Comparative toxicity of:

Coarse vs. Fine PM
&
Urban vs. Rural PM

Terry Gordon, PhD

NYU School of Medicine

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Objective

- To determine the contribution of coarse particles to the adverse effects associated with exposure to ambient PM.
  - We hypothesized that differences in the toxicity of coarse PM ($PM_{10-2.5}$) samples are due to the source contributions of the particles

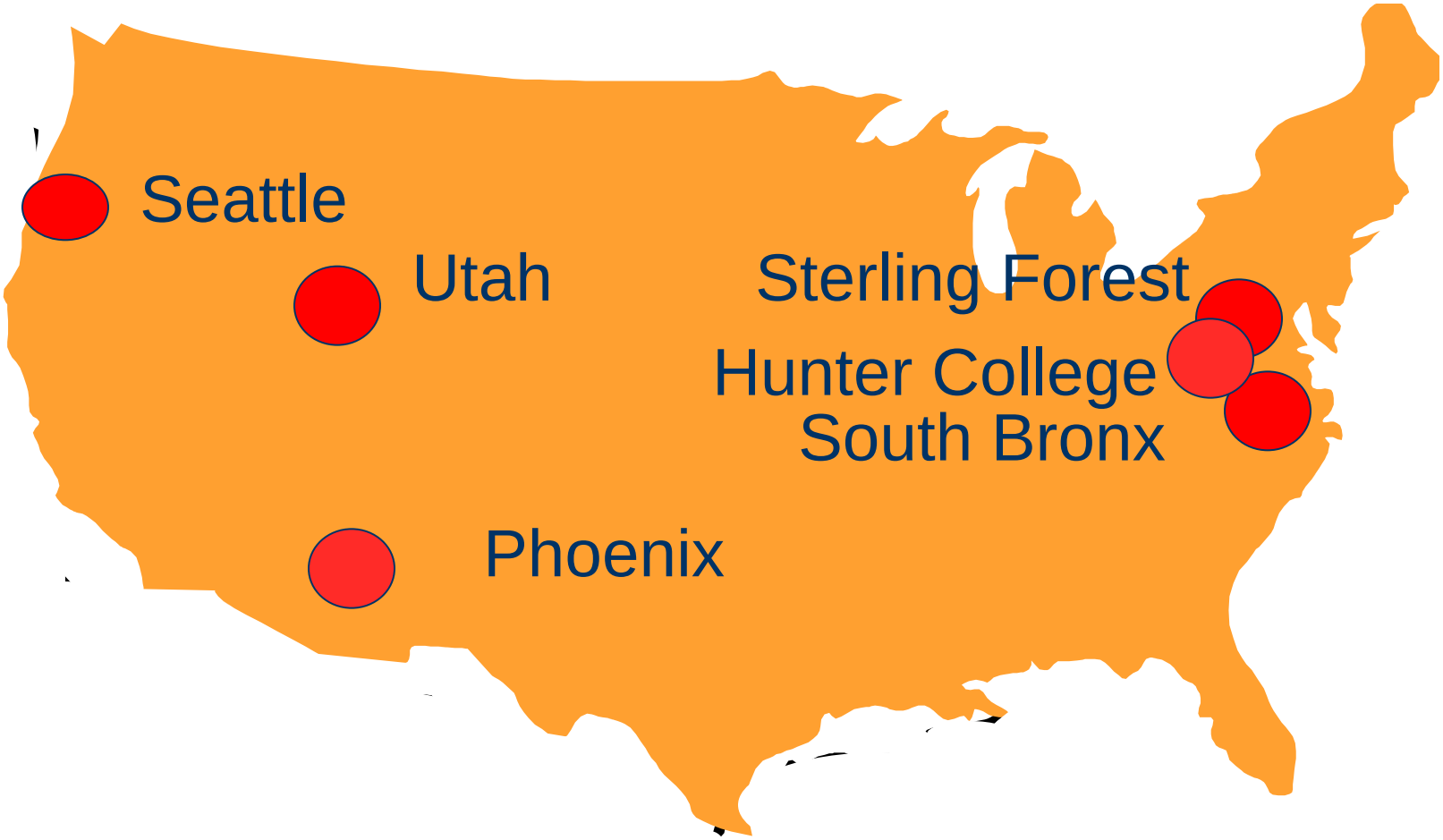
Experimental Design

1) To measure the differential toxicity of coarse and fine PM both *in vitro* and *in vivo*;
2) To identify whether coarse particles from urban and rural sources differ in toxicity.

Study Design

- Design was copied from European scientists (Netherlands/Germany)

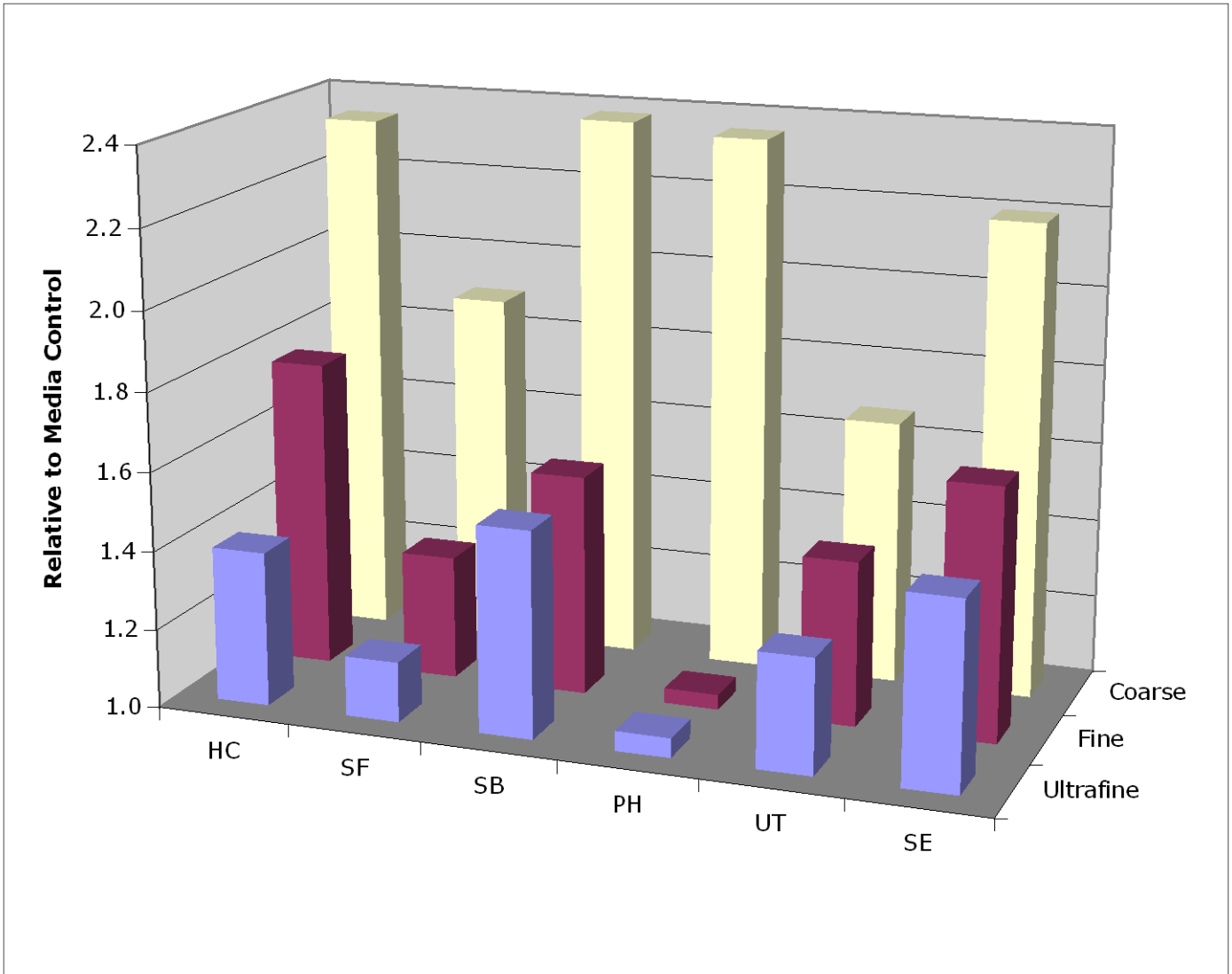
The Multi-City Ambient PM Study (MAPS)



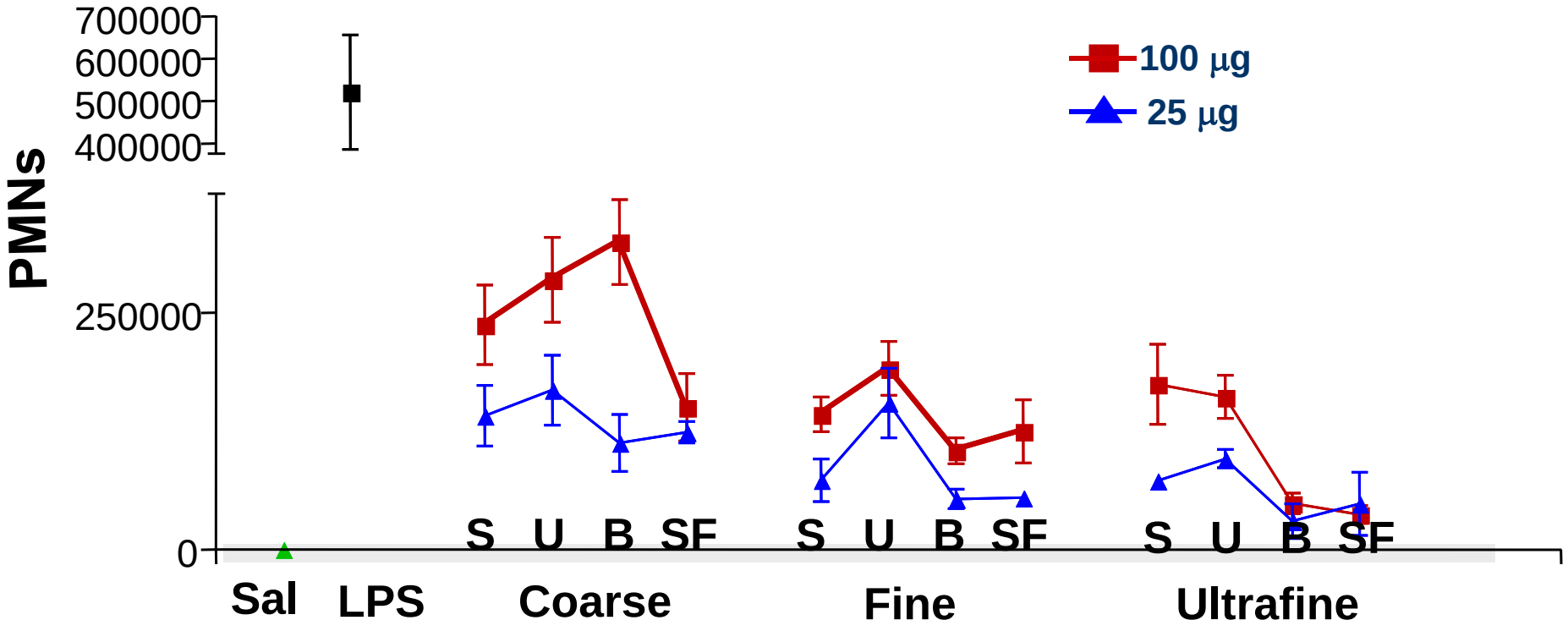
Effect of PM on Reactive Oxygen Species Production in Airway Epithelial Cells

