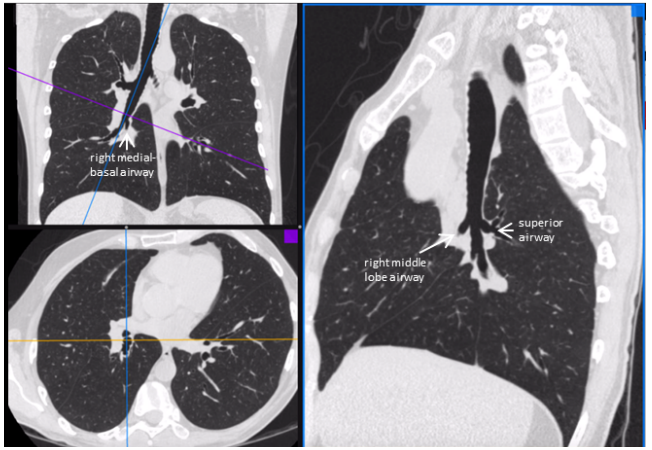
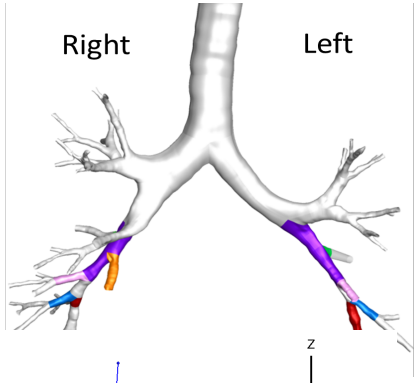
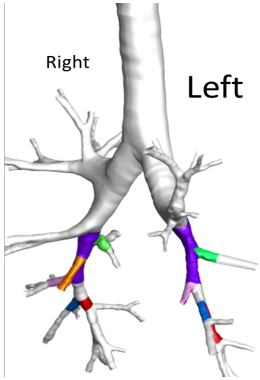
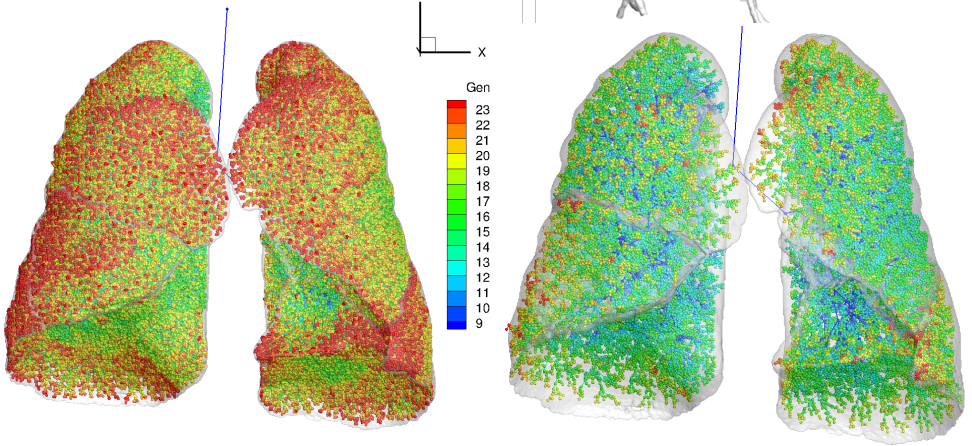
MESA Lung Non-Smokers

