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Molecular Biology of Human Prostrate Cancer

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MOLECULAR BIOLOGY OF HUMAN PROSTATE CANCER

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Work done at Case Western Reserve University, Dr. Sherron Helms*

In 1990 prostate cancer was the second leading cause of death of American males. My project involves the investigation of one aspect of the molecular biology of human prostate cancer which was to determine and characterize any changes in gene copy number and gene structure, and in gene expression that occur during short-term culture of human prostate tissue.

Genomic DNAs were extracted from tumorous tissue samples from 8 patients with prostate carcinoma or prostatic hyperplasia, then purified and quantified for Southern blot DNA analysis. The gene copy number and gene structure in fresh frozen tissue samples were compared with that in portions of the samples grown in culture for varying periods. Polyadenylated RNAs(mRNA) were selected from the cellular RNA from the tissue samples for Northern blot RNA analysis, which allows us to compare the pattern of gene expression in the fresh frozen tissue samples with that in cultured samples.

Two genes-c-myc and HUK have been examined in the samples. An increase in gene copy number of c-myc with increasing time in culture was observed in one of two patients with prostate carcinoma; this could either reflect the amplification of c-myc gene induced by culture conditions or could demonstrate that the c-myc gene is amplified in the epithelial cells prior to cultivation and the apparent increase in copy number is simply a result of the increase in the number of epithelial cells during culture. The samples were reprobbed with HUK gene and no amplification of this gene was detected with increasing time in culture. It suggests that the amplification may be specific for the c-myc gene and that there is no amplification of an unrelated gene on another chromosome.

Three messages were examined in RNA samples from the same patients. In one patient with prostatic hyperplasia, the expression of EGFR was not detected in the samples from the first three days, then it started to increase at Day 5 and reached a peak at Day 7, but it was not detected in the Day 11 sample. When the mRNA from these samples were probed with cytokeratin 19, no messages were detected in Day 0, 3, and 11 samples. It could have been that cytokeratin 19 is not expressed at an abundance which can be detected on this amount of RNA, or it may be that the mRNA was lost in the reprobbed process(unlikely).

The changes noted in gene copy number seem to support the idea that these changes result from the culture selection of a subgroup of cells with a specific pattern of genes. It is difficult to interpret Northern blot results because of the problems in quantification and degradation which are not encountered in Southern blot analysis. In addition, the yields of RNA have been very low. There is insufficient RNA for Northern blot analysis on many samples. No conclusive explanation can be given for the current observations.