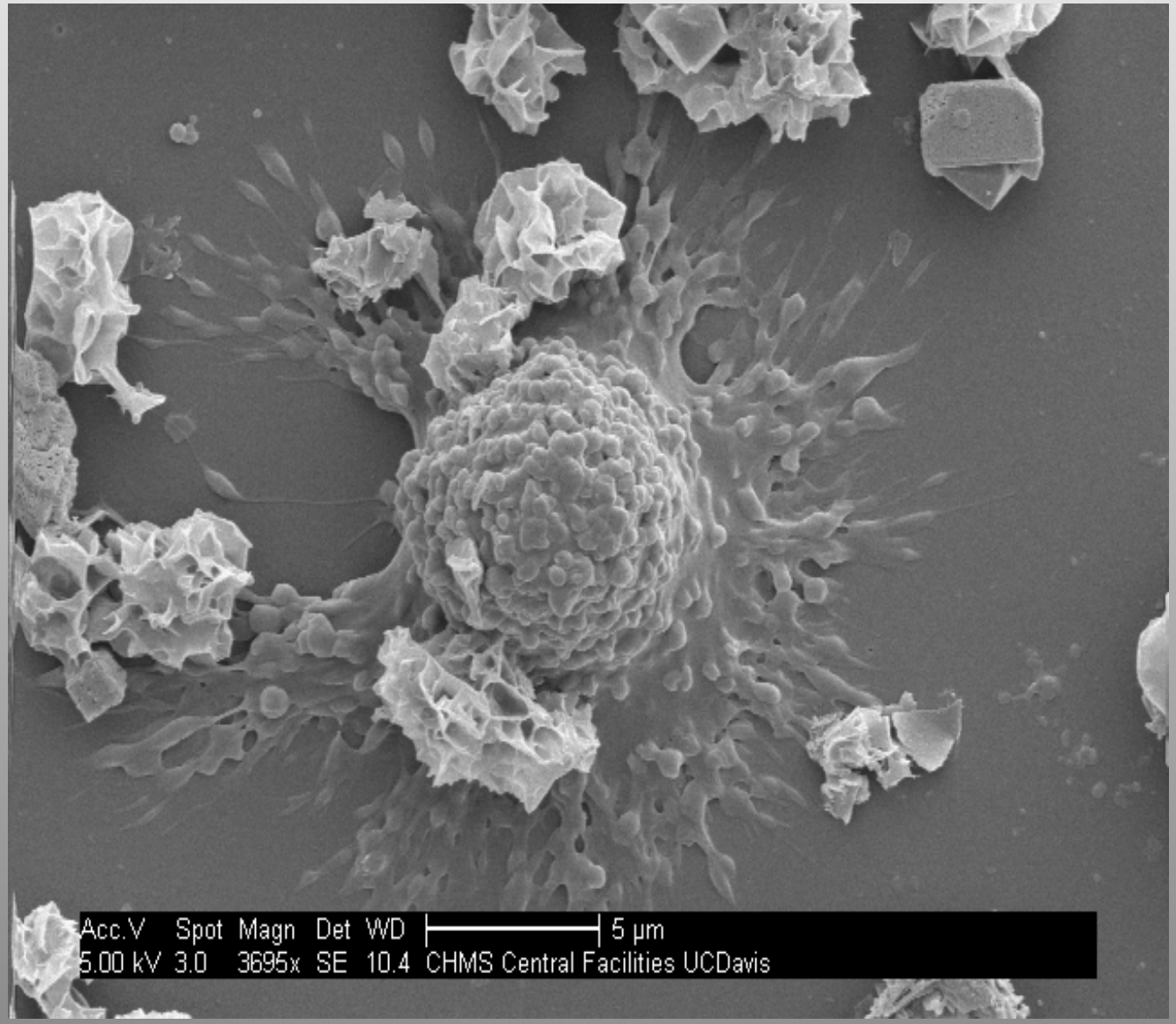
Macrophage Model

- Macrophage as a sensor of danger in the host
- Macrophages have remarkable plasticity and change their physiology in response to environmental stimuli
- Foam cell formation as precursor of CVD

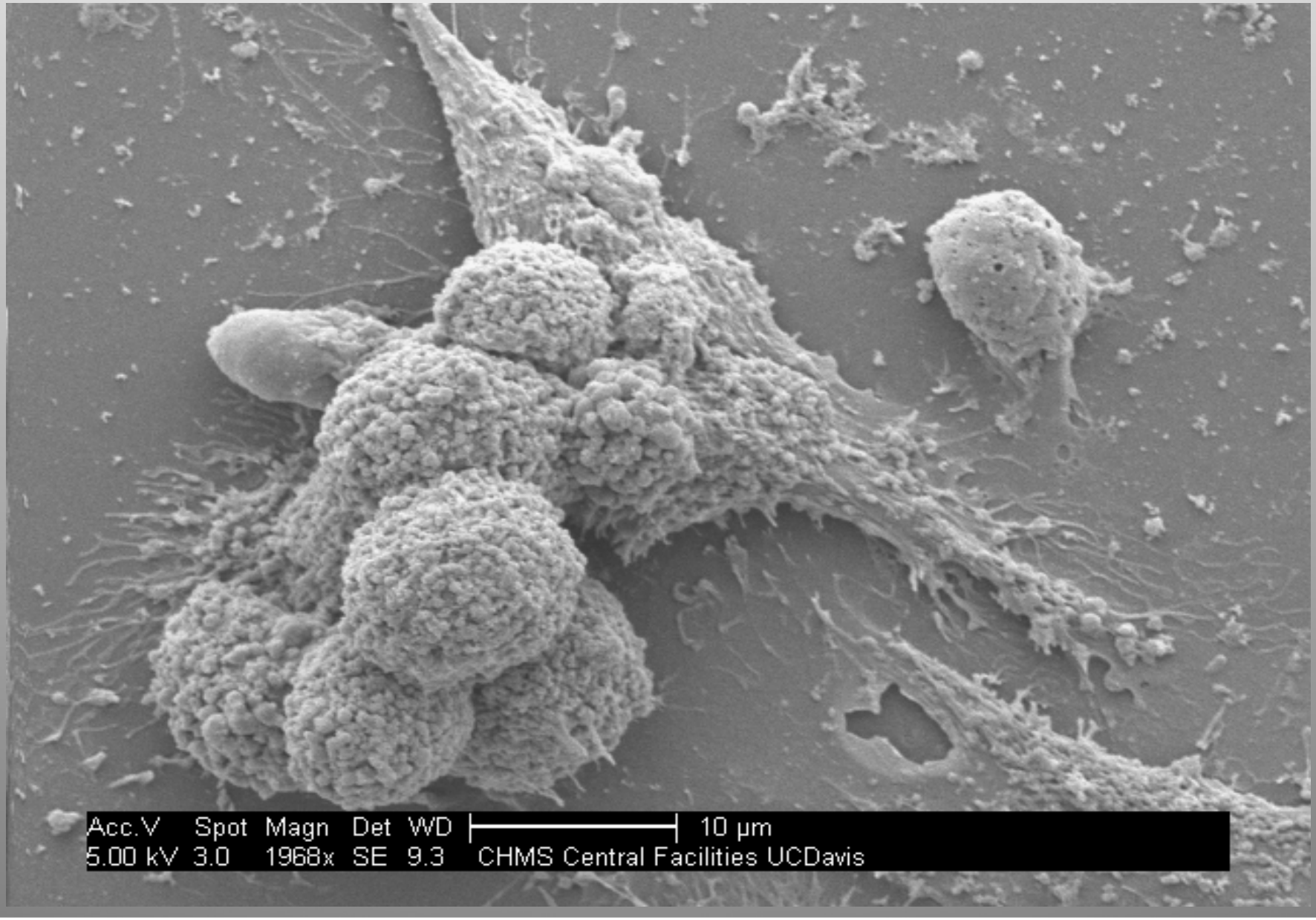
Macrophage model-U937 Monocyte



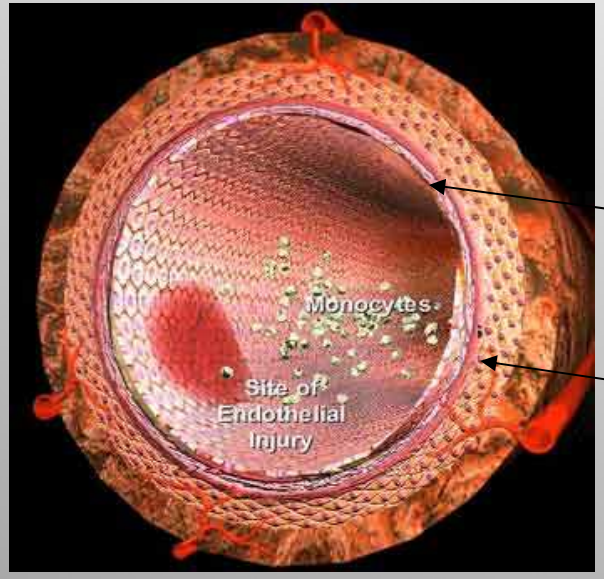
U937 macrophages



Activated U937 macrophages (Foam cells)



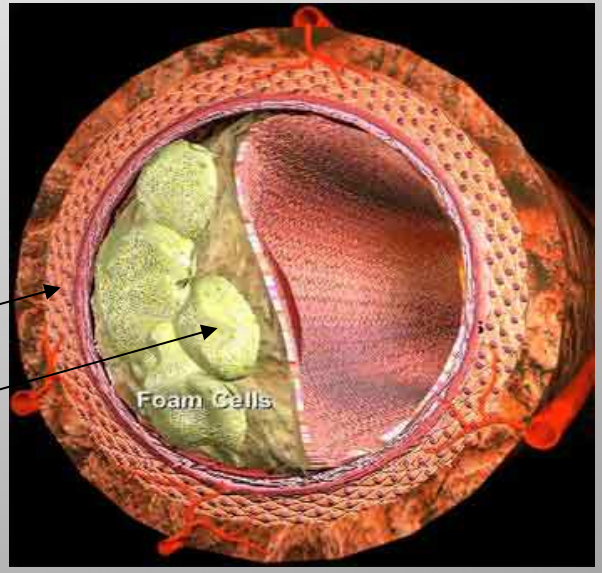
Formation of foam cells



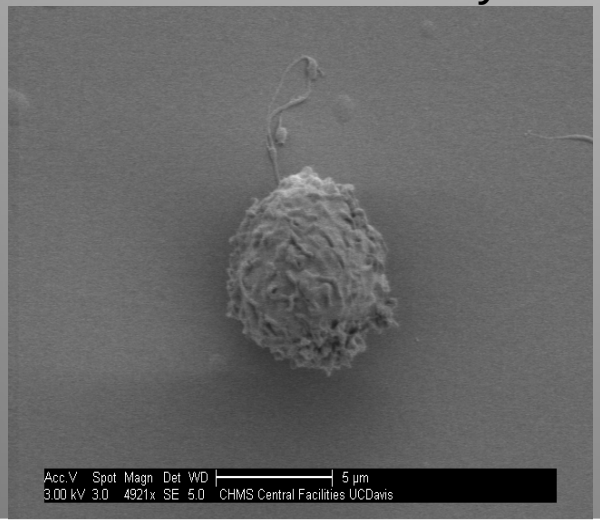
Swelling of the intima in the wall of the artery which pushes the endothelium into the lumen of the artery