Dose = 50 µg/ml

HC: Hunter College
SF: Sterling Forest
SB: South Bronx
PH: Phoenix
UT: Utah
SE: Seattle



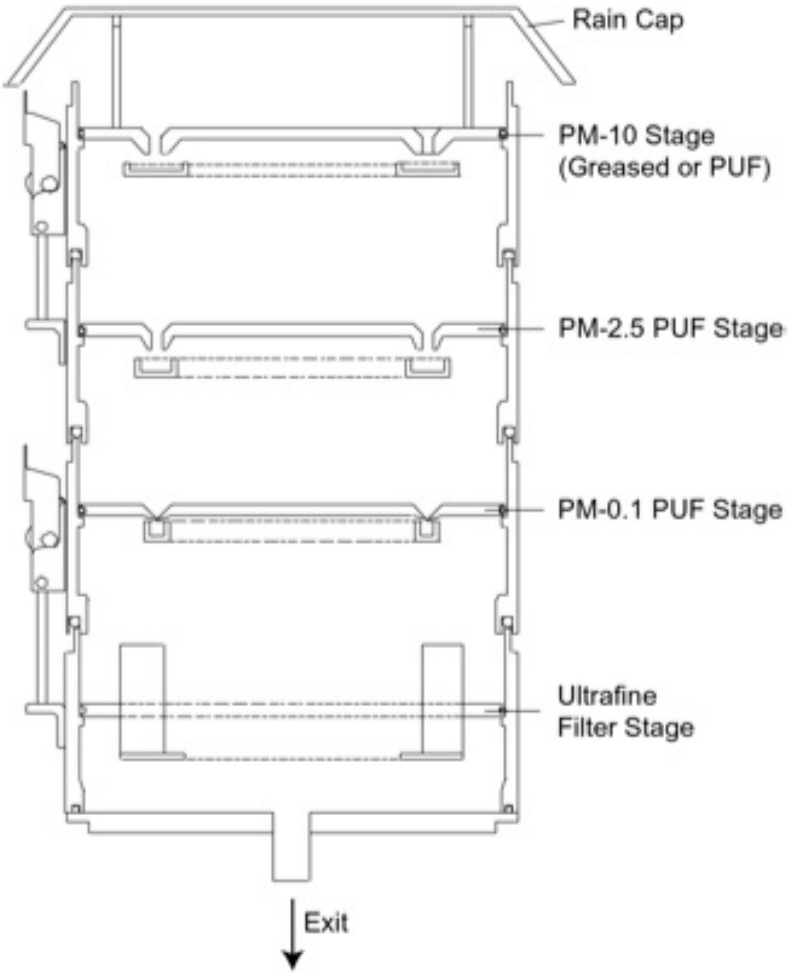
Effect of Aspirated PM in Mice

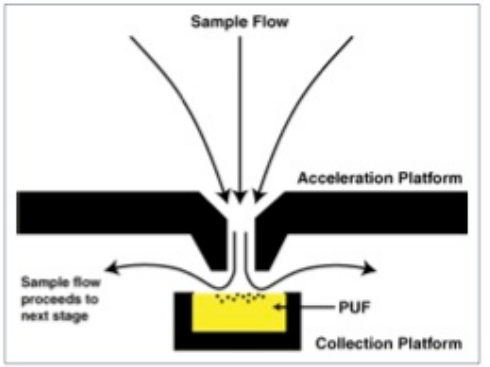


S = Seattle
U = Utah
B = Bronx
SF = Sterling Forest

Gilmour et al, 2007

Collection Apparatus





Foam Impaction Stage

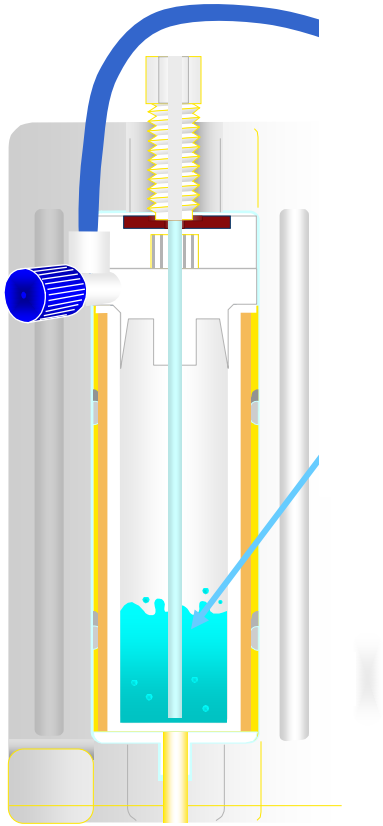
Study Design (cont….)

- Urban and rural PM sampling
  - NYC - winter and summer
  - San Joaquin Valley, CA – fall/winter
- 3 particle sizes (coarse, fine, and supercoarse)
  - Supercoarse samples only at some locations
- In vivo bioassay - mouse
- In vitro bioassay - 2 cell types
  - epithelial, vascular endothelial

Chemical Analyses

- Microwave Digestion
- ICP-MS
  - Chillrud and Ross @ Columbia's Lamont-Doherty
- Source Apportionment
  - Ito, Jin, Thurston

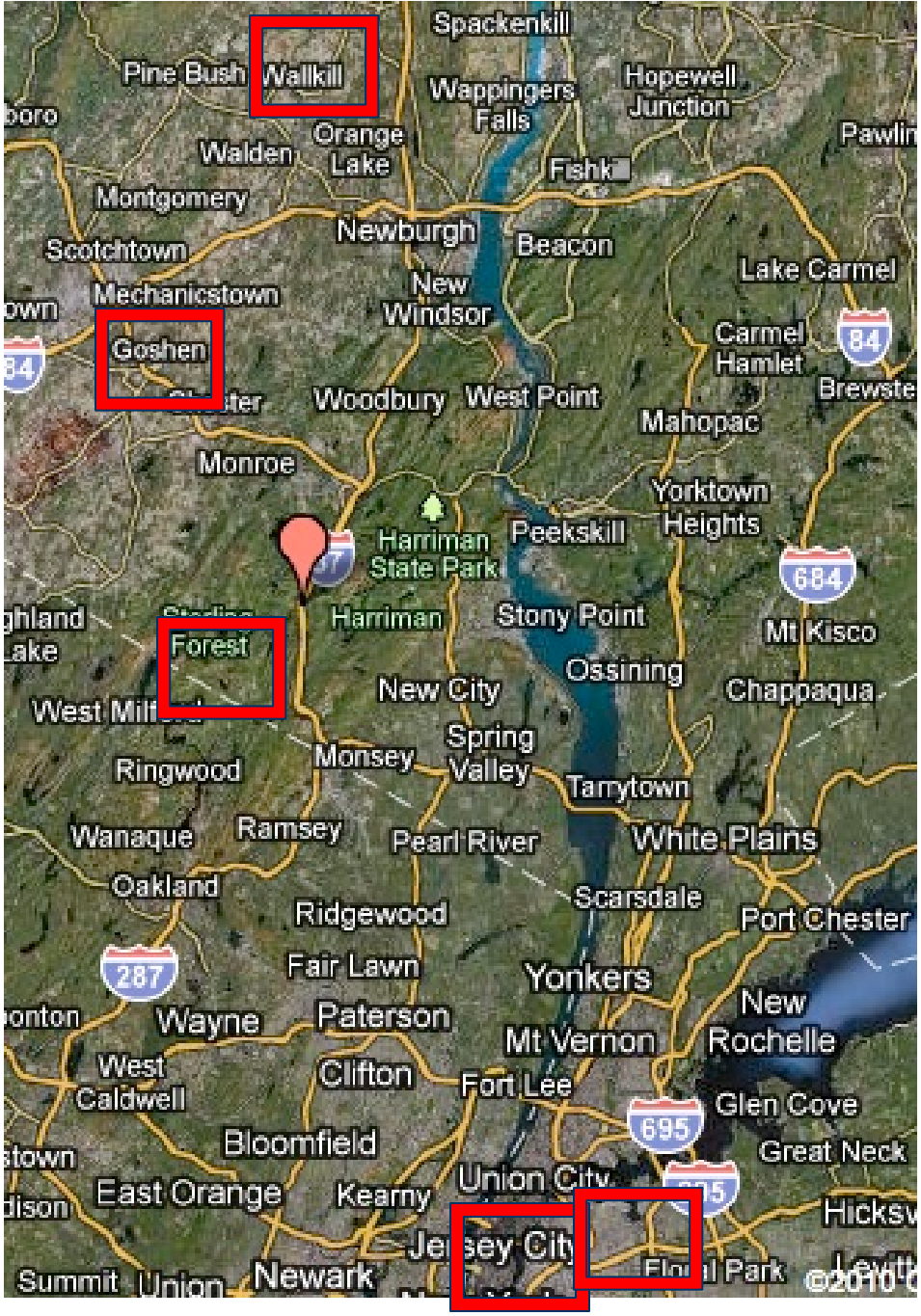
Microwave Digestion of PM Samples



- 48 samples/day
- As little as 50 µg PM
- No HF or perchloric acid
- Lose Si and Ti

NY Urban & Rural Study

NY Urban and Rural Sites



Urban Enough?

Rural Enough?

PM Mass Concentrations

($\mu g/m^3 \pm SD$)

		Super-coarse	Coarse	Fine
Wallkill (rural)	Summer	2.9 ± 0.5	5.2 ± 1.0	5.2 ± 1.7
	Winter	ND	4.7 ± 2.4	8.9 ± 5.1
Goshen (rural)	Summer	ND	5.8 ± 1.3	6.6 ± 2.5
	Winter	ND	6.5 ± 2.7	10.3 ± 5.4
Tuxedo (rural)	Summer	ND	5.0 ± 1.5	5.8 ± 2.5
	Winter	ND	4.4 ± 2.4	7.8 ± 5.1
Bronx (urban)	Summer	7.2 ± 2.5	7.3 ± 2.3	9.2 ± 3.9
	Winter	ND	8.9 ± 4.0	14.0 ± 7.1
Manhattan (urban)	Summer	ND	8.0 ± 2.4	9.5 ± 3.5
	Winter	ND	11.9 ± 5.1	14.0 ± 5.5

Individual Factors?

- Particle size?
- Sampling site?
- Urban vs. rural?
- Season?

