

# **Lovelace Respiratory Research Institute**

## **Legislative Tobacco Settlement Committee**

**Steven Belinsky, PhD**

**Senior Scientist, Vice President for Academic Research**

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**[www.LRRI.org](http://www.LRRI.org)**



# Joint LRRI Lung Cancer Program/UNM Comprehensive Cancer Center



## Introduction

- **Lung cancer is the number one cancer killer in the Western world. Tobacco products are linked to 90% of those afflicted.**
- **The Lovelace Respiratory Research Institute and the University of New Mexico Comprehensive Cancer Center have melded their cancer research programs together to join clinical research to basic science studies, all designed to come up with new treatments, diagnostics, and potential cures for this terrible disease.**
- **The Cancer Center provides patients and patient tissues for study by both organizations that allow the discovery of unique molecular markers of disease that can be used to tailor treatment and better design early diagnosis.**

# Approach



- **Cancer Center oncologists recruit patients into clinical trials that provide unique leading edge new treatments and offer the opportunity to Lovelace basic scientists to obtain tumor tissue samples along with control tissues for the development of molecular markers of disease.**
- **Lovelace, using tobacco settlement funding, has developed a large cohort of New Mexico smokers from which tissues, vital statistics, and disease progression data have been obtained.**
- **Thus, together the Cancer Center and Lovelace have been able to study smokers as they progress to disease onset and then throughout disease progression. They have been able to monitor and define the molecular markers that lead to disease and that define effective treatment.**

# Results and Future Work



- **The Cancer Center has been able to create a world-class treatment and assessment program for lung cancer patients here in New Mexico, and has for 10 years incorporated the Lovelace lung cancer basic science research program led by Dr. Steven Belinsky into the research agenda of the Center.**
- **I head up the lung cancer effort of the Cancer Center. This internationally recognized program uses basic research to understand the causes, and translates this knowledge into developing biomarkers for predicting cancer risk as well as the testing of novel agents for treatment and prevention.**
- **One major focus has been on developing unique, highly sensitive diagnostic biomarkers of early disease using sputum samples from Cancer Center patients.**

## Results and Future Work (continued)



- **With this data (and that obtained from the New Mexico Smoker's Cohort) he and other Cancer Center scientists have identified a number of DNA modifications that predict disease at a very early stage.**
- **Other markers are being sought that predict success of chemotherapy and other treatments. The physician-scientists treat the patient and study the results, which are provided to the basic scientists. The basic scientists suggest new approaches to early detection and point to new ways to intervene based on the molecular data.**
- **It is this back-and-forth interaction between the clinician scientists and the basic scientists that produce results that benefit patients. Over the years this interaction has produced a diagnostic test (DNA modification) that detects early disease from sputum obtained from smokers.**

## Results and Future Work (continued)



- **Further, these studies have also identified numerous molecular pathways that appear altered in lung cancer tumors and in the lungs of smokers prior to diagnosis.**
- **In the future, Cancer Center scientists hope to use these markers to predict who will respond best to which treatments, which smokers are at greatest risk of developing lung cancer, and what new chemotherapeutic drugs will be most effective.**

# Results and Future Work (concluded)



- **In addition, new avenues of research between LRRI and the Cancer Center are:**
  - **Testing novel therapies that awaken genes to kill tumor cells**
  - **Making old drugs better by aerosol delivery directly to the lungs**
  - **The repurposing of drugs used to treat other diseases that prove to be effective against lung tumor cells**
- **Additional exciting new avenues of work with this partnership will focus on the neurological basis of tobacco addiction and chemobrain.**

# Ben Lujan Lung Cancer Program



- **Through a recurring funding stream, the New Mexico UNM Comprehensive Cancer Center, along with its Lovelace partner, plan to extend and enhance the progress made so far to identify completely new approaches to treatment and diagnosis.**
- **In the past the funding for this work via the tobacco settlement mechanism has been intermittent and of inconsistent amounts.**
- **Our request for a yearly designated funding stream in Speaker Lujan's name to advance these goals will have a highly beneficial role in advancing the care and treatment of lung cancer patients in New Mexico.**
- **Basic and clinical scientists can be hired full time with the knowledge that their work will not be interrupted or ended by the vagaries of the funding cycle.**

