

Abstract

Motive

- Investigate the biological underpinnings of the respiratory system following aerosol exposure + its effect on pulmonary health
- Understand how e-cigarette exposure remodels lungs over time

Methods

- High-resolution computed tomography (CT) imaging data employed, generating comprehensive 3D models through SimVascular
- Image-J analysis software utilized to quantify mean intensities of alpha smooth muscle actin (aSMA) and epithelial cell mass in the airways of mice exposed to JUUL e-cigarettes for 8, 16, and 24 weeks

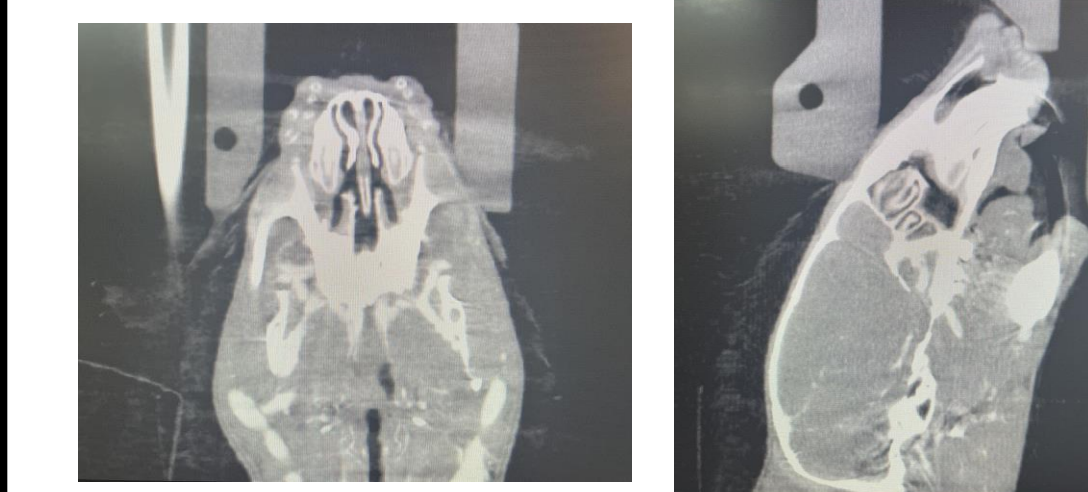
Results

- Examination of 3D models revealed undamaged nasal cavities and unobstructed airflow pathways
- Constriction examinations highlighted an increased response to methacholine leading up to 24 weeks of e-cigarette exposure, at which point there was no response to the drug at the highest exposure period

