A Novel Method to Capture Methylated Human DNA from Urine: Implications for Prostate Cancer Screening

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Abstract
Prostate cancer is the most commonly diagnosed male cancer and the second leading cause of death among men. Diagnosis and management are complicated by the lack of symptoms and the lack of cancer-specific diagnostic techniques to be used during early diagnosis. Novel approaches to prostate cancer diagnosis and management are therefore required to improve the detection of patients at risk of prostate cancer and therefore improve the detection of patients at risk of prostate cancer and therefore improve the treatment outcomes. In our previous studies we have developed a novel method for the isolation and enrichment of methylated DNA from whole prostate cancer tissues or cell lines. The isolation and enrichment of methylated DNA from prostate cancer tissues was achieved by hybridization on a solid matrix and using paramagnetic beads in order to isolate DNA片段具有甲基化的效应。

Results

Figure 1. Detection of extensive methylation changes involving the GSTP1 promoter in prostate cancer cell DNA. In prostate cancer cell lines, but not normal cell lines, extensive desigual hypermethylation would render the CG island encompassing the GSTP1 5′ regulatory region hypermethylated at HpaII. An acute increase in prostate cancer cell DNA but not normal cell DNA would result, and specific products would be detected when the HpaII digestion of the GSTP1 promoter harboring HpaII digestion by carcinogen (this case: a 300 bp product as the primer shown here).

Figure 2. Extension GSTP1 promoter methylation detected using PCR. The GSTP1 promoter in TPGO cells was methylated using the GST-2 method, but not unmethylated or control cells. This indicates the presence of extended GSTP1 promoter methylation in carcinogen-treated prostate cancer cell lines.

Figure 3. Hypomethylated GSTP1 isoforms of human urine samples obtained from Hepatic C patients with liver cancer. Norgen Biotek Corp. has previously isolated hypomethylated GSTP1 DNA from urine samples collected from individuals with hepatocellular carcinoma. The results presented in this study show that hypomethylated GSTP1 DNA was isolated from urine samples of patients with hepatocellular carcinoma. This suggests that hypomethylated GSTP1 DNA may be a potential biomarker for the early detection of hepatocellular carcinoma.

Conclusions and Future Work

- Although GSTP1 methylation was only detected in 35% of urine samples, this study has demonstrated that the long-distance correlation biomarker may be useful for early detection of hepatocellular carcinoma.
- The results presented in this study show that hypomethylated GSTP1 DNA was isolated from urine samples of patients with hepatocellular carcinoma. This suggests that hypomethylated GSTP1 DNA may be a potential biomarker for the early detection of hepatocellular carcinoma.
- Further work will focus on the isolation of urinary DNA, but also the isolation and enrichment of DNA hypermethylated over non-methylated DNA, and the sensitivity and specificity of detection of nucleosides from urine samples.
- We envision the development of a simple, non-invasive molecular method that may indicate the presence of prostate cancer in individuals with lesions underlying by currently existing methods, which is more specific for prostate tissue than smear I.C.
- This research should have broad applications for the diagnosis of a number of other cancers from urine, including breast, bladder and many kidney cancers.

References
8. Norgen Biotek Corp., 2001. Hypomethylated GSTP1 DNA was isolated from urine samples of patients with hepatocellular carcinoma. The results presented in this study show that hypomethylated GSTP1 DNA was isolated from urine samples of patients with hepatocellular carcinoma. This suggests that hypomethylated GSTP1 DNA may be a potential biomarker for the early detection of hepatocellular carcinoma.

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