Arterial wall

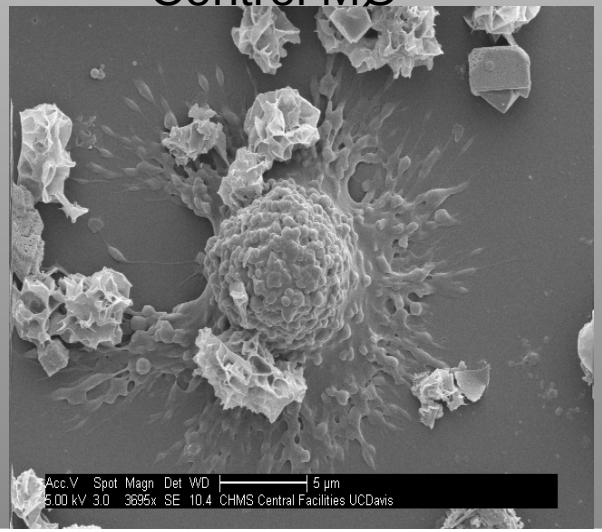
Foam cells



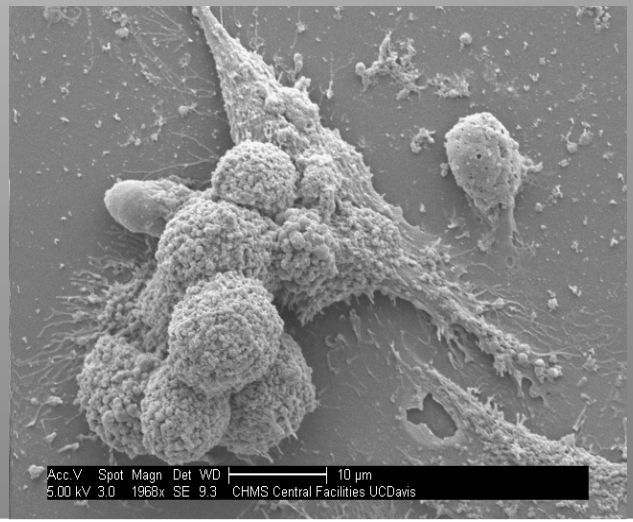
Control U937monocyte



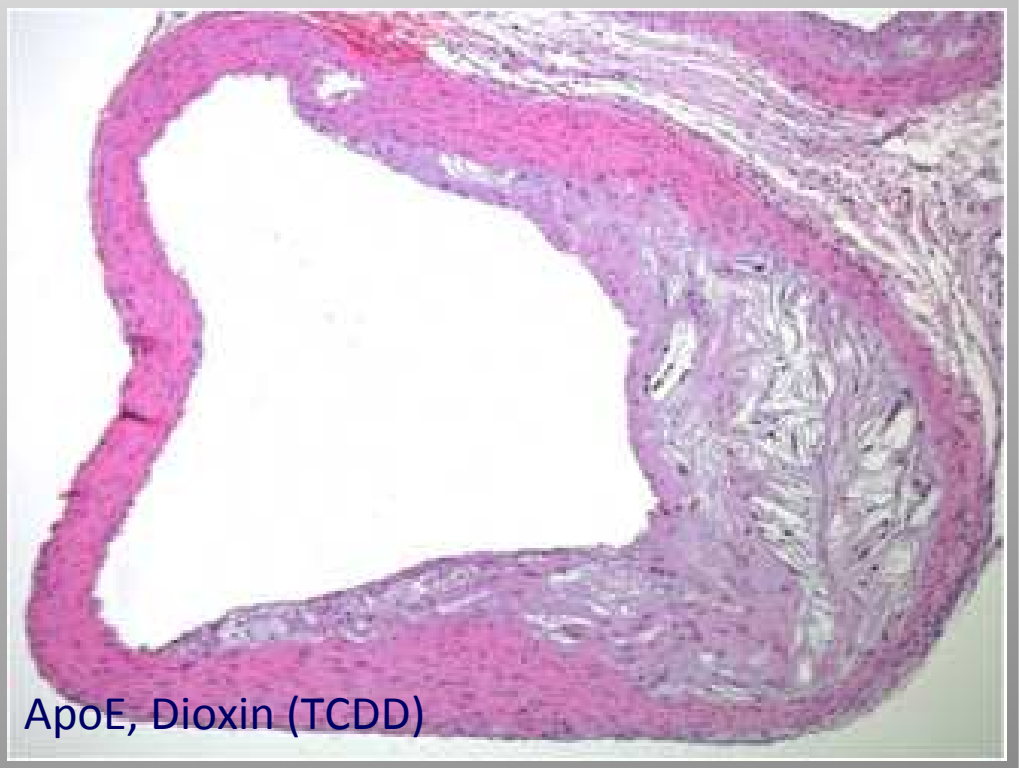
Control MØ



Dioxin MØ

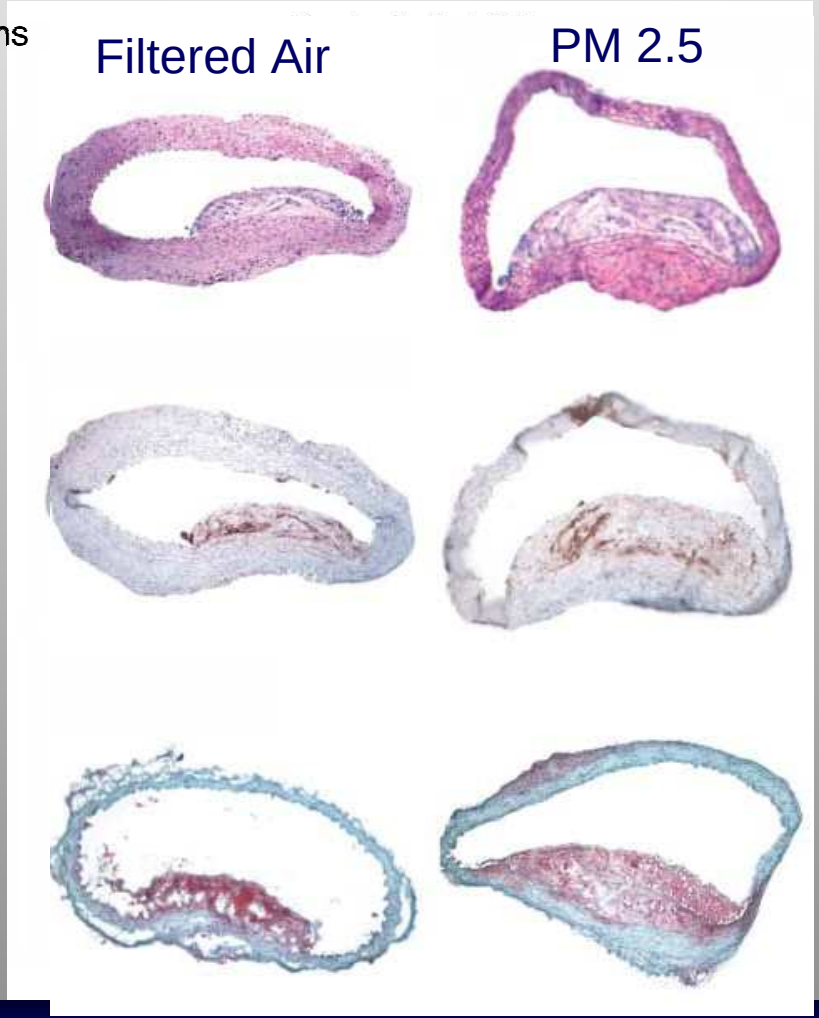


Development of atherosclerotic lesions in ApoE mice



Long-term Air Pollution Exposure and Acceleration of Atherosclerosis and Vascular Inflammation in an Animal Model

6 hrs/day, 5 days/wk x 6 months
Mean levels only 15.2 μg/m³



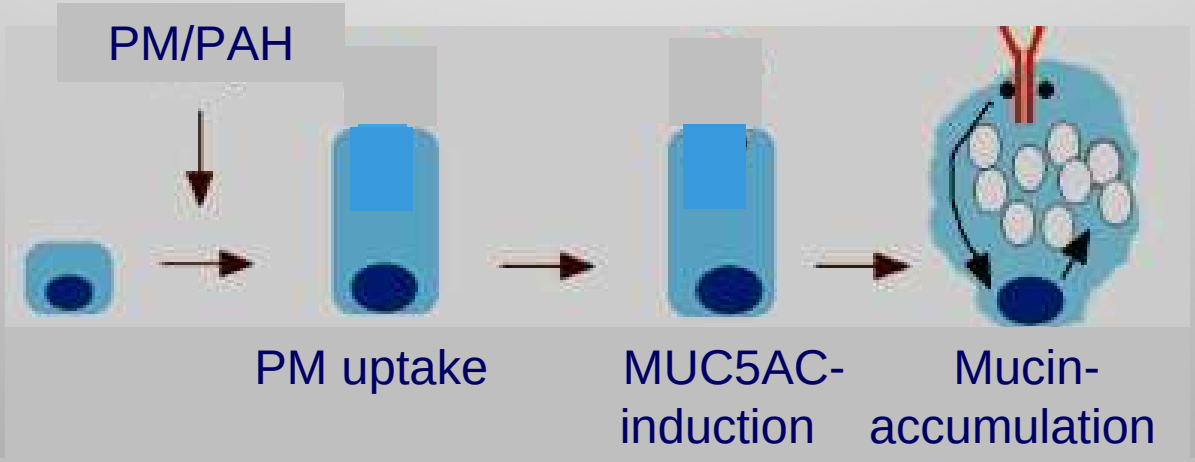
Air pollution exposed mice developed more ATHEROSCLEROSIS

JAMA. 2005;294:3003-3010

Lung Clara Cell Model

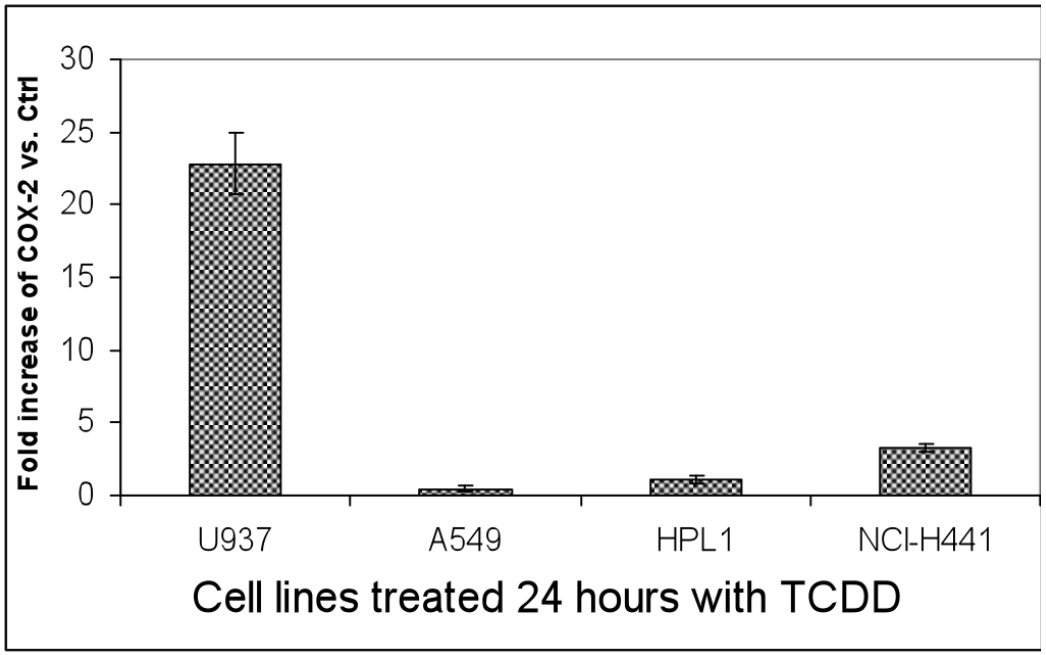
- NCI H441 Clara cell characteristics
- Primary secretory cells in small airways
- Clara cells can differentiate into mucin producing Goblet cells
- Pathological feature of asthma and COPD for adverse health effects

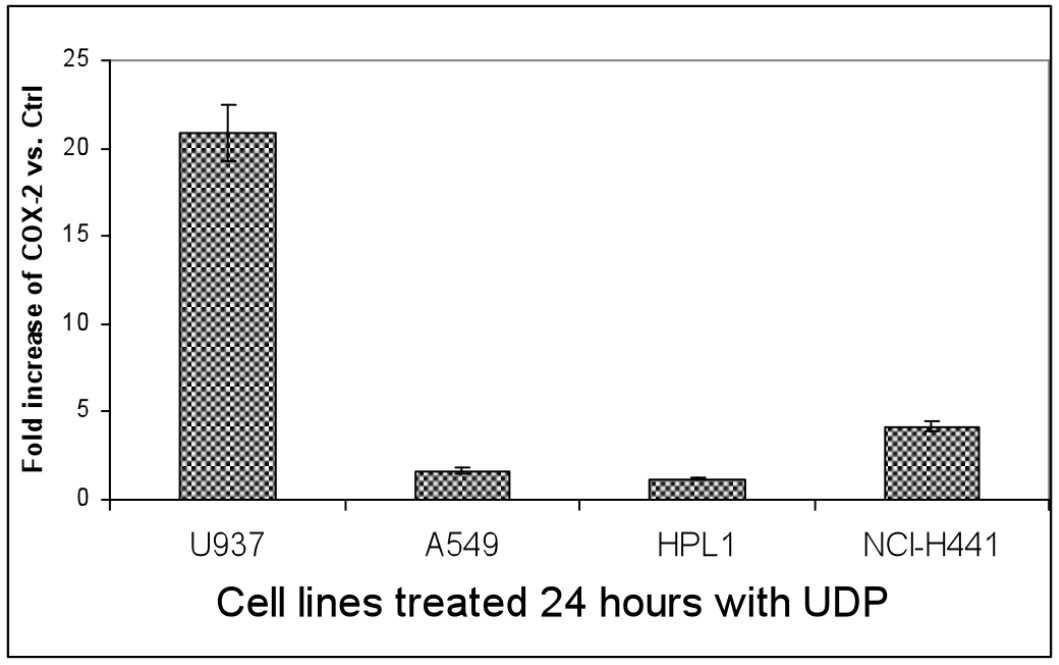
NCI H441 Lung Clara cell model



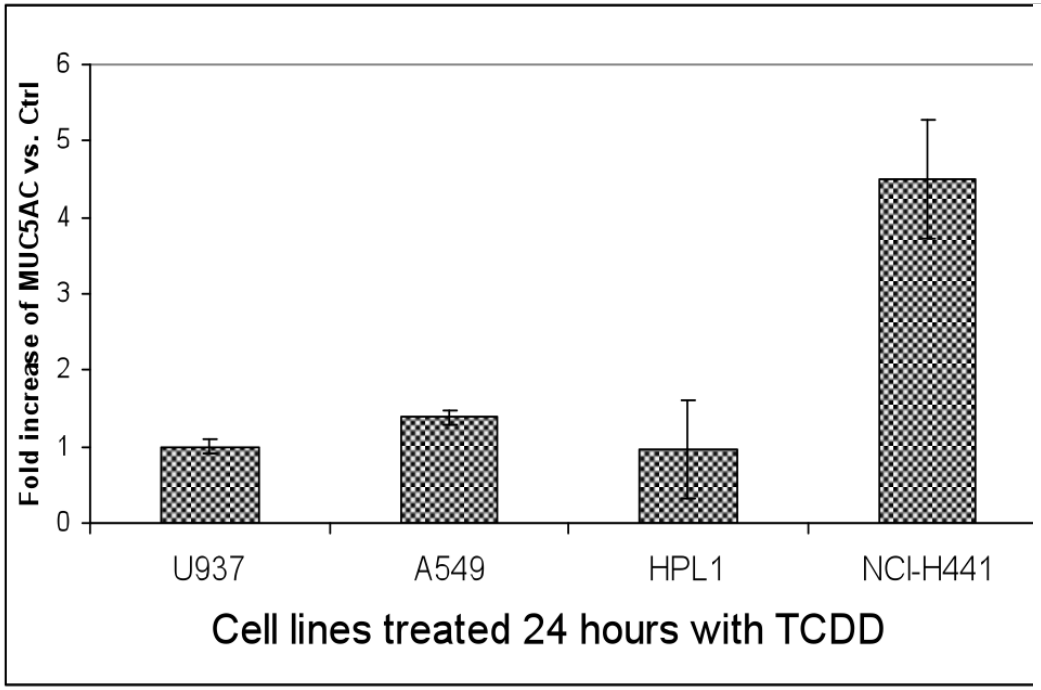
- Chronic obstructive pulmonary disease (COPD)
- Emphysema
- Asthma