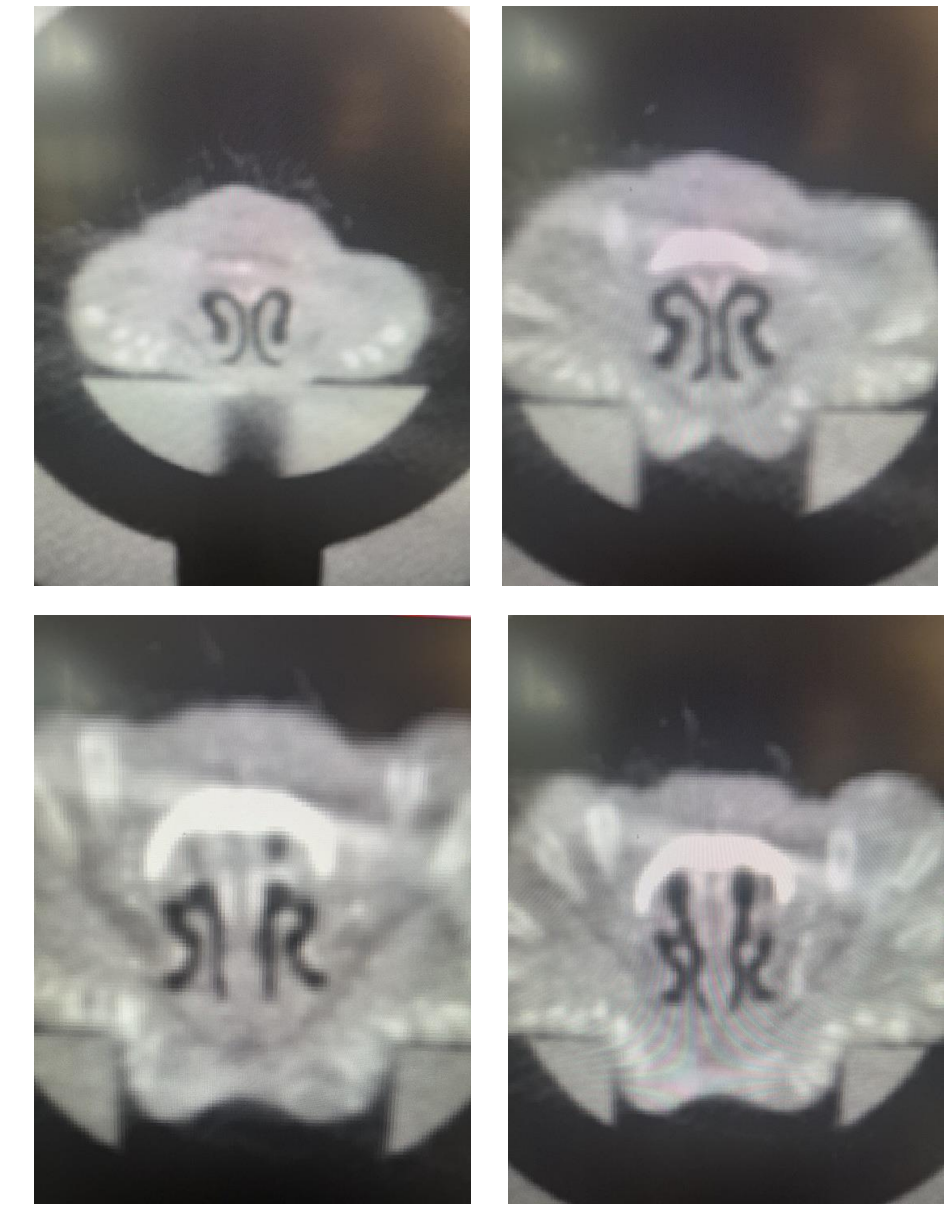
Results

Modeling Conclusions

- Using 3D modeling technology, researchers created detailed models of the mice nasal cavity, providing clear visualizations of its internal structures. They carefully included key features of the nasal cavity in the models, enabling a comprehensive examination.
- 3D models revealed all components of nasal cavity were in their expected positions, suggesting that the mice had healthy and normal nasal structures, essential characteristics for proper respiratory function



- Notable presence of clear, unobstructed pathways for airflow within nasal cavities; unhindered airflow is crucial for efficient breathing and ensures the effective exchange of oxygen in the respiratory system



