

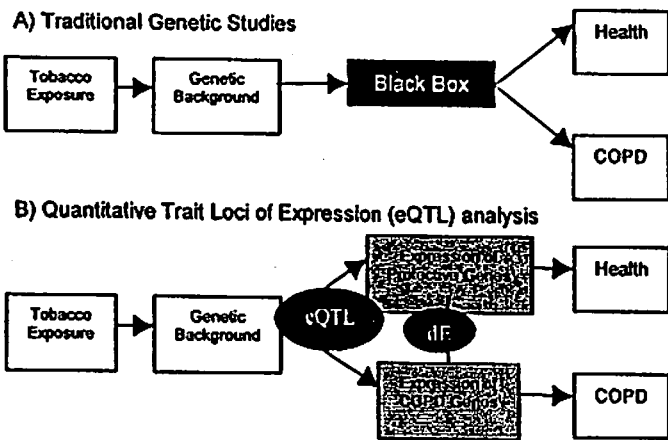
**GENETICS OF GENE EXPRESSION IN COPD
INVESTIGATORS**

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ABSTRACT

Lung diseases such as chronic obstructive pulmonary disease (COPD) result from a combination of environmental exposure and genetic susceptibility. For COPD (the fourth leading cause of death in the United States [1]) cigarette smoking is the major environmental risk factor and is present in > 80% of patients with the disease [2]; however, only approximately 20% of smokers develop COPD. Thus there must be other genetic risk factors. The only proven genetic risk factor is the α 1-antitrypsin gene, but this accounts for only 1-2% of COPD patients. Previous efforts to identify additional genetic risk factors have



used linkage studies and candidate gene approaches [3-5], but have not taken into account how genetic background modifies gene expression (Figure 1), despite pilot studies showing that gene expression is different in the lungs of those with COPD [6, 7]. We hypothesize that the genetic background of an individual determines how gene expression is altered in the lung in response to cigarette smoke and that the genetic loci (eQTLs) that control these gene expression differences (dE) are associated with the clinical diagnosis of COPD. In response to a new program announcement (PA-06-370) that seeks approaches to merge genetic and genomic techniques to find genes associated with human complex traits for lung disease, we propose to use a progressive filtering approach in multiple independent populations with previously banked DNA to identify and validate these novel eQTLs.

Figure 1: Traditional approaches (A) to identifying genetic risk factors for COPD do not take into account how genetic background influences differential gene expression (dE).

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