New Approaches to Prostate Cancer: Markers of Early Diagnosis, Prognosis, and Risk

Urologic cancers affect everyone, at every age, and every group in society. African American men have double the risk of dying from prostate cancer compared to any other group. In Hispanic men, prostate cancer is the most common cancer. From a personal standpoint, each and every one of the deaths due to prostate cancer is <u>unacceptable</u>. These men were sons, fathers, and grandfathers for their families.

Search for a "cancer test" and genetic markers:

Earlier diagnosis is a strategy we believe will increase the cure rates for prostate cancer since tumors diagnosed earlier are usually smaller and have not grown and expanded to other parts of the body. Ideally, early diagnosis would be done by using a "cancer test" that would be positive in all who have the cancer and negative in all who don't. Furthermore, the test should be low cost and we should be able to use it in large numbers to test the population — a process called "screening" for cancer. For example, there is evidence that use of PSA as a screening test has led to decreased mortality from prostate cancer. However, only one in four of the men who have a "positive" PSA blood test have cancer. In other words, three out of four men experience the anxiety and inconvenience of a biopsy, and they really don't even need the biopsy in the first place. Our goal is to develop one or more markers that can be used in tandem with those already present to greatly improve the accuracy of screening for cancer.

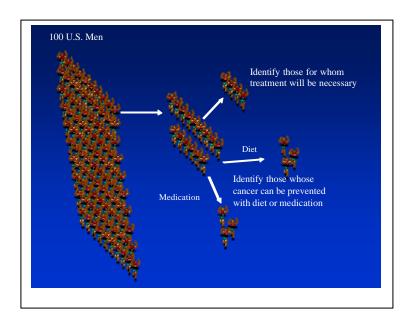
In addition to early detection, we believe genetic markers and nutritional studies can be used to determine the risk that an individual cancer will grow at a rapid rate. By looking "backwards" we know that some cancers do not need aggressive treatment. However, many of these tumors look alike, and it is very difficult to tell the "bad actors" from the more slow growing tumors. We believe that we are just entering an era when markers can be identified that will accurately predict the behavior of aggressive tumors. Instead of treating all patients alike, treatment will be customized using the information from these markers.

We assume it will take an enormous effort to understand all the details about cancer. Rather than waiting for this critical research to be accomplished, we are eager to develop ways to determine who is at risk for developing cancer. We believe there are genetic markers that will identify individuals at increased risk of developing cancer. These markers may not directly indicate genes that cause cancer, they may simply be, like our fingerprints, unique identifiers of risk. These genetic markers may be combined with other known markers of prostate cancer such as blood measurement of PSA to determine who is at greatest risk.

Unfortunately, we have far to go to find ideal *biomarkers* for cancer - *tests that identify the cancer early.* In <u>every case</u>, biomarkers are not perfect - they <u>miss some cancers</u> and also <u>tell some people without cancer that they might have disease</u>. Both of these problems are important!

Early Detection Research Network (EDRN):

The National Cancer Institute in 2001 awarded initiated the Early Detection Research Network (EDRN; web site http://www3.cancer.gov/prevention/cbrg/edrn/index.html). The goal of the EDRN is to discover, develop, and validate better ways to detect cancer early, generally through better biomarkers. In the brief time since its beginning, this consortium has initiated a large cooperative study to test whether a proteomic method can be used to screen men for prostate cancer by detecting differences in the profiles of proteins in patients with and without prostate cancer. Another promising development is the discovery that an alteration of the gene coding an antioxidant enzyme is an accurate marker for prostate cancer. These and other findings can be rapidly evaluated in the EDRN program since multiple medical centers participate and can bring large numbers of cases into the studies. This accelerates the discovery and validation processes required before testing is introduced into the general population. The following figure illustrates the strategies which can be used to determine risk of developing cancer, and to determine which cancers may be prevented and which need aggressive treatment.



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