# Appendix



# About LRRI



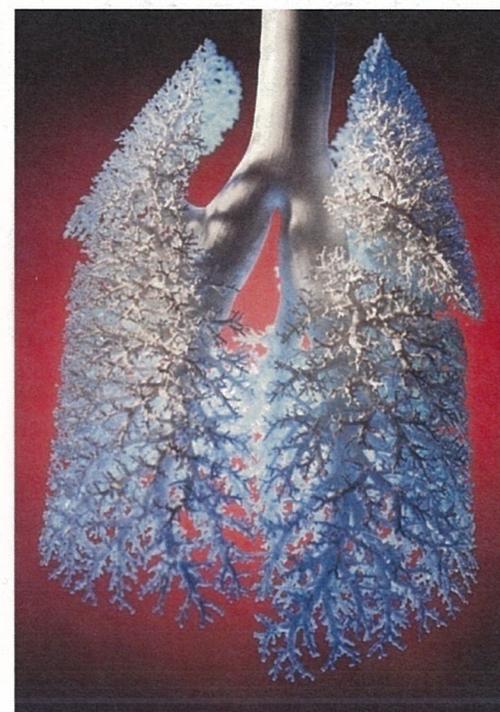
- **Founded in 1947 in the State of New Mexico, not-for-profit corporation**
- **170 PhDs, MDs, and DVMs**
- **\$125 million revenue**
- **\$43 million endowment**
- **500,000 square feet of facilities**
- **280,000-person clinical research population base**
- **1200 employees**
- **250 clients**
- **DOD Secure Facility; CBN defense focus**
- **Outlets in eight cities**

# Lovelace Respiratory Research Institute (LRRI)



**An independent, private, research institute serving humanity through research on the prevention, treatment, and cure of respiratory disease**

**LRRI is the only private basic-science, biomedical research organization totally dedicated to the study of respiratory diseases.**