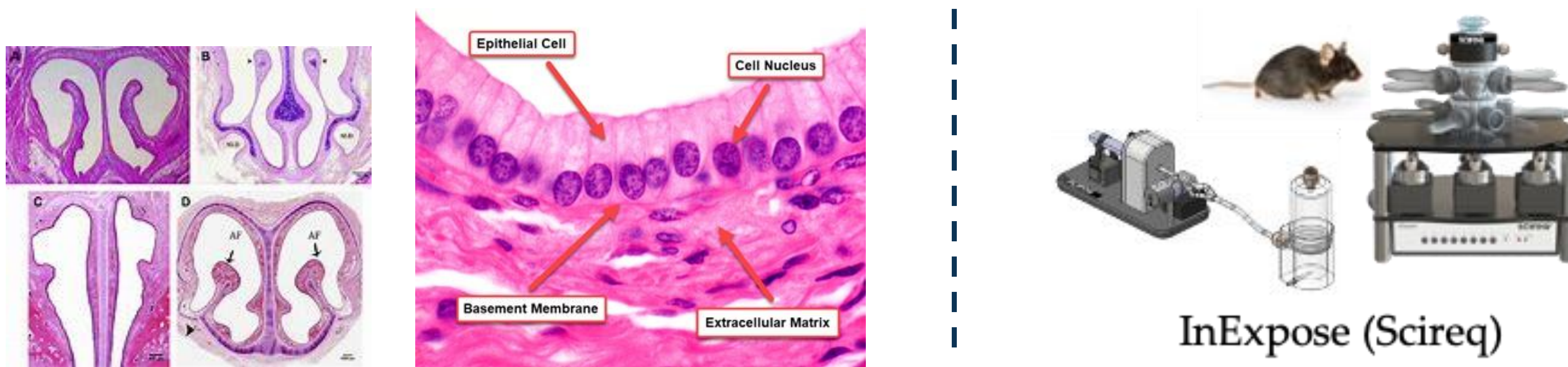
Background

SimVascular Modeling

- 3D modeling technology utilized to create detailed maps of the nasal cavity in mice.
- Enhanced understanding of airflow through nasal passages and particle filtration.
- Research aims to develop new respiratory treatments, including for asthma and allergies.

