



VIRGINIA PROSTATE CENTER Newsletter

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Kidney Cancer: Ranks as fifth most common malignancy in the U.S. male population

By Paul F. Schellhammer, M.D.

Renal cell carcinoma, or kidney cancer, is not as common as prostate cancer or bladder cancer but still is frequent enough to rank as the fifth most common malignancy in the U.S. male population and the ninth most common in the female U.S. population. For the past five years, evidence has been gathered that strongly implicates a genetic mutation as a causative factor. Patients with kidney cancer have an abnormality of the short arm of the third chromosome. This genetic abnormality can be inherited and, therefore, strategies for earlier detection of renal cell carcinoma will likely involve genetic testing which then would prompt radiologic imaging for subjects genetically predisposed.

Current medical practice requests abdominal imaging by ultrasound and/or computerized axial tomography (CAT) scanning to clarify the cause of abdominal pain. This has resulted in the detection of kidney cancers that are significantly smaller than those found a decade or more ago when symptoms, namely pain, bloody urine or an abdominal mass, called attention to the presence of a kidney cancer. The detection of smaller tumors coupled with the development of instrumentation and technology that permits laparoscopic, video controlled, incision-less surgery opens a new avenue for the treatment of kidney tumors. One innovative method for removing small kidney cancers is termed "hand assisted" laparoscopic nephrectomy. The surgeon's left hand is inserted through a small

abdominal incision. By visualizing hand movements as they relate to the kidney and its blood supply with a camera inserted through a separate insertion site and controlled by an assistant, and by manipulating instruments with his other hand, the surgeon removes the kidney with a much smaller incision than required for standard "surgery." Dr. Edwin Robey, in our practice group, Associate Professor of Urology at Eastern Virginia Medical School, has begun to employ this technique in appropriately selected patients.

The second option is to perform the entire procedure by laparoscopic means whereby a camera provides visualization and the surgeon, using both hands outside the body, employs instruments to dissect and free the kidney. The kidney is then placed in a special impermeable sac where it is dissolved to a pulp so that it can be brought through the tiny incision that had been used for placement of the camera. Dr. Robey and Dr. Michael D. Fabrizio, who will join our practice in July after a fellowship at Johns Hopkins Hospital, will provide this capability for the Department of Urology. It is important to recognize that these surgeries are not applicable to all kidney cancers but are employed in the appropriate circumstance so as to assure a cancer cure that equals that of standard open surgery. The advantages of the procedure, in addition to the cosmetic aspects, include reduction of pain (fewer muscle fibers are transacted) and thereby the shortened hospital stay and a more rapid return to routine activity.

The laparoscopic nephrectomy techniques described here have also been applied to renal transplantation. Patients who are donors may in the future have the opportunity for harvest of the kidney by laparoscopic means rather than by the standard abdominal incision, thereby benefiting from the cosmetic effects, more rapid return to preoperative employment and activity, and, possibly, reduced hospital stay. ■

VPC Researcher Receives Award

Roy R. Brown, Jr., M.D., a research fellow in the VPC, has recently received a Minority Scholar in Cancer Research Award from the



American Association for Cancer Research (AACR). Dr. Brown, a native of Norfolk, VA, has joined the VPC for eighteen months to receive advanced training in the area of immunotherapy of prostate cancer under the direction of Drs. Paul Schellhammer, Richard Ciavarrá and Kenneth Somers. Specifically, Dr. Brown will be investigating the effects of FLT3 ligand and other cytokines on the treatment of prostate cancer in animal models. Congratulations to Dr. Brown for receiving this prestigious AACR scholarship. ■

Immunotherapy: The saga continues

By Roy Brown, M.D.

Last spring, we informed you about research in the area of prostate cancer using immunotherapy in animal models. In that edition of the newsletter, there was a brief explanation about how cancer cells exhibit unique molecules called tumor associated antigens (TAA). These TAA are not expressed on normal body cells. Once recognized by the immune system, TAA can cause activation of the immune system to destroy tumors. Tumors are not destroyed upon TAA recognition because the immune system requires a second (activation) costimulatory signal in addition to the TAA for full activation. To that end, we continue to study the activation of the second costimulatory signal.

Currently, we and others around the

From the Laboratory

world are using immunotherapies involving Dendritic cells (DC) to help treat prostate cancer. DC are among specialized cells of the immune system that are termed antigen presenting cells (APC). These APC can activate the immune system by their ability to display TAA and other necessary costimulatory factors. This allows the immune system to now recognize the tumor as a foreign growth and eliminate it.

Scientists at the VPC are using FLT3 ligand to aid in DC research. FLT3 ligand is a growth hormone that dramatically increases the number of DC in a variety of organs. With the increase in the number of DC, it is hypothesized that there will be an increase in the anti-tumor response of the immune system.

At the VPC, we have used a mouse

model of prostate cancer to test this hypothesis. Mice with growing prostate tumors were injected with FLT3 ligand. After administration of the agent, there was dramatic change in the tumor size. Tumors that were initially palpable by hand decreased to undetectable levels. This therapy does not require dissection/removal of the tumor or identification of the specific TAA from a tumor. To date, we have not achieved a complete cure with this type of therapy, but we have observed stabilization of tumor growth and, in some cases, regression of tumors.

Our studies continue at the VPC and other cancer centers around the world using FLT3 ligand immunotherapy. The current research approach focuses on the use of FLT3 ligand alone or in combination with other cytokines/growth factors to treat all stages of prostate cancer. ■

In Memory of Charles Devine, Jr., M.D.

