Informed Prostate Cancer Support Group Inc.
"A 501 C 3 CORPORATION ID # 54-2141691"

September 2018 NEWSLETTER

P.O. Box 420142 San Diego, CA 92142
Phone: 619-890-8447 Web: http://ipcsg.org

We Meet Every Third Saturday (except December)

Tuesday, September 11, 2018

Volume 11 Issue 9

Next Meeting
Sept 15, 2018
10:00AM to Noon

Meeting at

Sanford-Burnham-Prebys Auditorium

10905 Road to the Cure, San Diego CA 92121

SEE MAP ON THE LAST PAGE

What We Are About

Our Group offers the complete spectrum of information on prevention and treatment. We provide a forum where you can get all your questions answered in one place by men that have lived through the experience. Prostate cancer is very personal. Our goal is to make you more aware of your options before you begin a treatment that has serious side effects that were not properly explained. Impotence, incontinence, and a high rate of recurrence are very common side effects and may be for life. Men who are newly diagnosed with PCa are often overwhelmed by the frightening magnitude of their condition. Networking with our members will help identify what options are best suited for your life style.

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Editor: Stephen Pendergast

PROSTATE CANCER IT'S ONLY 2 WORDS NOT A SENTENCE

Prostate cancer screening detection and treatment changes in 2018

Last Meeting Summary by Bill Lewis

Christopher J. Kane, MD; Professor and Chair of Urology Department at UC San Diego; CEO of UC San Diego Health Physicians.

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Video DVD's

DVD's of our meetings are available in our library for $10ea. Refer to the index available in the library. They can also be purchased through our website: http://ipcsg.org Click on the 'Purchase DVDs" tab.

The DVD of each meeting is available by the next meeting date.

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There have been many big changes this year.

1. Better screening and reducing/avoiding overtreatment.
2. Improve tests to enhance specificity, to provide fewer unnecessary tests, and more tests that will allow detecting risky cancers.
3. Big improvements in MRI technology and interpretation.
4. Treatment of localized disease improved, with lower side effects and improved outcomes by more use of large, experienced centers for surgery, and technology improvements for radiation to give higher doses with improved targeting.
5. Improved imaging of advanced disease, using PET scanning with various agents, and with clinical trials underway to determine how best to treat the various situations found.
6. New treatments for advanced disease.

Dr. Kane explained that as better imaging and more specific tests are used, patient populations for clinical trials are now more restricted to those most likely to benefit from a new therapy. So sometimes a new therapy may seem to give better results than an older one, when it is really just a result of "better" selection of candidates for the trial.

Risk issues. Prostate cancer is so common that nearly half of 70 year old men have low volume, low grade prostate cancer. Prostate cancer is the second leading cause of cancer death in American men, with over 30,000 deaths per year in 2016, but declining slightly since then. Some prostate cancer is indolent and others are deadly. So on the one hand, the indolent cancer should be called something else as it is not biologically dangerous, and on the other end of the spectrum, high-risk prostate cancer is a major contributor to deaths from cancer.

PSA stage and grade are powerful independent predictors of outcome. Low risk cancers – PSA under 10, Gleason score = 6 , and low "PSA density" (PSA divided by prostate volume) – if followed carefully under active surveillance guidelines, result in better than 99.5% survival for 10 years, per Johns Hopkins data. Including slightly more risky cancers gave 97% survival for 15 years, according to Toronto data. At the other end of the spectrum, high risk cancer, if untreated, results in only about 60-70% surviving after ten years. This prognosis can be improved by treatment, but such cases are harder to treat than lower risk, slower growing cancer.

To assess risk, we use PSA, Gleason grade, stage (i.e., local vs. metastatic disease), number of positive biopsy cores and extent/grade of positive areas in those cores, and genomic tests such as Decipher, Oncotype DX and Prolaris.

