Obesity Impact on Airway & Lung: Value of TNFα Receptor Blocker

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BACKGROUND

-In the US, more than 1/3 of adults are obese (1)

-Obesity has been linked to asthma, with abdominal obesity restricting lung volumes, lowering chest wall compliance and decreasing respiratory muscle efficiency (2)

-However, less is known about pulmonary inflammatory responses associated with raised levels of systemic inflammation often seen in the obese (2)

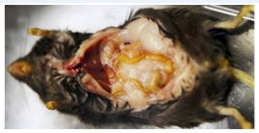
-Previous studies in lab animals have shown that lung inflammatory responses induce pro-inflammatory mediators (Leptin, IL6) from adipose tissue (2)

-This study investigates the role of obesity in pulmonary inflammation and aims to determine if obesity alone is related to greater lung inflammation

-We will compare degree of inflammation in control ob/ob mice (genetically obese, leptin knockout mice) and TNFα receptor blocker ob/ob mice

-We hypothesized that there would be a decrease in inflammation systemically and that both fat and lung would show lower inflammation

METHODS



GROSS OBESITY IN THE OB/OB MICE FED A NORMAL DIET, 8 WEEKS

-TNFα receptor blocker was administered 2x weekly X 8wks at a dose/kg (body weight)

-Abdominal fat and lung were paraffin embedded, sectioned and stained with H&E and with labeled with F4/80 antibody.

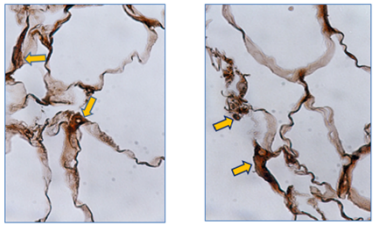
-9 high power fields were counted on each tissue section (400x)

-Sera from both groups were tested by ELISA for IL6 and TNFα

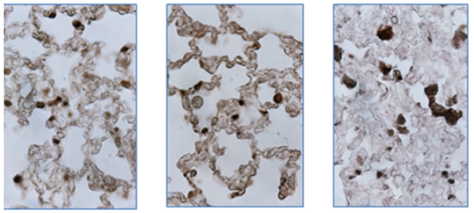
-Statistics utilized the Statistica program

RESULTS I

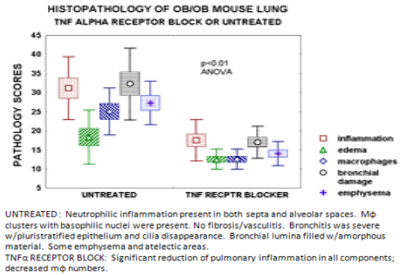
F4/80 stain: inflammatory macrophages in fat

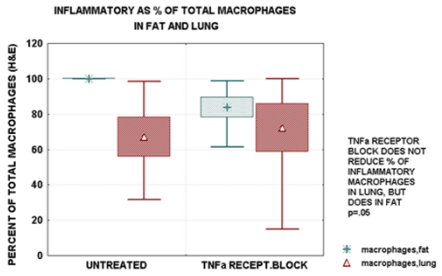


F4/80 stain: inflammatory mϕ in lung



RESULTS II





Ob/ob group	FAT		LUNG	
	Total tissue mϕ H&E stain	Inflammatory mϕ F4/80 stain	Total tissue mϕ H&E stain	Inflammatory mϕ F4/80 stain
UNTREATED	18.2 ± 0.83	21.16 ± 3.76	33.4 ± 21.2	38.7 ± 34.4
TNFαr-BLOCK	10.13 ± 3.1	9.5 ± 1.0	11.3 ± 9.5	28.8 ± 21.59

CONCLUSIONS

-Without intervention, inflammatory macrophages were found at high levels in lung as well as abdominal fat

-Mice receiving treatment had significant reduction of inflammatory macrophages in abdominal fat ($p < 0.01$)

-Treatment of mice did not lead to significant reduction of inflammatory macrophages in lung ($p = 0.32$)

Further Research Questions

-Do inflammatory macrophages originate in adipose tissue and distribute to other organ/sites?

-Since our intervention decreased only the abdominal inflammatory macrophages, can systemic effects of obesity be limited

Strengths and Weaknesses

-Use of appropriate genetically obese model

-Use of pictures to demonstrate procedures

-Size of group had been determined by a previous study and was adequate to find significant differences

-Count of inflammatory macrophages in fat and lungs of normal strain of mice would have furnished interesting data, but these would not be on obese mice

References

(1)Flegal KM et al. Prevalence and Trends in Obesity among US Adults, 1999-2008. JAMA. 2010 Jan 2012;303:235-41
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(3)Morris, AE et al. The Association between Body Mass Index and Clinical Outcomes in Acute Lung Injury, Chest. 2007 Feb;131(2):342-8