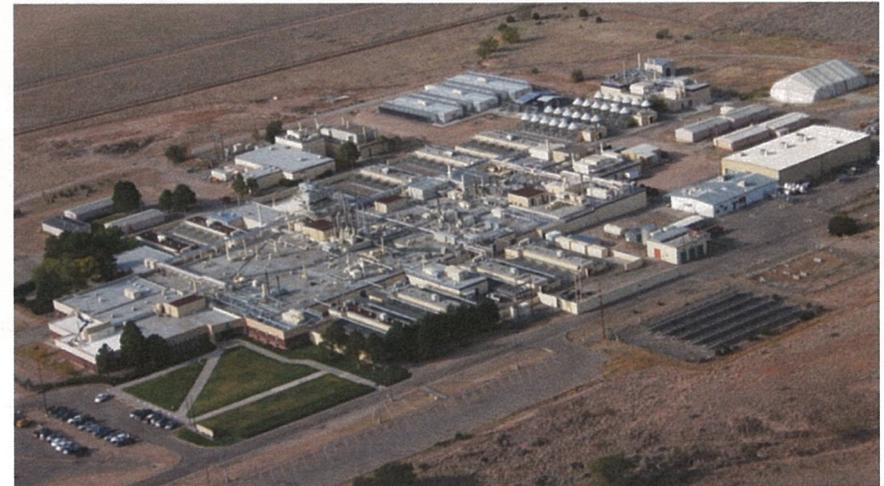




**LRRH Headquarters  
and Research Facility  
(125,000 sq. ft.)**



**Inhalation Toxicology  
Laboratory  
(325,000 sq. ft.)**



# Effect of Tobacco Settlement Support from the State to LRRI



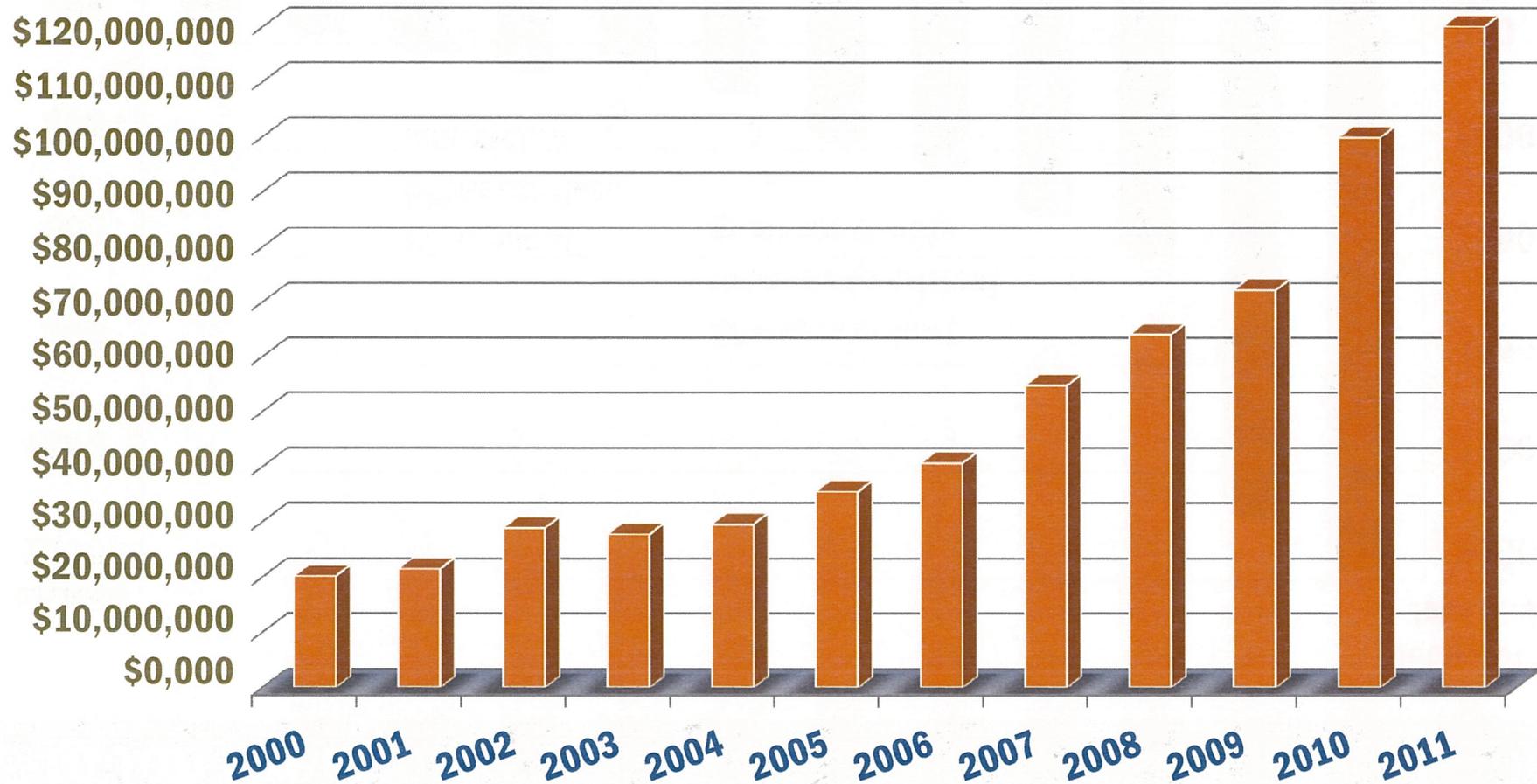
- **Supported the creation of a large infrastructure to test drugs on smoke-induced disease**
- **Created a clinical cohort of New Mexican smokers that has produced tens of millions of dollars of new federal funding**
- **Supported the development of infrastructure to allow for the study of new countermeasures to inhaled threats such as anthrax, dirty bomb aerosols, chemical threats (nerve gas, etc.).**
  - **This resulted in tens of millions of dollars of new commercial and federal funding coming to New Mexico**
- **Supported the creation of a clinical trial network and infrastructure that has undertaken >800 clinical trials in New Mexico and brought over \$30 million to the state from the pharmaceutical industry**