Single nucleotide polymorphisms are inherited variations in your DNA. By evaluating the pattern of these "SNP's," the risk of cancer can be predicted, for prostate cancer as well as for many other diseases. This is accurate enough to predict that a person's risk is anywhere in the range of ¼ to 5X the risk of the general population. It is very controversial as to whether such predictions should be given to people, since they could affect employment, insurance, and even emotional reactions. For now, such testing is only recommended for families with known prostate cancer, to test the next generation, and for families of African-American men (who are known to have higher risk of prostate cancer than other groups).

Mutations in tumors are called somatic mutations, and are useful for predicting the course of the cancer once it has started to grow.

Who should be screened? Should your sons and grandsons be screened? Having a primary relative diagnosed with prostate cancer, doubles your risk, but does not affect whether yours will be indolent or high-risk. Widespread adoption of PSA testing around 1990 resulted in a dramatic drop in findings of metastatic prostate cancer being the initial diagnosis. That is, cancers were found at earlier stages, due to

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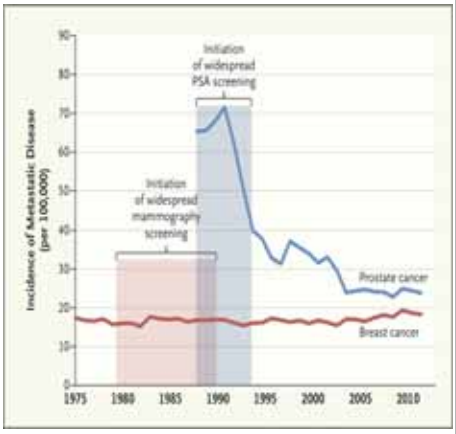

PSA screening. About 40% of men with newly diagnosed prostate cancer should go on active surveillance, and with the recent change in recommendations for screening, doctors are being reeducated to do more screening (but less immediate treatment).

Before, 2012, screening everyone and treating the prostate cancers found, cost 11 billion dollars a year and caused significant morbidity (i.e., obnoxious side effects). New recommendations from USPTF reduce costs to 8.7 billion by not screening and treating only symptomatic disease, but may increase mortality from 27,000 to over 40,000 men per year.

There are now many tests available to assess various biomarkers for the state of the disease, at various points in the course of the disease, and to determine which men may respond well to a given drug. These include 4K, ExoDX, phi, Select-MDX, ConfirmMDX, PCA3, Decipher, Oncotype, Prolaris, Promark, ARv7 and CTC's. See the video for more information. For example, Arv7 will indicate whether abiraterone (Zytiga) would be effective.

MRI is the standard of care prior to a repeat biopsy for men with a prior negative biopsy, and continuing concern for cancer. Since publication of the PRECISION trial in May of this year, MRI has become the standard of care prior to the first biopsy (so insurance companies have to pay for it). This improves accuracy but adds cost. The MRI is usually done with a 3T magnet, and an endorectal coil is not necessary. Interpretation of the MRI is not easy and it is difficult to standardize in community practice.

The RSI variant of MRI imaging, invented and developed for prostate cancer diagnosis at UCSD, in combination with the PIRADS score, gives strong correlation with the grade (aggressiveness) of the disease. The RSI image makes abnormalities seen in the T2 and ADC images of the MRI much more obvious, easing the identification and sizing of lesions.

Intermediate risk disease patients are challenging. Some end up "progressing" rapidly, others not. This is where genomic testing seems to be of most value, in determining who is really at higher or lower risk.

The changing "paradigm" in high risk and advanced cancer: Surgery is likely a bit superior to radiation therapy (RT) or ADT (hormone therapy) alone for high risk, clinically localized prostate cancer. Dr. Kane theorizes that the benefit is actually due to the availability of salvage radiation after surgery, whereas salvage surgery after radiation is almost never done. He also noted that surgery generally causes more side effects such as incontinence and impotence. The combination of ADT + RT definitely improves local control and overall survival in high risk, localized prostate cancer vs ADT alone. Addition of docetaxel (Taxotere) or abiraterone (Zytiga) to initial ADT prolongs survival in newly-diagnosed metastatic disease, as demonstrated/published in this past year. Previously, the combination was only approved for castration-resistant disease.

