PRELIMINARY DRAFT

DETECTION OF SYRIAN GOLDEN HAMSTER RAS FAMILY GENE. V I

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The ras proto-oncogene family is highly conserved across species lines, and its members (c-Ha-ras-1, c-Ki-ras-2 and c-N-ras) have been implicated in the carcinogenic process due to point mutations that activate them to transforming oncogenes. Experimental chemical carcinogenesis studies have consistently identified specific mutations at the 12th, 13th, or 61st codon as a direct result of treatment. We chose to examine the ras genes in Syrian Golden hamster lung. We have utilized human sequence designed oligonucleotide primers in the polymerase chain reaction (PCR) to amplify messages from exons 1 and 2 of hamster ras genes. We have confirmed the PCR products by (1) predicted size analysis and (2) by probing with non-radioactive (biotin labeled) oligonucleotides internal to the primer pairs. Furthermore, this approach has allowed us to generate clinically relevant sequence data from the hamster c-K-ras 2 gene. The c-K-ras-2 sequence exhibits close homology with the human sequence at the nucleotide level in this area. There are only 9 observed base differences in nucleotide sequence and non resulted in a change of encoded amino acid. We have applied this approach to the search for c-Ki-ras-2 point mutations in the Syrian Golden hamster small cell lung carcinoma (SCLC).
This study provides the background necessary to allow searches for oncogenically activated point
mutations in the c-Ki-ras-2 gene in experimental neoplasms of the hamster.

Key words: Lung cancer, oncogene activation, PCR.

INTRODUCTION

Lung cancer is the largest single cause of death among all cancer deaths [1]. The most important etiologic factor is smoking of cigarettes. In man, lung cancer can be divided into two major forms: small cell lung cancer and non-small cell lung cancer; the differentiation is important with regard to prognosis and therapeutic approaches.

Activated ras oncogenes have mainly been encountered in lung cell lines of non-small-cell origin [16]. The genes of this family code for 21 kilodalton (Kd) guanosine triphosphate-binding proteins (p21), which are related to G proteins and are thought to play