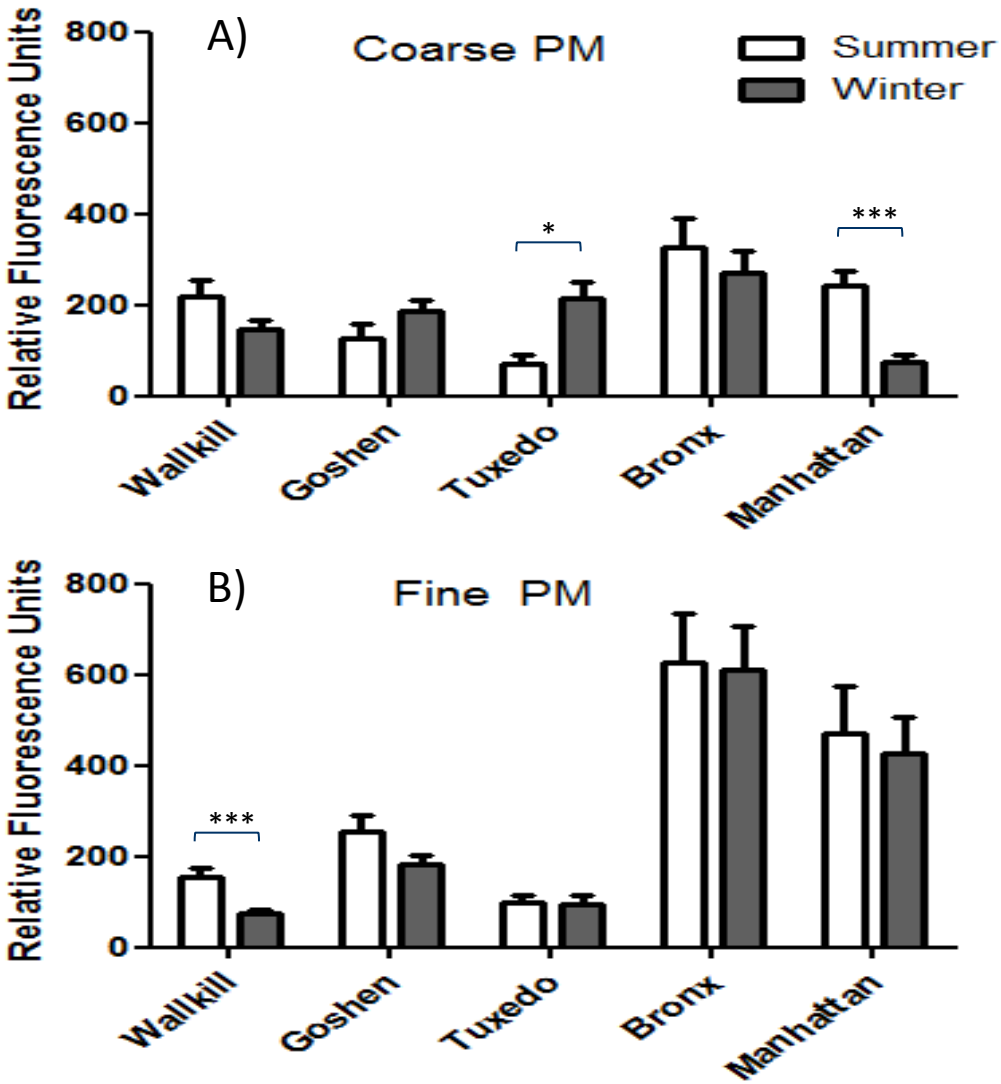
In Vitro Studies
Human Cell Lines

- Airway epithelial/vascular endothelial cells
- 50 µg/ml (96 well plate)
- Endpoints
  - Toxicity
  - ROS production (fluoroprobe)

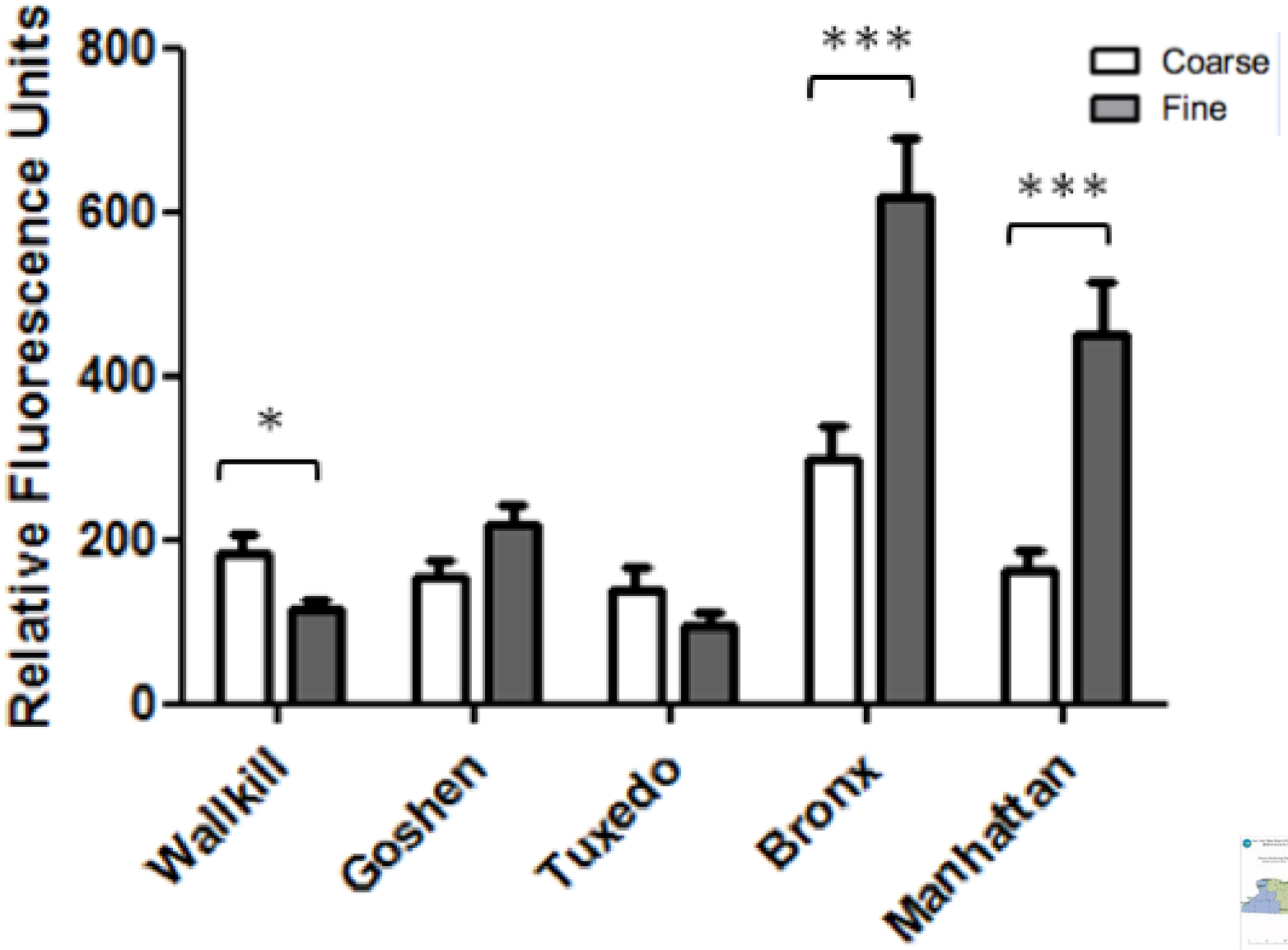
Effect of Particle Size, Location, Season, and Locale (U vs. R) in NY

	HPMEC –ST1.6R Endothelial Cells	BEAS-2B Epithelial Cells
Location	**<0.01**	**<0.01**
Season	0.11	0.64
Size	**<0.01**	0.86
Locale	**<0.01**	**<0.01**
Location: Season	0.27	0.96
Location: Size	**<0.01**	**<0.01**
Season: Size	0.66	0.24

Effect of Season and Size on ROS Activity in Endothelial Cells



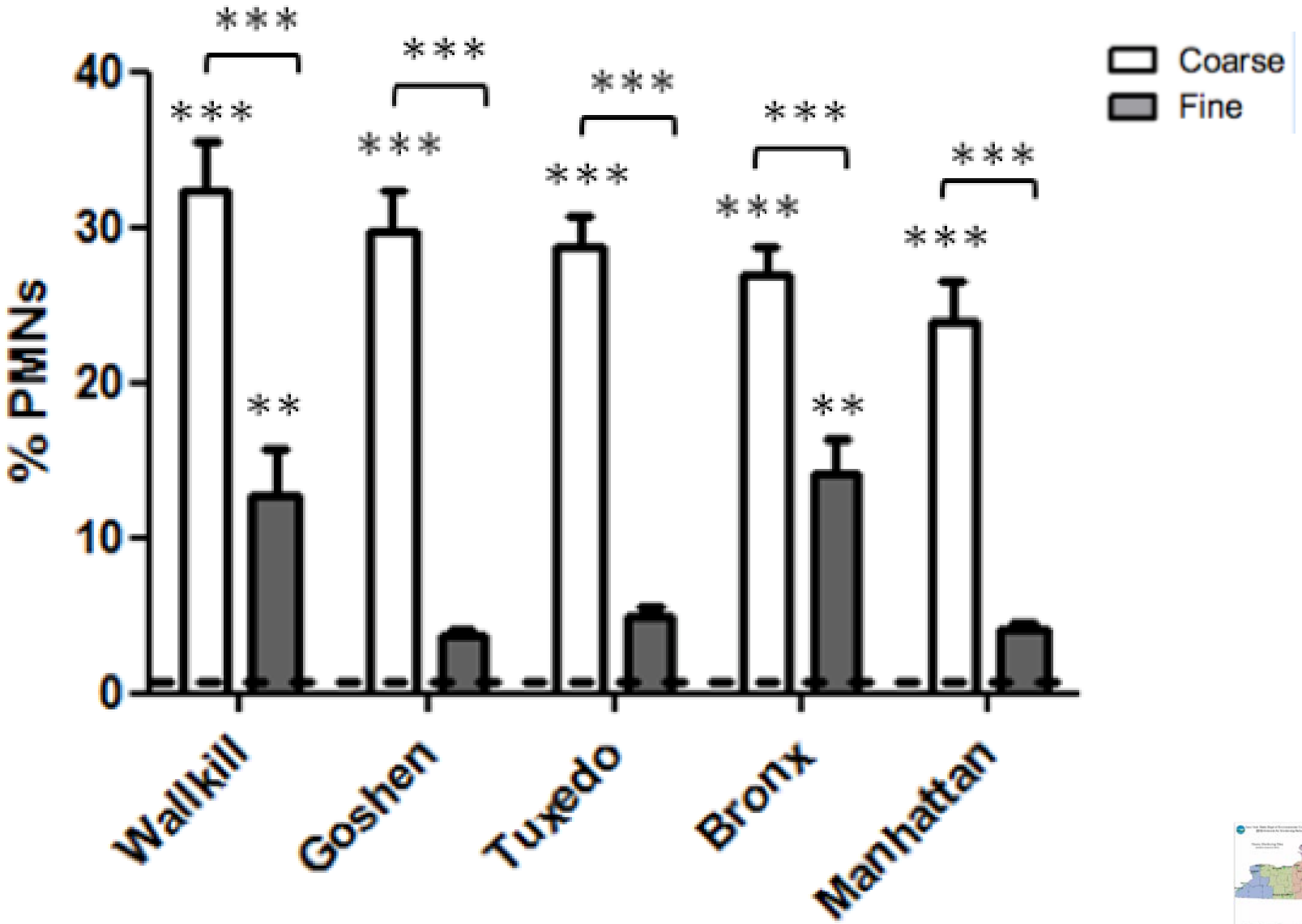
Effect of Size on ROS Activity



Does *in vitro* reflect *in vivo*?