# Valuable Emerging Information on Lung Disease as a Result of Funding

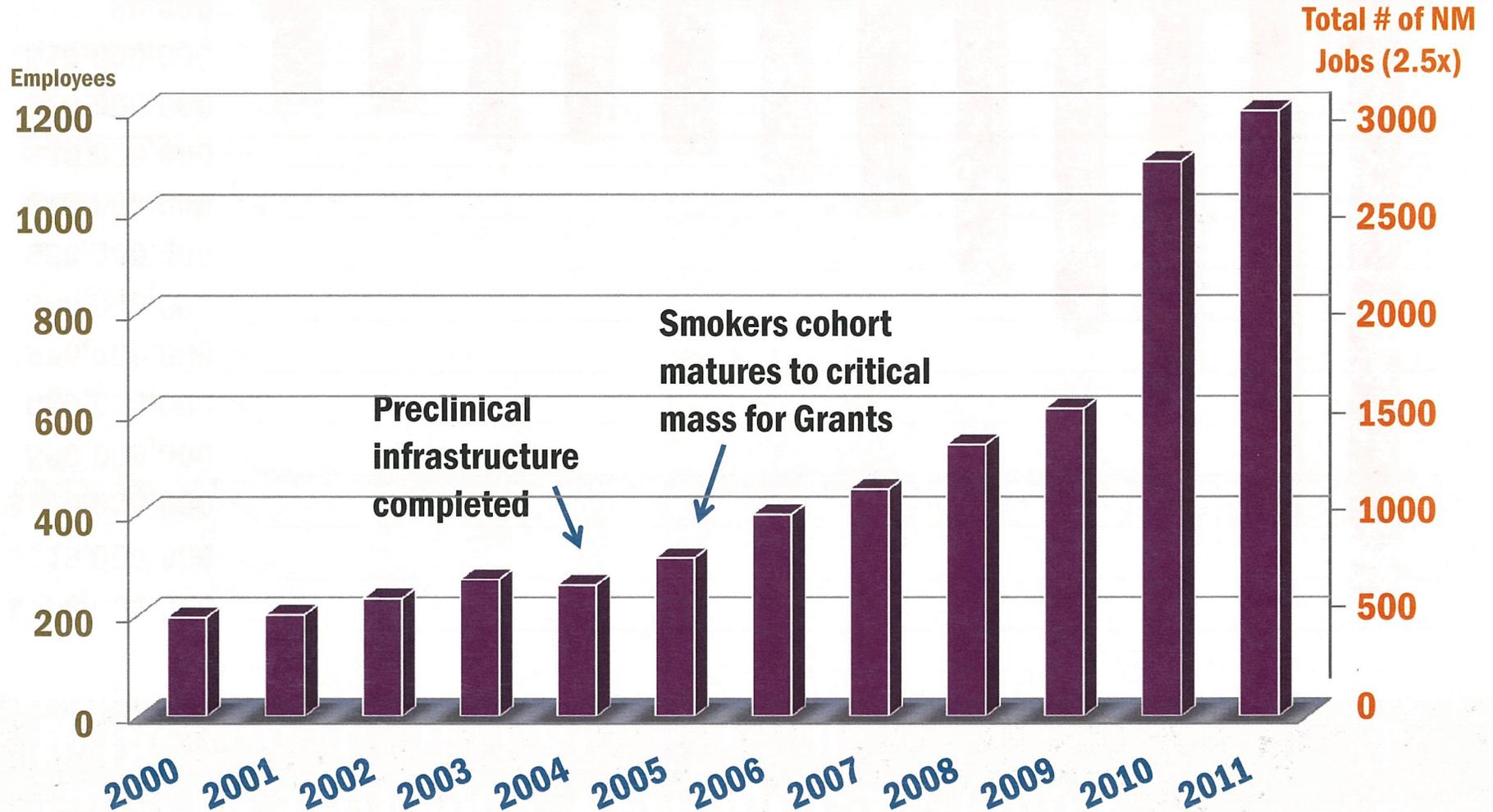


- **Yohannes Tesfaigzi and his colleagues have exciting new preliminary findings supporting the premise that lung infections may accelerate the development of COPD.**
- **Steve Belinsky and his laboratory are developing new classes of biomarkers that may allow for lung cancer screening in blood and nasal cells.**
- **Both Yohannes Tesfaigzi and Steve Belinsky are testing new drug approaches that could block COPD and lung cancer.**
- **The LSC cohort is unique in the nation because of the high percentage of Mexican/Hispanic participants and its longitudinal follow-up of subjects that facilitates the ability to identify factors that are responsible for the decline in lung function among smokers.**

# Tobacco Settlement Revenue Contributes to the Growth of LRRI's Revenue



# Tobacco Settlement Revenue Contributes to Job Creation



# Recent Publications as a Result of Funding



**Brehm JM, Hagiwara K, Tesfaigzi Y, Bruse S, Mariani TJ, Bhattacharya S, Boutaoui N, Ziniti JP Soto-Quiros ME, Avila L, Cho MH, Himes B, Litonjua AU, Jacobson F, Bakke P, Gulsvik A, Anderson WH, Lomas DA, Forno E, Datta S, Silverman EK, Celedón J. Identification of FGF7 as a Novel Susceptibility Locus for Chronic Obstructive Pulmonary Disease. *Thorax*, 66(12):1085-90, 2011.**

✓ **Bruse S, Sood A, Petersen H, Liu Y, Leng S, Celedón JC, Gilliland F, Celli B, Belinsky SA, Tesfaigzi Y. New Mexican Hispanic Smokers have Lower Odds of COPD and Less Decline in Lung Function than non-Hispanic Whites. *Am J Respir Crit Care Med*, 184(11):1254-60, 2011.**