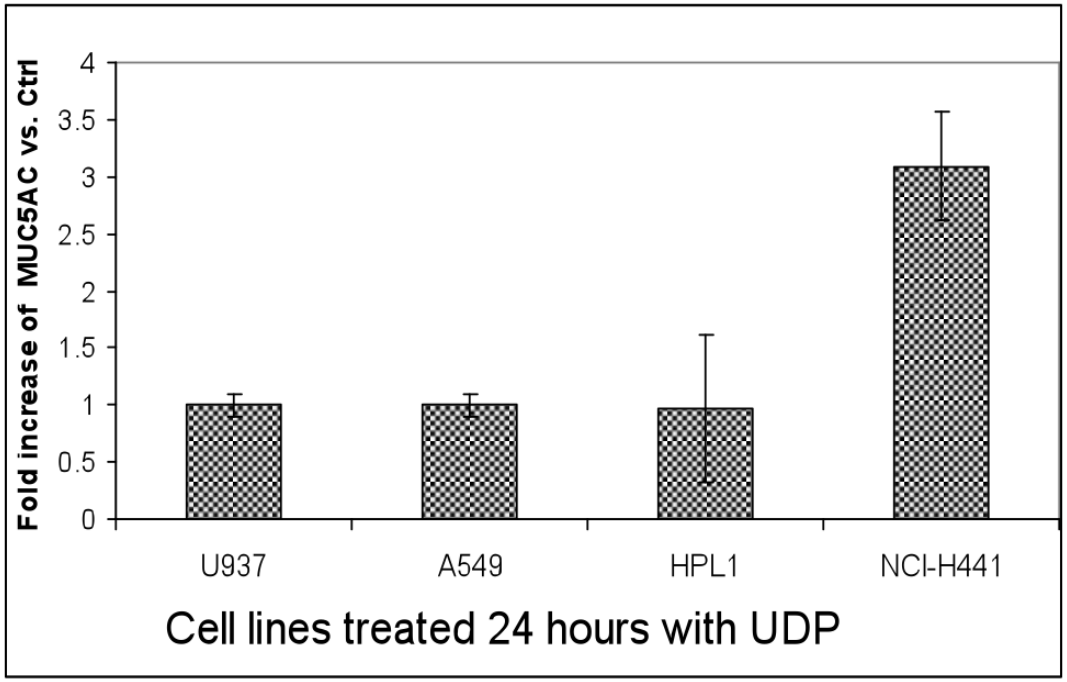
COX-2 Response of various cell lines





MUC5AC Response of various cell lines





Cooking

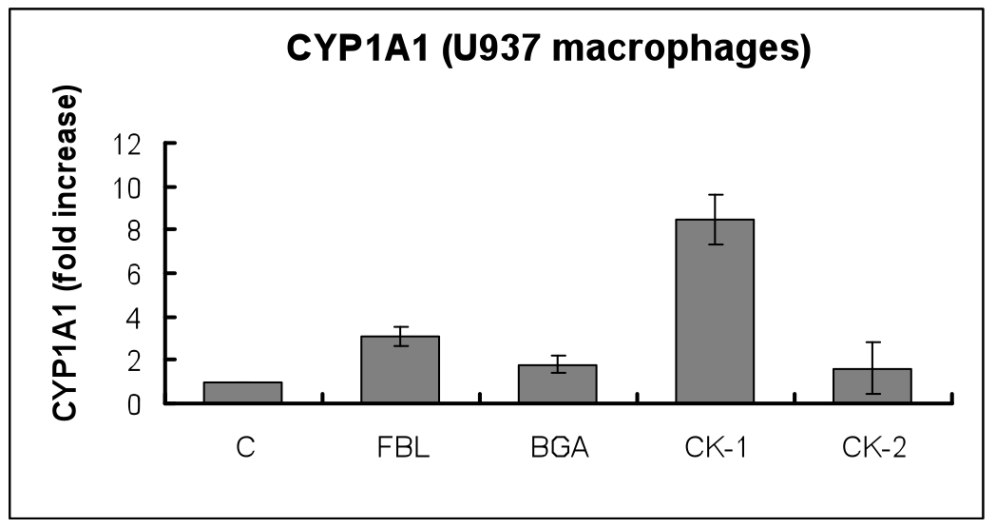
Cooking

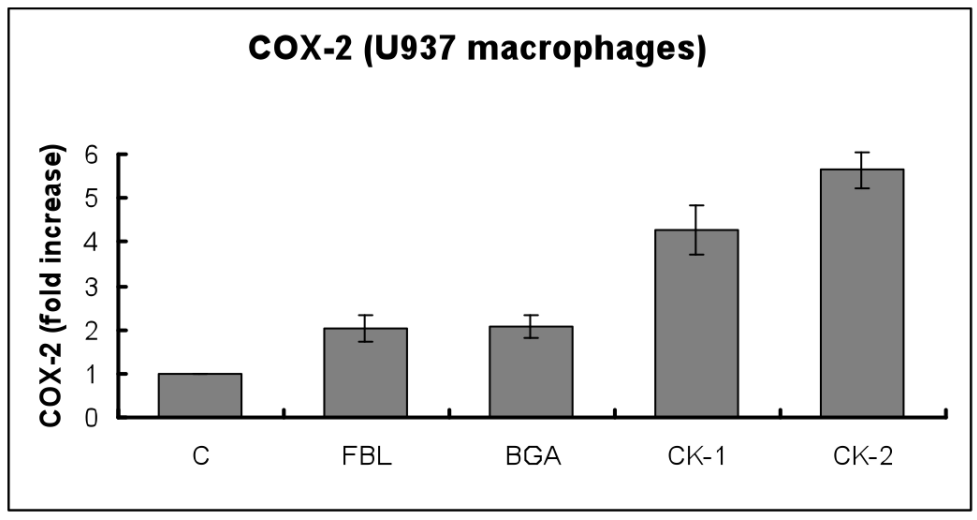
Cooking PM Sampling

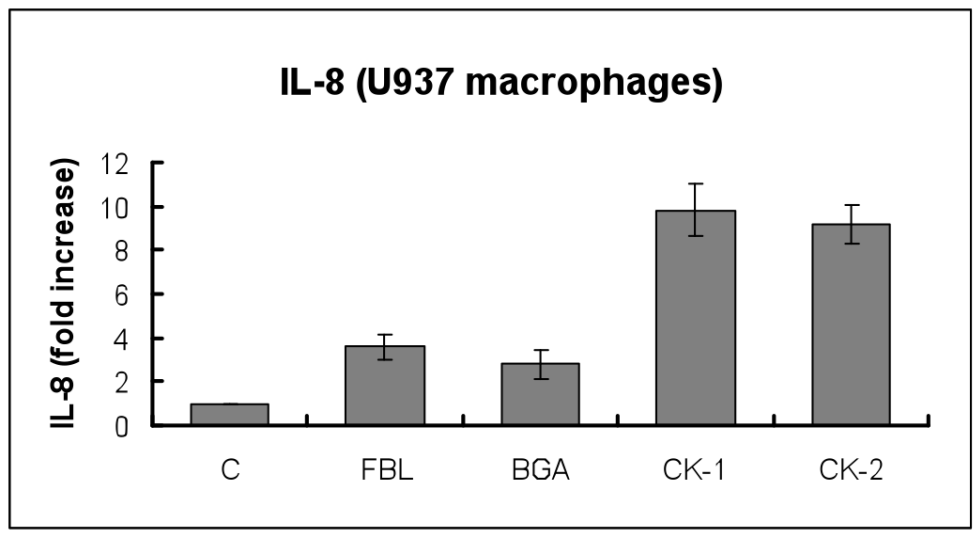
Stir-fry

Oven

Effect of cooking PM in Macrophages







C: Vehicle control

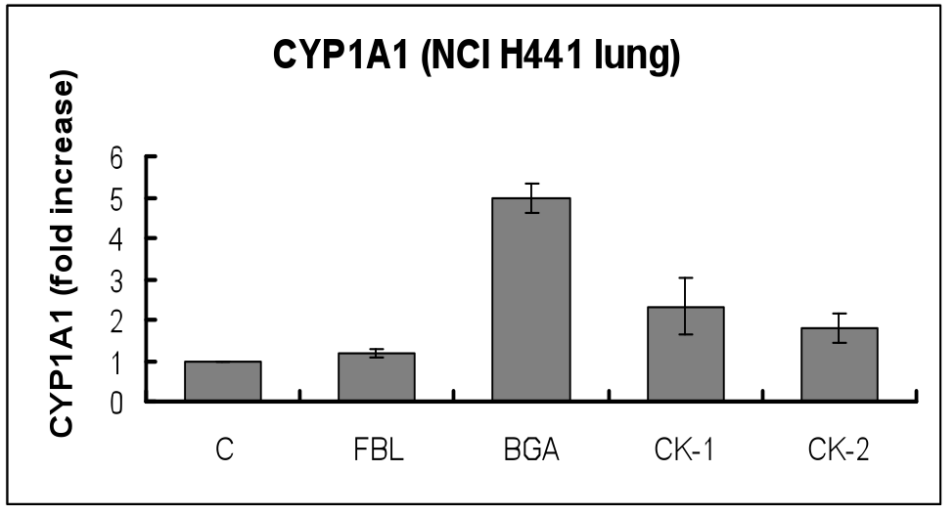
FBL-2: Field Filter Blank

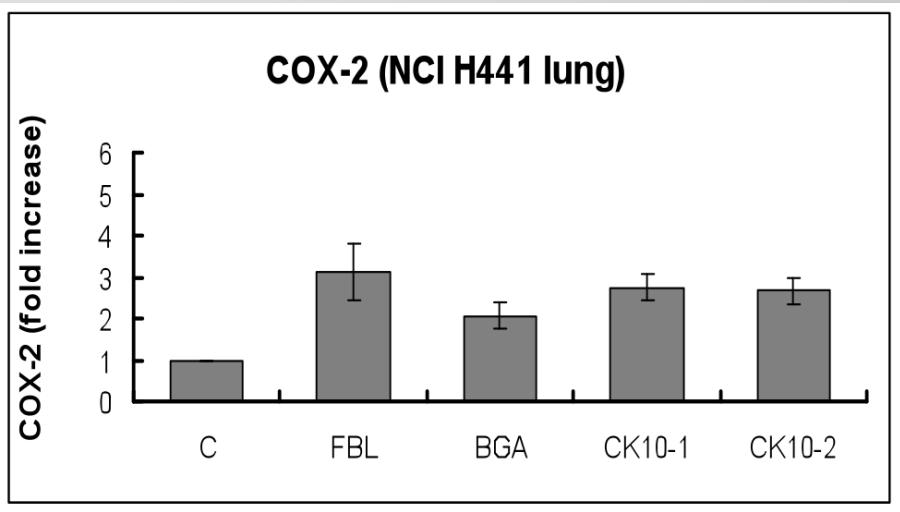
BGA: Background Air PM10 filter

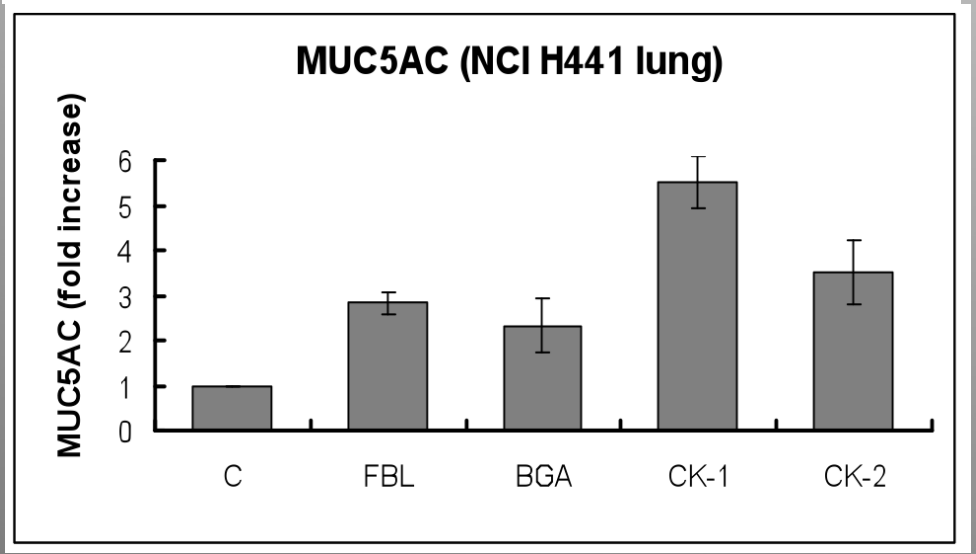
CK-1:Stir-fry cooking

CK-2: Oven cooking

Effect of cooking PM in Lung Cells







C: Vehicle control

FBL-2: Field Filter Blank

BGA: Background Air PM10 filter

CK-1:Stir-fry cooking

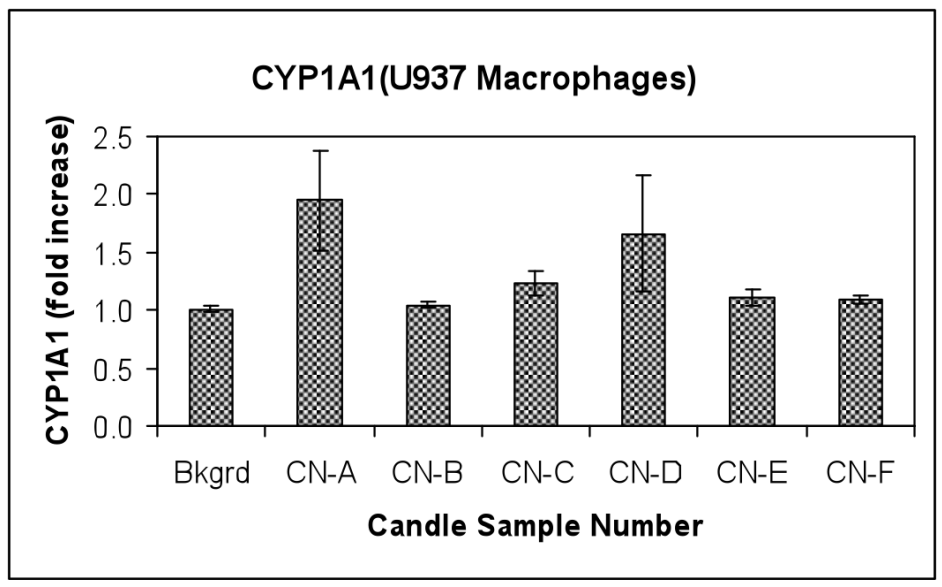
CK-2: Oven cooking

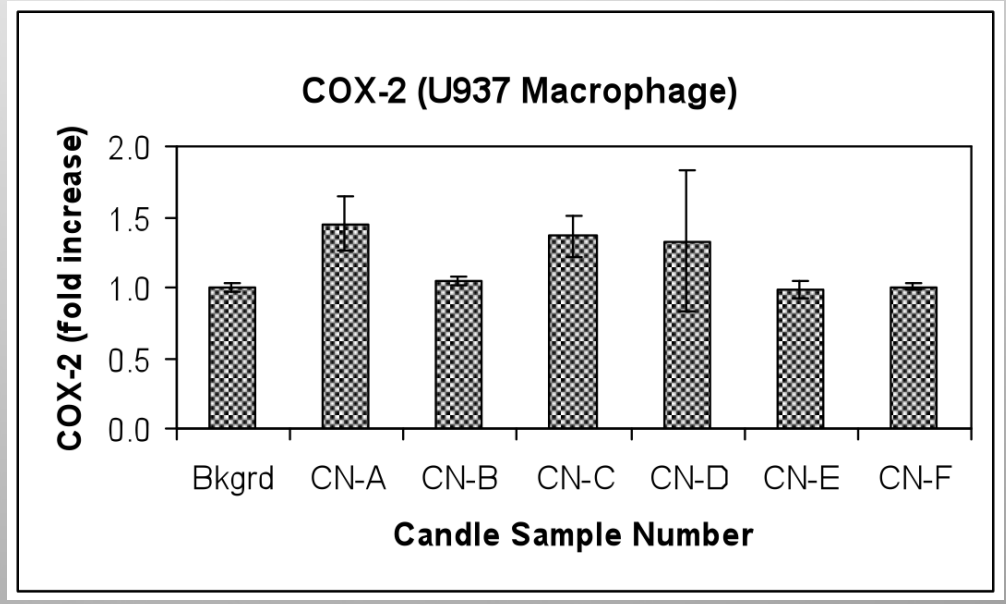
Candle

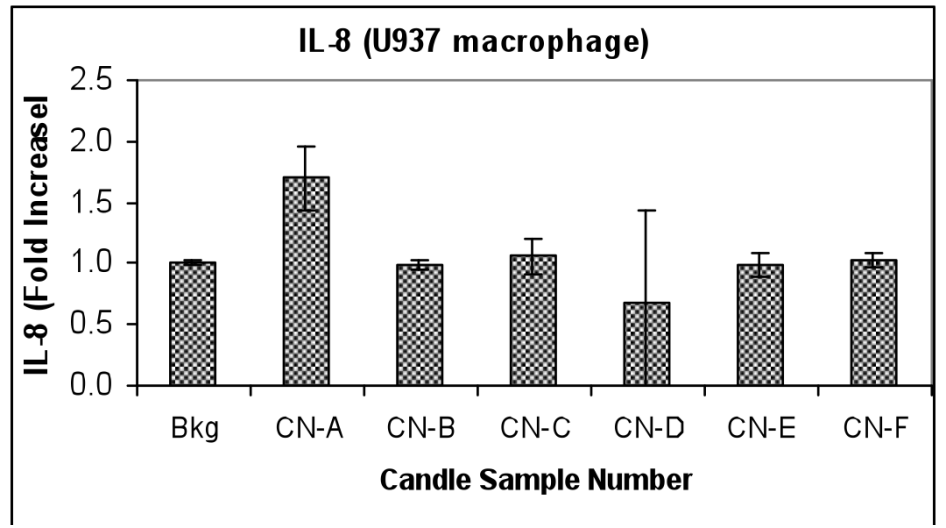
Variety of Candles

Candle ID	Name	Characteristics	Color/Style	Size	Store	Manufactured In
A	Tindra Ljuv	Scented Candle	Red, Filled Glass	2.5" dia X 1.8"	2	China
B	3" Fresh Cotton	Scented Candle	White, Pillar	2 3/4" (D) X 3"(H)	3	India
C	Botanica Candles	Scented and Handcrafted Candle, Mango Papaya	Orange Red, Pillar	260 g, 2 7/8" (D) X 3" (H)	4	Hong Kong
D	Paula Deen	Scented Candle, Pear Honey	Green, Filled Glass (Container)	16 oz (453 g)	1	USA
E	Scented Gold Ring Pink	Scented Gold Ring, Religious	Flamingo, Filled glass	2 1/4" (D) x 8 " (H)	2	USA
F	Renew	Hand poured, Jasmine & Tea Leaf	Coral, Pillar	8.8 oz/250 g, 2.75" x 3 "	4	Vietnam