- FVB/N mice
- 50 µg PM by aspiration
- Collect lavage fluid and serum at 24 hrs post treatment
- Subset of samples tested in mice
  - n = 60+ samples
  - n = 3/group

Effect of Size on Lung Inflammation in Mice

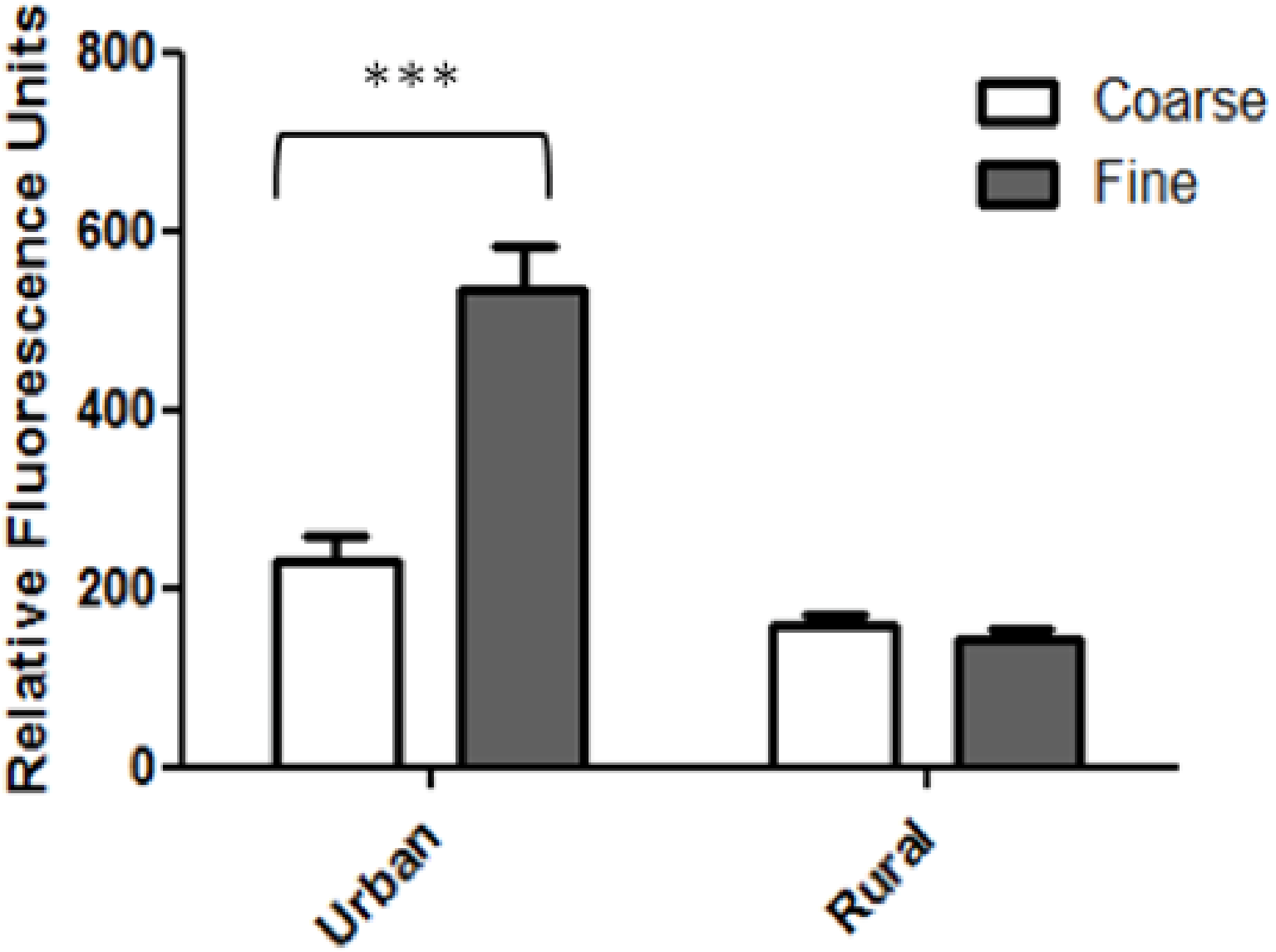


Size and Season In NY?

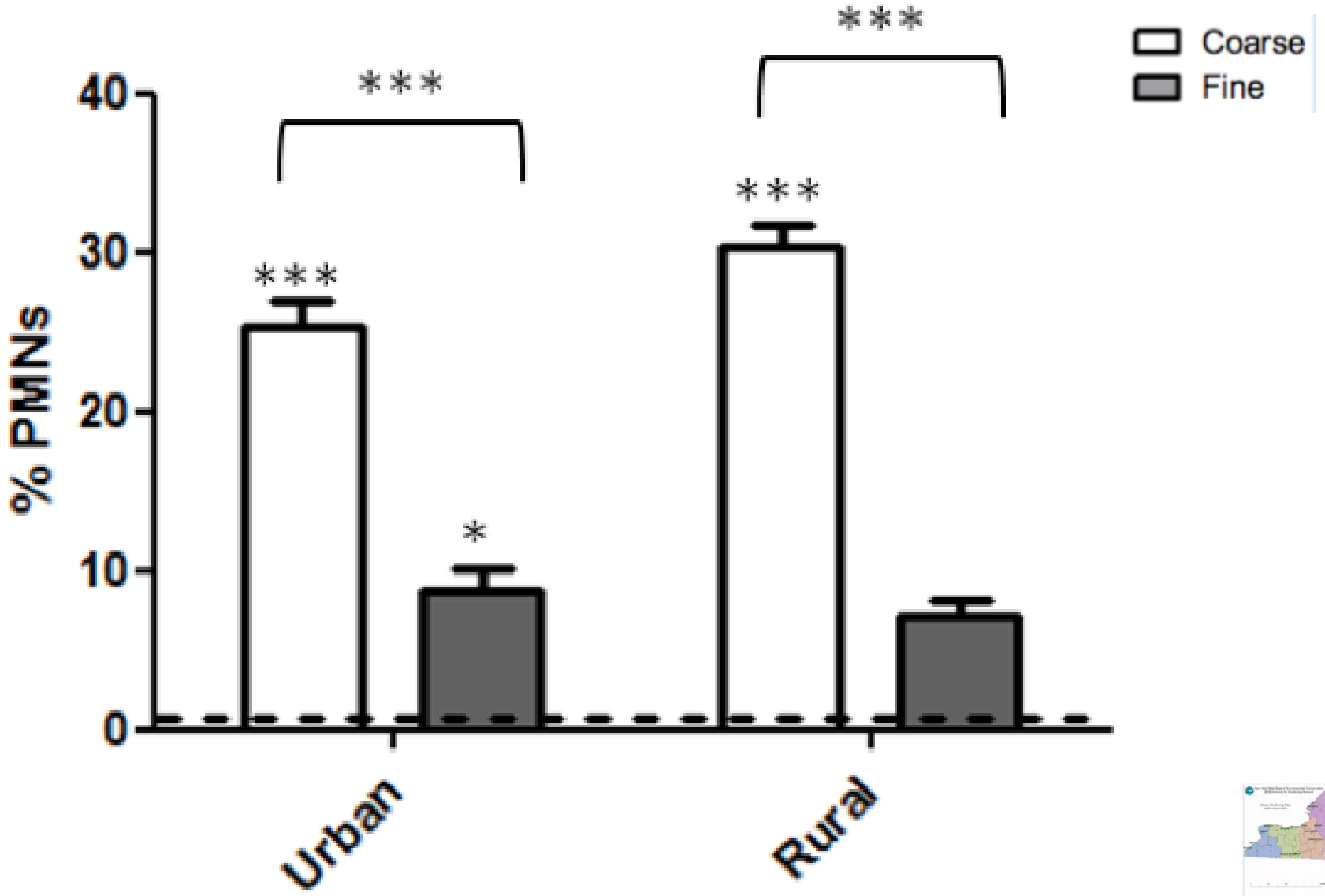
- Season had little influence on response
- Fine PM produced greater ROS *in vitro*
- Coarse PM produced greater inflammation *in vivo*

But what about a comparison of the toxicity of urban vs. rural PM?

Effect of Locale (Urban vs. Rural) on ROS



Effect of Locale (Urban vs. Rural) on Lung Inflammation in Mice

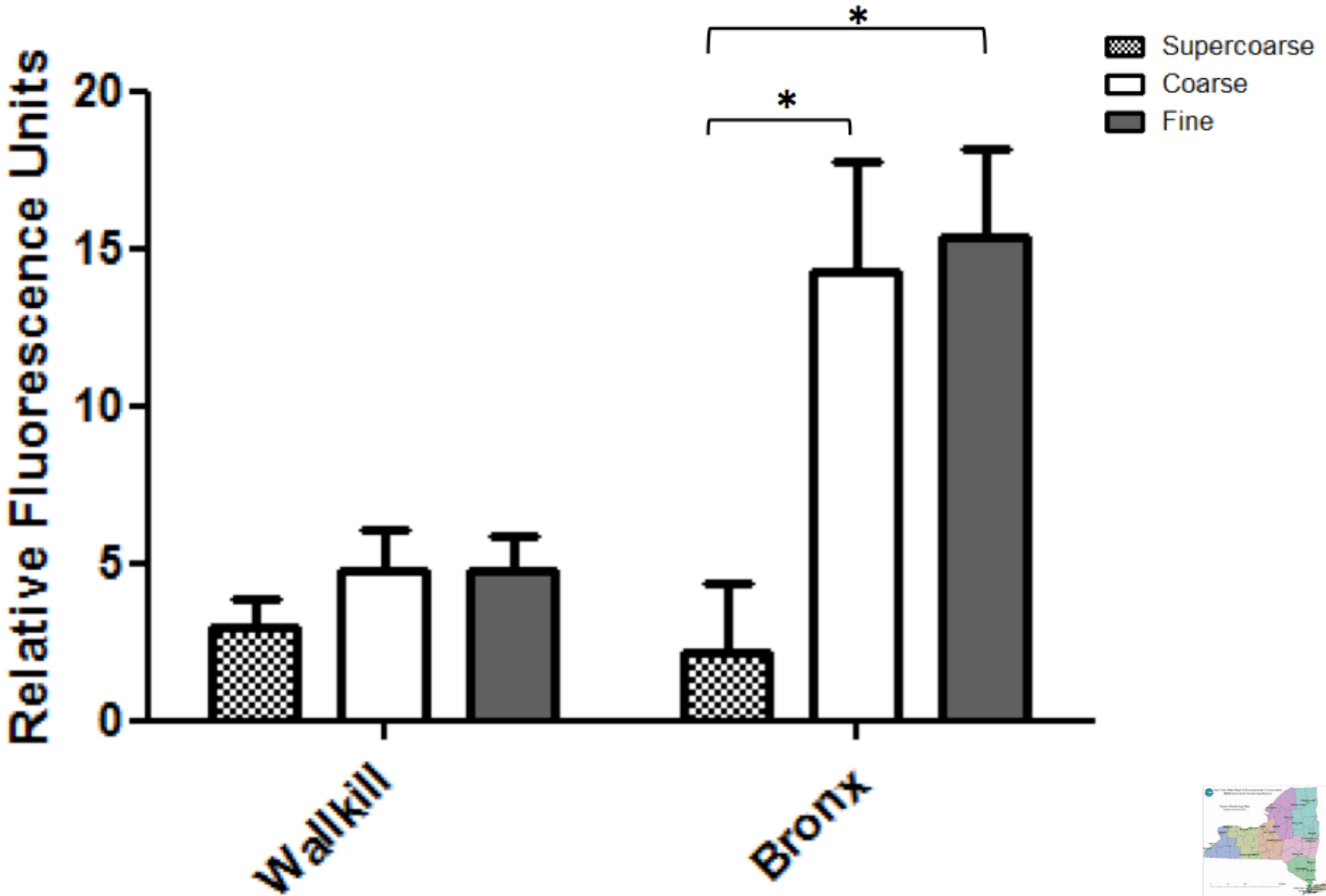


Effect of Locale In NY?

