Identification of PI3K activated pathway in cytological normal bronchial cell
may lead to early detection of the lung cancer

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Today, lung cancer still has a high mortality rate when compared with other types of cancer. Despite all the medical progress in methods of diagnosis and revolutionaries treatments, the medical tests to detect lung cancer have not a high sensitivity. Therefore, the patient is required, in most cases, to have multiple and invasive tests and many months pass before a diagnostic is final. The tests are expensive and sometimes a risk of other medical complications for the patient. Overall, this means a long delay for the medical treatment. The modern medical tests (CT, PET, MRI) are sensitive enough to detect malign growth that is not seen by conventional chest X-rays. However, the final and decisive test for lung cancer is the biopsy that reveals the cytological changes at cell level. Smoking is the first cause in lung cancer, but only a certain number of smokers will develop lung cancer. The diagnostic tests used for detection of lung cancer are not able to distinguish the smokers with highest risk for lung cancer or to determine the signaling pathways that are modified early in the lung cancer mechanism. Nowadays, smoking is not considered damaging only the lungs but also the rest of the respiratory tract creating a “field of injury”. Spira’s lab studied gene expression in the cytologically normal bronchial epithelium and they identified an 80-gene biomarker that is able to separate the smokers with cancer from those without cancer. The combined results of bronchoscopy (less invasive test) and gene expression on 129 smokers (60 individuals with lung cancer and 69 individuals without lung cancer) led to a 95% sensitivity in the individuals with cancer with 83% specificity (17% false positives) in those without cancer. Spira et al took the next step in their research and try to find the signaling pathways that are activated early in the lung cancer. They identified the PI3K signaling pathway to have an increased activity in different types of cancer tissues including lung cancer. The novelty of their discovery is that they detected the same pattern of increased activity of this PI3K pathway in the normal bronchial airway epithelium that was cytologically normal. The validation of the gene expression signature was made by comparison with the gene expression info from primary breast cancer tumors. The activation of the PI3K pathway was not related to other factors such as smoke exposure but specifically determined by the presence of the lung cancer. Furthermore, Spira et al determined that the dysplasia (considered a precancerous phase) regression due to the treatment with myo-inositol resulted also in the decrease of the PI3K activity and the hypothesis was sustained by the ability of the myo-inositol to inhibit PI3K activity. These results conduct to the conclusion that myo-inositol could be used in chemoprevention by using its inhibitory action on the PI3K activity.

The findings suggest that the PI3K deregulated activity is an early, measurable event in the starting of the mechanism of lung cancer. PI3K activity can be detected in the normal cytological cells after a flexible bronchoscopy (not so invasive test compared to others) and set apart this pathway from the already known signaling pathways that are active in cancer but can be identified only in the already grown malignant tissues. The PI3K increased activity can be used as a “marker” for lung cancer development avoiding biopsy. The inhibitory action of myo-inositol on the PI3K activity may offer solutions in lung cancer chemoprevention.
References

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National Cancer Institute, [www.cancer.gov](http://www.cancer.gov)

[www.lungcancer.org](http://www.lungcancer.org)