



FRED  
HUTCHINSON  
CANCER  
RESEARCH  
CENTER

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**FOR IMMEDIATE RELEASE**

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**FRED HUTCHINSON RECEIVES \$12.7 MILLION TO LEAD  
PROSTATE-CANCER RESEARCH CONSORTIUM**

*Funding underscores status of Pacific Northwest as major center of prostate research*

SEATTLE – The National Cancer Institute, a branch of the National Institutes of Health, has awarded \$12.7 million to the Fred Hutchinson Cancer Research Center to lead a multi-center, five-year investigation into the genetic mechanisms of prostate-cancer progression. Understanding how and why prostate cancer can turn deadly is key to developing therapies that may effectively treat men with recurrent or advanced prostate cancer, for which there is no cure.

Known as the Pacific Northwest Prostate Cancer Research SPORE (short for Specialized Program of Research Excellence), the initiative will involve more than 50 investigators in Seattle and Vancouver, B.C.

Participating institutions in Seattle are Fred Hutchinson, the University of Washington and the Institute for Systems Biology. Vancouver partners are the University of British Columbia and its affiliate, The Prostate Centre at Vancouver General Hospital.

The strong history of collaboration among these institutions – themselves all major contributors to prostate-cancer research – was key to getting the grant, said principal investigator Paul Lange, M.D., professor and chair of urology at the UW School of Medicine and an affiliate investigator in Fred Hutchinson's Public Health Sciences Division.

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“This highly competitive award exemplifies the high caliber of prostate-cancer research among the major medical-research institutions in the Pacific Northwest and the significant ongoing collaborations among researchers from each of the participating institutions,” Lange said.

During the past decade, for example, a working group of Seattle prostate-cancer investigators has met regularly to collaborate on projects focused on understanding the hereditary and lifestyle factors behind prostate cancer and developing innovative technologies to unravel the genetic mechanisms of the disease. Fruits of their labor include mapping the region of a gene associated with inherited prostate cancer and primary brain cancer, as well as better understanding the genes expressed in the more common forms of prostate cancer.

“The close relationship between these institutions and our long-standing track record of success was crucial to getting the grant,” echoes co-principal investigator Janet Stanford, Ph.D., a member of Fred Hutchinson’s Public Health Sciences Division and director of its Prostate Cancer Research Program.

The Pacific Northwest Prostate Cancer SPORE grant follows closely on the heels of another major prostate-cancer research coup for the Seattle researchers; in July, the University of Washington was awarded \$10.5 million from the National Institutes of Health to lead a multi-center, five-year investigation into the basic causes of why prostate cancer metastasizes, or spreads, to the bone. Participating institutions in this effort are Fred Hutchinson and the Institute for Systems Biology, co-founded by former UW geneticist Leroy Hood, M.D., Ph.D.

Together, the two hefty grants, totaling \$23.2 million, give area researchers unprecedented opportunities in their ongoing efforts to better understand prostate cancer and develop improved therapies, particularly for men with recurrent or advanced disease.

“There hasn’t been a lot of improvement in the survival of men with advanced prostate cancer over the past 30 years, so to focus on understanding the factors that may contribute to progression from clinically less aggressive to more aggressive disease is important if we’re to develop therapies that will effectively treat these men,” said Stanford, also a professor of epidemiology at the UW School of Public Health and Community Medicine.

As such, the overarching goal of the consortium is to bring, more quickly and efficiently, laboratory discoveries to patient bedsides throughout the Pacific Northwest. A variety of clinical partners throughout the Northwest will recruit and enroll patients for research studies to test the therapies that emerge. They will include the Seattle Cancer Care Alliance (the oncology patient-care arm of Fred Hutchinson, UW Academic Medical Center and Children’s Hospital and Regional Medical Center) and the Veterans Affairs Puget Sound Health Care System in Seattle; the Oregon Cancer Institute/Oregon Health & Science University in Portland; and Vancouver General Hospital/University of British Columbia in Vancouver.

Prostate cancer is the most common male cancer; an estimated 1.5 million Americans live with the disease, which affects one in six and is the second-leading cause of death from cancer in men. An estimated 189,000 men will be diagnosed this year and about 30,200 will die of the disease, according to the American Cancer Society.

Due to the prevalence of prostate-specific antigen, or PSA, screening, the majority of men are diagnosed early, before the disease has spread beyond the prostate. Only 6 percent of men first are diagnosed with advanced prostate cancer that has migrated to the bones.

While initial diagnosis of advanced prostate cancer is rare, recurrence after primary therapy is not. Several population-based studies have found that among men under age 70 who are diagnosed with localized prostate cancer, between 20 percent and 30 percent will develop a recurrence and many of them will die from the disease, Stanford said. Once the disease spreads to the bone, the median survival is 36 months.