Analytical Assessment of Methacholine and aSMA

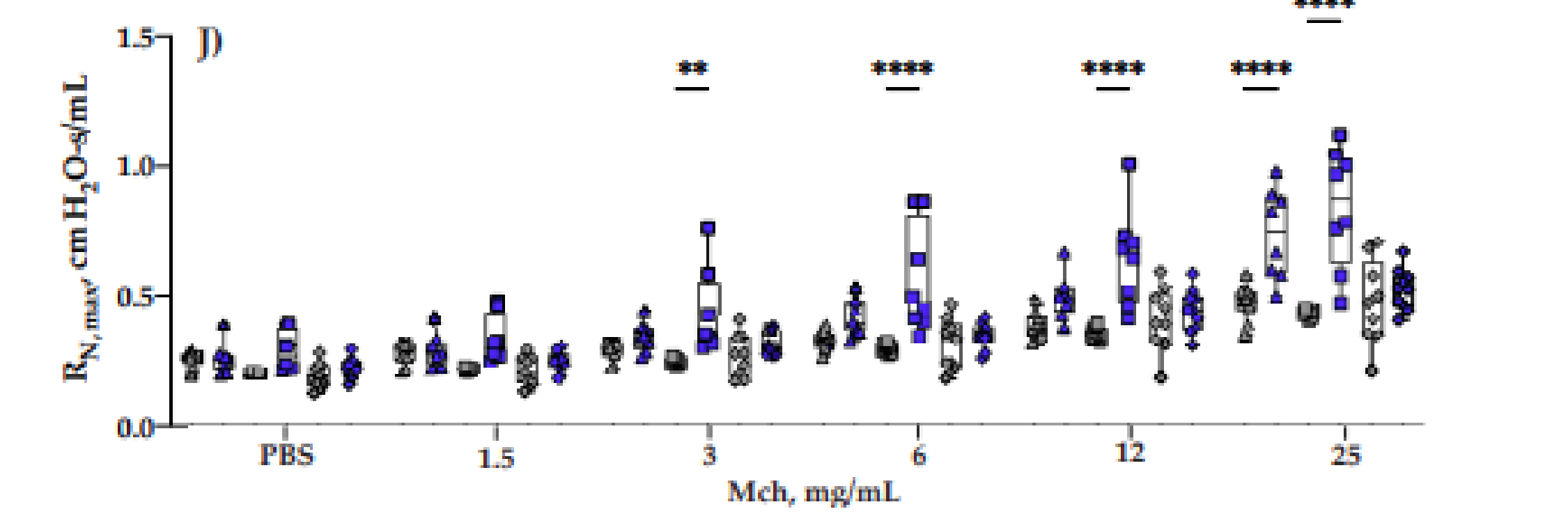
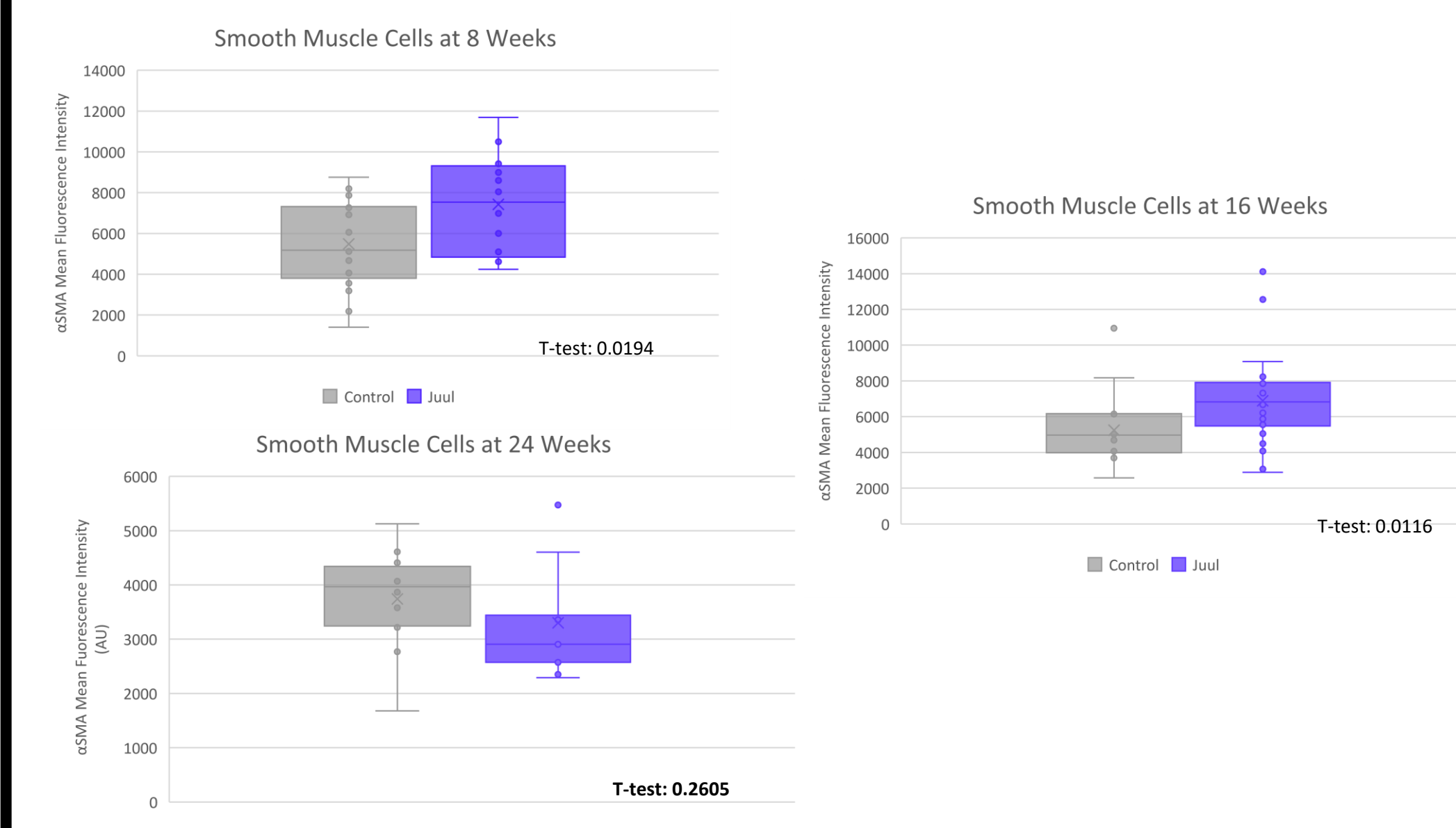
- Lung sections stained for smooth muscle actin to measure muscle content in airways, specifically epithelial cell nuclei and smooth muscle tissue
- Methacholine used to quantify constrictions of airways
- Hypothesized transient abnormalities in smooth muscle cells