What about treatment of the primary cancer (in the prostate gland) in low-burden metastatic castration-sensitive prostate cancer? A trial is underway. See below for existing info suggesting it may be helpful. What about salvage therapy of oligomets in low-burden metastatic castration-sensitive prostate cancer? A trial is underway.

Here is some supporting data:

A National Cancer Database retrospective study (2004-2011; published by **Lin C et al JNCI May 2015**) of patients with nearby positive lymph nodes, but no distant metastases, comparing ADT alone to ADT + RT of the prostate and nodes showed 50% lower risk of all-cause mortality. This suggests there is value in treating the prostate in "node-positive" disease.

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A randomized trial (**Fosså SD et al., The Scandinavian Prostate Cancer Group-7 Investigators,** Eur Urol. 2016 Mar 26) of 875 patients with locally advanced non-metastatic prostate cancer (with PSA up to 70), who were given hormone therapy with RT had half the risk of death from prostate cancer over 16 years, compared to those who received hormone therapy alone. Probably many of these men had microscopic metastases not seen with the imaging technology available at the start of the study. Radiating the prostate made the difference. Note that men with lower-risk prostate cancer did not have the same relative improvement.

Three other retrospective trials, also showing that control of the primary tumor is linked to longer survival in men with metastatic prostate cancer, were also discussed. See

Culp et al Eur. Urol, 2014 Jun;65 (6):1058

Engel et al Eur Urol, 2014 Sep;66 (3):602

Rusthoven et al JCO, 2016 epub

Now a multicenter, randomized, Phase 3 trial of standard systematic therapy vs. adding definitive treatment of the primary tumor in metastatic prostate cancer has started.

How about PET to identify oligometastases? PSMA-PET is expected to be approved this year or next.

Salvage lymph node dissection effectiveness: If done fairly early, when PSA is still low, about a third will become disease-free. Studies are included in the video/slides.

Trial	Patients	Treatment Arms	Overall Survival (months)
TAX-327	1006	Docetaxel vs. Mitoxantrone	19.2 vs. 17.6
IMPACT	512	Sipuleucel-T vs. Placebo	25.8 vs. 21.7
TROPIC	755	Cabazitaxel vs. Prednisone	15.1 vs. 12.7
COU-301	1195	Abiraterone vs. Placebo (Post-Chemo)	15.8 vs. 11.8
COU-302	1088	Abiraterone vs. Placebo (Pre-Chemo)	34.7 vs. 30.3
AFFIRM	1199	Enzalutamide vs. Placebo (Pre-Chemo)	18.4 vs. 13.6
PREVAIL	1717	Enzalutamide vs. Placebo (Post-Chemo)	32.4 vs. 30.2
ALSYMPCA	921	Radium-223 vs. Placebo	14.9 vs. 11.3

Dr. Kane's final comment is to recommend being treated by an expert/coordinated team with clinical trials available. This is the case at UCSD, and also at other local centers.

Q& A:

Complementary therapy? The most common result of alternative medical treatments is a delay in getting definitive treatment. However, he is in favor of complementary actions.

Coordination with UCSF and UCLA (and other UC campuses)? Working on the coordination. UCSD is as effective as any of the others. UCSF has a focus on research. We have proton therapy and UCLA refers patients here. UCSD refers patients to UCLA for high dose rate brachytherapy, since it's not yet available here. You need 60-80 patients for per year to be effective, and UCSD doesn't have that volume yet. UCSD does plan to add HIFU (high intensity focused ultrasound, another "focal therapy") technology, but first as a clinical trial, so as to not jump into it too fast.

Getting surgery with low-risk disease? Usually only if the patient has too much anxiety on active surveillance, with the doctor visits, imaging tests and repeat biopsies. If he had low-risk disease, he would go on active surveillance.

Is RSI-MRI now a standard test? Yes. UCSD has now done over 2000, and does about 600 a year.

Many images from various scans are shown in the video of this presentation, which, including the PowerPoint slides, will be available for purchase via the website shortly before the next meeting, or at the September meeting on the 15th.

