



The world's largest gathering of scientists and physicians working to solve the problem of prostate cancer -- the Ninth Annual CaP CURE Scientific Retreat -- was held in Washington, D.C., September 19-21, 2002. Moving this meeting from its traditional home, Lake Tahoe, Nevada, to Washington, D.C. put us in the very center of health policy and regulation with a specific goal: to more actively involve government in our urgent mission to end prostate cancer as a health threat to all men and their families.

To that end our meeting was enriched by the participation of Dr. Andrew von Eschenbach, Director of the National Cancer Institute (Dr. von Eschenbach is a 1993 CaP CURE research award winner and prostate cancer survivor); Dr. Richard Pazdur, Director of Oncology Drug Products at the Food and Drug Administration; United States Senator Ted Stevens; former Senate Majority Leader Bob Dole (both Senators Stevens and Dole are prostate cancer survivors); as well as key staff members from the National Institutes of Health, the National Cancer Institute and the Congress. These three days of scientific and clinical progress updates coupled with strategic panel discussions on policy topics, were productive: stimulating, rewarding, challenging and inspiring.

Here are highlights of the significant results, which you have made possible and that we find decidedly encouraging:

- **Dr. John Reed**, Director of the Burnham Institute in La Jolla California, is a leading expert in the area of programmed cell death. The normal progression of cellular aging and death is dysregulated in cancer cells and leads to unending growth of the tumor. Dr. Reed has studied the complex pathways of programmed cell death and has developed drug discovery strategies for restoring normal death pathways for malignant cells. He presented preliminary results for several lead compounds capable of restoring programmed cell death in cancer cells.
- **Dr. William Berg**, a physician-scientist from Aventis Pharmaceuticals discussed the very productive relationships his firm has established with academic prostate cancer researchers. Aventis is developing Taxotere for chemotherapy of prostate cancer. The multiple academic collaborations have been instructive in optimizing this important treatment in conjunction with other drugs. Many clinical trials currently ongoing with combinations of Taxotere and novel drugs are a direct result of Dr. Berg's program.
- **Dr. Leroy Hood** is a world leading biochemist and molecular biologist whose creation of instruments to sequence proteins and DNA have revolutionized science and enabled solution of the human genome. Dr. Hood is now focused on creating a new science he calls "systems biology". He has founded The Institute of Systems Biology in Seattle to tackle the problem of understanding the

interrelationships of cell systems that result in regulation of human cell growth. The work in Dr. Hood's laboratory is multidisciplinary and will require many years of effort to decipher the entire regulatory apparatus of the cancer cell. However, this integrated approach is novel and represents the most forward looking approach to solving the cancer problem.

- Two talks regarding the cellular mechanism for degrading proteins, the proteasome, were presented. One was by **Dr. Aaron Ciechanover** of the Technion Institute in Israel who discovered this dysregulated pathway and **Dr. Julian Adams** of Millennium Pharmaceuticals who discovered a drug in development to block the pathway. The drug under development is named Velcade and has demonstrated clinical activity in many solid tumors. Prostate cancer studies are currently in Phase II. Early academic support of this drug by CaP CURE made this possible.
- **Dr. Tomasz Beer**, of the Oregon Health Science Center, reviewed his data from a clinical trial of high-dose vitamin D (Calcitriol) in hormone refractory prostate cancer. These data show that response rate (PSA reduction) in these patients, treated weekly with the chemotherapy agent Taxotere plus high dose vitamin D is greatly improved compared to Taxotere alone. This work is being expanded into a major national trial by a biotechnology company, Novacea, in collaboration with Aventis Pharmaceuticals. We hope to have an update on this very important trial next year.
- **Dr. June Chan**, from the University of California, San Francisco, updated and projected future trends in prostate cancer epidemiology. Although these data are very preliminary and subject to some modification, her findings indicate an alarming trend of increased incidence and death from prostate cancer as the population at risk continues to age. These results reinforce the determination of CaP CURE to eliminate prostate cancer.
- **Dr. Eric Small**, from the University of California, San Francisco, presented a subset analysis of a clinical trial of Provenge, a prostate cancer vaccine for hormone refractory prostate cancer. His findings indicate that this vaccine may have activity in patients with lower grade disease (Gleason grade \leq 7). This analysis is from a Phase III clinical trial of Provenge where this subset had benefit and higher grade disease did not. Dr. Small will lead a national trial of this vaccine in the beneficial population.

