



Edward A. Frick

## From The Chairman's Desk

Cancer effects everyone, rich or poor, young or old. Over 1,000,000 people in the United States will be diagnosed with cancer this year. However there has been major progress in cancer research over the past few years. We are beginning to understand the causes of cancer and to initiate new methods of prevention, diagnosis, and treatment. The "war on cancer" is far from being won, but some of the battles are beginning to turn our way.

**This year's forum** addressed a key topic, "Differentiation as Cancer Therapy", and was chaired by *Dr. Raymond Warrell* from Genta, Incorporated in New Jersey. It was one of the best sessions ever. **The 2002 Forum** topic will focus on "Cellular Senescence and Cancer" and will be chaired by *Dr. Ron DePinho* from the Harvard Medical School and *Dr. Charles Sherr* from St Jude Children's Research Hospital.

In 1999 the foundation established the "Focus on the Future" program where grants are awarded to allow the recipients to hold meetings similar in content and format to the very successful annual Hilton Head Forums. **The 2001 Focus grant** was awarded to *Dr. Donald McDonald* from the University of California, San Francisco to address the topic of "Mechanisms, Consequences, and Therapeutic Implications of Blood Vessel Leakiness in Cancer." **2002 Focus grants** have been awarded to *Dr. Michael Seiden* from Massachusetts General Hospital, to focus on "Developing Bioradiomics for the Evaluation of Biologically Targeted

Therapies" and to *Drs. Volker Schirmmacher and Philipp Beckhove* from the German Cancer Research Center (Heidelberg, Germany) to address "Exploiting the Patient's Immunological Memory."

In August, *Jim and Jennifer Buchanan* sponsored the fifth **Homefront Bike Tour** to benefit the Forbeck Foundation. They biked 140 miles from Manchester, Massachusetts to Harrison, Maine and raised \$128,000 (\$345,000 over 5 years).

We want to welcome *Jamie Forbeck* to the Foundation's Board of Trustees. She has been associated with the foundation since it was established. We also want to thank the following Emeritus Board Members for their many years of guidance, direction and assistance: *Dr. Joe Black, Dr. William Frackelton, Richard Goodemote, Robert Smyth and Howard Wright.*

This is the time of the year when we ask for your renewed support to maintain the momentum that has been established. It is through your generous help that continuing progress will be made.

Thank you for your continuing assistance to the Foundation.

Edward R. Frick  
Chairman, Board of Trustees

## Cancer Therapeutics— A Model for the Future

It is possible that we are on the verge of a new era in cancer medicine. Most of the drugs that we have available to us today have been developed by a process of trial and



John T. Kenshead, PhD

error. Many come from natural sources such as plants and fungi. The search for these compounds continues with ever more exotic regions, such as the sea-bed, being screened for sources of drugs that can kill cancer cells. The candidate drugs are tested in laboratories for their ability to kill cancer cells that grow in culture. If they show some degree of selectivity they will go on to be tested in animals; for both efficacy against tumor as well as toxicity to normal body organs. Those compounds that pass these screens they will enter Phase I clinical studies that are usually open to patients who have relapsed from normal therapeutic strategies. In these studies the optimal dose

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# 2001 Forbeck Forum: XVII<sup>th</sup> Annual Forum

November 2–3, 2001 Hilton Head Island, South Carolina

## Differentiation as Cancer Therapy

- I: Hematology I
- II: Pediatric Neoplasia
- III: Hematology II
- IV: Solid Tumor Neoplasia

