MAYO CLINIC
Cancer Center

Volume I

Lung Cancer Research Update

Greetings from the staff of the Mayo Clinic Lung Cancer Research Program

Our purpose with this update is to inform you about the progress of our Lung Cancer Research Program. The success of our ongoing research program depends on the support of you and your family members. Therefore, all of us who work in lung cancer research at Mayo Clinic wish to acknowledge and thank all of our study participants.

Over the past four years, more than 1,000 lung cancer patients and their relatives have participated in our study. The efforts of these participants and our research team have led to three national grant awards for research and more than 10 scientific publications. These achievements would not have been possible without your participation and support.

We believe that communication between you and the research team is essential. Through this newsletter, we hope to serve two main goals: 1) provide you with information about lung cancer gained from our research, and 2) encourage your continued interest and participation in the ongoing research.

Q&A Answers to questions frequently asked by participants in our study

During the study years, we have received many questions from our participants about lung cancer and our research program. Here are answers to the 10 most frequently asked questions:

Q "I smoked cigarettes all of my life and I know this is why I have lung cancer. Why do you want me to participate?"

A This statement is only partly correct. At least eight out of 10 (80%) lung cancer patients have used tobacco products. This is why many people believe that most smokers will develop lung cancer at some point in their life. In reality, only two out of 10 (20%) long-term heavy smokers will eventually develop lung cancer.

Based on this fact, one of our research goals is to identify the people who are susceptible to the disease (that 20% of people who smoke and develop lung cancer) and to learn why they are susceptible. Our second goal, based on what we learn about an individual's susceptibility, is to improve disease outcome by finding the best treatment plan for each patient. Your participation can contribute to researchers achieving both goals.

Q "Do we know what gene it is? Do I have the affected gene? Will I get any of my test results back? If you find something important, will I be notified?"

A So far, no lung cancer-specific gene has been identified. The main roadblock when trying to identify such a gene(s) is obtaining a sufficient number of lung cancer families with multiple living relatives willing to participate and complete the study.

Our study is one of the most hopeful for hunting down the gene(s) responsible for lung cancer development because we are screening many people and investigating a large number of genes. If any major lung cancer gene is discovered, we will let study participants know by an update similar to this one.

To protect the privacy and confidentiality of every participant involved in our study, we do not link test results to participant's identifications. Therefore, our study results are not retrievable for each patient.

Continued inside

MCCC
Mayo Clinic Cancer Center

Q "Are my children at high risk for getting lung cancer?"

A Based on published findings, your children are at a greater risk than the general population for developing lung cancer because you had it. If they are also tobacco smokers, their risks increase further.

Q "There are no other cancers in my family, so you would not get much information from me. What can you learn from my siblings? Do other family members need to be aware of the possibility of inherited factors? What do they need to do?"

A Even if you are the only person in your family to have lung cancer, it is important for your close relatives (for example, siblings) to participate in our study. We will compare your results to your family members' results. We value their participation because the difference between you and your relatives, including both environmental and personal factors, could provide important information on the cause of lung cancer.

If your relatives choose to participate, they will be asked to fill out a two-page questionnaire and donate a small sample of blood.

Q "I want to participate but do not want my family involved in this study."

A Your participation is very helpful even when your family is not involved. For example, your participation helps us study the progress and the prognosis of the disease and its relationship to genetic and other factors, (such as different treatment plans).

Q "Will my insurance company get hold of any of my study information?"

A Your insurance company will not see any information from this study. We assure all participants that the information provided is kept strictly confidential, and test results are not identifiable with any participant.

Q "What caused my cancer? Being around chemicals such as asbestos or radon–is that what gave me my cancer?"

A Based on published findings, direct exposure to asbestos leads to a higher risk of lung cancer. This elevated risk depends on the nature and length of exposure, and more importantly, on whether the person was also a tobacco smoker. Tobacco smoke is much more powerful than any other exposures for causing lung cancer.

Q "How long is the study and what do you expect from me?"

A It varies. Our participants can be in the study for up to five years. During that time, they fill out a written questionnaire every year starting six months after diagnosis. Some patients may have an initial telephone interview because of certain features of their lung cancer diagnosis or family cancer history. During the interview, most participants are asked if their relatives may be interested in participating in the research. Relatives' participation is one-time only, in that they are requested to fill out a two-page questionnaire. From both patients and relatives, a sample of blood (4-6 tablespoons) is needed for various tests.

Q "I am already in another study, why should I participate in this one? I am tired of them."

A We know of the inconvenience, and sometimes redundancy patients go through when participating in multiple studies. However, each study has unique goals. We hope you will consider our study, but we understand if you choose not to participate. In some situations, we may ask your permission to use the blood sample that you donated in other studies to minimize the inconvenience.