ON THE LIGHTER SIDE

The famous question is asked for the first time.

"It would be nice if you could check for a pulse next time."

"One day you'll realize that the people most capable of running the country are too smart to get into politics."

"The whole surgical team worked really hard on him, but we reached a point where it was really gross-looking, so we quit."

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FUTURE MEETINGS

- Meeting Date SPEAKERS
  September 15 - Dr. Carl Rossi Update on Proton Therapy

Dr. Rossi has personally treated more than 9,000 prostate cancer patients with proton radiation over the last 26 years—more than any other physician in the world.
Internationally recognized for his achievements in cancer treatment, Dr. Rossi is a radiation oncologist with a research focus on the quality of life and cure rate in prostate cancer and lymphoma. Specializing in proton beam therapy, he has been treating prostate cancer patients with proton therapy since 1991. Prior to serving as the Medical Director of California Protons, he was the Medical Director of the Scripps Proton Therapy Center and was an Associate Professor in the Department of Radiation Medicine at the Loma Linda University Medical Center.

- **For further reading:**
  http://spendergast.blogspot.com/2018/03/prostatecancernews-2018-03.html
- **For Comments, Ideas and Questions,**
  email to Newsletter@ipcsg.org

INTERESTING ARTICLES

New genetic marker could help diagnose aggressive prostate cancer
Date: August 30, 2018
https://www.sciencedaily.com/releases/2018/08/180830100805.htm
Source: University of Turku

Summary: A new link has been found between certain genetic mutations, the aggressiveness of prostate cancer, risk of developing the disease and poorer survival rates of patients.

Scientists have discovered a link between certain genetic mutations, the aggressiveness of prostate cancer, risk of developing the disease and poorer survival rates of patients. The gene, called ANO7, could play a vital role in improving diagnosis of prostate cancer patients.

There is currently no clear way to diagnose aggressive prostate cancer at an early-stage. Genetic mutations, such as those revealed in this study, could lead to the development of accurate diagnostic tests that will ultimately mean patients receive the best possible treatment, sooner.

The researchers studied the DNA from over 1,700 prostate cancer patients and a comparable number of healthy men to look for genetic mutations that were associated with the disease. They were particularly interested in studying mutations to the ANO7 gene because their previous research suggested this could be a gene of interest for prostate cancer.

"We found that small genetic changes to the ANO7 gene increase a patient's risk of aggressive prostate cancer. One of the current biggest unmet needs in prostate cancer care is being able to diagnose aggressive cancers at an early stage. Genetic testing for ANO7 could help identify these patients sooner and may bring new opportunities for precision oncology in prostate cancer," says the leading author of the study, Professor Johanna Schleutker from the Institute of Biomedicine of the University of

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Turku, Finland.

The researchers found one particular genetic mutation that correlated with an increased risk of developing prostate cancer as well as the severity of the disease. They also found a separate mutation that correlated with shorter survival.

Analysis of tissue samples from prostate tumours revealed that mutations to ANO7 were associated with the gene being more active, suggesting that the biological function of ANO7 may play an important role in why these cancers are more aggressive. The function of ANO7 is not fully understood, but further research could lead to new ways to treat the disease.

Although the study involved a large population, it is limited by the fact that it is primarily a Caucasian population from Northern Europe. Further research involving other demographics is needed to validate the findings. The research was published in the International Journal of Cancer. The study was funded by the Worldwide Cancer Research in Britain, the Cancer Foundation, Academy of Finland, Sigrid Jusélius Foundation, and Government research funding granted by Turku University Hospital.

Story Source:

Materials provided by University of Turku. Note: Content may be edited for style and length.

Journal Reference:

Elina Kaikkonen, Tommi Rantapero, Qin Zhang, Pekka Taimen, Virpi Laitinen, Markku Kallajoki, Dhanaprakash Jambulingam, Otto Ettala, Juha Knaapila, Peter J. Boström, Gudrun Wahlström, Csilla Sipeky, Juha-Pekka Pursiheimo, Teuvo Tammela, Pirkko-Liisa Kellokumpu-Lehtinen, Vidal Fey, Lovise Maehle, Fredrik Wiklund, Gong-Hong Wei, Johanna Schleutker. ANO7 is associated with aggressive prostate cancer. International Journal of Cancer, 2018; DOI: 10.1002/ijc.31746

Why does hormone therapy worsen some prostate cancers?