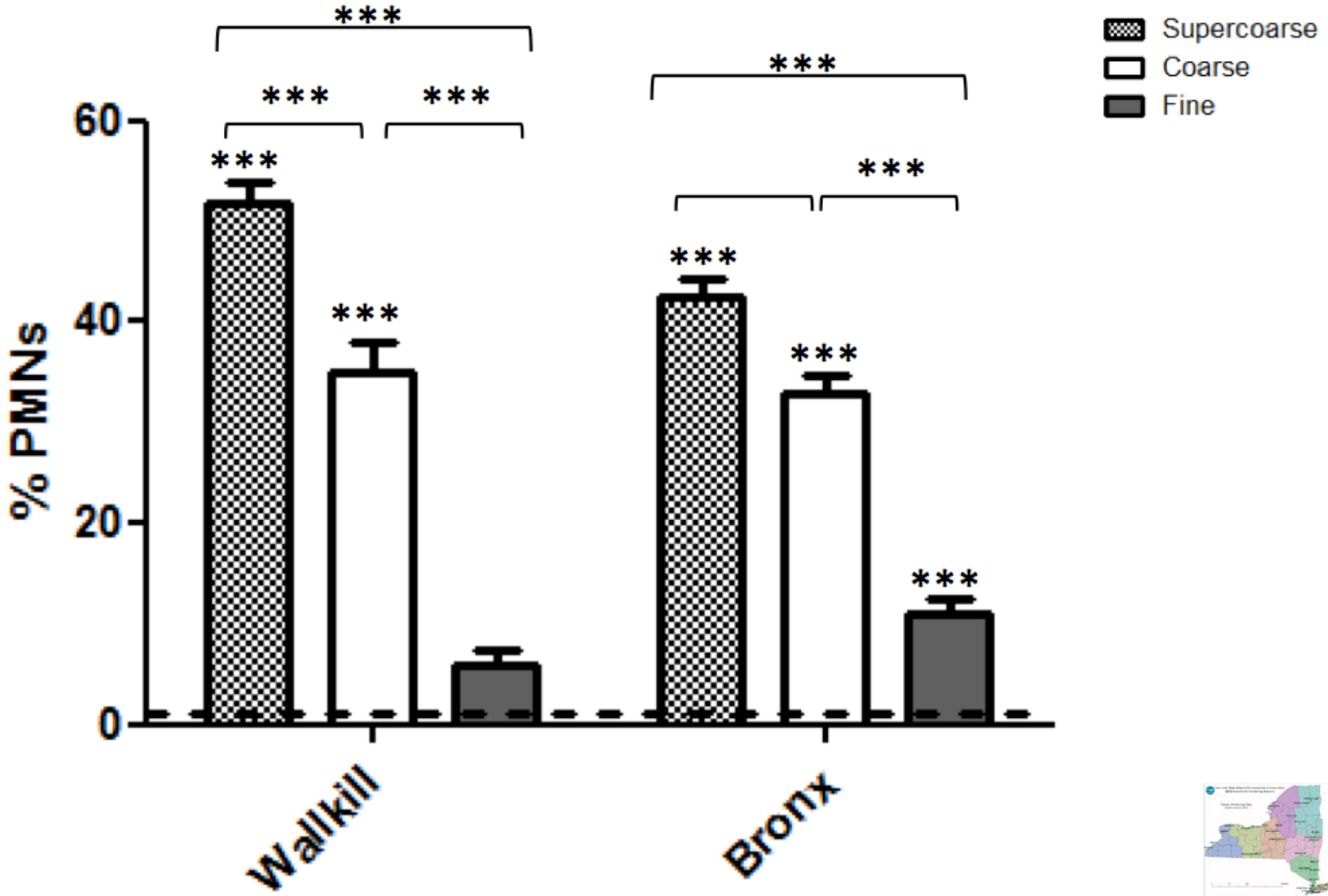
- Urban fine PM produced a greater ROS *in vitro*
- There was no difference between urban and rural PM for inflammation *in vivo*

But what about supercoarse PM (> 10 µm) ?

Effect of Supercoarse, Coarse, and Fine PM on ROS



Effect of Supercoarse, Coarse, and Fine PM on PMNs



Conclusions (NY only)

- Size and site (urban vs. rural) were shown to be significant factors influencing ROS production *in vitro*.
- The fine fraction collected at urban sites elicited a greater ROS response than either coarse or 'supercoarse' PM.
- Generally, urban PM produced greater ROS effects than rural samples.
- Coarse PM produced greater pulmonary inflammation in mice regardless of collection site
- Analysis of PM composition needs to be considered to gain a better understanding of these effects.

Did *in vitro* predict *in vivo*?

- NO!
- Despite clear differences *in vitro*, urban and rural PM samples produced similar effects *in vivo*.

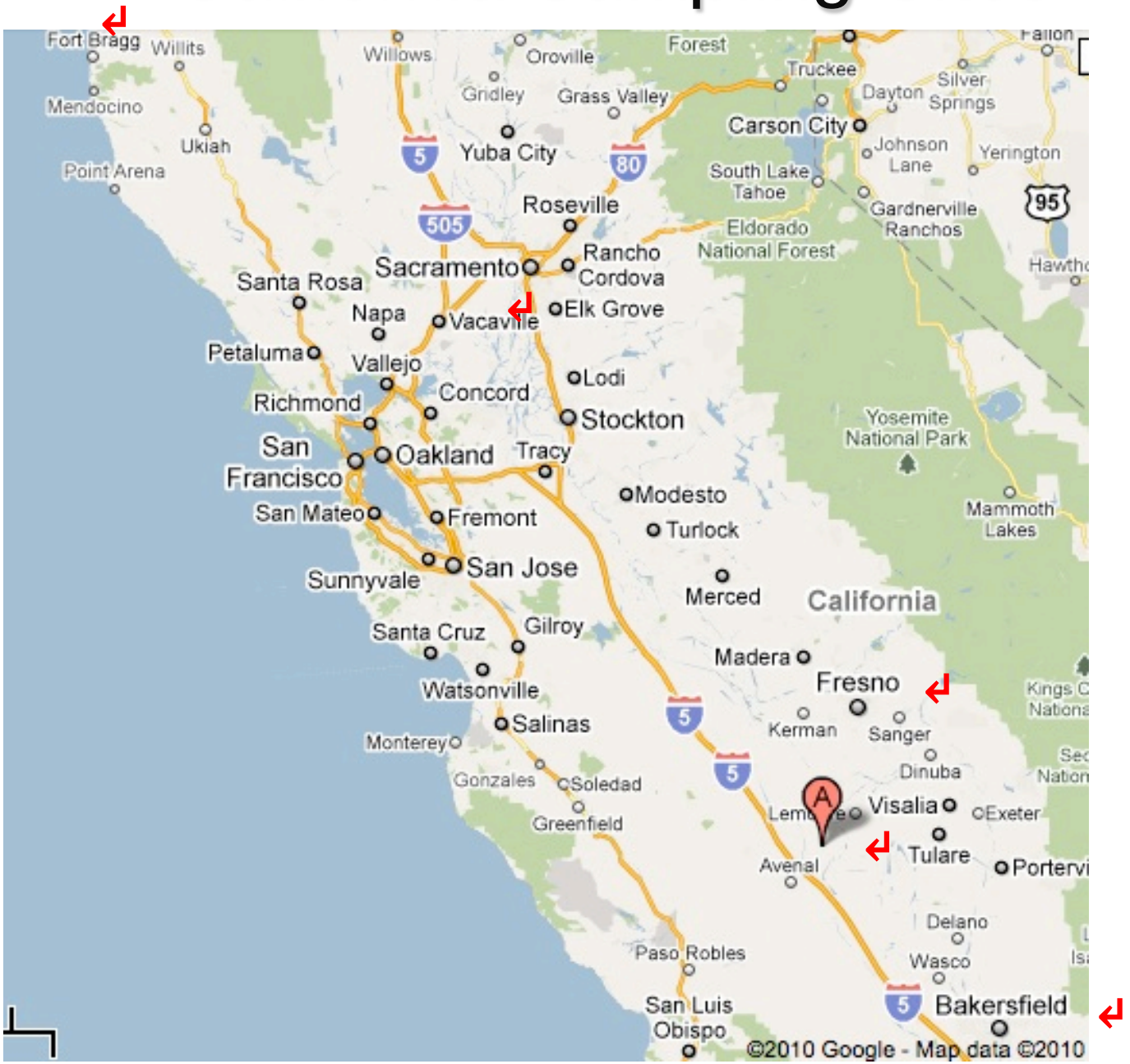
Correlation - Bioassay & Trace Elements in NY

	in vitro response		in vivo response	
	HPMEC	BEAS-2B	% PMNs	Protein
Mg	**-0.17**	-0.10	**0.37**	0.12
P	**0.16**	0.00	**0.61**	0.07
S	**0.35**	0.05	**-0.72**	-0.09
K	0.02	0.08	**0.31**	-0.17
Ca	**-0.14**	-0.12	0.21	0.20
Sc	-0.01	-0.03	0.25	0.16
V	**0.52**	0.00	**-0.36**	0.15
Cr	0.01	0.02	0.02	-0.01
Mn	-0.03	-0.06	0.25	0.13
Fe	-0.08	0.02	-0.05	-0.02
Co	**0.51**	0.02	-0.15	0.18
Ni	**0.53**	0.03	-0.21	0.16
Cu	**0.25**	0.12	0.06	0.07
Zn	**0.50**	0.04	**-0.30**	0.17
As	0.16	-0.02	**-0.62**	-0.18
Se	0.14	0.05	**-0.63**	0.09
Ag	-0.05	0.02	-0.05	0.16
Pb	0.06	0.10	**-0.68**	-0.16
Endotoxin	0.05	-0.13	**0.56**	0.18