Male hormones, or androgens, are known to fuel prostate-cancer growth, so current treatments for advanced prostate cancer focus on slowing the progression of the disease through surgical or chemical castration, also known as androgen-deprivation therapy. Prostate cancer consists of both “hormone-sensitive” and “hormone-insensitive” cells, and everyone’s ratio of such cells is different. Eliminating the body’s major source of androgens, such as testosterone, interrupts the pathway of hormone production that speeds the growth of hormone-sensitive cancer cells. While such therapy works for a while to increase the length of life, it is not considered curative, as androgen deprivation is only effective in controlling the growth of the cancer cells that feed on male hormones.

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Eventually, these hormone-sensitive cells are crowded out by hormone-insensitive cancer cells, which don't depend on male hormones to proliferate.

Improving the treatment options for men faced with recurrent prostate cancer that no longer responds to androgen-deprivation therapy is the unifying mission behind the consortium's four scientific projects, all of which seek to apply the insights of laboratory and epidemiological research to better understand how and why prostate cancer spreads. Below are brief descriptions of each project:

**Project 1: Identifying genetic variants linked to prostate-cancer progression and mortality** – This study aims to identify genetic variants that are linked to prostate-cancer recurrence and mortality with the goal of developing a simple blood test to determine which prostate-cancer patients are most likely to progress to advanced disease. The researchers will follow more than 700 Seattle-area men, all of whom were diagnosed with prostate cancer before age 65, to see if those who relapse share common genetic markers of disease progression. *Project leaders: Janet Stanford, Ph.D., member, Fred Hutchinson Public Health Sciences Division; and David Penson, M.D., M.P.H., assistant professor of surgery, UW School of Medicine.*

**Project 2: Understanding the genetic differences between men who relapse and men who remain cancer-free after initial therapy for localized prostate cancer** – Previous studies have found that many men with early-stage prostate cancer, even those who are cured with localized therapy such as surgery or radiation, in fact have prostate-cancer cells in their blood and bone marrow very early in the disease process. It is not known why some of these circulating cells turn into deadly metastatic cancer while others die or remain dormant. This study will examine blood samples from men who undergo surgery for early-stage prostate cancer to try and determine the genetic differences between those who remain cancer free and those whose cancer recurs. The ultimate goal would be to develop a genetic screening tool to identify which men are most likely to relapse and may benefit from more aggressive therapy upon initial diagnosis. *Project leaders: Robert Vessella, Ph.D., professor and associate chair of urology; William Ellis, M.D., assistant professor of urology, both of the UW School of Medicine; and Barbara Trask, Ph.D., member and director, Fred Hutchinson Human Biology Division.*

**Project 3: Developing new treatments for men with advanced prostate cancer who no longer respond to androgen-deprivation therapy** – The goal of this project is to develop new treatments for men with advanced prostate cancer who no longer respond to androgen-deprivation therapy. The idea is to harness antisense technology, which inhibits gene expression, to coax hormone-insensitive prostate-cancer cells to commit suicide – a process called apoptosis, or programmed cell death. Such antisense drugs, when combined with novel chemotherapeutic agents or combinations of existing drugs, also may block the cellular processes that allow cancer to grow. *Project leaders: Martin Gleave, M.D., professor of surgery and director of clinical research; and Colleen Nelson, Ph.D., assistant professor of surgery and head of the Gene Array Facility, both of the University of British Columbia/The Prostate Centre at Vancouver General Hospital.*

**Project 4: Understanding the molecular biology of prostate cancer throughout all stages of its progression** – This project will analyze gene and protein expression in the entire spectrum of prostate tumors – from those that are clinically localized and slow-growing to those that are advanced and highly aggressive. The goal is to create a genetic blueprint, of sorts, to help understand the molecular biology of prostate cancer at all stages of its progression. A particular focus will be to understand the mechanisms that cause tumors to progress from being androgen-dependent and treatable to androgen-independent and drug-resistant. Deciphering the molecular pathways that allow disease progression could help identify new drug targets and new genes that are linked to tumor metastasis. *Project leaders: Leroy Hood, M.D., Ph.D., co-founder and president, Institute for Systems Biology, and UW affiliate professor of bioengineering, immunology, and computer science and engineering; and Peter Nelson, M.D., assistant member, Fred Hutchinson Human Biology and Clinical Research divisions and assistant professor of medicine and biotechnology at the UW School of Medicine.*

These projects will be supported by an infrastructure of SPORE-funded research cores that will provide resources and expertise in a variety of areas: administration, bioinformatics, biostatistics, specimen collection and tissue banking, and clinical-trial design, recruitment and management. Below are the cores and their leaders:

**Leadership and administrative core** – The administrative core will consist of a variety of interacting committees, such as internal and external advisory boards, which

will oversee the scientific direction and progress of the SPORE. *Core leader: Paul Lange, M.D., professor and chair of urology, UW School of Medicine; co-leader: Janet Stanford, Ph.D., member, Fred Hutchinson Public Health Sciences Division.*

**Tissue and specimen core** – The tissue and specimen core will provide specimen collection, storage, distribution and clinical/research-information dissemination. *Core leader: Robert Vessella, Ph.D., professor of urology; co-leader: Lawrence True, M.D., associate professor of pathology, both of UW School of Medicine.*