Published 9/6/18 By Catharine Paddock PhD

Fact checked by Jasmin Collier

Hormone therapy for prostate cancer does not always work; the tumor can become resistant and continue to spread. Now, new research reveals how the therapy alters the environment of tumor cells to make this happen.

Hormone therapy can actually make some prostate cancers worse, but how?

Scientists at the Cedars-Sinai Medical Center in Los Angeles, CA, suggest that their study could lead to a "simple blood test" to identify prostate cancer cases that are likely to become resistant and aggressive if they are treated with hormone therapy.

They report their findings in a study paper that now features in the Journal of Clinical Investigation.

Prostate cancer starts in the prostate, which is a gland that lies between a man's bladder and his penis, next to the rectum. The gland surrounds the urethra, which is the tube that carries urine from the bladder to the penis. It makes and adds fluid to semen as it passes through this tube.

The cancer begins when cells in the prostate grow out of control and form a tumor. It arises mostly in men aged 65 and older and rarely before the age of 40.

In the United States, prostate cancer is the most common cancer in men after skin cancer. The American Cancer Society (ACS) estimate that the U.S. will see around 164,690 new cases of prostate cancer and 29,430 deaths to the disease in 2018.

Hormone therapy for prostate cancer

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Although it can be serious, most men diagnosed with prostate cancer will not die of it. This is why today in the U.S., there are 2.9 million men living with or who have survived the disease.

In general, prostate cancer survival rates are higher the earlier the cancer is detected and treated. However, many other factors can also affect a man's outlook, including how well his cancer reacts to treatment.

A research project lasting 6 years has identified dozens of genes that could help identify men at higher risk of prostate cancer.

The male sex hormone androgen stimulates tumor growth in prostate cancer. Hormone therapy — also known as androgen deprivation or androgen-targeting therapy — aims to halt tumor growth by reducing androgen levels or by blocking its effect on tumor cells.

The treatment can be used, for example, to shrink tumors before radiation therapy, or to treat men in whom surgery or radiation therapy has been ruled out.

Hormone therapy can be successful, but there are cases when the tumor develops resistance to the treatment and then comes back or spreads.

Transforms cancer into more aggressive type

In their study paper, the Cedars-Sinai researchers reveal that a possible reason for this is that the hormone therapy triggers a fundamental change in the tumor.

It causes some cancer cells, which are mainly of the common adenocarcinoma type, to transform into a much rarer type called neuroendocrine, which occurs in less than 1 percent of cases.

"This transformation is a problem," says senior study author Neil A. Bhowmick, who is the co-director of the Cancer Biology Program at Cedars-Sinai, "because neuroendocrine prostate cancer is especially aggressive, metastasizes more readily, and is more resistant to both androgen-targeted therapy and chemotherapy."

He explains that there is evidence to suggest that around a quarter of men treated with hormone therapy can experience a return of their cancer in which the tumors look like neuroendocrine prostate cancer and become treatment resistant.

So, working mainly with mice, he and his colleagues decided to focus on the interaction between prostate cancer cells and their microenvironment inside the tumor. The microenvironment is supported by cells called stromal cells.

The team found that androgen deprivation therapy can influence genetic programs in the stromal cells to cause prostate cancer to progress to "a more aggressive differentiation state."

Rise in glutamine

They also observed that the cell transformation was accompanied by a rise in glutamine, an amino acid that is known to hasten the growth of cancer.

The glutamine was being produced in the genetically altered stromal cells and "served as a source of energy" for the cancer cells, as well as helping transform the adenocarcinoma cells into neuroendocrine ones.

Finally, the scientists confirmed the glutamine finding in humans. In a small group of men who had prostate cancer, they found that those whose cancer was resistant to treatment had higher levels of glutamine in their blood than those whose cancer responded to treatment.