### Chairman

**Raymond Paul Warrell, Jr. MD**  
Genta, Incorporated  
Berkeley Heights, NJ

### Participants

**Stephen B. Baylin, MD**  
Johns Hopkins Oncology Center  
Baltimore, MD

**James R. Downing, MD**  
St. Jude Children's Research Hospital  
Memphis, TN

**Gary Gilliland, PhD, MD**  
Howard Hughes Medical Institute  
Boston, MA

**Calvin B. Harley**  
Geron Corporation  
Menlo Park, CA

**H. Philip Koeffler, MD**  
CLA School of Medicine  
Los Angeles, CA

**Scott M. Lippman, MD**  
M.D. Anderson Cancer Center  
Houston, TX

**Malcolm A. S. Moore, D.Phil.**  
Memorial Sloan Kettering Cancer Ctr  
New York, NY

**Makio Ogawa, MD, PhD**  
Medical University of South Carolina  
Charleston, SC

**Pier Paolo Pandolfi, MD**  
Memorial Sloan-Kettering Cancer Ctr  
New York, NY

**Professor Leo Sachs**  
Weizmann Institute of Science  
Rehovot, Israel

**Daniel G. Tenen, MD**  
Harvard Institutes of Medicine  
Boston, MA

## 2001 Conference Report

by Raymond Paul Warrell, Jr. MD

The Year 2001 Forum of the William Guy Forbeck Research Foundation dealt with the topic of *Differentiation in Cancer Therapy*.

While the concept has obviously evolved to reflect scientific advances, the general idea of differentiation goes back almost 100 years. Within this framework, cancer is viewed as a disease of relatively immature cells that are occasionally dividing at an accelerated rate, but whose major defect is a decrease in the rate of cell death. The imbalance of dividing cells versus dying cells results in tumor growth that ultimately overwhelms the patient. The relative longevity of cancer cells owes to their being trapped in a prolonged state of adolescence in which their ability to grow up is blocked due to genetic abnormalities. Conceivably, drugs that could eliminate this maturation block might enable these cells to grow up, grow old, and die off. Thus, treatments that reverse this dividing vs. dying imbalance—however slightly—should over time eventually extinguish the disease.

*Leo Sachs*, the Forum's keynote speaker, provided an expansive view of cellular capabilities. The general proposition was that both normal and malignant cells were enormously "plastic", an idea that implies cancer cells can be reprogrammed to behave normally. All cells communicate via networks of factors that are continually cross-talk. Dr. Sachs pointed out that simply because we do not yet know how to interfere

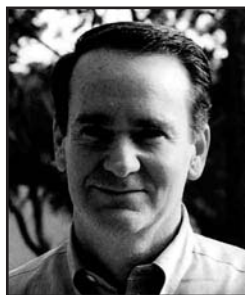
does not mean that it cannot be done. Moreover, given their criticality, these pathways are likely to multiply redundant, and this "power of redundancy" will increase the

likelihood of making chance observations that would yield major insights.

*Pier Paolo Pandolfi* has created mouse models of several human diseases, particularly acute promyelocytic leukemia (APL), his group has genetically engineered mice that express proteins that are known to give rise to human leukemia. These models have yielded insights into both the cause and biology of leukemia, and they are being used to determine mechanisms of drug action, as well as targets for new treatments.

*Malcolm Moore* presented information regarding self-renewal properties of hematopoietic stem cells (i.e., cells that continually give rise to new blood-forming cells). He described a number of factors that normally regulate this key process in healthy cells, along with those that deregulate the processes in cancers such as leukemia, lymphoma, and myelodysplasia. *Makio Ogawa* then reviewed how these early cells make their own transition from the earliest stages of immaturity into adolescence, and also how these cells that are nominally "blood cells", have been used to rebuild damaged liver tissue. Following on these ideas, *Calvin Harley* discussed work in using such stem cells as a mechanism of novel gene discovery (so-called "pharmacogenomics"), as well as a source of cells for transplantation or replacement therapy. This incredibly powerful technology could eventually be used to provide new nerve cells for patients with Parkinson's disease or stroke, cardiac cells for patients with heart attacks, pancreas cells for patients with diabetes, and bone or muscle cells for patients with crippling diseases.