**Biostatistical core** – This core will link study design with data collection and analysis, and it will assist investigators in designing studies that feasibly address questions of scientific interest, are amenable to statistical analysis and will yield statistically valid and interpretable results. *Core leader: Ruth Etzioni, Ph.D., associate member, Fred Hutchinson Public Health Sciences Division.*

**Informatics and gene expression core** – This core will provide gene-chip technology and data analysis tools to facilitate large-scale gene-expression studies. *Core leader: Peter Nelson, M.D., assistant member, Human Biology and Clinical Research divisions; co-leader: Nigel Clegg, Ph.D.; senior fellow, both of Fred Hutchinson.*

**Clinical core** – This core will work to bring promising research findings into the clinic as quickly as possible by providing tissue samples for analysis, establishing a unified clinical database, and designing and conducting clinical trials. The goal of this core is to facilitate the flow of information not only from the laboratory to the clinic but also from the clinic to the laboratory and back. In addition, this core will work with a patient-advocacy group to engage patients in SPORE activities. *Core leader: Celestia Higano, M.D., associate professor of medical oncology, UW School of Medicine.*

The SPORE grant also will fund up to four pilot projects each year as part of a developmental-research program to support innovative translational research aimed at improving survival in prostate-cancer patients. Research proposals will be solicited from investigators within the four participating institutions.

Established by Congress in 1992, the organ-based SPORE program was created to promote collaboration between basic and applied scientists to speed the testing of new approaches to the prevention, early detection, diagnosis and treatment of a variety of

cancers. Other recipients of prostate SPOR funding this year are Harvard University and the University of California at Los Angeles.

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#### **About the Fred Hutchinson Cancer Research Center**

The Fred Hutchinson Cancer Research Center, home of two Nobel Prize laureates, is an independent, nonprofit research institution dedicated to the development and advancement of biomedical technology to eliminate cancer and other potentially fatal diseases. Fred Hutchinson receives more funding from the National Institutes of Health than any other independent U.S. research center. Recognized internationally for its pioneering work in bone-marrow transplantation, the center's four scientific divisions collaborate to form a unique environment for conducting basic and applied science. Fred Hutchinson is the only National Cancer Institute-designated comprehensive cancer center in the Pacific Northwest and is one of 41 nationwide. For more information, visit the center's Web site at [www.fhcr.org](http://www.fhcr.org).

#### **About the University of Washington**

The University of Washington's faculty includes five Nobel Prize-winners, five MacArthur Fellows, and more than 40 members of the prestigious National Academy of Sciences. Its highly regarded School of Medicine has been ranked first in the nation in training primary-care physicians, and several of its graduate and professional programs are rated among the top 10 in their fields. Since 1975, the UW has been among the top public universities in receipt of federal research funds. Web site: [www.washington.edu](http://www.washington.edu).

#### **About the Institute for Systems Biology**

Systems biology is an emerging discipline that takes a more global look at complex biological functions. The Institute for Systems Biology is one of the most visible and pioneering research organizations in the world dedicated to this new approach that requires the integration of science, technology and bioinformatics in ways that would have been impossible only a few years ago. The Institute is also committed to pioneering new approaches to science education and increasing public awareness of biotechnology issues.

The Institute was founded by Dr. Leroy Hood, Dr. Ruedi Aebersold and Dr. Alan Aderem in 2000 and rapidly grew to a faculty of eight and a staff of more than 170. Hood, the Institute's president and director, led the development of the automated DNA-sequencing technology that enabled the Human Genome Project and was among the small group that advocated for the effort in 1985. Aderem, a prominent immunologist and cell biologist and pioneer in the study of innate immunity, has provided scientists with fundamental insights into the functioning of the macrophage. Aebersold, who is widely recognized for his work in analytical protein biochemistry and proteomics, leads a research group at the ISB that is focused on developing new methods and technologies for understanding the structure, function and control of complex biological systems. Web site: [www.systemsbio.org](http://www.systemsbio.org).

#### **About the University of British Columbia and The Prostate Centre at Vancouver Hospital**

The Prostate Centre at Vancouver General Hospital, an affiliate of the University of British Columbia, is the largest comprehensive research and treatment centre of its kind in Canada with a focus exclusively on prostate disease. Home to Canada's largest gene array facility and Western Canada's only Training and Education Centre for Prostate Research, the Centre is a University of British Columbia Academic Centre of Excellence. The Prostate Centre is one of three centres of excellence located at Vancouver General Hospital, the primary adult referral and teaching hospital in Western Canada and a part of the Vancouver Coastal Health Authority, the largest network of health organizations and services in Canada. Prostate Centre Web site: [www.prostatecentre.com](http://www.prostatecentre.com). UBC researchers, who conduct more than 4,000 investigations annually, attracted \$260 million in research funding in 2001/2002. UBC Web site: [www.ubc.ca](http://www.ubc.ca).

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