R01-HL130506
Progress Report
MESA Steering Committee
April 19, 2017



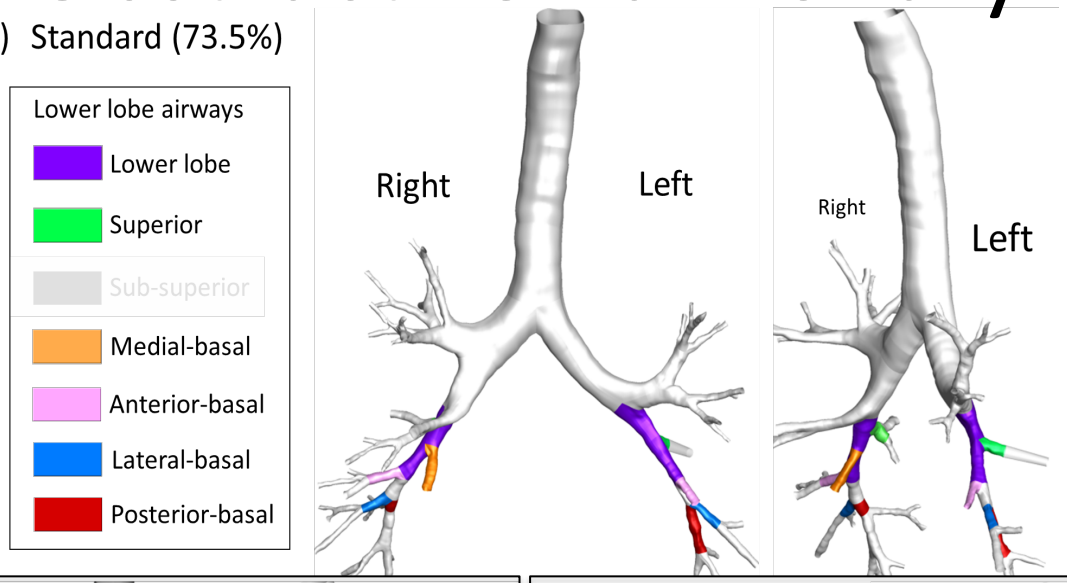




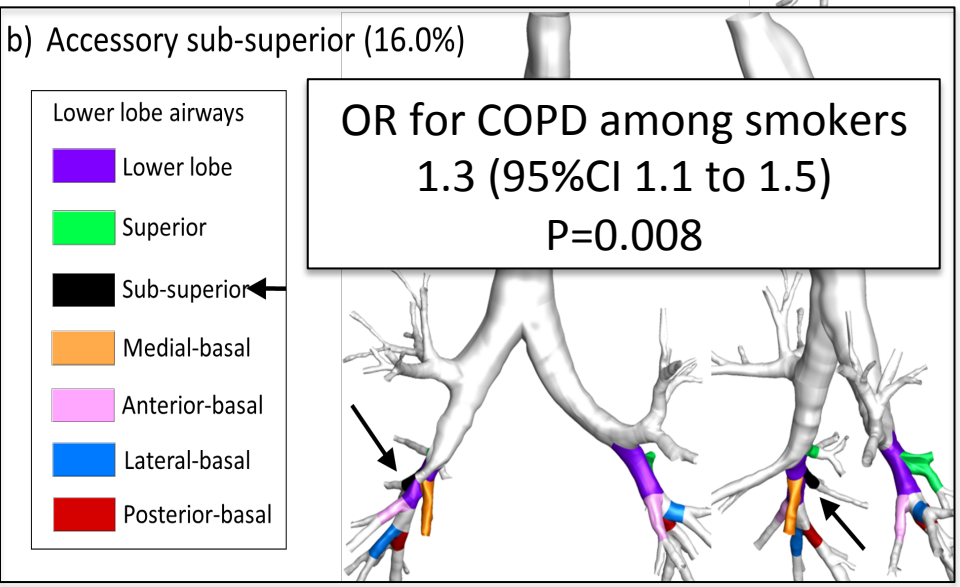


Airway Branching Variation and Chronic Obstructive Pulmonary Disease

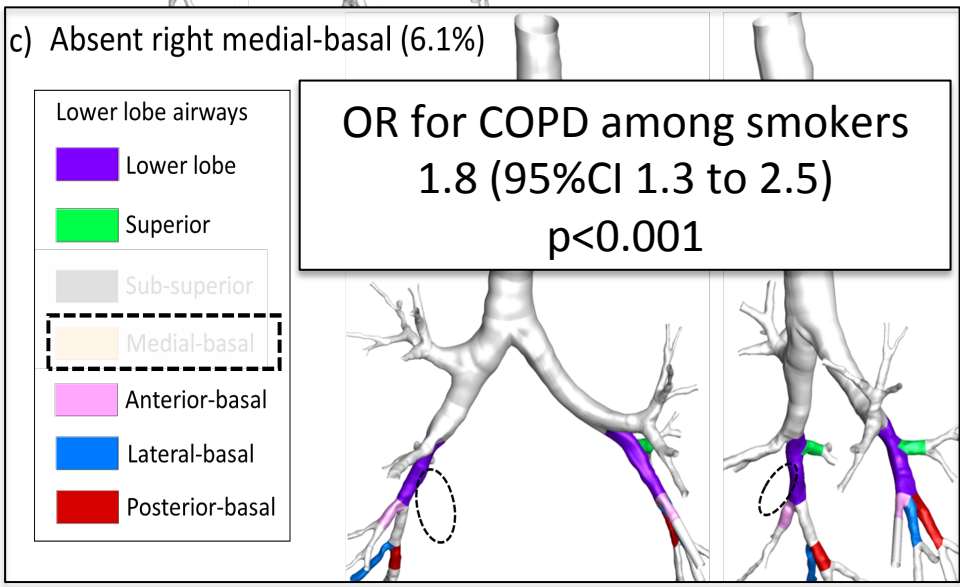
a) Standard (73.5%)