Effect of candle PM in Macrophages



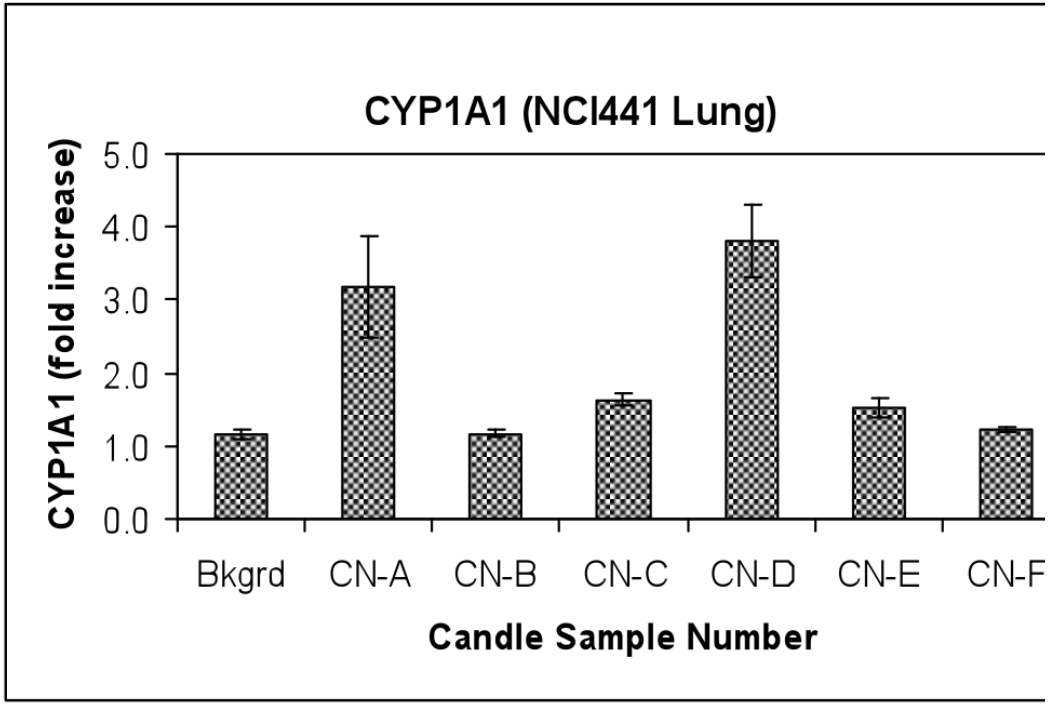


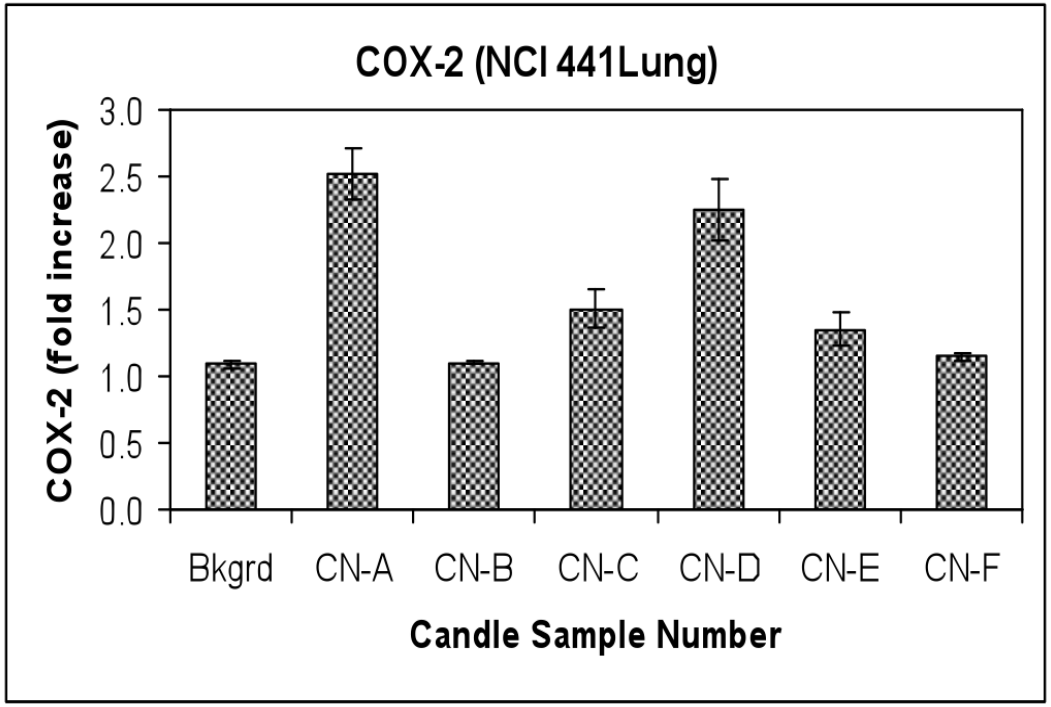


Bkgrd: Background Air

CN-A to CN-F: Candle samples

Effect of candle PM in Lung cells

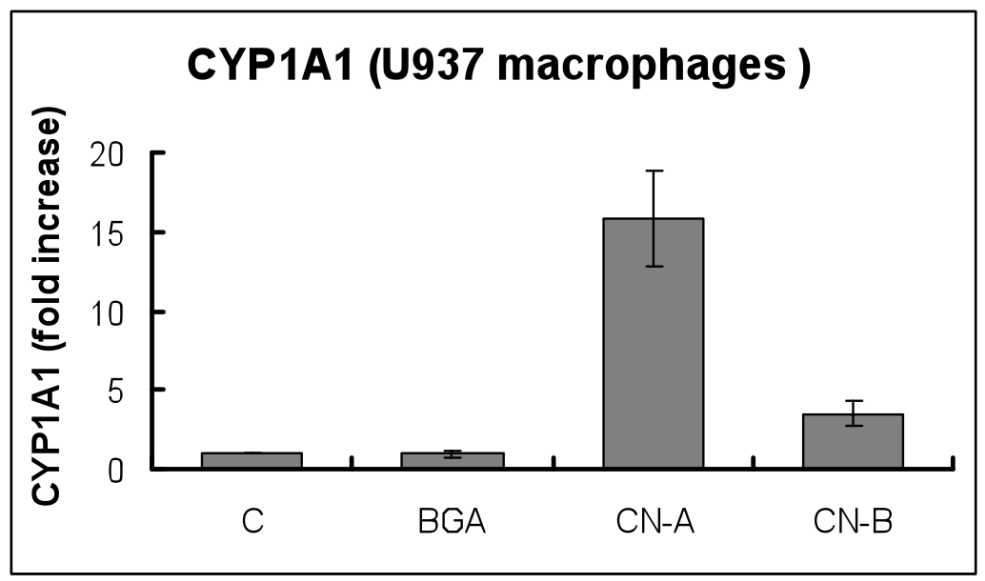


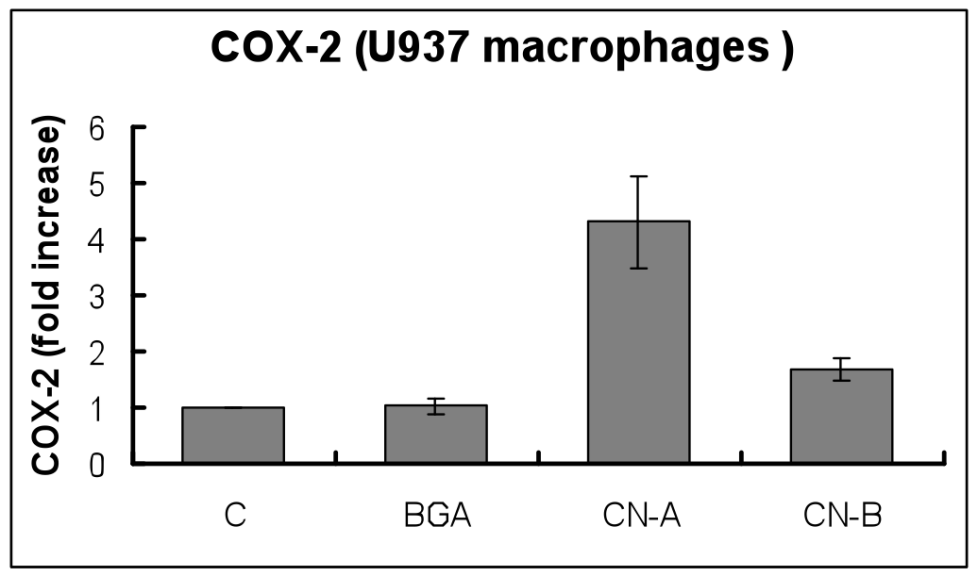


Bkgrd: Background Air

CN-A to CN-F: Candle samples

Effect of candle PM Retest



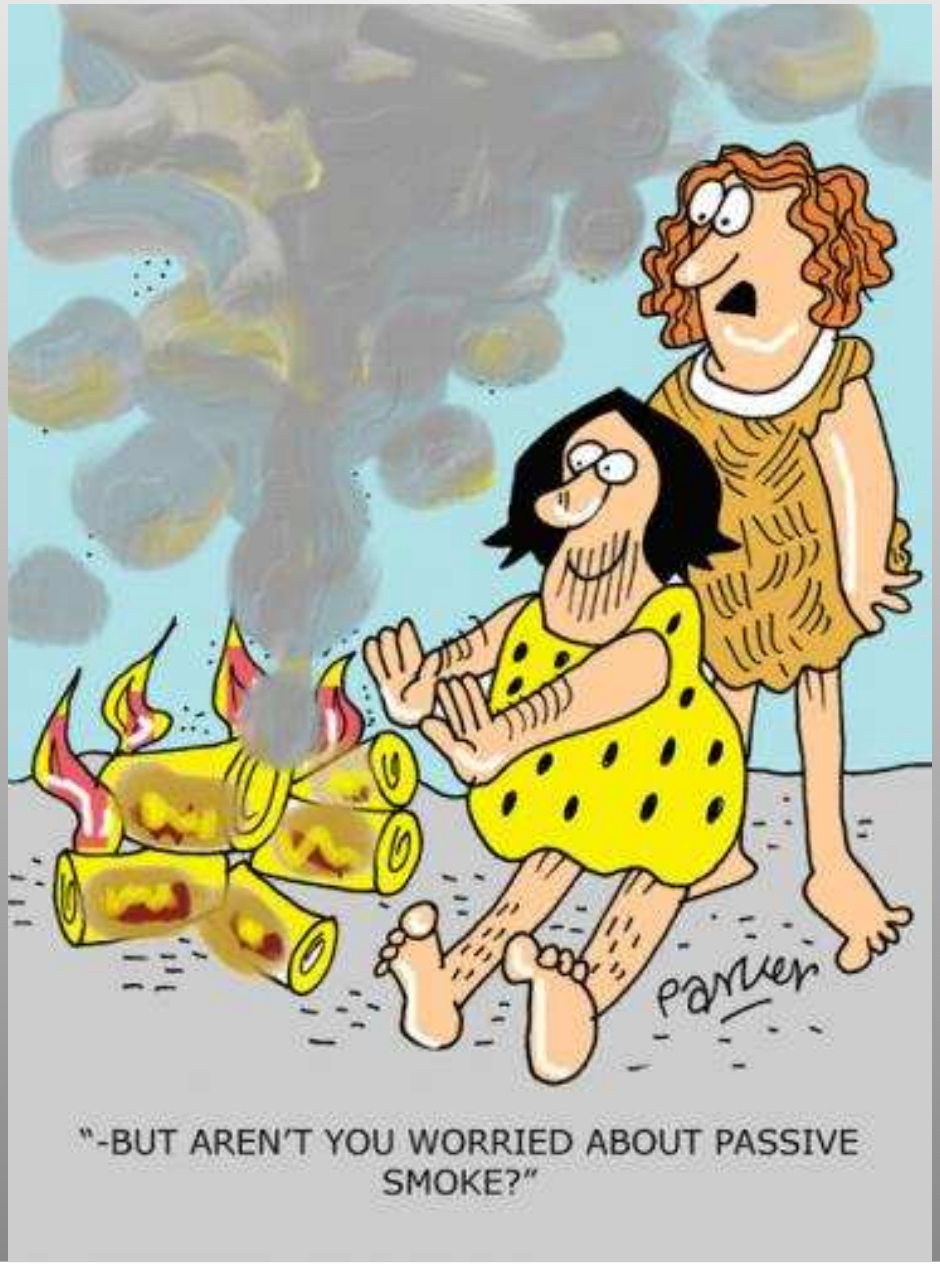


C: Vehicle Control

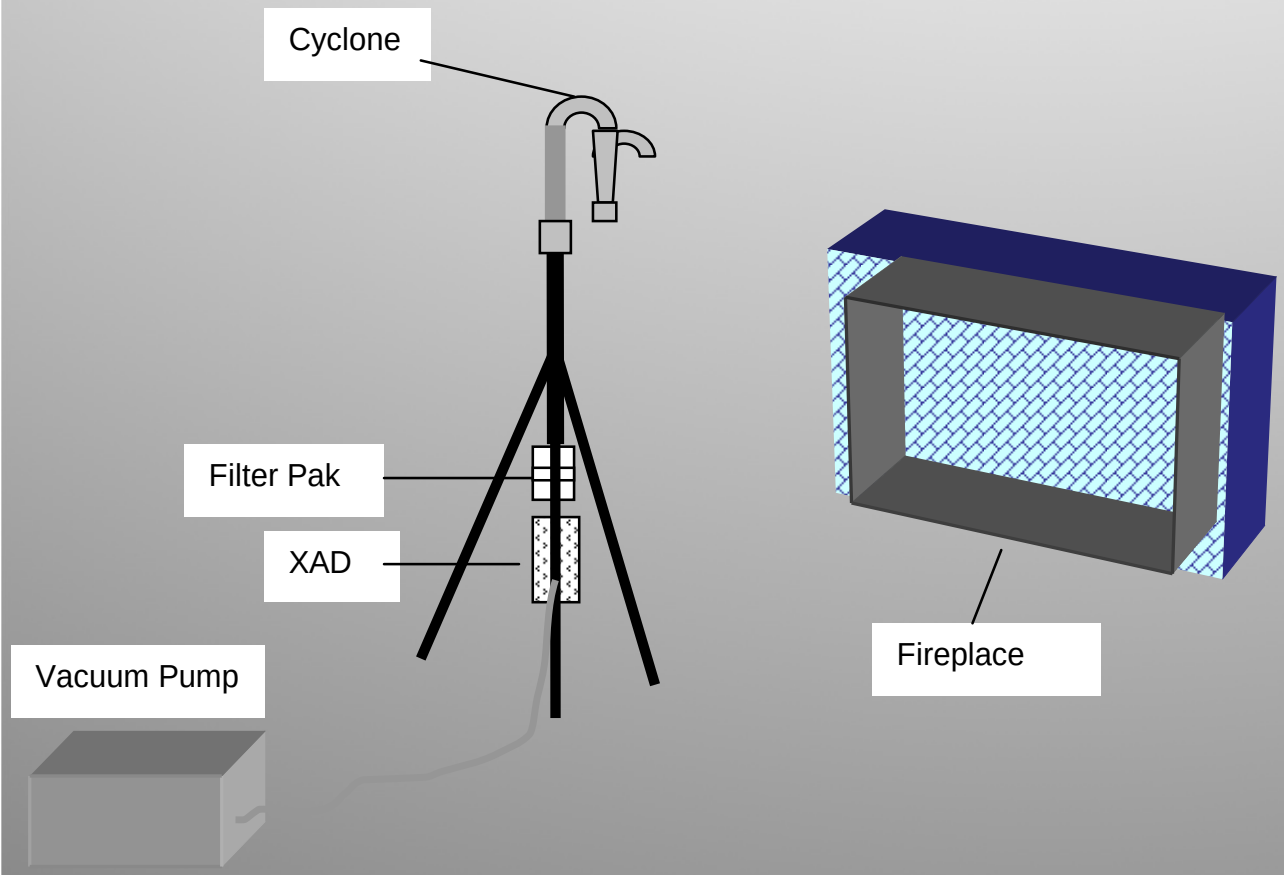
BGA: Background Air

