Expressed Prostate Secretions Biomarker NIH Grant Awarded

The research team lead by Dr. Richard Drake and Dr. Raymond Lance received two grants from the NIH to further ongoing studies using expressed prostate secretions to identify individual prostate cancer proteins able to more precisely categorize these cancers by outcome. The problem for prostate cancer patients is the lack of precise molecular biomarkers that can guide how each man's cancer should be managed based upon the individual cancer's biology. To combat this problem we currently use multiple pieces of information such as PSA , clinical stage, Gleason grade of the biopsy, and the percent of biopsy cores involved with cancer to create an individual risk stratification. This approach represents our best guess about the true extent of the cancer and its ability to spread beyond the prostate gland or even if it is confined to the prostate at diagnosis. The work funded by these grants takes us away from traditional PSA type blood samples and to the closest body fluid to the prostate we can obtain in the form of the so call expressed prostate secretions or EPS. EPS fluid is harvested from the urine following a digital rectal exam (DRE). The prostate is a spongy gland wrapped around the urethra with multiple tiny tubes that connect directly into the urethra so that when the doctor pushes on the prostate EPS leaks into the urethra which is then voided into a cup moments after the exam. In the case of PSA, blood spends very little time in the walnut sized prostate gland before circulating through much larger organs on its way to a needle stick in an arm vein and thus represents a more confusing biomarker arena to study prostate cancer. We believe that in the 21st century, the key to better prostate cancer treatment must begin with the most accurate initial understanding of each man's cancer. To illustrate this consider the vastly different cases of two recent patients. In the first case "Bill" was found to have a PSA of 5.7 and a normal DRE, but the biopsy showed 3 samples out of 12 with Gleason 3+4 prostate cancer. "Bill" underwent a robotic prostatectomy and the final pathology showed a completely confined cancer (all margins negative) with only 5% of his gland involved with cancer. This is what most men hope for when they receive the diagnosis. Contrast this with the case of "Roger" who had a PSA of 5.2, normal DRE, biopsy showed 4 of 12 biopsy cores with Gleason 3+4 prostate cancer. When his prostate was analyzed after radical prostatectomy it was found that 40% of the prostate was involved and that the cancer had already spread outside the gland and into a lymph node. The traditional risk stratification did not help us understand that Roger was in trouble while Bill was in great shape. Our project seeks to clearly delineate from the EPS fluid just before biopsy what is truly going on with a given man's prostate cancer. Better information early will allow for better treatment choices to be made. Additionally, there are cases of prostate cancer that do not have the capability to take a man's life. This type of prostate cancer is called, "insignificant disease." You may be thinking, wait a minute how can cancer be "insignificant"? Insignificant prostate cancer does not have the capacity to spread and thus does not pose any risk of taking the man's life. It has been well demonstrated that

many men who are diagnosed with prostate cancer in the PSA era harbor insignificant disease. Unfortunately the only precise way to know for sure who has insignificant disease is to take out the prostate gland with surgery and then it can be tested to see if it is significant or not. We must do better than that.

Dr. Drake's research will focus upon a protein modification called glycosylation in which different sugars are applied to individual proteins. We have evidence that cancer cells, in fact, have unique sugar changes in their proteins and our work will focus upon using that information to go much deeper than PSA to provide answers immediately after the diagnosis of prostate cancer to create more precise clinical treatment plans. These projects require teamwork between the urology clinic, the operating room, and laboratory at EVMS. We depend upon precise information gleaned from the medical records and placed in our powerful CAISIS database by our clinical data managers. Working together we are able to carefully categorize the specimens with true outcome following radical prostatectomy such as cancer free or PSA recurrence or worse metastasis (spread of the cancer to other parts of the body). So far we have more than 500 specimens and are working diligently to identify the glycoproteins that in the future will better serve our patients in the quest to be cured of prostate cancer with the least damage to their quality of life, a goal we all share.