b) Accessory sub-superior (16.0%)



c) Absent right medial-basal (6.1%)



Odds ratios adjusted for age, gender, height, race, smoking status, pack-years of smoking

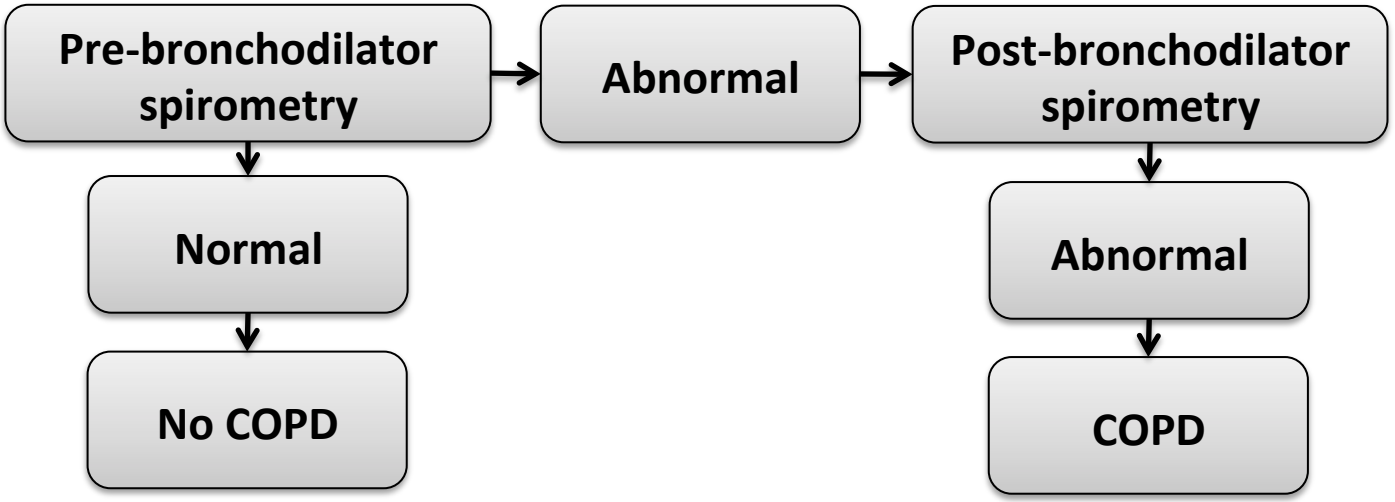
MESA Lung Non-Smokers

- ***Aim 1:*** Variant airway anatomy is independently associated with COPD and respiratory symptoms cross-sectionally among 2,635 non-smokers and with incident COPD and decline in lung function among 2,000 non-smokers followed for a median of 10 years

NON-SMOKERS	**KEY PROCEDURES: Lung questionnaire, CT, and Spirometry****
MESA Exam 6	258 of 650 (39% of target)
MESA Exam 5	1,445
CanCOLD	540