CN-A to CN-B: Candle samples

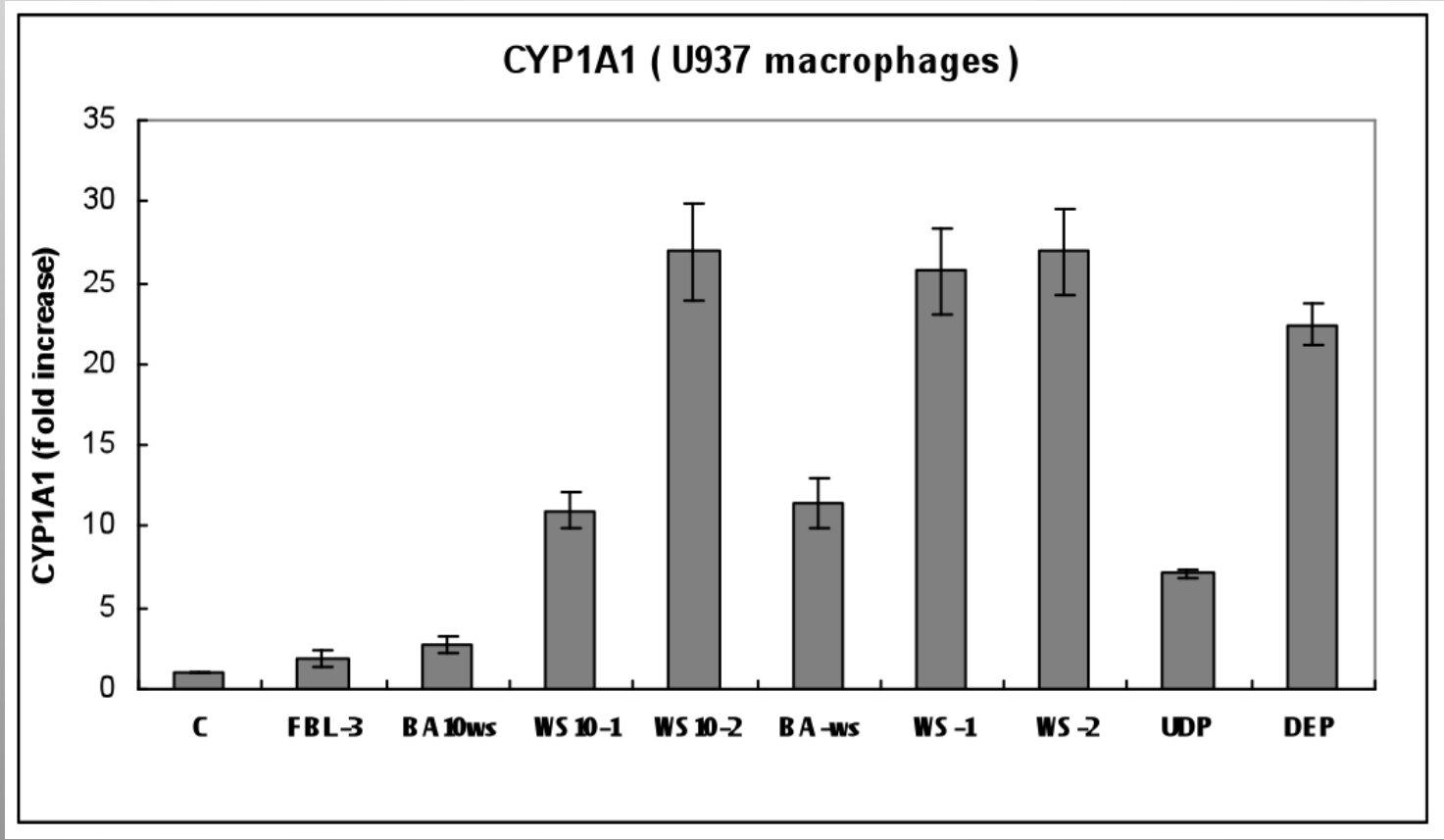
Wood Smoke



Wood Smoke PM Sampling

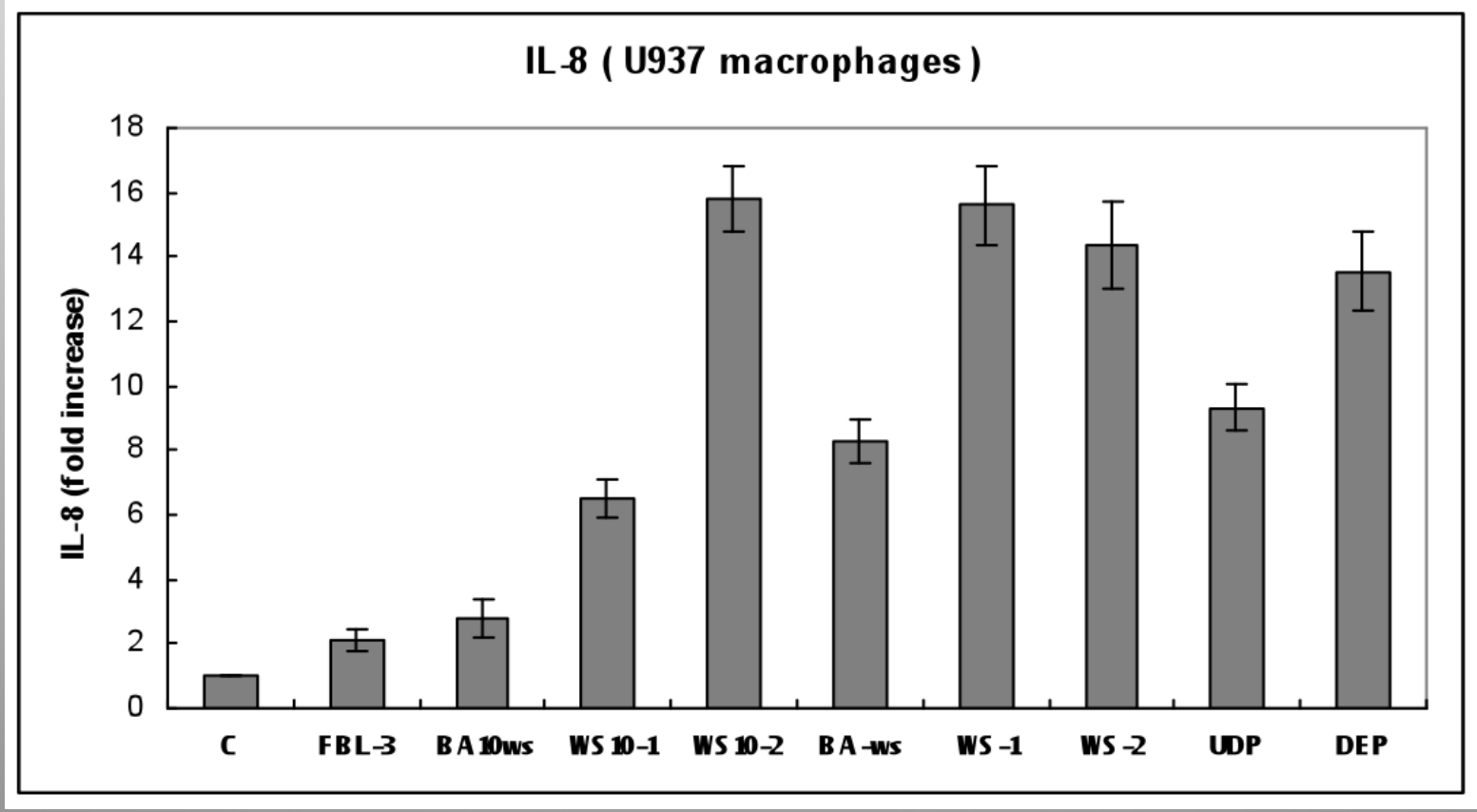


Effect of Wood smoke PM on CYP1A1 in Macrophages



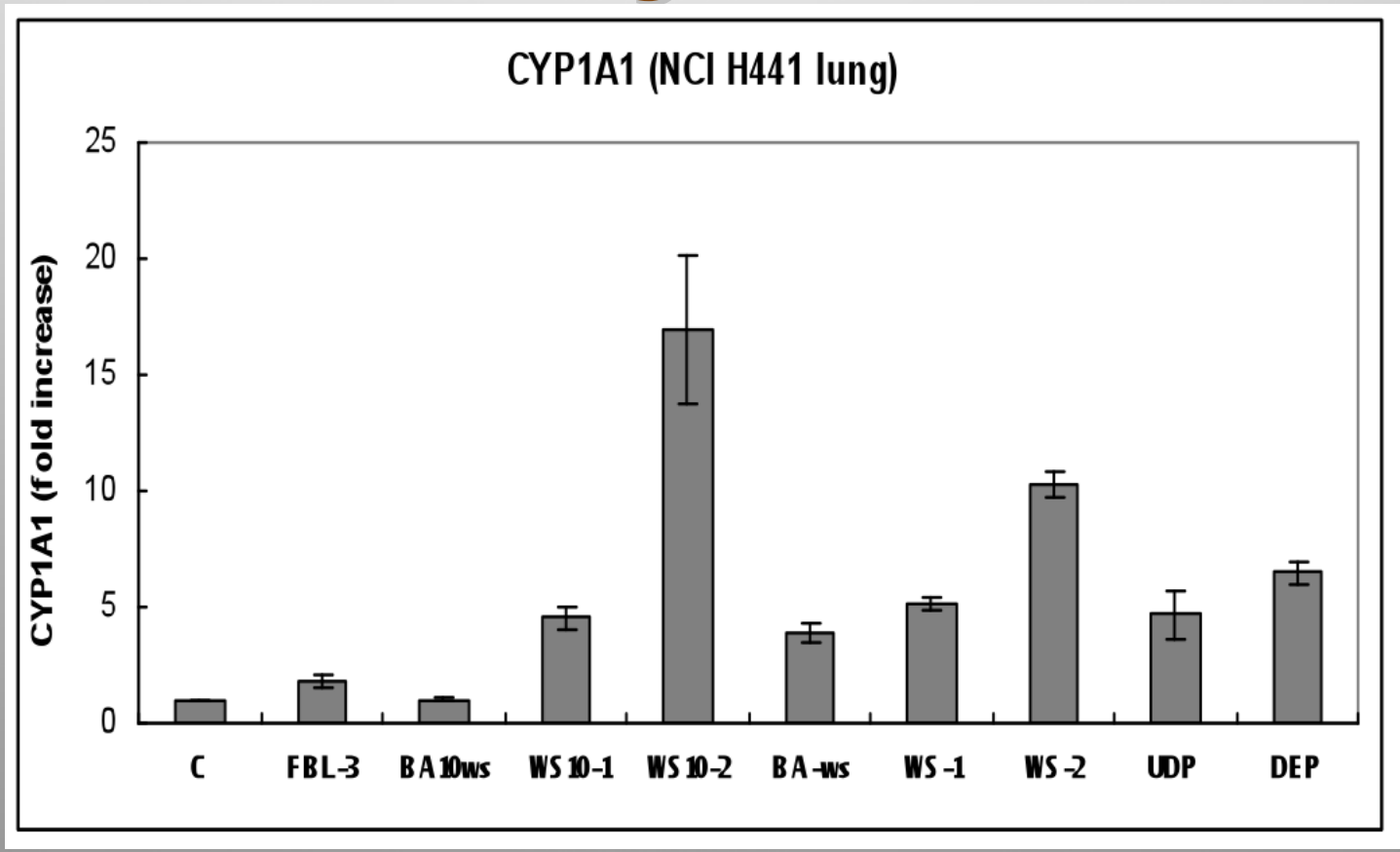
FBL: Filter Blank, BA ws: Background Air PM 2.5, BA10ws: Background Air PM10
WS-1: Woodsmoke PM2.5 run#1, WS10-1: Woodsmoke PM10 run # 1
WS-2: Woodsmoke PM2.5 run#2, WS10-2: Woodsmoke PM10 run # 2
UDP: Urban Dust NIST SRM 1649, DEP: Diesel PM NIST SRM2975