They suggest that this means that it should be possible to develop a simple blood test to detect those prostate cancers that are not responding to hormone therapy and perhaps even predict resistance.

"To our surprise, we found this type of therapy further changed the cellular environment in a way that caused adenocarcinoma cells in the prostate to transform into neuroendocrine cancer-type cells."

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Team Identifies Possible Cause of Resistance to Prostate Cancer Treatment

A Roswell Park-led research team has linked the development of castration-resistant prostate cancer and resistance to treatment to a lack of androgen receptor expression in prostate cancer cells, identifying a new therapeutic target.

BUFFALO, N.Y. (PRWEB) September 06, 2018

A collaborative research team has linked the development of castration-resistant prostate cancer and resistance to treatment to a lack of androgen receptor (AR) expression in prostate cancer cells, identifying a new therapeutic target for one of the deadliest forms of cancer among men. Results of this research, which was led by scientists at Roswell Park Comprehensive Cancer Center, were published today in the journal Nature Communications.

Prostate cancer is one of the most common and treatable types of cancer in men. Most patients respond well to hormone therapy or chemotherapy, and five-year survival rates have reached nearly 100% thanks to advances in detection and treatment. However, prostate cancer remains the second-leading cause of male cancer deaths, because those with more advanced or aggressive forms of the disease eventually experience progression or recurrence despite treatment.

For men with advanced disease and tumors that cannot be surgically removed, standard therapy involves drugs that target and block AR, a protein that binds to androgens (male hormones). AR-targeted therapies stop or inhibit the growth of prostate cancer cells, but for unknown reasons, their effectiveness is usually short-lived. Within a year or two of antiandrogen therapy, many patients will develop castration-resistant prostate cancer, an aggressive and treatment-resistant form of the disease.

In an effort to uncover the mechanisms of treatment resistance and progression in prostate cancer, a team of scientists led by Dean Tang, PhD, Chair of Pharmacology and Therapeutics at Roswell Park Comprehensive Cancer Center, in collaboration with scientists at other cancer centers and research institutions in the United States and China, examined AR expression patterns in 89 patients with castration-resistant prostate cancer and found three distinct types: AR in the nucleus of the cancer cell, AR in both the nucleus and cytoplasm, and near or complete absence of AR from all parts of the cell.

Further research confirmed that cells lacking AR did not respond to treatment with enzalutamide (brand name Xtandi), an AR blocker commonly used to treat patients with castration-resistant prostate cancer. These prostate cancer cells were also more likely than AR-containing cells to grow, regenerate and proliferate. Through deep RNA-Seq analysis, the team identified BCL-2, a stem-cell-enriched prosurvival molecule, as a critical regulator and important therapeutic target in castration-resistant prostate cancer cells.

“In order to survive the pressure of chemical castration and antiandrogen therapy, prostate cancer cells overexpress, redistribute or lose androgen receptor,” explains Dr. Tang, the senior author of the study. “Our study offers new proof-of-principle therapeutic strategies to not only treat advanced and metastatic prostate cancer but also prevent castration resistance.”

The research team also reports new evidence that combination treatment with enzalutamide and ABT-199 (brand name Venetoclax), a newly FDA-approved BCL-2 inhibitor, markedly inhibits experimental castrate-resistant prostate cancer. Dr. Tang has initiated a phase Ib/II clinical trial based on these findings, in collaboration three Roswell Park clinical colleagues: Gurkamal Chatta, MD, James Mohler, MD, and Igor Puzanov, MD, MSCI, FACP, who are also co-authors on the new published research.

The study, “Linking prostate cancer cell AR heterogeneity to distinct castration and enzalutamide responses,” is available at https://www.nature.com/articles/s41467-018-06067-7.

NETWORKING

Please help us in our outreach efforts. Our speakers bureau consisting of Lyle LaRosh, Gene Van Vleet and George Johnson are available to speak to organizations of which you might be a member. Contact Gene 619-890-8447 or gene@ipcsg.org to coordinate.