**COPD classification requires post-bronchodilator spirometry

MESA Lung Non-Smokers

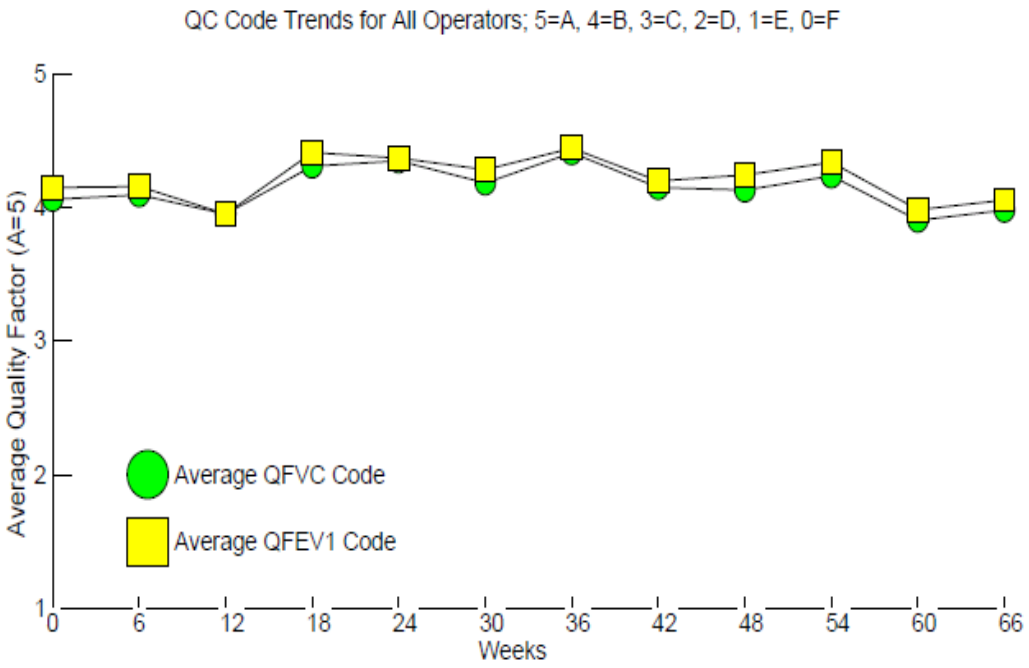


Site	Exam 6 Visits (n)	Selected for spirometry (%)	Consented of those selected (%)	Completed pre-BD spirometry of those consented (%)	Completed post-BD spirometry of those selected (%)
3 Wake	143	90	98	87	**55**
4 CU	210	86	93	93	**81**
5 JHU	207	92	98	97	**83**
6 Minn	317	98	99	95	**27**
7 NWU	327	90	96	84	**39**
8 UCLA	246	91	98	94	**61**
Total	1450	92	97	92	**56**

**COPD classification requires post-bronchodilator spirometry

MESA Lung Non-Smokers

- **Exam 6 Spirometry**
  - Good, but could be better
  - Completion rate and quality varies by site



**Post-bronchodilator spirometry required to determine COPD status

MESA Lung Non-Smokers

SPIROMETRY TAKE-HOME POINTS
- Spirometry is an essential outcome measure for the MESA Lung Studies
- High quality pre- and post-bronchodilator spirometry is possible in Exam 6

TIPS
- Remind your staff that spirometry is well-tolerated, even in the elderly
- Perform spirometry early in visit when participants when are less tired
- Questionnaires can be completed between pre- and post-bronchodilator spirometry
- Perform spirometry (or post-bronchodilator spirometry) on return visit
- QC committee is sending site-specific recommendations to improve spirometry quality