Effect of Wood smoke PM on IL-8 in Macrophages



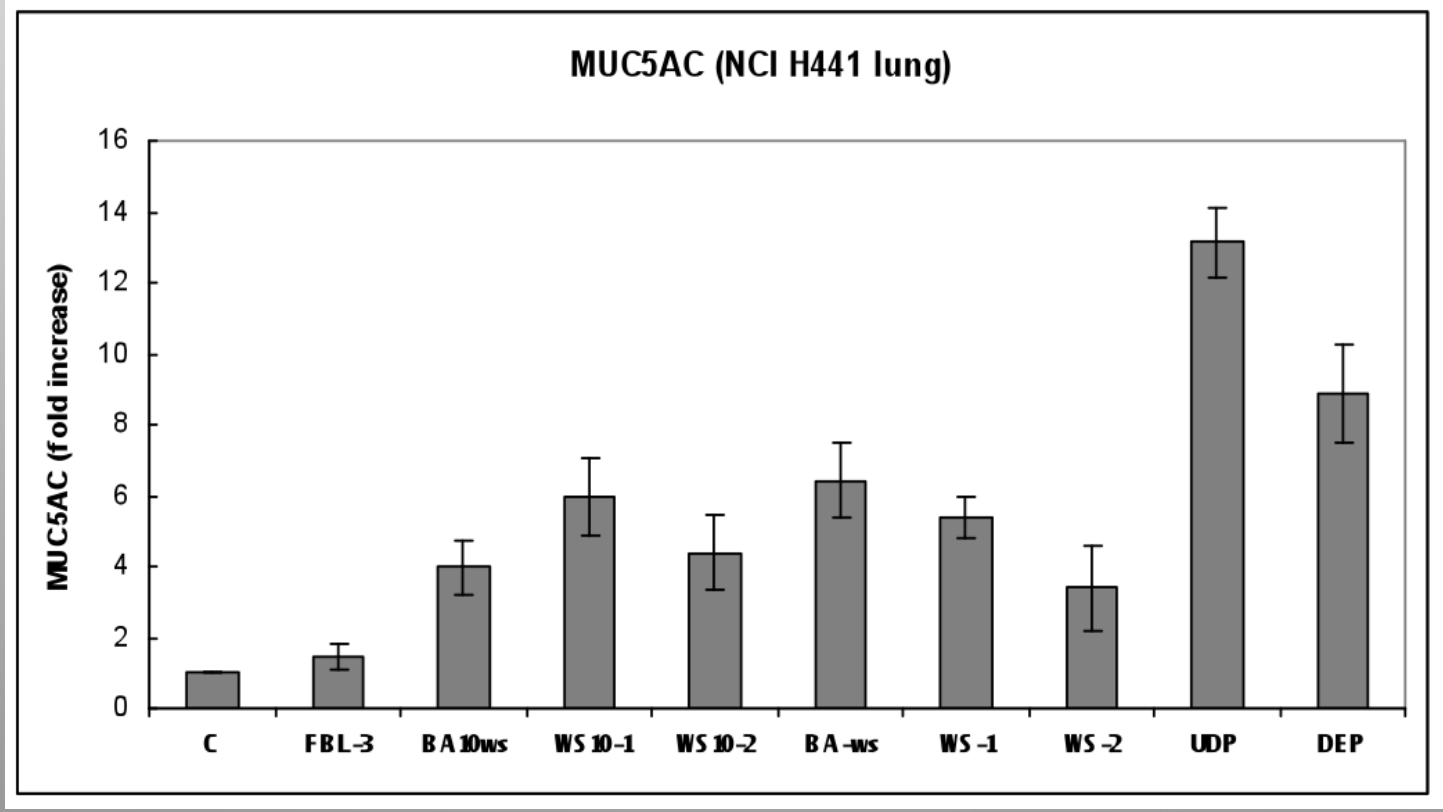
FBL: Filter Blank, BA ws: Background Air PM 2.5, BA10ws: Background Air PM10
WS-1: Woodsmoke PM2.5 run#1, WS10-1: Woodsmoke PM10 run # 1
WS-2: Woodsmoke PM2.5 run#2, WS10-2: Woodsmoke PM10 run # 2
UDP: Urban Dust NIST SRM 1649, DEP: Diesel PM NIST SRM2975

Effect of Wood smoke PM on CYP1A1 in Lung Cells



FBL: Filter Blank, BA ws: Background Air PM 2.5, BA10ws: Background Air PM10
WS-1: Woodsmoke PM2.5 run#1, WS10-1: Woodsmoke PM10 run # 1
WS-2: Woodsmoke PM2.5 run#2, WS10-2: Woodsmoke PM10 run # 2
UDP: Urban Dust NIST SRM 1649, DEP: Diesel PM NIST SRM2975

Effect of Wood smoke PM on MUC5AC in Lung Cells



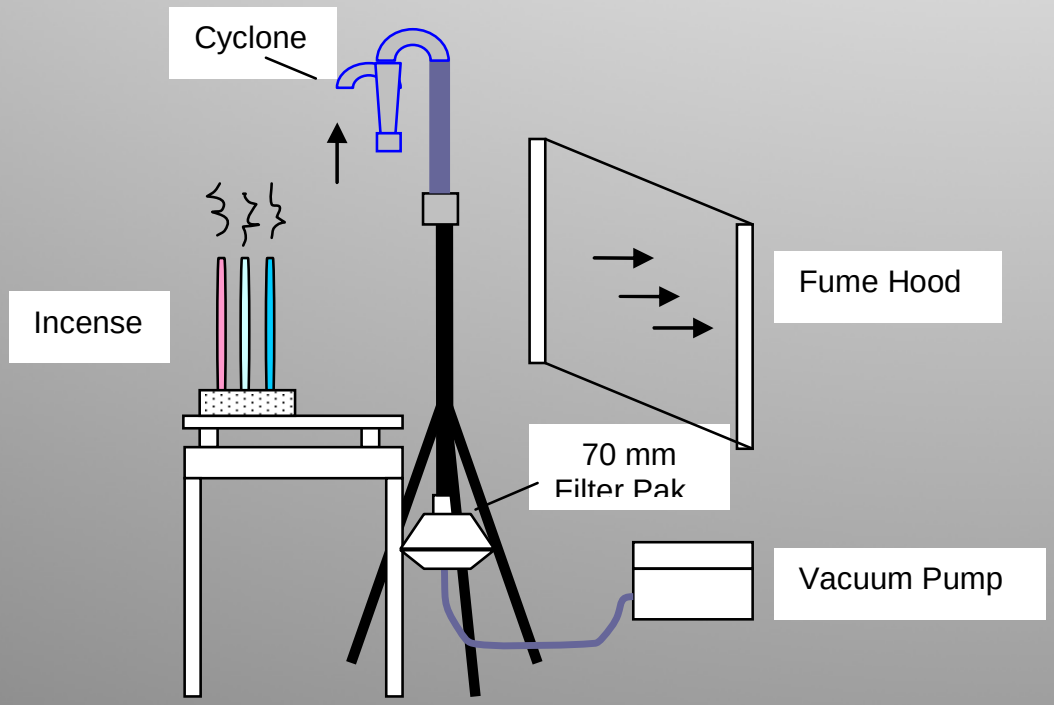
FBL: Filter Blank, BA ws: Background Air PM 2.5, BA10ws: Background Air PM10
WS-1: Woodsmoke PM2.5 run#1, WS10-1: Woodsmoke PM10 run # 1
WS-2: Woodsmoke PM2.5 run#2, WS10-2: Woodsmoke PM10 run # 2
UDP: Urban Dust NIST SRM 1649, DEP: Diesel PM NIST SRM2975

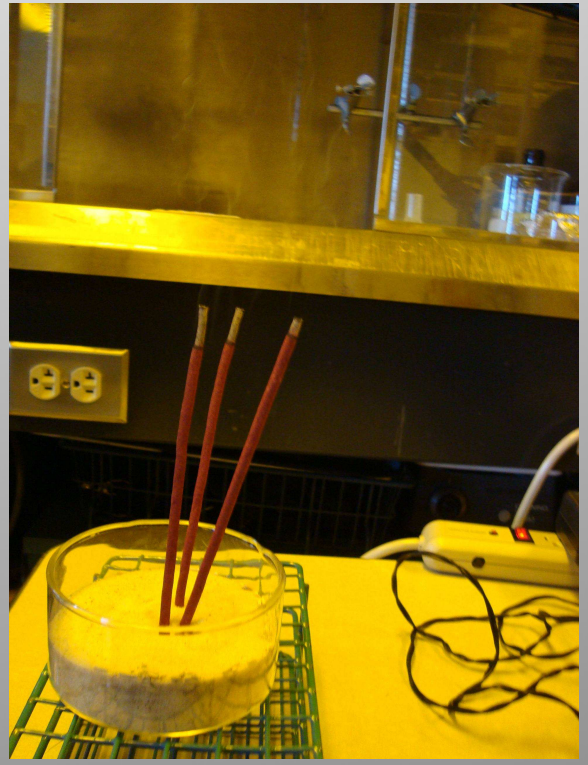
Incense

Variety of Incenses

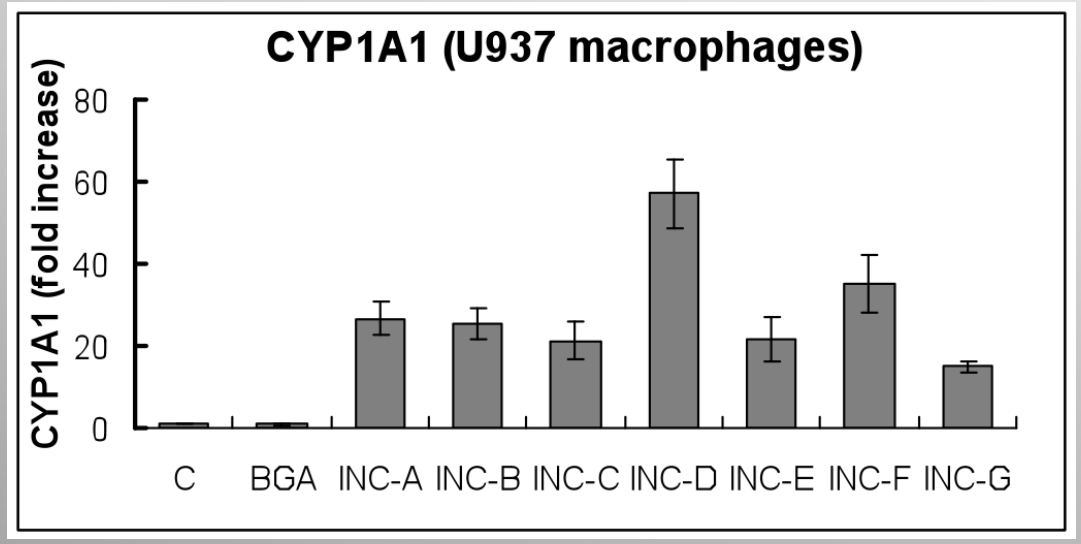
Sample ID	Name	Color	Size	Type	Store	Manufactured
A	Nag Champa	Brown	15g Net weight	Wood core	1	Bangalore, India
B	Pure Tibetan-Herbal Medicine	Brown	N/A	No Core	1	Kathmandu, Nepal
C	Shoyeido Traditional Japanese	Multi	.017 oz per stick, 10 sticks/Pack	No Core	1	Kyoto, Japan
D	Pure Tibetan-Potala	Red	N/A	No Core	1	Nepal
E	Aromatherapy variety	Multi	10 in, 24 sticks/Pack	Wood core	2	Mumbai, India
F	Joss Sticks Mainichikoh	Green	107 sticks	No Core	3	Japan
G	Floral variety	Multi	10 in, 24 sticks/Pack	Wood core	2	Mumbai, India