Q "Will there be any costs for me to participate in this study? I don't have the money to travel to the Mayo Clinic for this study."

A There is no cost to you except time. We generally ask for a 20 to 40 minute telephone interview or for you to fill out a short questionnaire. In most cases, we ask that you go to the Mayo Clinic or your local health care facility to give a blood sample. If you choose to go to your local clinic, we will send you a kit to take to the facility so they can send the blood sample directly to us and also bill us for any costs incurred.

Progress of our major research projects

The following information explains the major directions of our research program and lists references of selected publications. One of our goals is to identify individuals who are susceptible to lung cancer. Besides active or passive (second-hand) tobacco smoke exposure, lung tissue damage makes individuals vulnerable to the cancer. Researching biological markers to measure lung tissue damage is our major research focus.

Project 1

Chronic lung diseases in lung cancer development and progression

About 15 years ago, researchers at Mayo Clinic and other research centers reported that people with lung tissue damage and decreased lung function have an increased risk of lung cancer. Emphysema and chronic bronchitis are examples of diseases that result from lung tissue damage over time and cause problems with lung function.

One reason for lung damage is the imbalance between two proteins normally found in the lungs. One of the proteins, called neutrophil elastase, is capable of damaging lung tissue, and the second protein, alpha-1 antitrypsin, neutralizes neutrophil elastase, and thus protects lung tissue.

We are investigating whether we can use genetic markers to measure the levels of these proteins to predict a person's risk of lung cancer. The goal is to find patients at increased risk for lung cancer who can be screened aggressively to detect lung cancer at a very early stage. Lung cancer is most curable when found early enough. This research is ongoing.

Yang P, Wentzlaff KA, Katzmann JA, Marks RS, Allen MS, Lesnick TG, Lindor NM, Myers JL, Wiegert E, Midthun DE, Thibodeau SN, Krowka MJ. Alpha1-antitrypsin deficiency allele carriers among lung cancer patients. Cancer Epidemiol Biomarkers Prev 1999;8(5):461-465.
Yang P, Taniguchi K, Deschamps C, Bass E, Meyer R, Liu W. Neutrophil Elastase Gene in Lung Cancer Development: Evidence From Molecular Genetics and Clinical Epidemiology. Genetic Epidemiology 2001; 21(2):12.

Project 2

Passive (second-hand or environmental tobacco) smoking exposure among lung cancer patients who never used tobacco products

Among lung cancer patients, it is a known fact that female patients are more likely never to have smoked. We have shown through our study that the majority of these women who had never used tobacco products but got lung cancer have had long-term and heavy exposure to second-hand smoke from spouses, parents, and/or co-workers.

Our study conclusion is, for female lung cancer patients, the cumulative amount of tobacco smoke exposure may be significantly under-estimated if only personal smoking history is considered. Therefore, it is essential to include passive smoking history when assessing carcinogen dose and gene-environmental interaction's in studies of tobacco-related disease.

de Andrade M, Miller DL, Bass E, Marks R, Croghan G, Jatoi A, Sellers TA, Yang P. Second-Hand Smoke Exposure Among Female Lung Cancer Patients. American Society of Preventive Oncology Conference 2001.

Continued on back

Progress of our major research projects *(continued)*

Lung cancer will continue to be a major medical and public health burden for several decades. Very little improvement has been made on how to treat the disease, particularly among patients with advanced disease. Many of our patients have the same clinical disease and the same treatment plans, but vary significantly in their response to treatment.

Because of this, another direction of our research program is to improve the outlook of lung cancer patients by finding individual treatment plans. Our goal is to discover a group of inherited markers that can be easily tested in every patient before treatment. These markers will assist physicians in choosing a patient-specific plan to achieve the best possible outcome. Project 3 is an example of that effort.

Project 3 Genetic determination of lung cancer survival

Most patients with advanced stage lung cancer receive chemotherapy as a single or a combination of drugs including platinum-based compound. Certain enzymes in the body interact to break down these drugs.

Genetic tests can determine in which individuals the drugs will break down faster or slower. By checking for the presence or absence of relevant genes, we hope to predict which drugs will work best for which lung cancer patients. This research is ongoing.

Yang P, Yolomizo A, Tazelaar HD, Marks RS, Lesnick TG, Miller DL, Sloan JA, Edell ES, Meyer RL, Jett J, Liu W. Genetic Determinants of Lung Cancer Short-Term Survival: The Role of Glutathione-Related Genes. Lung Cancer, March 2002.

Comments and suggestions are welcome

Please feel free to contact our program coordinator, Sheila McNallan at 507-266-1065 for additional information about this research program or to submit comments and suggestions.

MAYO CLINIC
Cancer Center

200 First Street SW
Rochester, Minnesota 55905
www.mayoclinic.org

MC1205-05rev0404