**Post-bronchodilator spirometry required to determine COPD status

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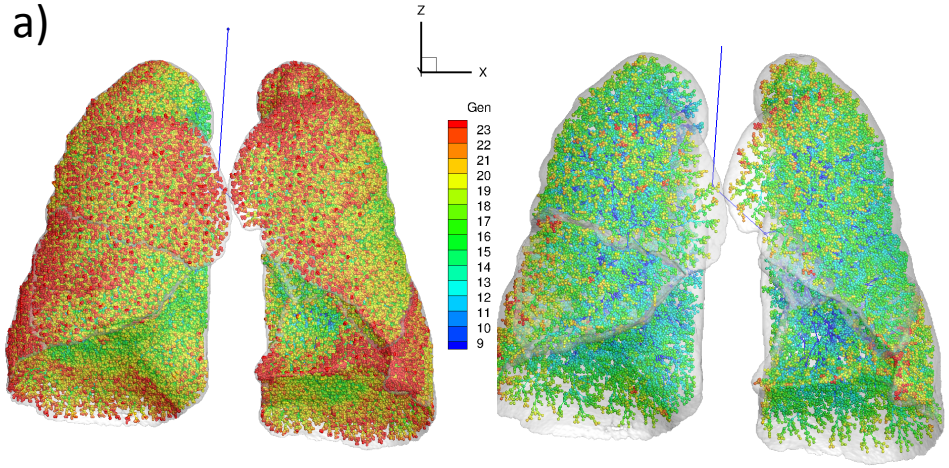
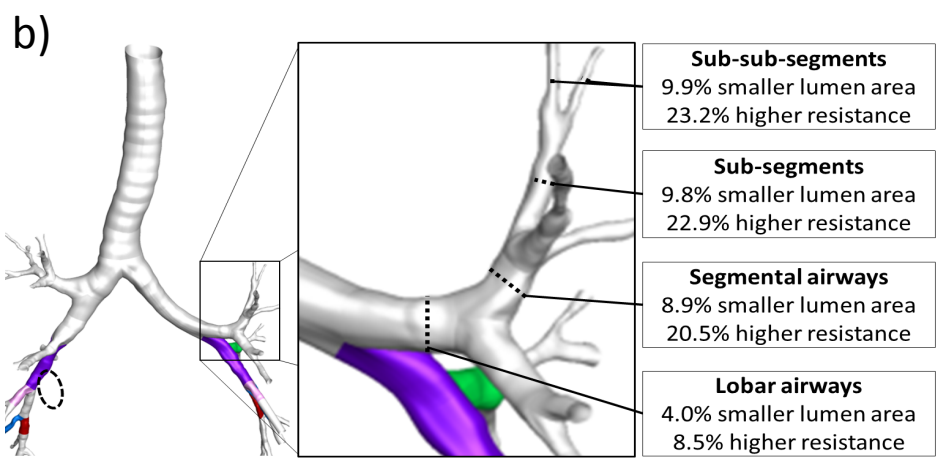
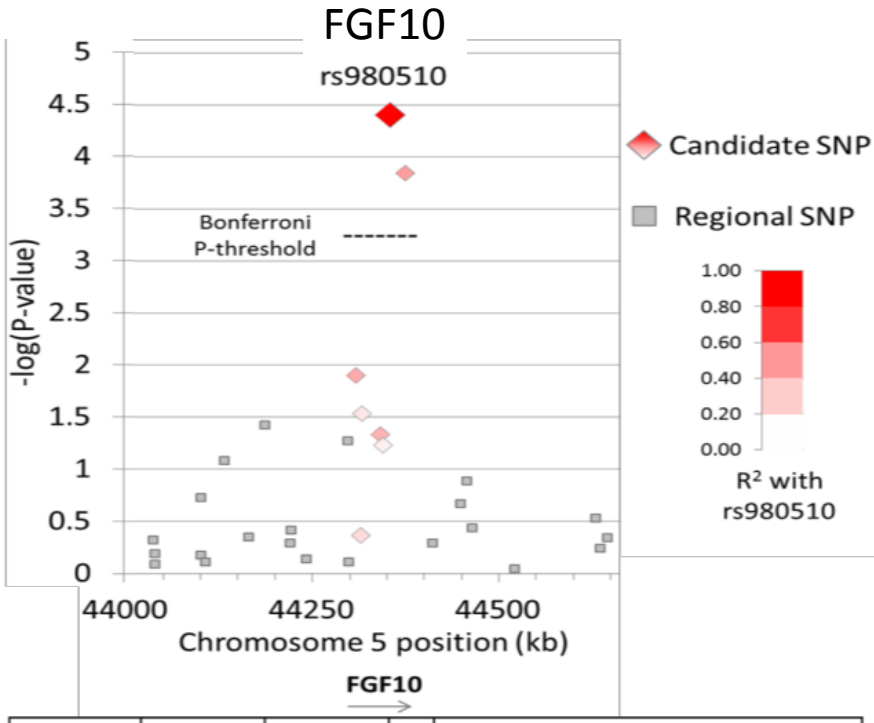
- ***Aim 2:*** The mechanisms of COPD risk differ by common airway variant among non-smokers and smokers in a CFD model of participant-specific geometry
  - Accessory airway variant: higher bifurcation density (a), and higher particle deposition in a CFD model of participant-specific geometry
  - Absent airway variant: globally narrowed lumens (b), and higher airway resistance





MESA Lung Non-Smokers

- ***Aim 3:*** GWAS will discover genetic variants underlying the common airway variants in MESA, MESA Family and SPIROMICS, with replication in an independent sample (CanCOLD)
  - Anatomy phenotyping (years 1-2)
    - 6,076 of 11,269 participants (54%) complete
  - Candidate gene analysis of absent airway variant