**Bruse S, Petersen H, Tesfaigzi Y. The Hispanic Paradox and Chronic Obstructive Pulmonary Disease. *Reply Am J Respir Crit Care Med*, 185 1246-47, 2012.**

**Flores KG, Stidley CA, Picchi MA, Mackey AJ, Stabler S, Byers T, Berwick M, Belinsky SA, Leng S. Gender Specific Association of Sequence Variants in CBS and MTRR with Risk for Promoter Hypermethylation in non-Hispanic White Smokers. *Carcinogenesis*, in press.**

## Recent Publications as a Result of Funding (continued)



**Leng S, Bernauer AM, Hong C, Do KC, Yingling CM, Flores KG, Tessema M, Tellez CS, Willink RP, Burki EA, Picchi MA, Stidley CA, Costello J, Gilliland FG, Crowell RE, Belinsky SA. The A/G Allele of Rs16906252 Predicts for MGMT Methylation and is Selectively Silenced in Premalignant Lesions from Smokers and in Lung Adenocarcinomas. *Clinical Cancer Res*, 17:2014-2023, 2011.**

**Leng S, Bernauer AM, Zhai R, Tellez CS, Su L, Burki EA, Picchi MA, Stidley CA, Crowell RE, Christiani DC, and Belinsky SA. Discovery of Common SNPs in miR-200/205 Family-regulated Epithelial to Mesenchymal Transition Pathway and their Association with Risk for Lung Cancer. *Int J Molec Epid & Gen*, 2:145-155, 2011.**

**Leng S, Do KC, Yingling CM, Picchi MA, Wolf HJ, Kennedy TC, Feser WJ, Baron AE, Franklin WA, Brock MV, Herman JG, Baylin SB, Byers T, Stidley CA, Belinsky SA. Defining a gene promoter methylation signature in sputum for lung cancer risk assessment. *Clin Cancer Res*, 18: 3387-3395, 2012.**