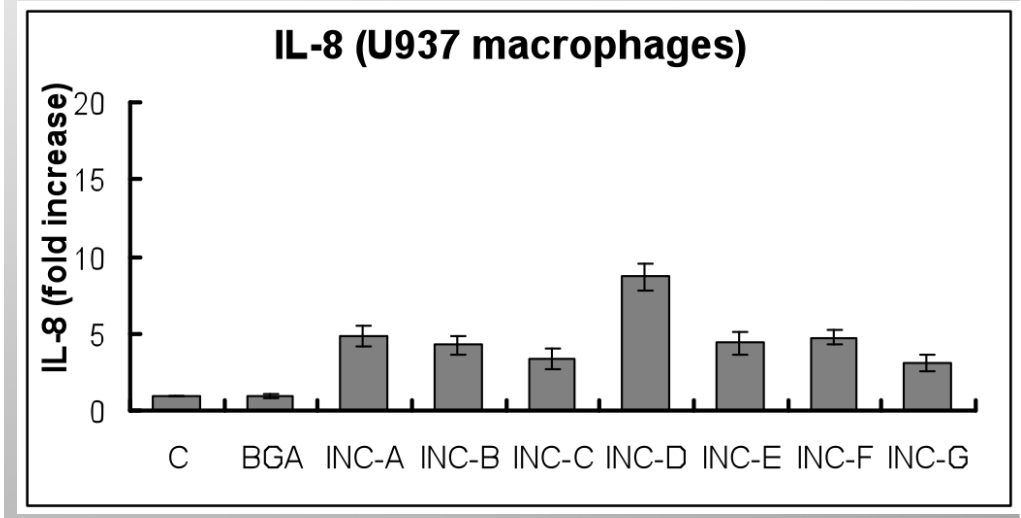
Incense PM Sampling

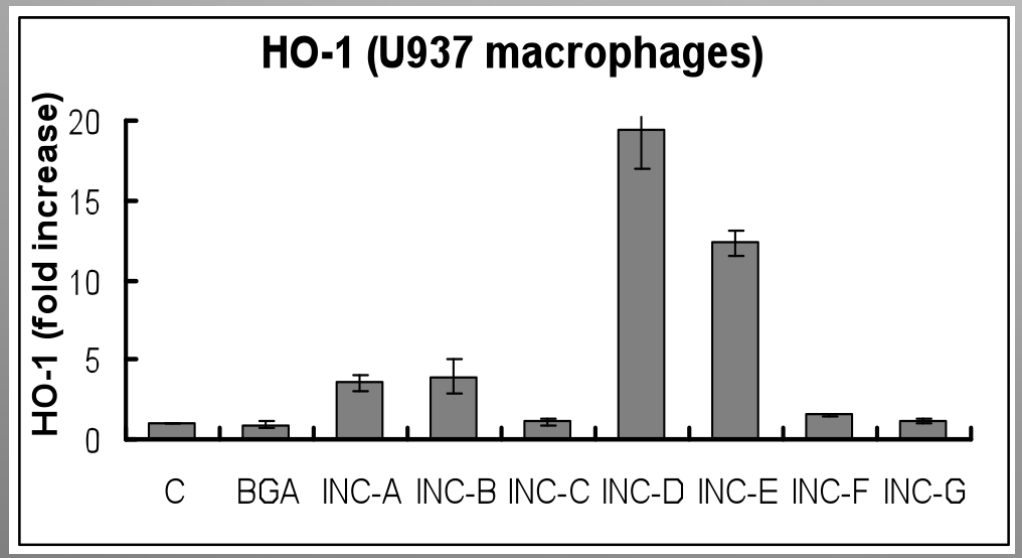




Effect of Incense PM in Macrophages

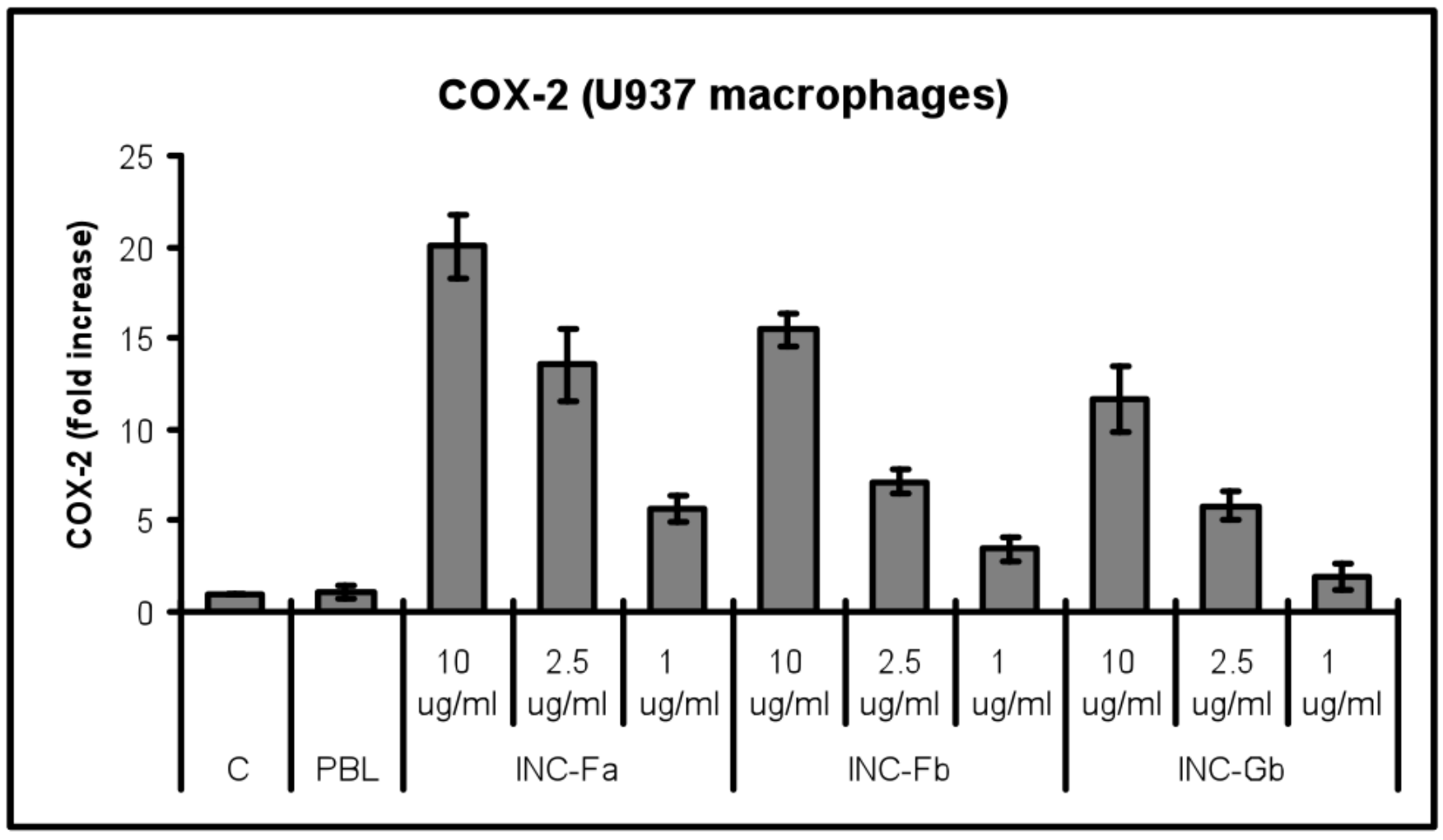






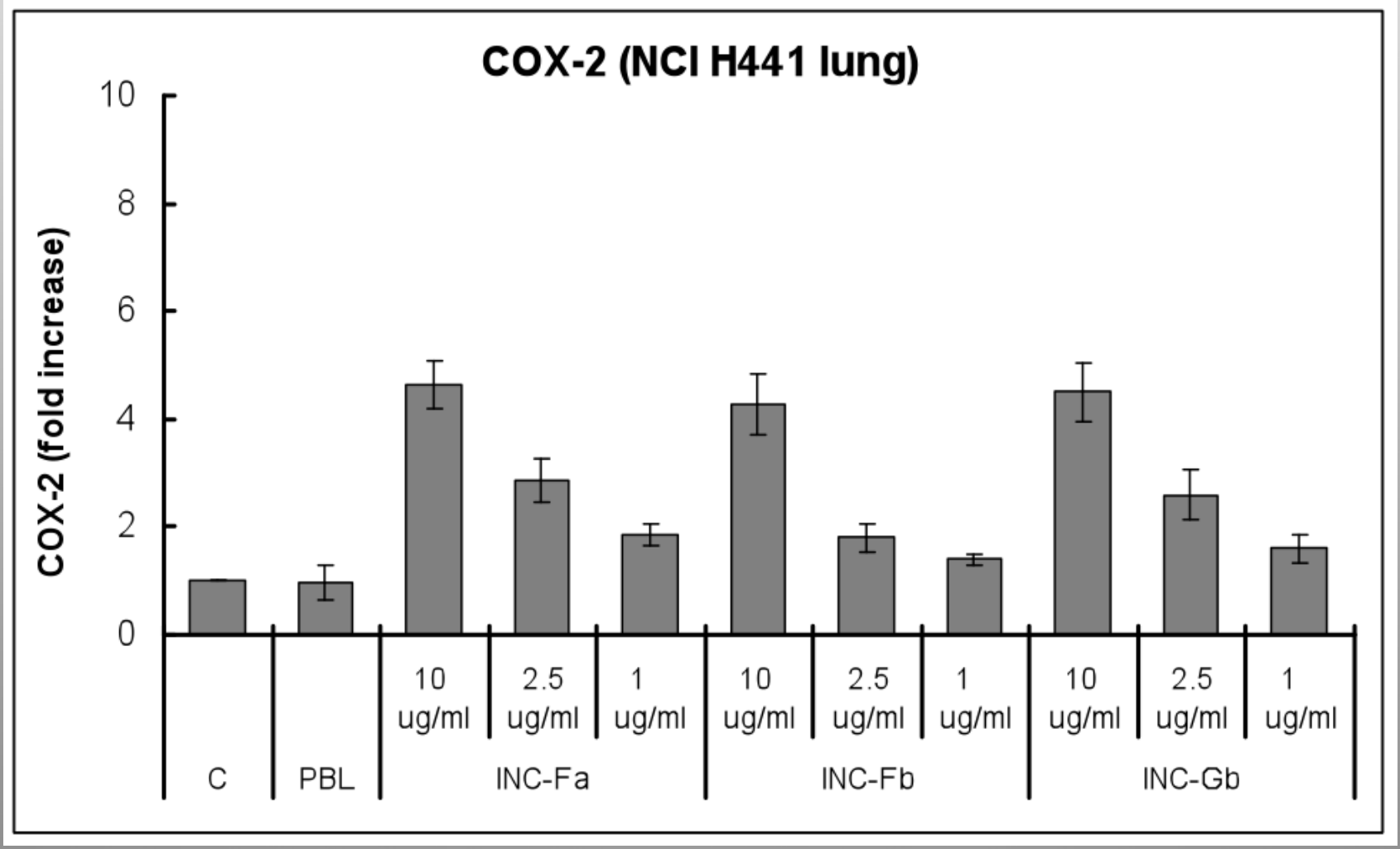
C: DMSO Control
BGA: Background Air
INC-A: Incense Nag Champa
INC-B: Incense Tibet
INC-C: Incense Shoyiedo
INC-D: Incense Potala
INC-E: Incense Aromatherapy
INC-F: Joss Stick green
INC-G: Floral Variety

Dose-response of Incense PM in Macrophages



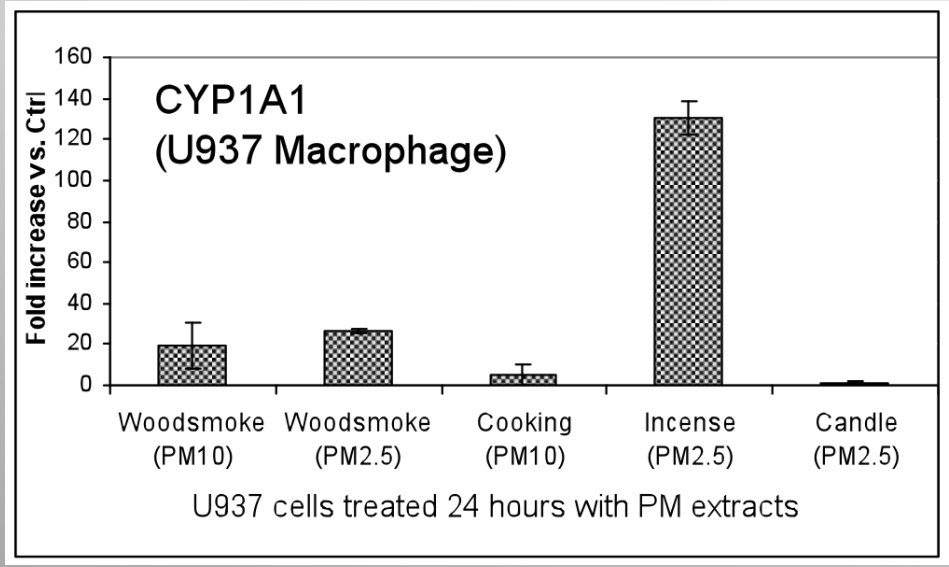
C: DMSO Control, PBL: Process Blank, INC-Fa: Joss Stick green PM10
INC-Fb: Joss Stick green PM2.5, INC-Gb: Floral Variety PM2.5

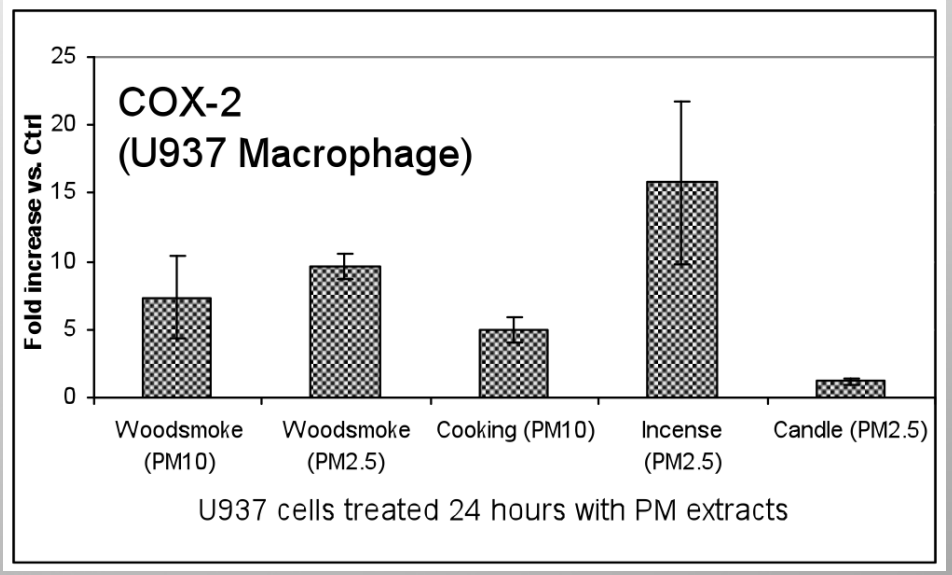
Dose-response of Incense PM in Lung Cells

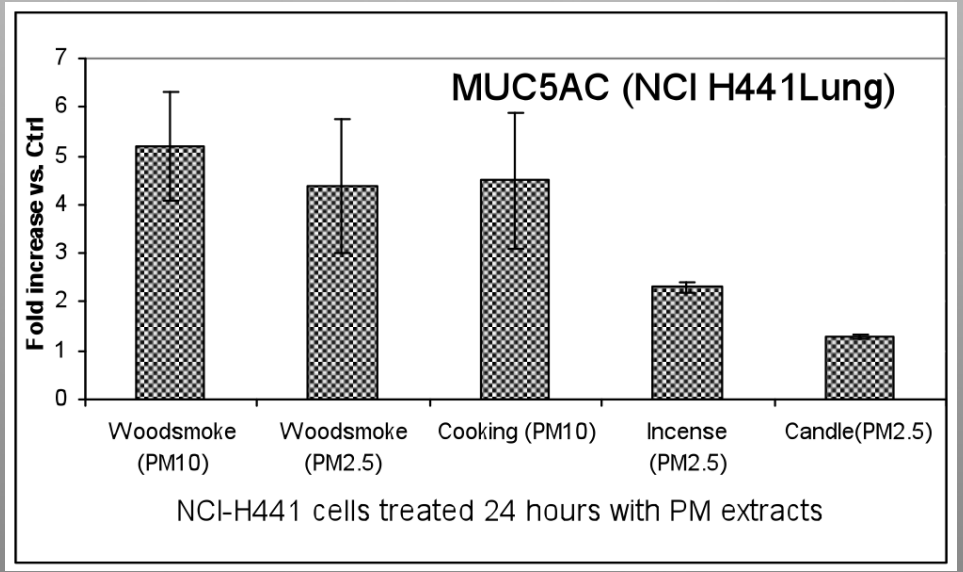


C: DMSO Control, PBL: Process Blank, INC-Fa: Joss Stick green PM10
INC-Fb: Joss Stick green PM2.5, INC-Gb: Floral Variety PM2.5