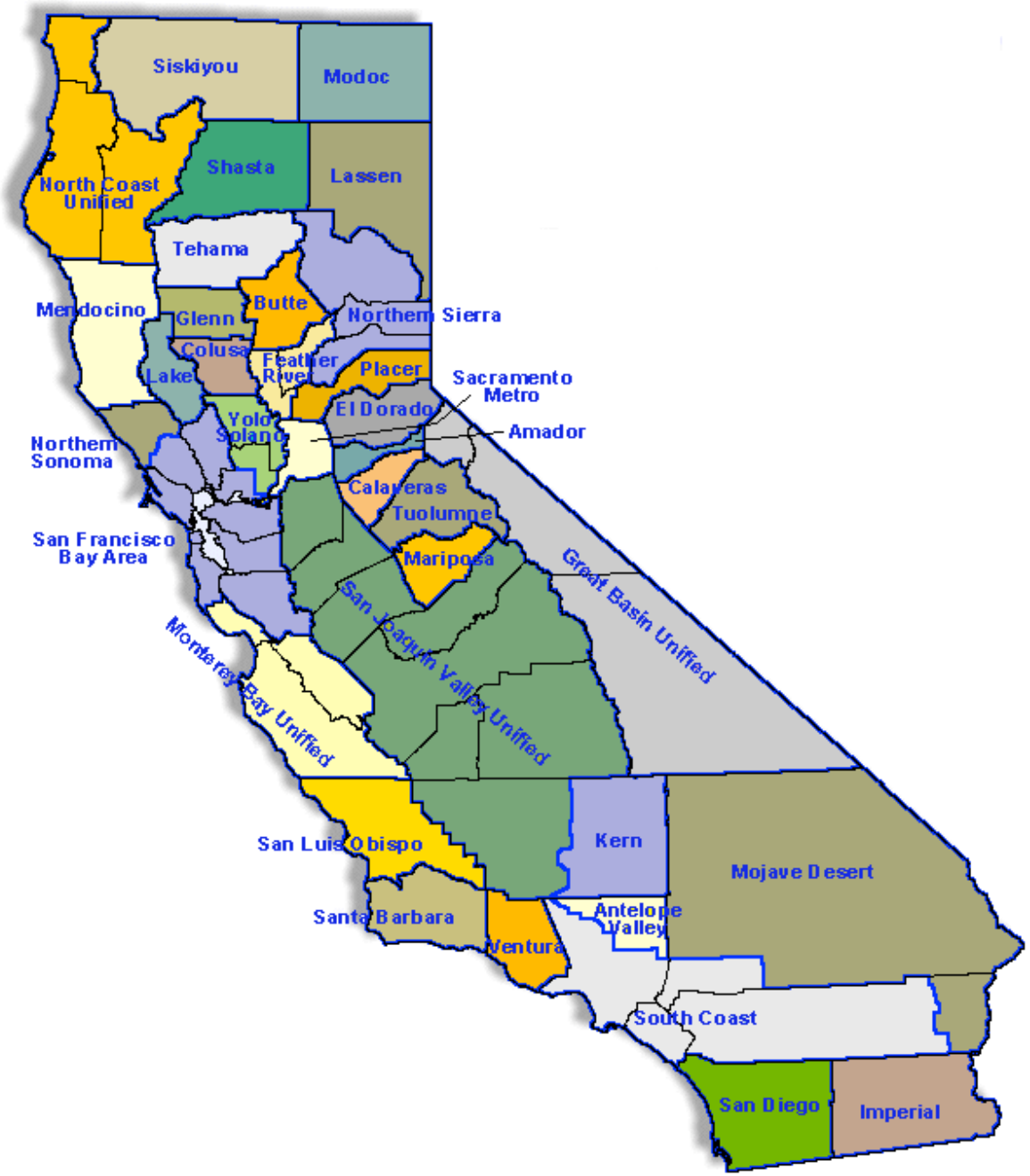
Endotoxin Dose-Response in Mice

Endotoxin (ng/50 μL)	Average % PMNs
0.1	0
0.5	0
1	1
5	13
10	15

California Sampling Sites



California Air Districts



PM Mass Concentration in CA

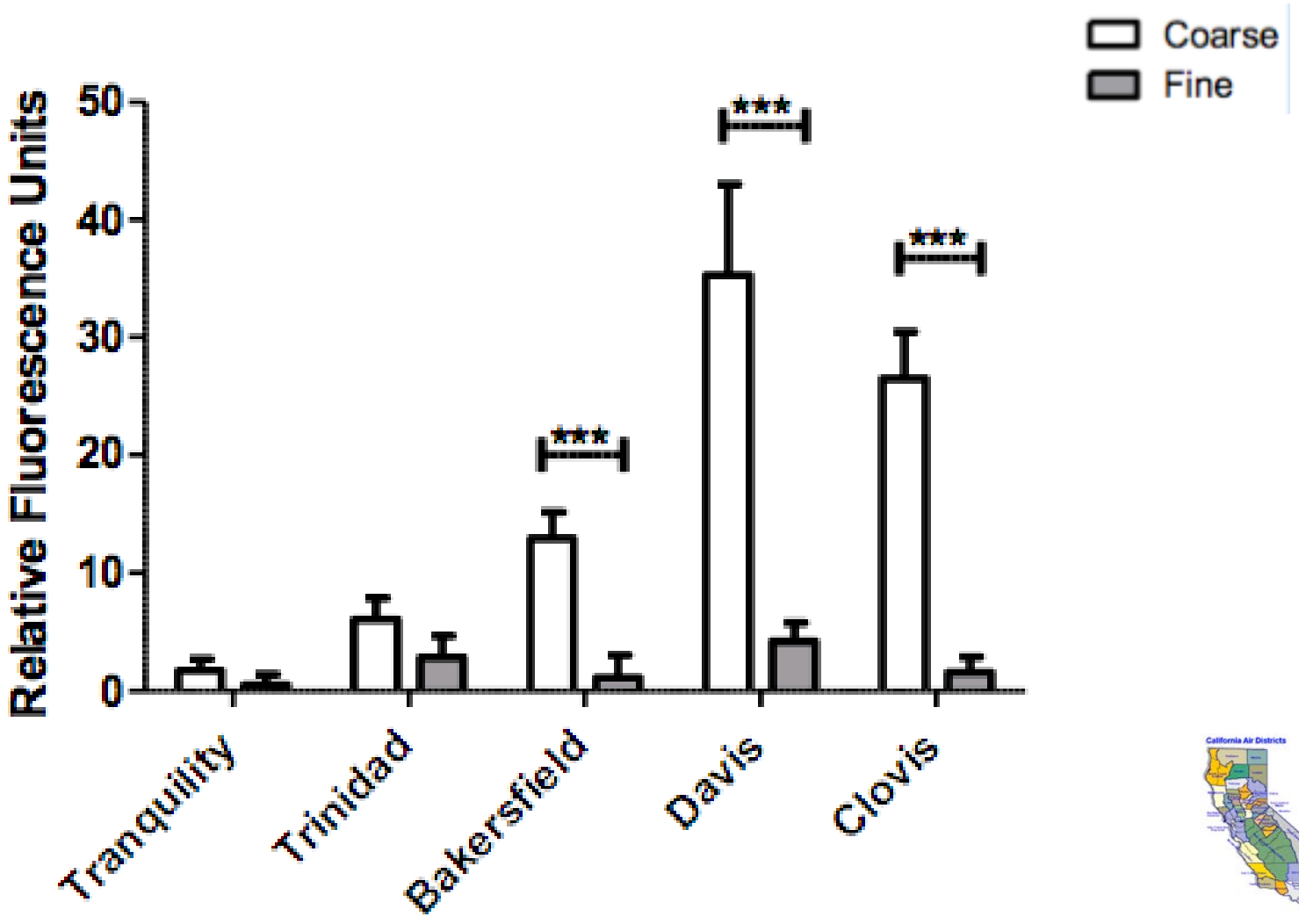
($\mu g/m^3 \pm SD$)

	Super-coarse $PM_{>10}$	Coarse $PM_{10-2.5}$	Fine $PM_{2.5}$
Tranquility	20.1 ± 37.6	15.0 ± 14.6	15.2 ± 9.9
Bakersfield	37.2 ± 23.6	37.0 ± 17.6	31.2 ± 16.4
Davis	ND	15.5 ± 3.7	11.5 ± 5.6
Clovis	ND	23.7 ± 0.1	29.1 ± 11.8
Trinidad	ND	71.4 ± 18.8	5.7 ± 2.8

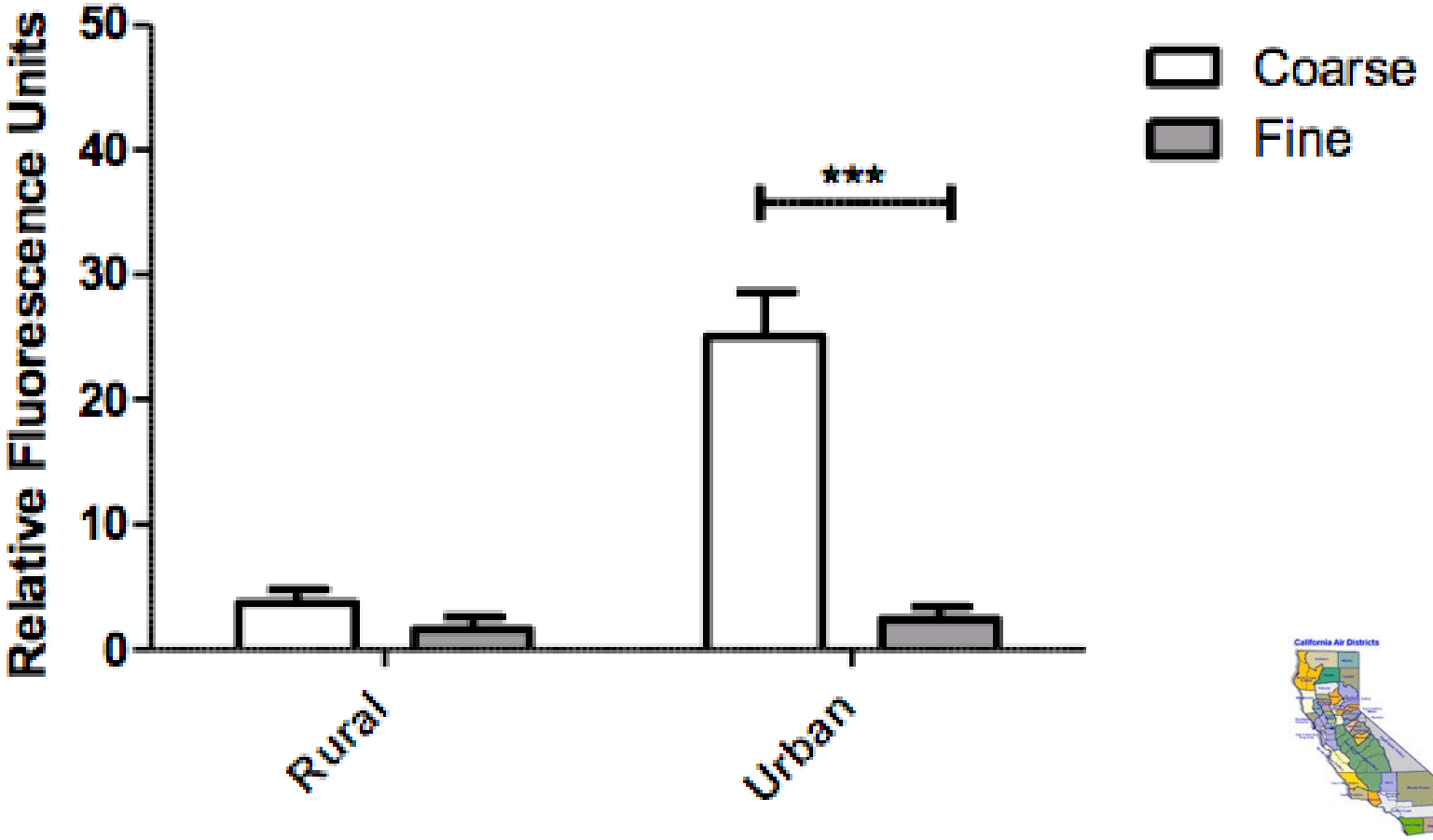
Effect of Particle Size, Location, and Locale (U vs. R)

	in vitro ROS	*in vivo* %PMNs
Size	<0.001	<0.001
Location	<0.001	<0.001
Locale	<0.001	0.02
Location:Size	<0.001	<0.001
Locale:Size	<0.001	<0.001