Member and Director, John Tassi is the webmaster of our website and welcomes any suggestions to make our website simple and easy to navigate. Check out the Personal Experiences page and send us your story. Go to: https://ipcsg.org/personal-experience

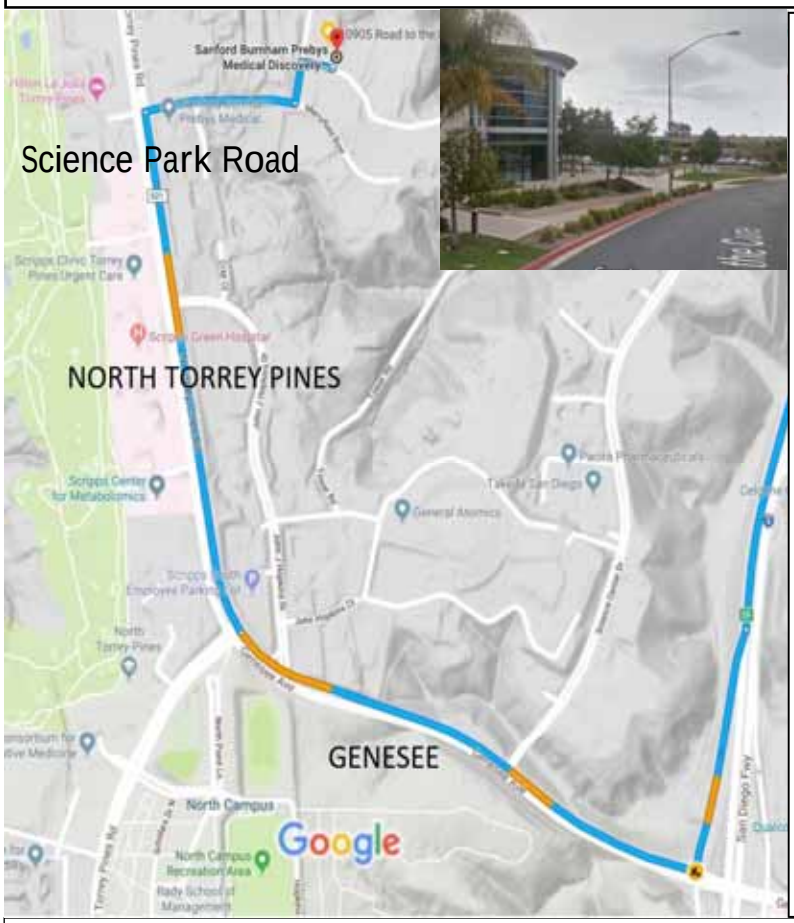
Our brochure provides the group philosophy and explains our goals. Copies may be obtained at our meetings. Please pass them along to friends and contacts.

FINANCES

We want to thank those of you who have made special donations to IPCSG. Remember that your gifts are tax deductible because we are a 501(c)(3) non-profit organization.

We again are reminding our members and friends to consider giving a large financial contribution to the IPCSG. This can include estate giving as well as giving in memory of a loved one. You can also have a distribution from your IRA made to our account. We need your support. We will, in turn, make contributions from our group to Prostate Cancer researchers and other groups as appropriate for a non-profit organization. Our group ID number is 54-2141691. Corporate donors are welcome!

If you have the internet you can contribute easily by going to our website, http://ipcsg.org and clicking on "Donate" Follow the instructions on that page. OR just mail a check to: IPCSG, P. O. Box 4201042, San Diego CA 92142



Directions to Sanford-Burnham-Prebys Auditorium
10905 Road to the Cure, San Diego, CA 92121

Take I-5 (north or south) to the Genesee exit (west).

Follow Genesee up the hill, staying right.

Genesee rounds right onto North Torrey Pines Road.

Do not turn into the Sanford-Burnham-Prebys Medical Discovery Institute or Fishman Auditorium

Turn right on Science Park Road. Watch for our sign here.

Turn Left on Torreyana Road. Watch for our sign here.

Turn Right on Road to the Cure (formerly Altman Row). Watch for