

# Emphysema And Macrophages

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## A. Statement of study and purpose rationale

Emphysema is a debilitating disease of the lung characterized by an abnormal dilation of the distal airways of the lung. Millions of Americans suffers from this condition. The consequences range from mild shortness of breath to significant exercise limitation and even death. The major risk factor for this disease is smoking. However, only approximately 30% of smokers will develop significant signs of the disease. Why some smokers develop emphysema and others do not is not entirely clear. Traditionally, it has been thought that the disease is a result of an imbalance between proteases (enzymes that break down important structural proteins of the lung like elastin) and antiproteases. It has long been thought that neutrophils attracted by cigarette smoke produce neutrophil elastase. This enzyme has been thought to be the main culprit responsible for the breakdown of elastin and the disruption of the lung's architecture. However, recent studies have begun to show that other cells namely the macrophage may be playing the primary role in the progression of the disease. the studies have shown that in patients with emphysema, the relative concentration of macrophages increases in the lung whereas the relative concentration of neutrophils decreases. In addition, research has shown that the macrophages of emphysematous lungs have greatly enhanced elastinolytic activity. In my study, I will assess the qualitative and quantitative action of macrophages by looking at lung samples from patients who have undergone lung reduction surgery. The goal of this research would be to further categorize the role of the macrophage in this disease. If the study demonstrates that the macrophage has a prime role in the disease, this may help to focus research and possibly strategies for combating the disease.

## B. Description of study design and analysis

The study subjects would be obtained from those patients who would be undergoing lung reduction surgery for emphysema.

### a. Eligibility Criteria

- 1) Significant dyspnea on six minute walk test
- 2) FEV1 < 500
- 3) Radiographic evidence of hyperinflation of the lungs
- 4) Poor diaphragmatic movement
- 5) PFT's with TLC, RV increased above 2 SID and FEV1 and FEV1/VC decreased below 2 SID

### b. Exclusion Criteria

- 1) Presence of other lung disease: sarcoid, IPF and other restrictive lung diseases
- 2) Patients on immunosuppressive drugs or steroids > 10mg/day

All the study and control subjects will be selected from cases here at CPMC. As Columbia is one of the two major lung reduction centers in the metropolitan area, the patient would be referred from practicing pulmonologists and outside hospitals. As this is a disease which affects males to a greater degree, the population of patients is likely to be predominantly male. Attempts to educate outside physicians and institutions about the potential benefit of the surgery would also help to improve the recruitment of minority subjects.

Control subjects would be obtained by analyzing lung samples from patients who underwent lung resection for other reasons (i.e. tumors).

### c. Eligibility Criteria

- 1) Pre-op CT of the chest to evaluate for radiographic evidence of

emphysema

- 2) Pre-op PFT's which did not demonstrate significant changes of emphysema
- 3) Must meet criteria for thoracic surgery and have sufficient V/Q to tolerate the procedure
- 4) Not smoking for at least six months

**d. Exclusion Criteria**

- 1) Radiographic or physiologic evidence of significant emphysematous disease (i.e. TLC, RV increase above 1 SID; FEV1, FEV1/VC decrease below 1 SID).
- 2) Patients on immunosuppressive drugs or steroids >10mg/day

**C. Study Procedures**

With informed consent, the resected lungs of both the subjects and controls would undergo light microscopy and immunohistochemical testing to look for numbers of neutrophils and macrophages. The immunohistochemical stains would be repeated to minimize the underestimation of cell numbers. Once sufficient data was collected, a comparison would be made between the percentages of cells in the controls patients versus our study subjects.

The second phase of the study would involve procuring macrophages from the resected lungs of the controls and subjects via saline lavage. The macrophages would be separated out from other cells in the lavage by density centrifugation and by selecting those fluid samples with >85% macrophages and <5% polys. Radioactive elastin would then be incubated with the macrophages for 72 hours and the amount of radioactive peptides release in the supernatant would be measure and a comparison between the macrophages of emphysematous patients and controls could be made.

**D. Location of study**

The study would involve only subjects and controls from CPMC..

**E. Confidentiality of study data**

All samples used in this study will be numerically coded so as to protect the identity of participants. A secure file will be kept correlating numerical codes to individual patients.

**F. Risks and benefits**

The study will incur no additional risk to the patients; however, it may enhance understanding of the disease and serve as a focus for guiding research into potential therapies.

**G. Compensation and costs to subjects**

The patients will neither receive additional costs nor compensation during this study.

**H. Study drugs**

The study would not require any change in the drug regimens patients were taking.

**I. Radioactive substances**

Approval by the Joint Radiation Safety Committee would be obtained prior the use of radioactive elastin in this study.