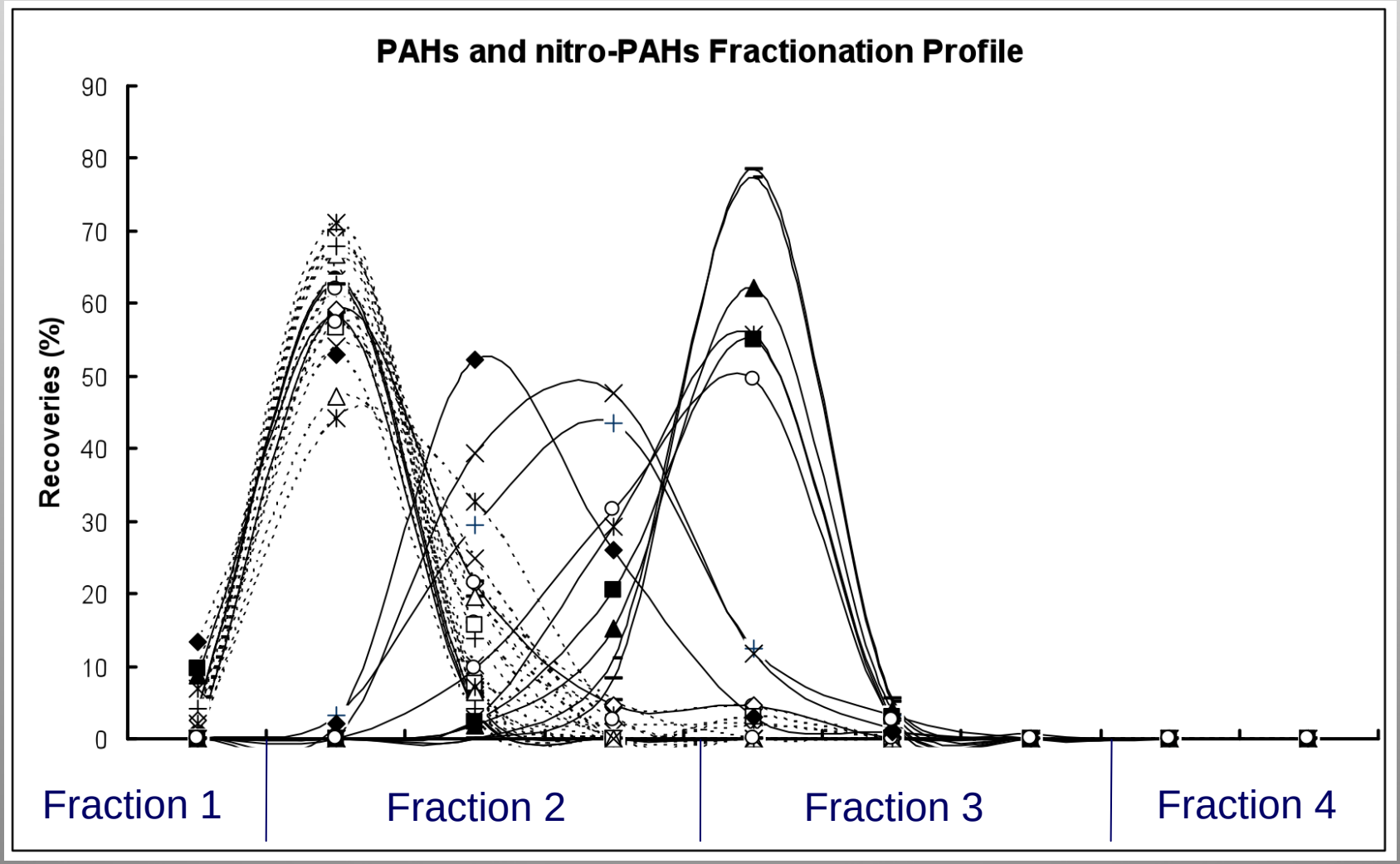
Comparison of PM sample groups





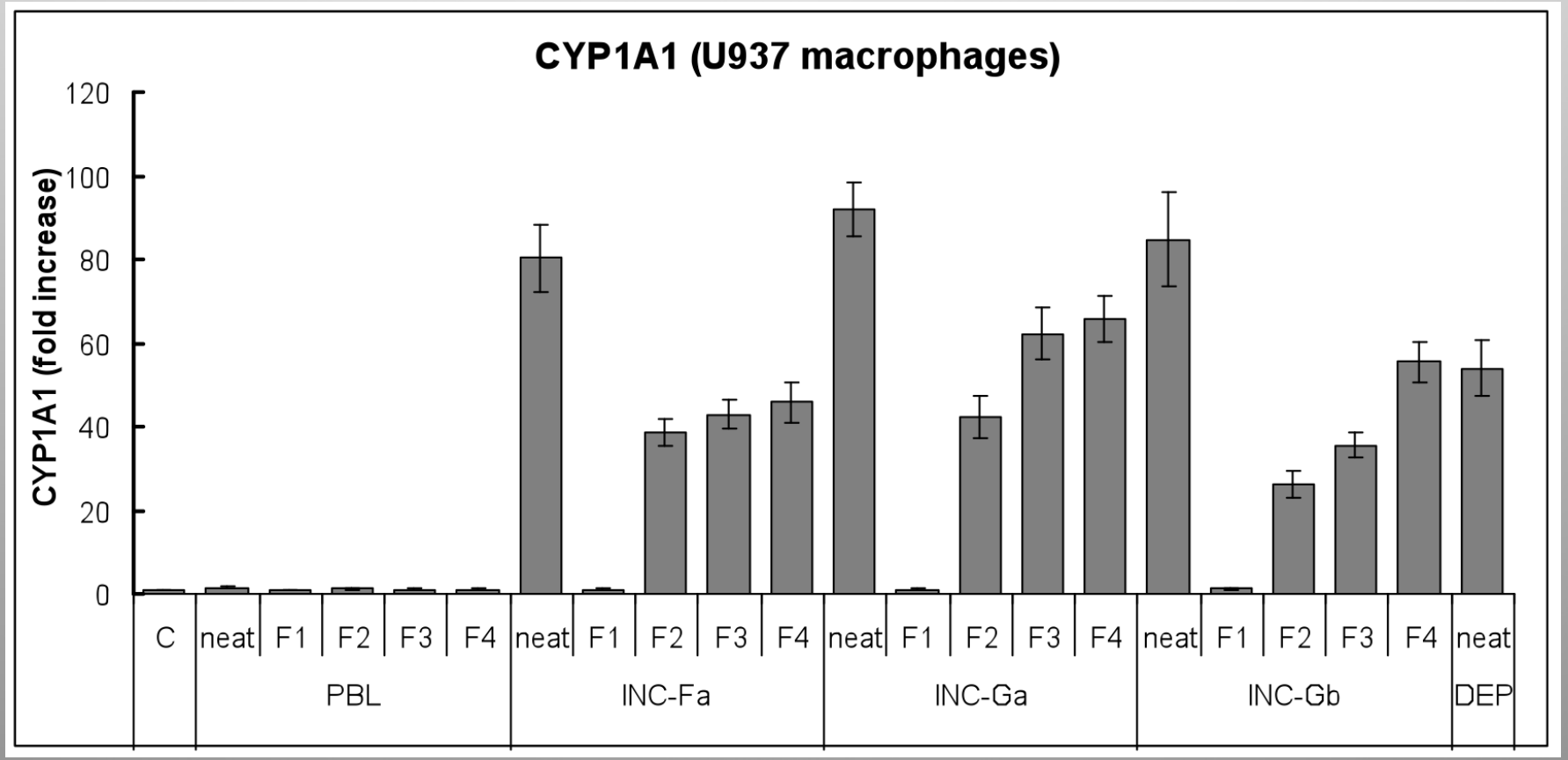


PAHs in Incense PM Fractions



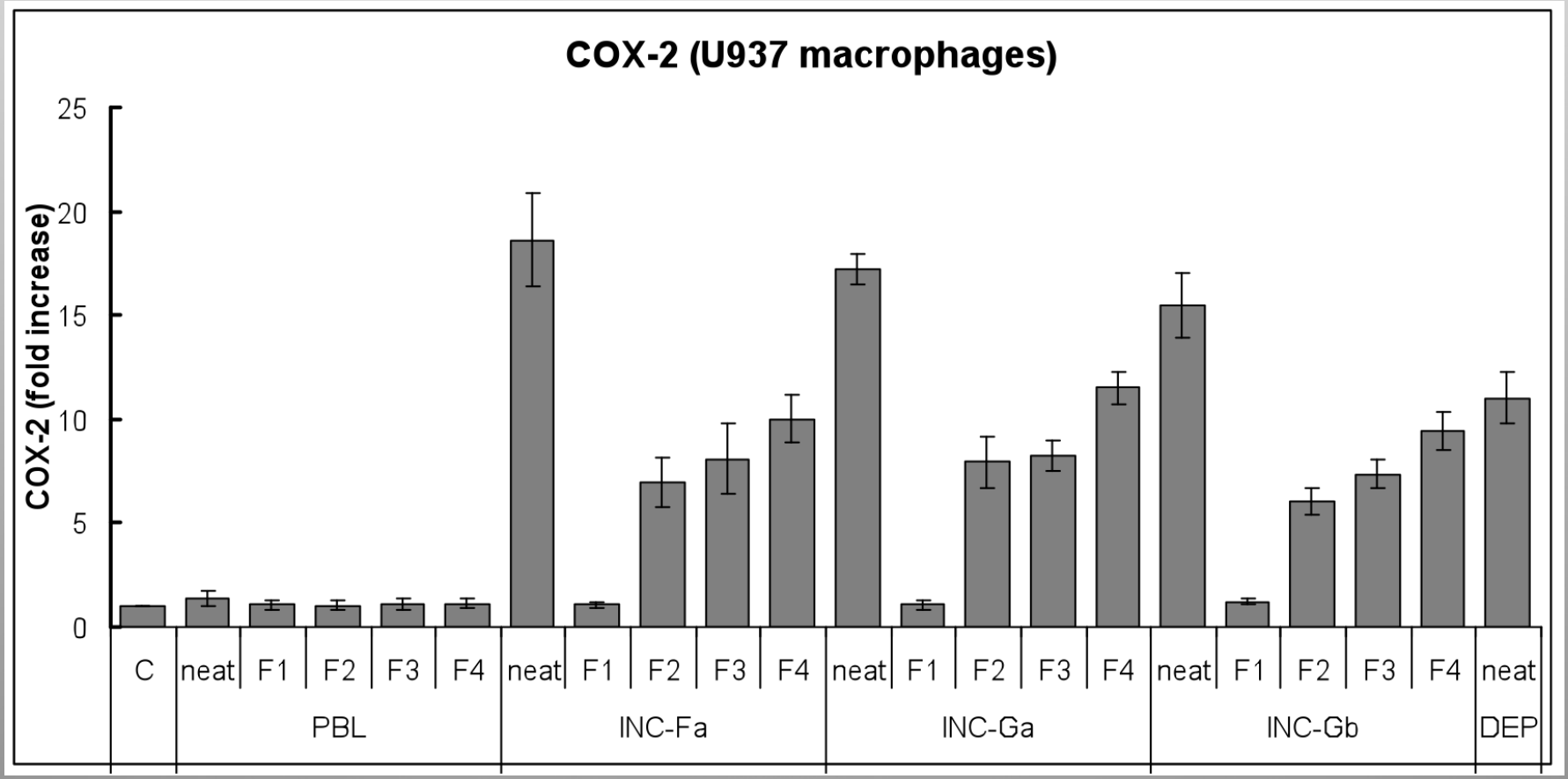
Chemical fractions F1 to F4: non-polar > polar

Effect of incense PM fractions on CYP1A1



Chemical fractions F1 to F4: non-polar > polar; neat: un-fractionated
INC-Fa: PM2.5 Incense, Mainichi-koh Japanese-1, INC-Ga: PM2.5 Incense, Floral India-1, INC-Gb: PM2.5 Incense, Floral India-2 duplicate
DEP: Diesel engine exhaust particles (NIST 2975)

Effect of incense PM fractions on COX-2



Chemical fractions F1 to F4: non-polar > polar; neat: un-fractionated
INC-Fa: PM2.5 Incense, Mainichi-koh Japanese-1, INC-Ga: PM2.5 Incense, Floral India-1, INC-Gb: PM2.5 Incense, Floral India-2 duplicate
DEP: Diesel engine exhaust particles (NIST 2975)

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CORRESPONDENCE

Radicals in the church

It was found that PM10 concentrations before candle/incense burning are three-fold higher as compared with the outdoor values (table 1), and clearly exceed the 24-h average European Union standard of 50 $\mu g \cdot m^{-3}$. Moreover, incense and candle burning were found to increase PM10 concentrations up to levels exceeding 1,000 $\mu g \cdot m^{-3}$. The average oxygen

Table 1. – PM10 concentrations, radical-generating capacity and polycyclic aromatic hydrocarbons (PAH) concentrations

	PM10 $\mu g \cdot m^{-3}$	Oxygen radicals# AU·m^{-3}	Carbon-centred radicals# AU·m^{-3}	Unidentified radicals# AU·m^{-3}	Total PAH concentration¶ $ng \cdot m^{-3}$
Church pre-service	163	52.3	0	0	16.4
Church post-service	658	19.8	12.5	3.9	52.9
Chapel before candle burning	233	53.7	0	0	11.2
Chapel after candle burning	1013	60.8	0	45.6	110.0
High-traffic outdoor locations+	53	6.3	0	0	7.4

PM10: particulate matter passing through a size-selective inlet with a 50% efficiency cut-off at a 10-μm aerodynamic diameter. #: radical-generating capacity, detected and identified as 5,5-dimethyl-1-pyrroline-*N*-oxide spin-trapped radical adducts, expressed in peak area (arbitrary units (AU)) per m^3; ¶: sum of 16 individual compounds analysed by HPLC, expressed in $ng \cdot m^{-3}$; +: >45,000 motorised vehicles per day.

Summary 1

- The human Macrophage Cell line (U937)and Lung Clara cell (NCIH441) suitable in vitro model for PM testing
- All indoor PMs tested generated a response in at least one or both cell types
- Wood Smoke samples increase CYP1A1 and COX-2 significantly in Macrophages
- All incenses were tested very active in the induction of biomarkers (polar fractions more active)

Summary 2

- Effective and inexpensive indoor air monitoring
- Assessment of mixture toxicity (combined effect of exposure)
- Assessment of exposure and evaluation of health effects

Cleaner Indoor Air

Thank you

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