## Recent Publications as a Result of Funding (continued)



**Leng S, Stidley CA, Liu Y, Edlund CK, Willink RP, Han Y, Landi MT, Thun M, Picchi MA, Bruse SE, Crowell RE, Van Den Berg D, Caporaso NE, Amos CI, Siegfried JM, Tesfaigzi Y, Gilliland FD, Belinsky SA. Genetic Determinants for Promoter Hypermethylation in the Lungs of Smokers: A Candidate Gene-Based Study. *Cancer Res*, 72(3):707-715, 2012.**

**Leng S, Stidley CA, Willink RP, Liu Y, Picchi MA, Edlund CK, Van Den Berg D, Tesfaigzi Y, Crowell RE, Gilliland FD, Belinsky SA. Sequence Variation in DNA Replication and Apoptosis Genes Affects Promoter Hypermethylation in Sputum from Lung Cancer-free Smokers. *Cancer Res*, 72: 707-715, 2012.**

**Mebratu YA, Schwalm K, Smith KR, Schuyler M, Tesfaigzi Y. Cigarette Smoke Suppresses Bik to Cause Epithelial Cell Hyperplasia and Mucous Cell Metaplasia. *Am J Respir Crit Care Med*, Jun 1, 183(11):1531-8, 2011.**

**Meek P, Sood A, Petersen H, Belinsky SA, Tesfaigzi Y. GATA-4 Gene Methylation is Associated with Health Status in Chronic Obstructive Pulmonary Disease. *J COPD*, submitted.**

## Recent Publications as a Result of Funding (continued)



**Nyunoya T, March TH, Tesfaigzi Y, Seagrave J. Antioxidant Diet Protects Against Emphysema, but Increases Mortality in Cigarette Smoke-Exposed Mice. *COPD*, 8(5):362-8, 2011.**

**Petersen H, Sood A, Meek P, Shen X, Cheng Y, Belinsky SA, Celli B, Tesfaigzi Y. ACE Inhibitor Use is Associated with Less Decline in Lung Function in Smokers. submitted.**

**Silverman EK, Vestbo J, Agustí A, Anderson W, Bakke PS, Barnes KC, Barr RG, Bleecker ER, Boezen HM, Burkart KM, Celli BR, Cho MH, Cookson WO, Croxton T, Daley D, DeMeo DL, Gan W, Garcia-Aymerich J, Hall IP, Hansel NN, Hersh CP, Kalsheker N, Kiley JP, Kim WJ, Lambrechts D, Lee SD, Litonjua AA, Lomas DA, London SJ, Nishimura M, Nørdestgaard BG, O'Donnell CJ, Postma DS, Puhon MA, Tesfaigzi Y, Tobin MD, Vogelmeier C, Wilk JB, Wouters E, Young RP, Ziegler-Heitbrock L, MacNee W, Crapo JD. Opportunities and challenges in the genetics of COPD 2010: an International COPD Genetics Conference report. *COPD*, Apr, 8(2):121-35, 2011.**

## Recent Publications as a Result of Funding (concluded)



**Smith KR, Leonard D, McDonald JD, Tesfaigzi Y. Mucous Cell Metaplasia, and Bcl-2 Expression in Response to Inhaled Lipopolysaccharide Aerosol and Effect of Rolipram. *Tox Appl Pharmacol*, Jun 15, 253(3):253-60, 2011.**

**Sood A, Petersen H, Blanchette CM, Meek P, Picchi MA, Belinsky SA, Tesfaigzi Y. Methylated Genes in Sputum among Older Smokers with Asthma. *Chest*, in press, 2012.**

**Tessema M, Yingling CM, Thomas CL, Klinge DM, Bernauer AM, Dacic S, Siegfried JM, Dahlberg SE, Schiller JH, Belinsky SA. SULF2 Methylation is Prognostic for Lung Cancer Survival and Increases Sensitivity to Topotecan Via Induction of ISG15. *Oncogene*, in press.**