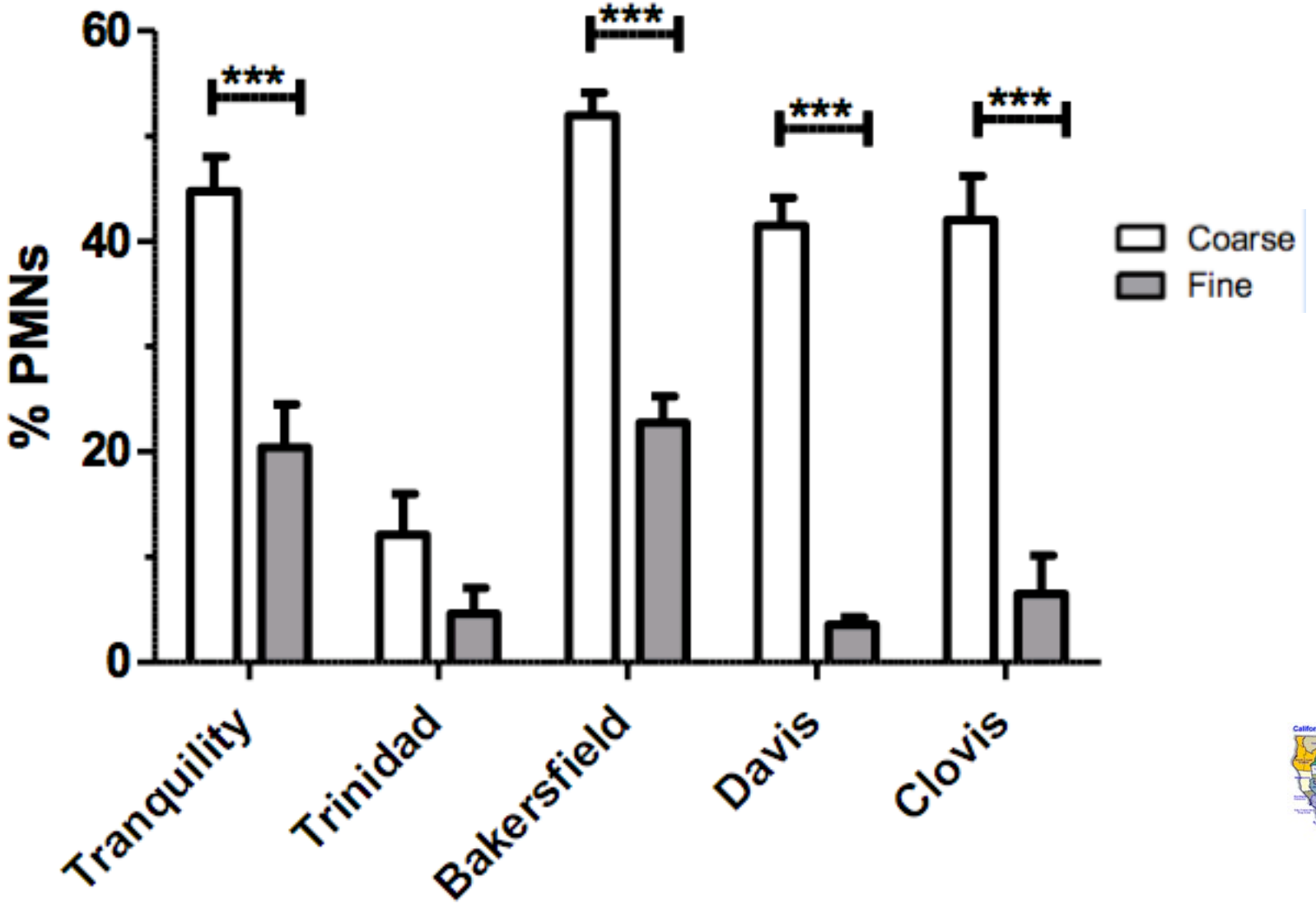
Effect of Coarse and Fine PM on ROS Activity in Endothelial Cells



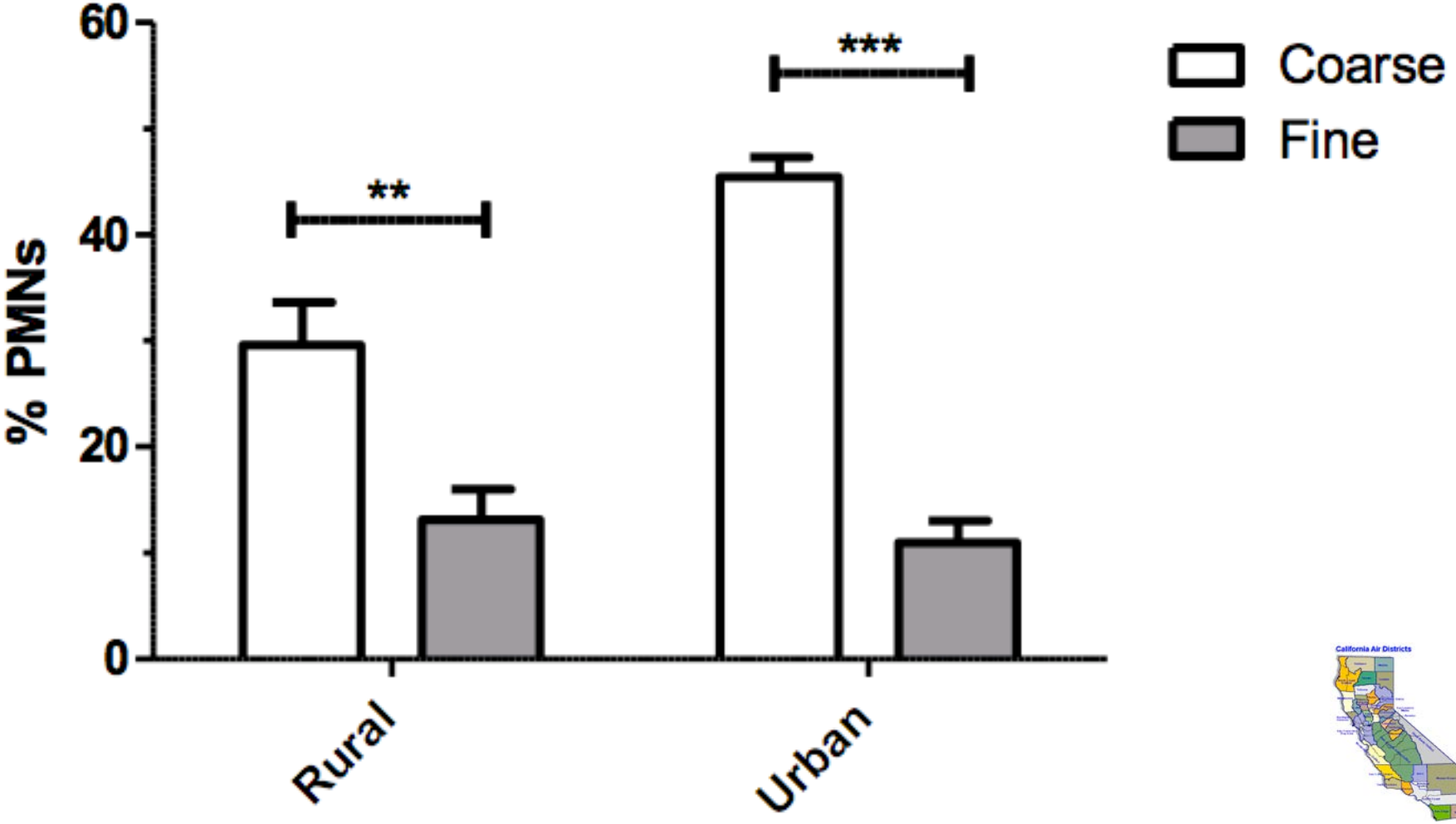
Effect of Urban and Rural PM on ROS activity



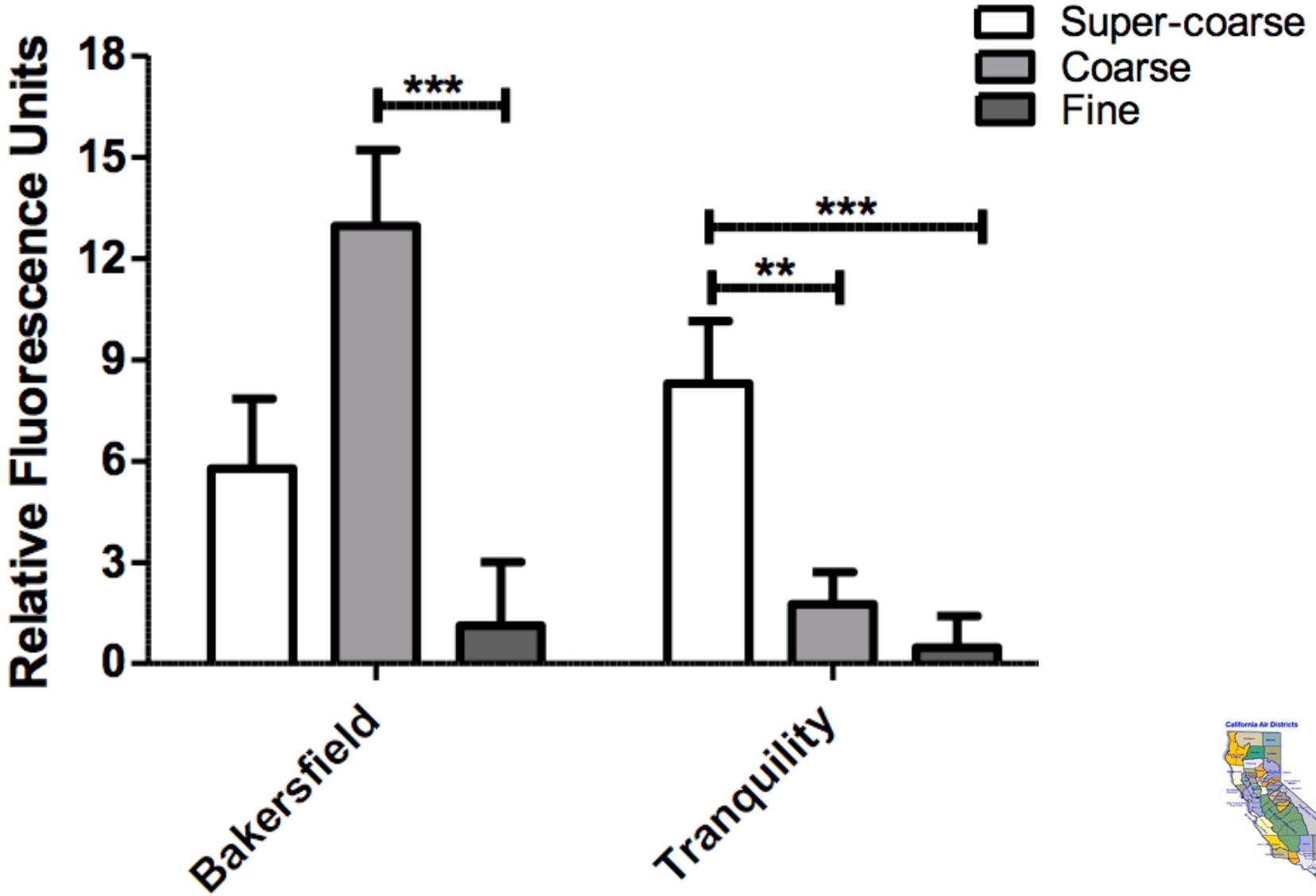
Effect of Fine and Coarse PM on Lung Inflammation in Mice



