The grant was initially funded in May 1994 to St. Mary’s Hospital and Medical Center located in Grand Junction, CO (Agreement No. DE-FG03-94-ER61842). When the Principal Investigator, Marshall Anderson, relocated to the University of Cincinnati, a continuation of the initial grant was awarded to this institution with Dr. Anderson as Principal Investigator for one year and a no cost extension for another year. This report summarizes the research results obtained with this grant.

Lung cancer is one of the leading causes of death in the United States and in Western Europe. The incidence of lung cancer in developing countries is rising as their cigarette smoking habits increase. The objectives of this grant were to analyze genetic alterations associated with the development and progression of non-small cell lung carcinoma (NSCLC). Endpoints that may be realized from the research accomplished are: 1) detection of early genetic and/or cellular alterations which ultimately could lead to diagnostic modalities for the early detection of lung cancer; and 2) detection of a novel tumor suppressor gene(s) on chromosome 9p. This proposal analyzed both tumor specimens and sputum samples.

A major focus of the research was to examine lung tumors for the presence of tumor suppressor genes (TSG) on 9p. The p16/CDKN2 gene, a cyclin dependent kinase inhibitor, is a well-known TSG on 9p21. Our data strongly suggest the existence of at least one additional TSG on 9p (Wiest et al, Cancer Research 57, pp 1-6, 1997; and Wiest et al, Journal of Cellular Biochemistry Supplement 28, pp64-73, 1997). This was the major accomplishment of this grant. We have subsequently narrowed the chromosomal region of this putative TSG and presently are examining this region for candidates. Based on our results and published reports by other investigators, a high frequency loss of heterozygosity is observed in each major histologies subtype of human lung cancer. We will continue to attempt to identify a novel TSG(s) on 9p.

Mutations in the p53 TSG gene are detected in approximately 50% of human lung non-small cell carcinomas (NSCLC). This gene is also overexpressed in preinvasive lesions of the bronchial epithelium. p53 overexpression may serve as a biomarker for high-risk assessment of lung cancer. A study was conducted to analyze p53 overexpression in cells from sputum samples collected prior to histological tumor diagnosis. The rationale was based on the observation that preinvasive cells of the bronchial epithelium can be exfoliated into the airways and detected in sputa based on morphology. Our data suggested that sputa cells which overexpress p53 and/or cytokeratin in conjunction with morphological criteria may define a new class of atypical cells which are predisposed to cancer development (Anderson et al, Journal of Cellular Biochemistry 64 pp185-190, 1996). We will continue to explore this new potential class of atypical cells to be utilized in early detection of lung cancer by analysis of sputum samples (Anderson et al, Analysis of Sputum Specimens for the Presence of Atypical Cytanophilic Epithelial Cells, submitted for publication).
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We also conducted an extensive study to examine a new procedure to prepare slides of
sputum specimens. These new types of slides are referred to as “Megafunnel slides” and
the procedure is outlined in our published manuscript (Michels et al, Acta Cytologica, 41,
pp1774-1780, 1997). The objective of this study was to compare Megafunnel slides to
Saccomanno smear slides of sputum samples. We demonstrated that Megafunnel slides
compared favorable to Saccomanno smear slides in the quality of specimen. The
Megafunnel slides are more expensive and labor intensive to prepare. However, the
reduction in screening time by cytotechnologists may be advantageous. Moreover, their
potential for immunocytochemical analyzing, FISH, and other special clinical and
research analyses is enormous since they exhibit better cell adhesion, a more uniform
monolayer of cells and decreased background staining.