SNP	P-value	Pooled OR	I^2	OR by race-ethnicity			
				White	Asian	Black	Hispanic
rs980510	3.95E-05	1.63	0	1.75	1.69	1.27	1.67

Fig. 5: Regional association plot of candidate SNPs within *Fgf10* and absent right medial-basal airway (n=2,522). SNPs selected *a priori* based on location within genes implicated in airway morphogenesis (11 genes, 107 SNP). Genotyping: Affymetrix 6.0, excluding MAF<0.05, missingness per SNP>0.1, missingness per subject>0.1, and linkage disequilibrium>0.7. Analysis stratified by race-ethnicity, adjusted for gender, and principle components of ancestry, pooled by random effects meta-analysis. I^2 is heterogeneity index by race-ethnicity. OR denotes odds ratio. Bonferroni P-threshold 4.67E-04, indicated by dashed line.

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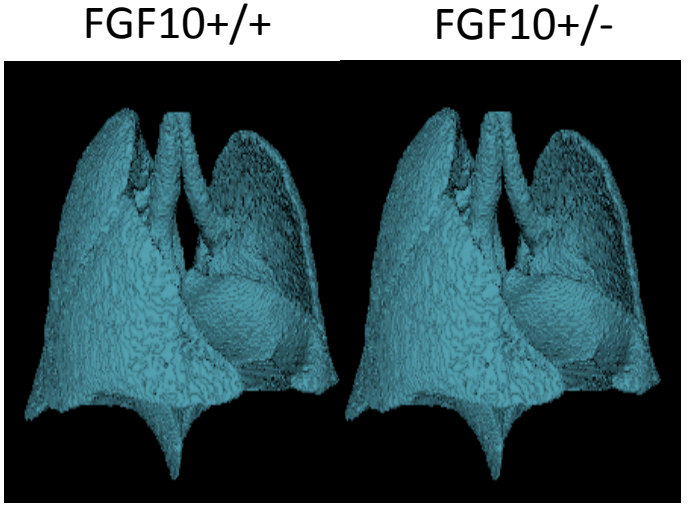
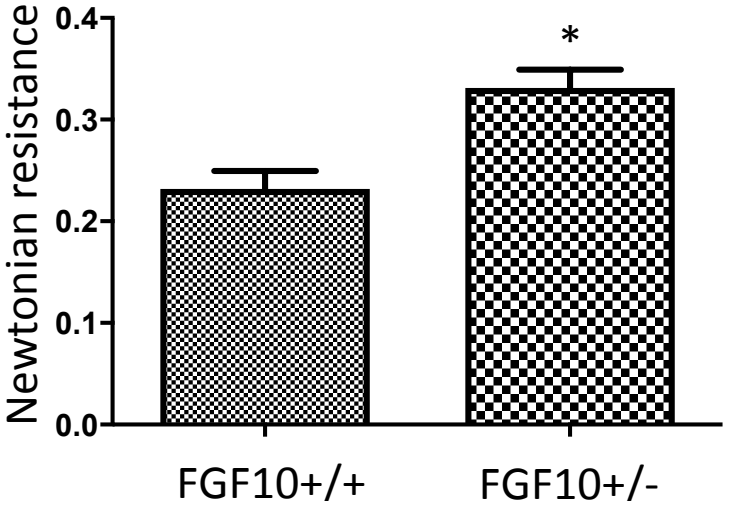


18% smaller airway lumens (p<0.001)



* p=0.01; 12 mice (het=6, wt=6)

Thank you MESA, NIH/NHLBI

- Project officer, Steering committee, OSMB, Operations committee, Ancillary study committee
- R. Graham Barr
- Clinical Site PIs,Coordinators, Staff
  - CU (S Shea, C Casto-Diehl), JHU (W Post, Erin Michos, I Benayache), NWU (K Liu, G Ho), UCLA (K Watson, S Tadros), UMN (A Folsom, J Munoz), WF (G Burke, C Nunn)
- Coordinating center
  - Dick Kronmal, Craig Johnson, Karen Hinckley Stukovsky, Kayleen Williams
- CT reading center
  - Eric Hoffman, Melissa Saylor
- Spirometry reading center
  - John Hankinson
- Computational fluid dynamics
  - Ching-Long Lin, Eric Hoffman
- Genetics
  - Steve Rich, Ani Manichaikul
- P&P committee, QC committee
- CanCOLD
  - Jean Bourbeau, Wan Tan

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