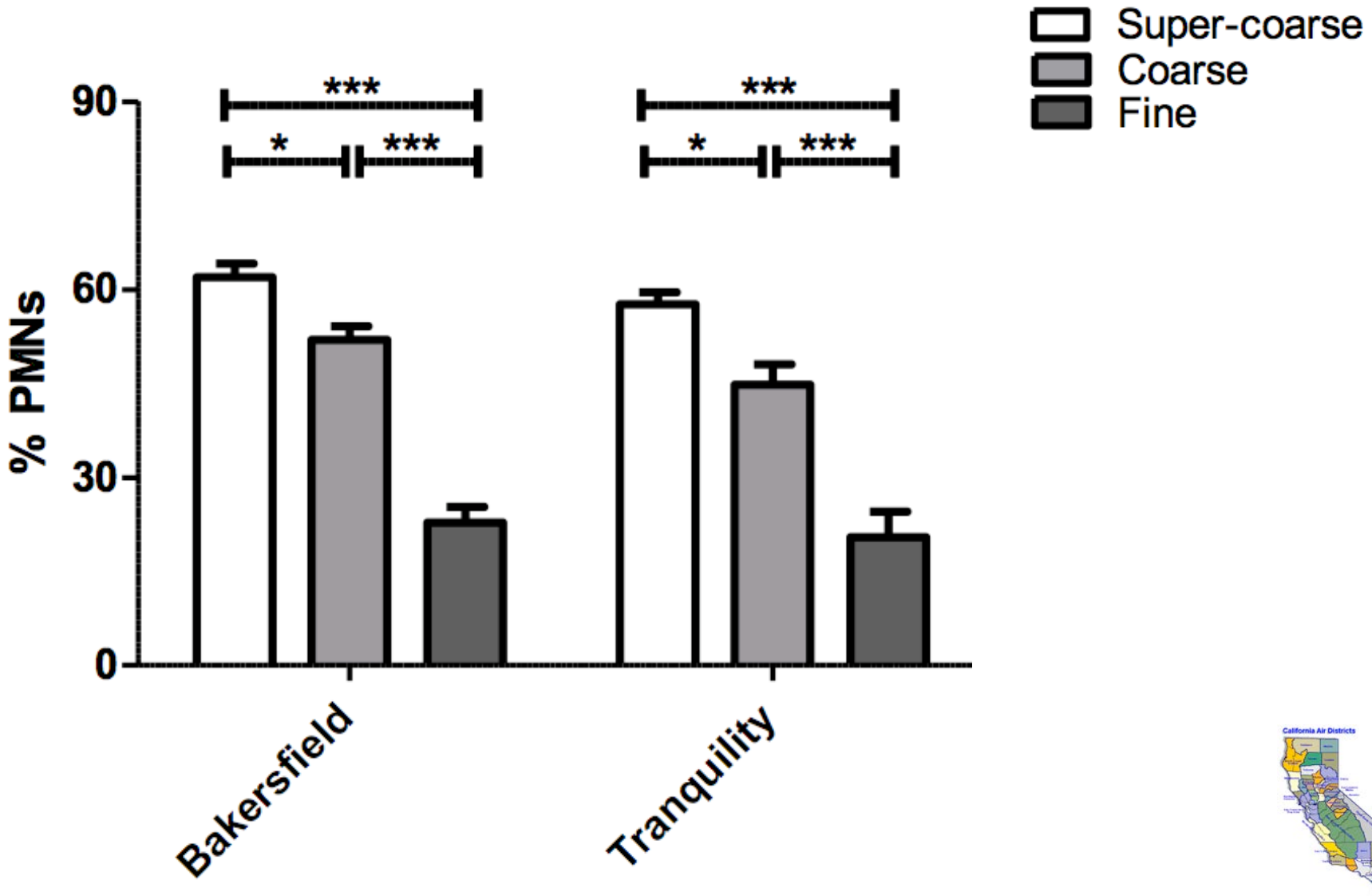
Effect of Urban and Rural PM on Lung Inflammation in Mice



Effect of Supercoarse, Coarse, and Fine PM on ROS



Effect of Supercoarse, Coarse, and Fine PM on PMNs



Correlation - Bioassay & Trace Elements

	in vitro ROS	*in vivo* %PMNs
Co	0.47***	0.75***
Cd	-0.01	-0.09
La	0.30***	0.73***
As	-0.30***	-0.27**
Se	-0.14	-0.10
V	0.33***	0.65***
Sb	0.42***	0.42***
Ni	0.14	0.19*
Sn	0.27**	0.37***
Cu	0.44***	0.60***
Mn	0.44***	0.77***
Ti	0.33***	0.76***
Zn	0.06	-0.04
P	0.29**	0.72***
Mg	0.14	0.07
K	-0.04	-0.01
Fe	0.41***	0.80***
Ca	0.27**	0.66***
S	-0.27**	-0.51***
Endotoxin	0.54***	0.27

Positives

- Simultaneous sampling at all 5 sites
  - Urban and rural within a single region
- 48 hr samples for time resolution
- ICP-MS analysis for all samples
- Looked at PM > 10 μm
- Have ~1000 samples available for collaboration

Study Limitations

- Extracted PM only – aqueous but archived 1/3 of each substrate
- Not daily samples or even shorter time resolved
- Biologics
- Coarse and supercoarse PM reach lung?

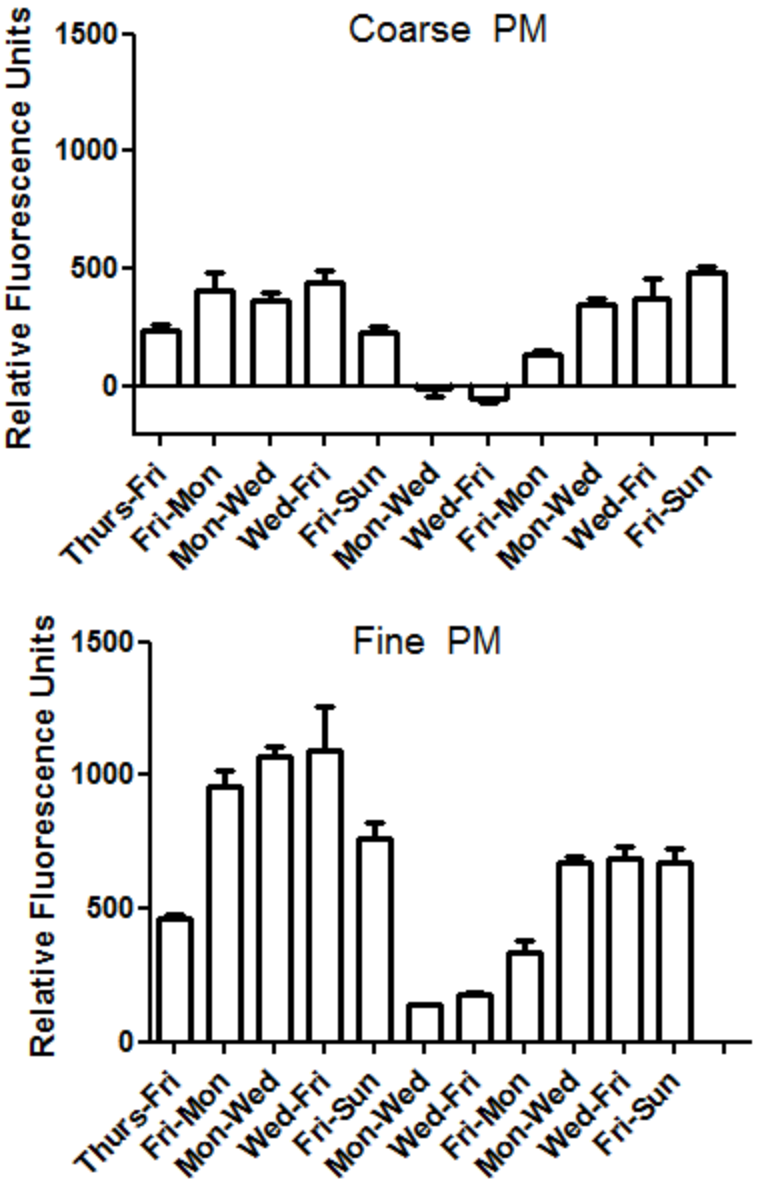
CA vs. NY Summary

- ROS (in vitro)
  - Fine >> Coarse for NY
  - Coarse >> Fine for CA
  - Urban >> Rural for both NY and CA
- PMNs (in vivo)
  - Coarse >> Fine for both NY and CA
  - Equal for Site and Locale (urban vs. rural) – same for NY and CA with exception of Trinidad
- Supercoarse PMNs
  - Coarse >> Fine for both NY and CA

Conclusion

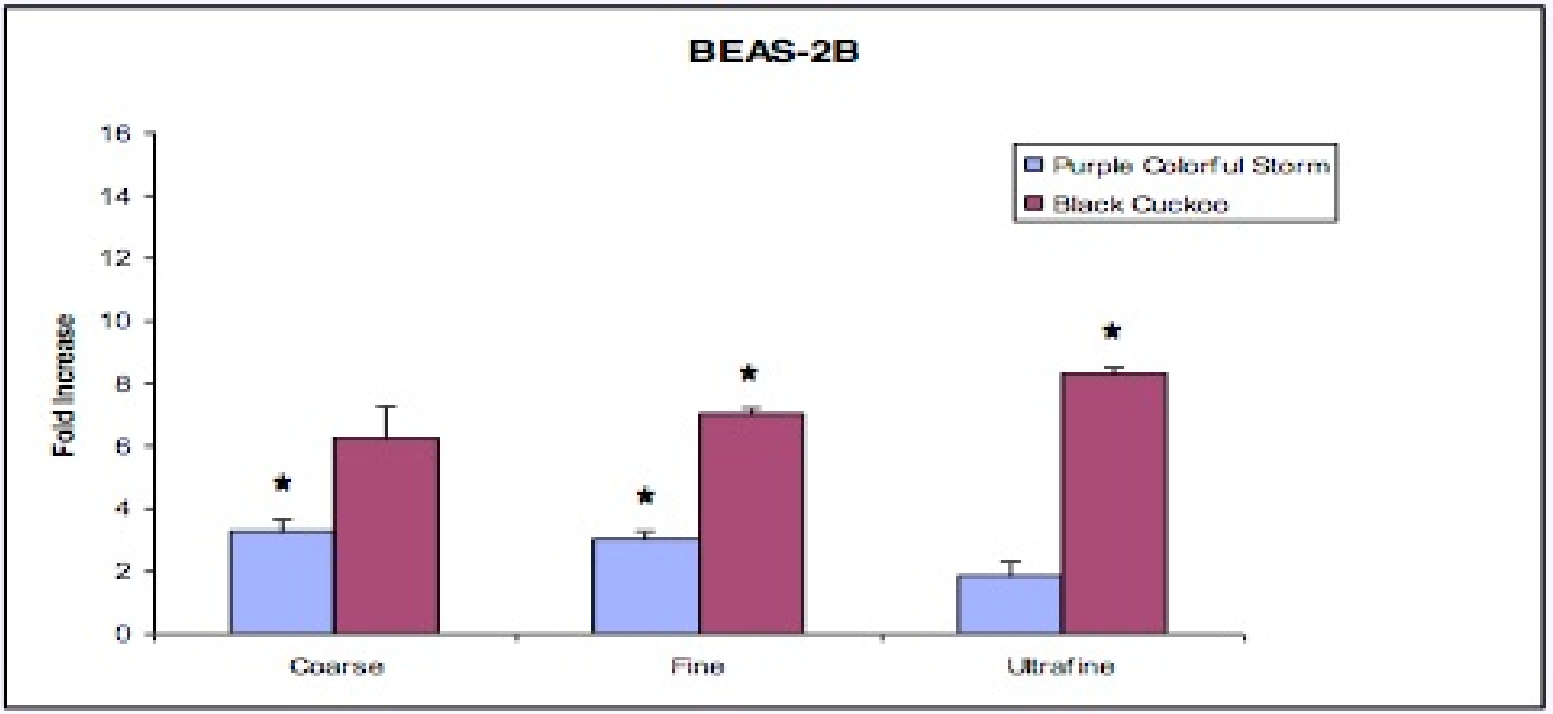
- PM composition matters

Daily Variability



Fireworks - Does Size Matter?

ROS Production by Size-fractioned PM
3hr after Exposure



Conclusion

- PM composition matters

Collaborators

David Lighthall, Tim Tyner, Jaime Contrares, James Sweet, Scott Nester, Corinne Bartlett, Chris Ruehl

Mike Kleeman, Toshihiro Kuwayama, and Kent Pinkerton (UC Davis)

Michael Ives and Brian Vasel (NOAA)

Bob Devlin, Ian Gilmour – U.S. EPA

Steve Ferguson, Petros Koutrakis – Harvard SPH

NYU - Christina Hickey, Jaime Mirowsky, Lori Horton, Martin Blaustein, Karen Galdanes, Lung Chi Chen, Mort Lippmann, Rick Peltier

w/ the help of HEI