Results

Epithelial and Smooth Muscle Cell Data

- T-tests employed to analyze statistical differences
- Hypertrophic muscle, indicated by increased aSMA, is associated with airway reactivity**
- 8 and 16 weeks showcased statistical differences between the exposed and control groups, 24 weeks showed none



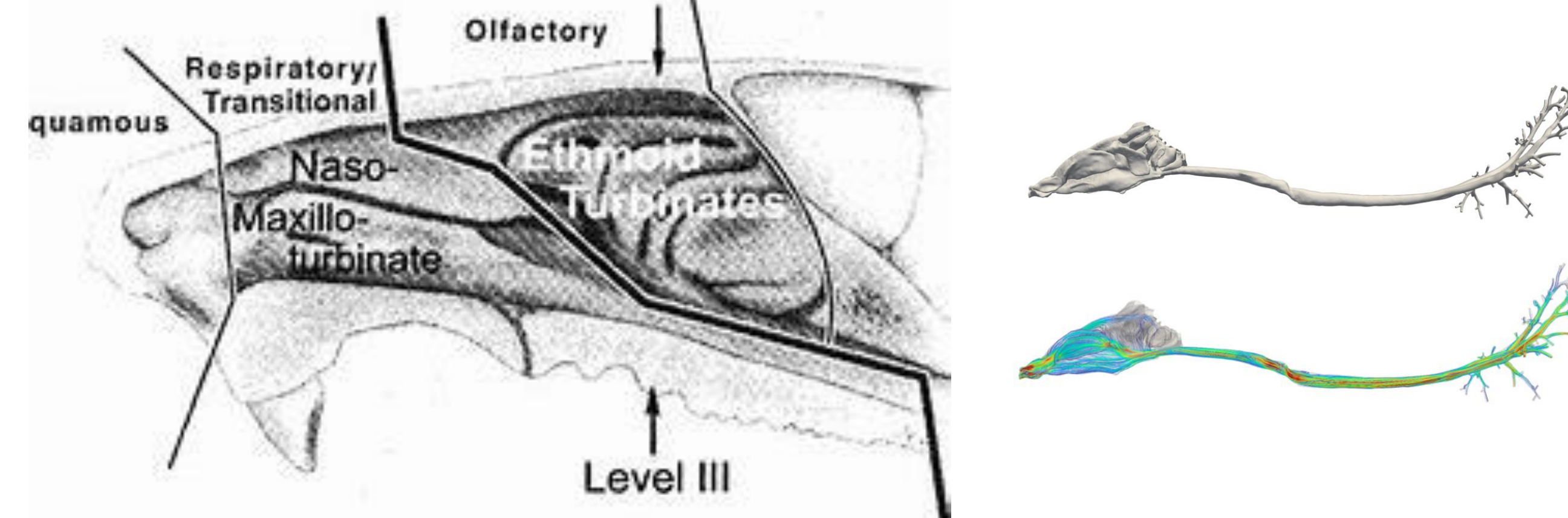
Methacholine Resistance

- Following exposure, mice produce excess collagen in attempts to compensate for the damage the smoke causes, consequently constricting the airways and making it more difficult for them to expand
- Imaging revealed mice exposed for 8 weeks responded to the drug at highest dose, 16 weeks responded much lower dose, 24 weeks didn't have a change in their response (resistance same as control)
- Demonstrates hyperreactivity across 8 weeks and 16 weeks, none at 24 weeks