Dr. Anthony D'Amico, of the Dana-Farber Cancer Institute, is studying the changes in PSA in prostate cancer patients to determine if there is a resulting prediction of outcome. He has pooled data from his own radiation patients as well as patients treated by Dr. Peter Carroll at UC San Francisco and the Uniformed Services University of the Health Sciences (the U.S. Army) prostate cancer database maintained by Dr. Judd Moul. The preliminary data presented at the Retreat shows that patients with PSA doubling times of less than 12 months have a high risk of mortality due to prostate cancer. This is a very enabling finding for clinical trial design. Dr. D'Amico will also test the viability of PSA as a surrogate marker

- for survival following treatment in this cohort. This is the most critical factor lacking in prostate cancer clinical trial design. A surrogate marker to survival would reduce the time and complexity of testing new drugs and would attract more experimental drugs to the clinic.
- **Dr. Christopher Logothetis**, Chairman of Genitourinary Medical Oncology at M.D. Anderson Cancer Center in Houston, provided a keynote address. His group is making great progress in optimizing treatments of prostate cancer in bone. The recently completed chemotherapy plus strontium bone-targeted therapy has now advanced to a national study and was reviewed. An interesting observation is that Gleevec plus chemotherapy (Taxotere) appear to have significant activity against prostate cancer in bone. This elegant translational science project is now in clinical trials and appears promising.
 - **Dr. Howard Scher**, Chairman of Genitourinary Medical Oncology at Memorial Sloan-Kettering Cancer Center in New York, provided a keynote address. In addition to a brilliant positioning presentation on prostate cancer clinical trial methodology, Dr. Scher discussed and updated his clinical programs. Of note is the broad prostate-specific membrane antigen (PSMA) program that was also discussed in a presentation by **Dr. Neil Bander** from Cornell Medical School, NY Hospital. Trials are now proceeding on several fronts using monoclonal antibodies to PSMA and DNA vaccines that will cause an individual patient to produce antibody to PSMA. PSMA antibody, when bound to prostate cancer cells, results in the death of the cancer cell. This is one of the highest priority clinical development programs. Results will be forthcoming soon.
 - **Dr. Philip Needleman** is Chief Science Officer at Pharmacia Corporation and discoverer and developer of Celebrex. This drug, first developed and successfully marketed for arthritis and pain, appears to reduce incidence of colon cancer in high risk patients and may be subsequently approved for prevention of colon cancer. Studies are also ongoing in treatment and prevention of other solid tumors, including prostate cancer. While studies are very early, reducing the inflammatory response associated with cancer might be a powerful strategy for this very low toxicity drug.
 - **Dr. David Agus**, of Cedars-Sinai Hospital in Los Angeles, presented results of a Phase I clinical trial of a monoclonal antibody being developed by Genentech. This antibody has a mechanism of action similar to but distinct from the breast cancer drug, Herceptin. Dr. Agus did the translational research that generated strong rationale for development of 2C4 in prostate cancer. Genentech is planning development of 2C4 in Phase II for prostate cancer.
 - It has become a CaP CURE tradition that the final session of the meeting is on nutrition. The migration from observational studies of food habits to strongly science-based nutrition research funded by CaP CURE is of note.

- **Dr. Ron Evans**, of the Salk Institute in La Jolla, presented data to show how dietary fats might promote prostate cancer by activating receptors in the cell nucleus that promote growth.
- **Dr. William Nelson**, from Johns Hopkins Medical School, showed a linkage between cooked meat and damage to DNA, a cancer promoting event.
- **Dr. Peter Nelson**, from the Fred Hutchinson Cancer Research Institute, presented gene expression results for an herbal supplement PC SPES. His results demonstrated different gene activation when prostate cancer cells were stimulated with PC SPES or DES, a contaminant of PC SPES.
- **Dr. David Heber**, from the University of California at Los Angeles, presented his latest findings on obesity. His team has discovered that cells associated with fat tissue, especially in the gut, secrete chemicals that promote the growth of tumor cells. This strongly argues for caloric restriction to prevent initiation and propagation of cancer.
- **Dr. Leonard Marks**, a Los Angeles-based urologist, has collected prostate specimens from a cohort of prostate cancer patients living in Japan and Los Angeles. These samples will now be analyzed for molecular differences that might help explain why the disease is more aggressive in the western world compared to Asia.

The progress reported at this meeting is the result of your continued generosity and support of CaP CURE. With your help, we will solve this problem. We will not rest until advanced prostate cancer is transformed from an acute and life-threatening disease to a treatable chronic disorder. There is much work to do. We applaud your ongoing commitment to our cause – it is invaluable.

Do not hesitate to contact us if you have comments or questions about this extraordinary event. I can be reached by email (capcure@capcure.org) or by phone 800-757-2873.

Best personal regards,
Howard R. Soule, Ph.D.

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