

## GENOMIC RESEARCH IN SARCOIDOSIS

### Purpose

This project is designed to address the following hypothesis:

Distinct patterns in lung microbiome are characteristic of sarcoidosis phenotypes and reflected in changes in systemic inflammatory responses as measured by peripheral changes in gene transcription.

The Specific Aims are:

- 1.To identify peripheral blood mononuclear cell (PBMC) gene expression patterns that characterize distinct sarcoidosis phenotypes.
- 2.To determine whether patterns in the lung microbiome are associated with sarcoidosis severity and disease phenotypes
- 3.To correlate mRNA and microRNA expression patterns in sarcoidosis affected organs with changes in microbiome, clinical parameters and PBMC gene expression patterns
- 4.To integrate clinical, transcriptomic, and microbiome data to identify novel molecular phenotypes in sarcoidosis.

### Eligibility

Ages Eligible for Study: 18 Years to 85 Years

### Study Population

Subjects will be prescreened for predefined clinical phenotypes of sarcoidosis. Those who meet initial criteria and ERS/ATS criteria for a sarcoidosis diagnosis will be recruited and phenotyped by questionnaire, physical exam, research chest CT exam, pulmonary function tests, and blood and urine tests with a total recruitment goal of 400.

A subset of participants who have suspected pulmonary sarcoidosis, but who have not undergone a biopsy, will be recruited so that material may be obtained during their clinically indicated biopsy. If a diagnosis of sarcoidosis is confirmed, they will be enrolled and followed. If an alternative diagnosis is made, they will not undergo any further testing

Inclusion Criteria:

- 1.Age between the ages of 18 and 85.
2. Have a diagnosis of sarcoidosis established by consensus criteria (ATS/ERS), confirmed by either biopsy or by manifestations consistent with acute sarcoidosis (Löfgren's syndrome) in absence of other known diagnosis.

OR Have a suspected diagnosis of sarcoidosis and is scheduled to undergo a biopsy procedure to confirm a diagnosis of sarcoidosis using the same consensus criteria (ATS/ERS).

3. Able to tolerate and willing to undergo study procedures.

4. Be capable of understanding study forms.

5. Provide signed informed consent.

Exclusion Criteria:

1. History of comorbid condition severe enough to significantly increase risks based on investigator discretion.

2. Currently an active smoker.

3. Undergoing bronchoscopy (clinical or research) with any one of the following:

a. severe pulmonary impairment (<50% predicted FVC, <1 L FEV1; DLco <40% predicted, resting hypoxemia <92% with or without supplemental oxygen)

b. other co-morbid disease that would preclude bronchoscopy.

c. hypersensitivity to or intolerance of any of the drugs required for sedation during conscious sedation bronchoscopy.

4. Known systemic autoimmune disease such as rheumatoid arthritis, lupus, scleroderma, Sjögrens, etc.

5. Found to have an alternative interstitial lung disease during evaluation and/or screening.

6. Diagnosis of unstable cardiovascular disease including myocardial infarction in the past 6 weeks, uncontrolled congestive heart failure, or uncontrolled arrhythmia

7. Use of anticoagulation (patients on warfarin or clopidogrel will be excluded, patients on aspirin alone can be studied even with concurrent use)

8. Dementia or other cognitive dysfunction which in the opinion of the investigator would prevent the participant from consenting to the study or completing study procedures

9. Non-Sarcoidosis pulmonary disease (e.g., rheumatoid arthritis, lupus, scleroderma) that, in the opinion of the investigator, limits the interpretability of the analysis of sarcoidosis pulmonary disease

10. Primary biliary cirrhosis or autoimmune hepatitis

11. Crohn's disease

12. Chronic beryllium disease

13. Have an active bacterial or viral infection at time of screening.

14. Have an active or ongoing serious infection, including HIV, HBV and HCV
15. Active tuberculosis or are taking any medication for tuberculosis
16. Have a history of demyelinating diseases, lymphoproliferative diseases, or other malignancies other than presumed cured non-metastatic skin cancer
17. Have evidence of a likely malignancy on chest x-ray
18. Are currently pregnant at time of screening
19. Currently institutionalized (e.g., prisons, long-term care facilities)
20. Hypersensitivity to or intolerance of albuterol sulfate or propellants or excipients of the inhalers
21. History of Lung volume reduction surgery, lung resection or bronchoscopic lung volume reduction in any form.
22. History of lung or other organ transplant
23. Unable to comprehend consent document and/or questionnaires

Participating centers:

University of Pittsburgh

Johns Hopkins

National Jewish Health

University of California San Francisco

University of Pennsylvania

Vanderbilt University

Yale University

Arizona Health Sciences Center

Medical University of South Carolina