Experimental Methods

Model Construction

- 3D model created using SimVascular
- Allowed for a detailed visualization of mice nasal cavity
- Key anatomical structures observed and analyzed: turbinates, olfactory epithelium
- Cross-sectional views + virtual tours used to enhance understanding



Data and Graphical Analysis

- Brightfield fluorescent microscope
- Image-J Fiji Analysis Software; measure intensity of smooth muscle tissue
- Cross sections analyzed ranging from 8 weeks, 16 weeks, and 24 weeks of exposure
- Measures intensities of smooth muscle tissue to be later compiled in an excel sheet

		epithelial + smooth muscle cells				just smooth muscle cells					
		Area	Mean	Min	Max	Area	Mean	Min	Max		
8 wk Control	M1 bronchi a	7016.8	3270.5	9	85535	0.8689	3288	4056.8	9	65535	12344
	M1 bronchi b	6403.6	4460	9	65535	0.8286	4053.4	4636.9	9	65535	11831
	M1 bronchi c	4534.8	8086.3	14	65535	1.2075	16831	8054.1	18	65535	35842
	M1 bronchi d	7380.9	6123.1	14	65535	0.8286	2427.3	6994.1	20	65535	23484
	M2 bronchi a	6773.1	3192.7	14	65535	0.4636	4076	2932	14	65535	6153
	M2 bronchi b	5827.9	3575.9	17	65535	0.6143	2334.3	3182.8	17	65535	12635
8 wk Juul	M2 bronchi c	6270.3	3895.3	4	65535	0.362	3755.3	1434.9	4	35911	0.2127
	M2 bronchi d	6080.2	5675.3	9	65535	0.3482	5338.9	3555.4	9	65535	0.6686
	M3 bronchi a	4044.1	7391.3	14	65535	1.6262	1045	7201.1	20	65535	6.8229
	M3 bronchi b	6272.4	6697.8	12	65535	0.934	1636	5177.6	12	65535	2.0709
	M3 bronchi c	10837	8278.1	14	65535	0.6604	952.5	7671.4	15	62462	0.8206
	M3 bronchi d	10900	3182.6	14	65535	0.7306	10300	3182.6	14	65535	0.7306
16 wk Control	M1 bronchi a	6420.5	7932.7	0	65535	1.8027	3302.9	7255.6	0	65535	2.2636
	M1 bronchi b	6405.4	8436.6	0	65535	1.6004	3904	7250.2	0	65535	1.862
	M1 bronchi c	5700	9361.1	0	54172	1.4393	2363.1	8790.7	2	54172	3.7031
	M2 bronchi a	6125.3	5581.5	4	48895	0.3785	1430.5	5117.1	4	30767	3.5722
	M2 bronchi b	14808	8636.6	2	47290	0.2802	3895.9	4327.2	2	47290	1.1805
	M2 bronchi c	7199	3127.2	12	65535	1.1432	3216.2	6004.7	19	65535	1.8876
16 wk Juul	M2 bronchi d	3274.1	6556.6	9	65535	0.7068	4756.4	4710	9	65535	0.8888
	M3 bronchi a	7095.1	8045.8	14	65535	1.134	5411.6	8042.7	19	65535	2.2574
	M3 bronchi b	59796	8462.3	17	65535	1.4294	1832.2	8789.6	27	58832	4.7527
	M3 bronchi c	65801	10556	17	65535	0.9425	1627.2	4750.4	20	42167	2.2656
	M3 bronchi d	3083.3	7651.7	14	65535	0.8423	3658.4	8534.6	19	65535	2.3429
	M4 bronchi a	4653.4	6748.3	7	58874	1.4763	3538.8	6579.1	20	63626	4.5384
24 wk Control	M2 bronchi b	4571.7	31025	4	65535	2.247	1584.6	1688	14	65535	8.9512
	M3 bronchi a	3234.6	3458.8	7	27683	1.6883	673.91	4618.1	20	23549	6.8542
	M3 bronchi b	3688.6	3898.8	9	37174	1.054	1622.8	4237	19	23576	2.7823
	M3 bronchi c	4327.9	8695.6	12	57878	1.794	1976	5452.3	14	57955	4.7867
	M3 bronchi d	5853.6	5032.6	7	65535	0.87	5853.6	5032.6	7	65535	0.87
	M4 bronchi a	5236.1	12060	10	65535	1.2628	2486.2	10494	27	62702	4.2003
24 wk Juul	M4 bronchi b	7383.9	19267	10	65535	1.6848	4167	9417.6	12	55904	2.2931
	M4 bronchi c	4687.4	8989.8	12	65535	1.8261	4467.4	8989.8	12	65535	1.8261
M4 bronchi d	7451.7	6981.1	7	80836	0.5275	4003.2	7027.8	9	3884	1.7959	

