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**Lung Cancer in Uranium miners: A Tissue resource and Pilot Study**

*Annual Report for 1993*

**Progress Report  
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### *Abstract*

This project involves two related activities directed toward understanding respiratory carcinogenesis in radon-exposed former uranium miners. The first activity involves a continuation of the tissue resource of lung cancer cases from former underground uranium miners and comparison cases from non-miners. The second activity is a pilot study for a proposed longitudinal study of respiratory carcinogenesis in former uranium miners. The objectives are to facilitate the investigation of molecular changes in radon exposed lung cancer cases and to develop methods for prospectively studying clinical, cytologic, cytogenetic, and molecular changes in the multi-event process of respiratory carcinogenesis, and to assess the feasibility of recruiting former uranium miners into a longitudinal study that collects multiple biologic specimens.

During the first nine months, the collection of tissue for the resource continued at five hospitals in Albuquerque and at St. Mary's Hospital in Grand Junction, Colorado, and was expanded to include collection of blood, induced sputum, bronchial brushing, washings, and mucosal biopsies from participants at two of the hospitals. In regard to the extended study, a questionnaire was developed and all protocols for specimen collection and tissue handling were completed. To date, tissue has been collected from X cases, including 10 using the expanded collection protocol. Tissue utilization has begun at ITRI and methods are being developed to study molecular and cellular changes in exfoliated cells contained in sputum.

The pilot study will be launched in the Albuquerque and Grants regions during June, 1993 and will subsequently be implemented in Grand Junction, Colorado. Protocols have been developed and approved for the New Mexico phase of the pilot study and are under development for Grand Junction. We anticipate that the pilot phase will include 100 participants from New Mexico and 25 from Grand Junction and be completed by early 1994.

### ***Introduction***

This project involves two related activities directed toward understanding respiratory carcinogenesis in radon-exposed former uranium miners. The first activity involves a continuation of the tissue resource of lung cancer cases from former underground uranium miners and comparison cases from non-miners. The objective of the tissue resource is to facilitate investigation of the molecular and cellular biology of lung cancer, particularly radon-associated lung cancers. The second activity is a pilot study for a proposed longitudinal study of respiratory carcinogenesis in former uranium miners. The objectives are to develop methods for prospectively studying clinical, cytologic, cytogenetic, and molecular changes in the multi-event process of respiratory carcinogenesis, and to assess the feasibility of recruiting former uranium miners into a longitudinal study that collects multiple biologic specimens.

The project was funded in September 25, 1992. Development of the tissue resource and collection of tissues was continued and a new protocol for collection of additional specimens including blood, induced sputum, and bronchoscopically obtained mucosal biopsies and washings was implemented. During the first nine months of support, the principal tasks for the pilot investigation were to establish community networks to identify and recruit former uranium miners, to identify study venues and resources in Albuquerque and Grants, New Mexico, to strengthen the collaborative efforts between St. Mary's Hospital and the University of New Mexico, and to develop and test interview and tissue handling protocols.

### ***Project activities***

***Community cooperation:*** The investigators have made ongoing efforts to maintain full medical community cooperation with the tissue collection protocol. In regard to the pilot study, Drs. Samet and Gilliland have met with and obtained support for the project from Drs. Arnolfo and Arnold Valdivia of the Grants clinic and other Grants area physicians involved in the care of former uranium miners. During the first week in May, a planning meeting of collaborating investigators from the University of New

Mexico, Lovelace Inhalation Toxicology Research Institute (ITRI), and St. Mary's Hospital newly formed Cancer Research Center was held in Grand Junction.

*Tissue collection:* To date 127 cases have been collected in Albuquerque and Grand Junction. An extended tissue collection protocol was approved by the Institutional Review Boards of the University of New Mexico School of Medicine and Albuquerque Veteran's Administration Hospital and implemented. As part of the extended tissue collection protocol, blood, induced sputum, bronchial brushings, washings and biopsy specimens have been collected on 10 individuals undergoing diagnostic bronchoscopy. Two of these individuals were former uranium miners.

*Tissue utilization:* 29 tissue specimens are currently under analysis by Dr. Lechner's group at ITRI and Dr. Curt Harris's group at NCI. In addition, Dr. Lechner is using 10 sputum specimens to develop molecular techniques to be used in the longitudinal study.

*Pilot study for proposed longitudinal cohort study:* Protocols were developed for collecting and handling specimens and conducting interviews. The study protocols was approved by the Institutional Review Board of the University of New Mexico School of Medicine. A request to use the University of New Mexico's Clinical Research Center as the Albuquerque study venue was submitted and approved. The outreach program of Miner's Colfax Medical Center has agreed to make their miner's screening van and personnel available for screening in Grants. Recruiting materials and methods have been developed including a bilingual recruiting brochure, a toll-free telephone number for responses, and telephone eligibility screening criteria and script. The School of Medicine's Public Relations Department has agreed to facilitate the media aspects of recruiting.

*Future Activities:* Tissue collection will continue at the five hospital in Albuquerque and at St Mary's Hospital in Grand Junction. In addition, the extended tissue collection protocol will continue at the University of New Mexico and the Albuquerque V.A. hospitals. The development of methods

for molecular analysis of sputum, as well as use of collected tissue to identify cytogenetic and molecular changes will continue.

Recruitment in New Mexico for volunteers willing to participate in the pilot study will begin in June,1993. In the pilot phase, 100 miners from New Mexico will be entered into the study protocol, 50 in Albuquerque and 50 in Grants. We will seek 10 volunteers to undergo bronchoscopy based on clinical indications and exposure status. The Grand Junction phase will begin in the summer of 1993 and build on the experience gained in New Mexico. If the pilot phase indicates a longitudinal study of former uranium miners is feasible, an application for funding for will be made in 1994