Dr. Charles Devine died on February 12, 1999, of advanced prostate cancer. Charlie, as he was known to us, was born in Norfolk, Virginia, in 1923. He attended college at Washington and Lee University and received his doctorate in medicine from George Washington University School of Medicine. He completed an internship at Johns Hopkins Hospital and a fellowship in urology at the Cleveland Clinic. It was in Cleveland that he met Rae Ellis. They were married on September 30, 1950. Rae and Charlie were a perfect complement to one another and the two were always a delight. Everyone was comfortable in their company. They had 5 children -- 3 sons and 2 daughters -- and a host of grandchildren.



They established a residency; they were the driving force behind the establishment of a medical school, Eastern Virginia Medical School; they pioneered the field of reconstructive urology.

Charlie was recognized for his accomplishments - his membership in the Association of Genitourinary Surgeons, his receipt of the Distinguished Contribution Award from the American Urologic Association, and in 1997, his receipt of the highest honor of the American Urologic Association, the Ramon Guiteras Award. A month before his death, an endowed chair, The Devine Chair in Genitourinary Reconstructive Surgery, was established at Eastern Virginia Medical School.

I will conclude with two events that occurred during his funeral service. The first included the words of the eulogist who reminded us that the full exercise of Charlie's creativity and talents had introduced surgical concepts that would provide hope for many patients past and future.

The second event, at the end of the service, brought Charlie's youngest daughter,

Rachel, to the lectern. She reminded the congregation of her father's love of family, and medicine. She also recalled her father's passion for sailing by reciting verses from Tennyson's "Crossing the Bar" to commemorate his journey.

*Sunset and evening star,
And one clear call for me!
And may there be no moaning of the bar,
When I put out to sea,
Twilight and evening bell,
And after that the dark!
And may there be no sadness of
farewell,
When I embark;
For tho' from out our bourne of
Time and Place
The flood may bear me far,
I hope to see my Pilot face to face
When I have crossed the bar.*

With Charles Devine's death, Norfolk, Virginia, lost a first citizen, his family a devoted father and husband, urology a pioneer and urologists everywhere a loyal comrade. ■

American Foundation of Urologic Diseases Awards Fellowship to EVMS Instructor

John W. Davis, M.D., to study prostate cancer biomarkers at the Virginia Prostate Center

Dr. John W. Davis, chief resident and instructor in urology, has been awarded a research fellowship from the American Foundation of Urologic Diseases to study prostate cancer biomarkers. Dr. Davis will work in the prostate cancer research laboratory of George L. Wright, Ph.D., who is Chairman of Microbiology and Molecular Cell Biology at EVMS and the Scientific Director of the Virginia Prostate Center. Dr. Paul F. Schellhammer, clinical director of the VPC, will serve as co-sponsor.

Prostate cancer (CaP) and benign prostatic hypertrophy (BPH) continue to be significant health problems for men. The prostatic specific antigen (PSA) test has greatly improved our ability to screen for CaP. However, BPH and age can elevate the PSA to above the normal upper limit of 4.0 ng/ml. in men without CaP. Approximately 75% of men with PSA 4.0-10 ng/ml. will have a negative biopsy for CaP. Therefore, there is much need for even more powerful screening markers. It is also hoped that markers can be found to help identify prostate cancers that are likely to cause metastatic disease.

Drs. Davis and Wright plan to identify such biomarkers that can improve

cancer screening and provide prognostic information. The hypothesis that BPH and CaP secrete different proteins is not novel, but two new exciting technologies are now available to hasten the search. Prior efforts to compare BPH to CaP have been complicated by the difficulty of isolating pure populations of cancer versus non-cancer cells. A new device called the Laser Capture Microdissector allows researchers to take prostate tissue under a microdissector and isolate pure cell populations of BPH and all grades of CaP.

These pure cell populations will then be studied to find proteins that are uniquely expressed in BPH versus CaP that could lead to a new clinical test. Another new technology in protein analysis is called Surface-Enhanced Laser Desorption/Ionization Protein Chip Analysis (SELDI). This computer-driven technology captures proteins from a given tissue sample (BPH or CaP) and performs an extremely thorough identification of proteins present based on molecular weight. Using the Virginia Prostate Center's vast



Dr. John W. Davis, chief resident and instructor in urology at EVMS

prostate tissue bank, samples will be analyzed and proteins unique to BPH versus cancer will be identified and further studied. The SELDI device allows creation of bioassays that can be evaluated for clinical use.

In summary, the Laser Capture Microdissector and SELDI technologies will allow Drs. Davis and Wright to work at a fast pace towards improving our ability to diagnose and predict the metastatic potential of prostate cancer. ■

Clinical Trials of Interest Conducted at the VPC

PROSTATE CANCER

- **Abarelix-Depot vs. Lupron Depot 1-Month Plus Daily Casodex in Patients with Prostate Cancer Who Are Candidates for Initial Hormone Therapy.**
- **Bicalutamide (CASODEX) 150 mg as a Second Line Therapy for Patients with Asymptomatic Metastatic Prostate Cancer.**
- **Antiandrogen Withdrawal in Patients with Progressive Prostate Cancer.**
- **Total Androgen Blockade versus Total Androgen Blockade plus Pelvic Irradiation for Adenocarcinoma of the Prostate.**

BLADDER CANCER

- **DFMO in Low Grade Superficial Bladder Cancer.**
- **Single Adjunctive Instillation of Intravesical AD 32 Immediately Following Transurethral Resection for Multiple Superficial Bladder Tumors.** Anthra Pharmaceuticals. Open Trial.
- **BCI-Immune Activator or Adriamycin for the Treatment of Refractory Carcinoma in Situ.**
- **Retinamide 4HPR for Transitional Cell Bladder Carcinoma.**