- Find differences that are meaningful with exposure to pollutants
- Brightfield and Polarized images taken to analyze Picrosirius red collagen stains

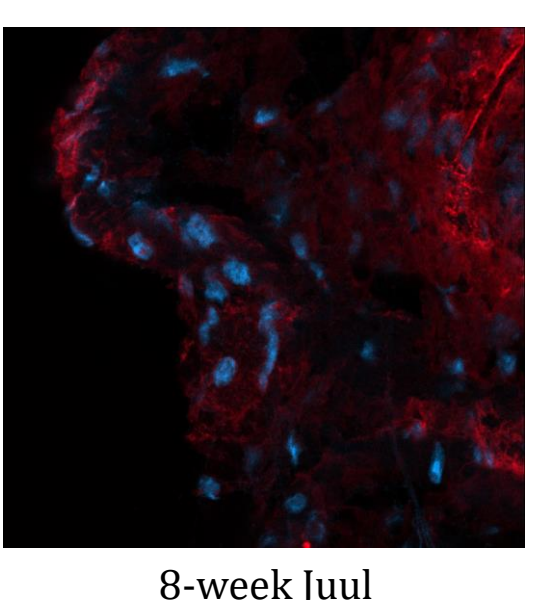
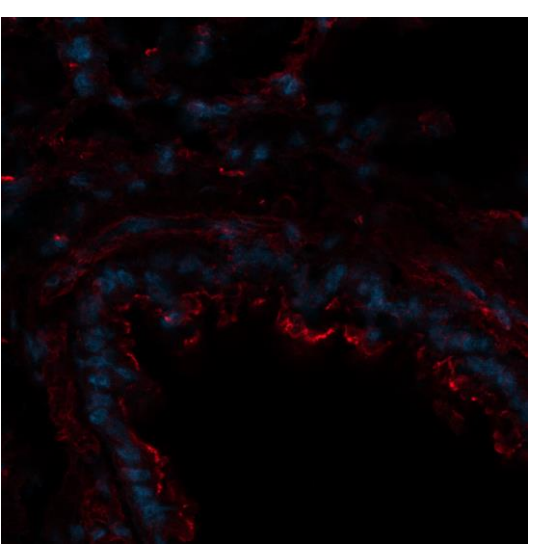
Conclusion + Moving Forward

Modeling in the Future

- Studies to be conducted on the mice nasal cavities post-aerosol exposure, making this a long-term project utilizing different researchers to build upon each other
- Our final project helps researchers understand how smoke inhalation affects the mice nasal cavities
- Sketches of nasal cavities drawn before and after exposure, giving researchers a visual means of comparing the discontinuities to better understand the effects of smoke exposure on the respiratory system
- Essential for understanding how smoke might impact the respiratory health of both mice and humans

Data Continued

- Continuing investigation on the 24-week exposure group, to be studied to develop deeper understandings of the long-term effects of aerosol exposure
- These findings suggest that regulating airway muscle hypertrophy could be a potential therapeutic target in asthma
- Study emphasizes the importance of understanding the mechanisms underlying ASM remodeling in asthma



References

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