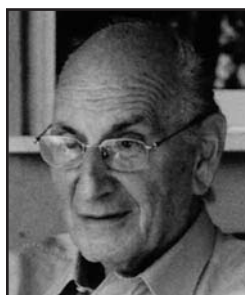
*Gary Gilliland* proposed a simplified grouping of the more than 100 gene mutations that are responsible for leukemia into two broad types: those that confer advantages with respect to



Raymond Paul Warrell, Jr. MD



Malcolm Moore



Leo Sachs

increased cell division or prolonged survival, and those that impair differentiation. This concept then refines those methods of attack that can be targeted to these broad categories of disease. For example, Gleevec® would be viewed as a prototype drug useful for the first class, and retinoic acid or arsenic as drugs for

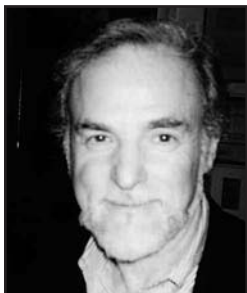
these approaches, which have included vitamin approaches, have been strikingly unsuccessful despite their intuitive attractiveness. Newer approaches, such as the use of Advil®-like drugs to prevent colon cancer in high-risk patients, have been considerably more promising. He suggested that future



2001 Forum

the second class. *Daniel Tenen* presented a somewhat different concept wherein several types of leukemia share abnormalities that center on disrupted differentiation. These abnormalities should be potentially reversible by targeting a specific gene product (known as C/EBP- $\beta$ ). *Phillip Koeffler* then showed that addition of certain older drugs in a new sequence could reactivate many genes thought to be dormant in leukemias. Moreover, restoration of these normal gene functions could lead to extinction of the leukemic cells.

*Stephen Baylin* focused on novel approaches to solid tumors that similarly involve reactivation of normal genes that are abnormally shut down in cancer cells. This silencing is caused by specific chemical changes (known as methylation and acetylation), both of which can now be manipulated by drugs. Because of its potentially broad applicability to gene regulation, this area



Stephen Baylin

is one of the most exciting in biomedicine. Finally, *Scott Lippman* closed the Forum by taking a macro view of these developments from a public health viewpoint, particularly focusing on translation of these ideas into very large (and long) trials of interventions for cancer prevention in large U.S. populations. He noted that the first generation of

approaches to cancer prevention must first carefully identify patient populations who are at highest risk, rather than attempting to broadly study healthy people with agents that need to be taken for decades in order to determine their benefit (or additive risks).

“It takes good people to attract good people”, and the high level of scientific quality in this year’s Forum reflected the world-class caliber of our speakers. We again saw very high enthusiasm for the Forum’s format by all participants. The idea of ‘differentiation therapy’ has yielded several spectacular successes in the last 10 years. In 1992, APL was a lethal disease primarily in young adults, and less than 25% of patients survived. By the end of the decade, this leukemia had been transformed. A new patient with APL in 2002 should expect to be cured with greater than 85% probability. As Chair of the 2001 Forum, I speak for the excitement of all the attendees that this type of progress can only be accelerated in the future. I was honored to lead this group, and we are all most grateful to the Forbeck Foundation for continuing its sponsorship of this wonderful event.

Raymond Paul Warrell, Jr. MD  
Chairman, 2001 Forbeck Forum  
Genta, Incorporated  
Berkeley Heights, NJ

## Comments From 2001 Participants

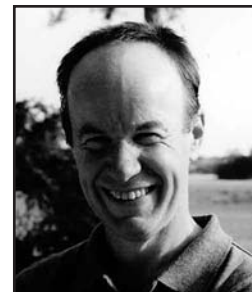
“All of my private conversations with the invited speakers were uniformly positive. I believe they especially appreciated the ability to interact with scientists from fields that were quite different from their own focus. It was a great pleasure to have served as this year’s organization chair.”

—Raymond Paul Warrell, Jr. MD  
Chairman and CEO, Genta, Inc

“It was a scientifically excellent meeting and gave me a chance to reunite with old friends and to create new friendships. Dr. Moore and I are planning to exchange fellows for possible collaboration and I may be visiting the laboratory of Dr. Gilliland in the future.”

—Makio Ogawa, MD, PhD  
Medical University of South Carolina  
Charleston, SC

“The small closed group setting and the format did allow for ample discussion and off-line interactions that a lot of larger meetings lack. I liked the 5-slide format. The purpose of the meeting was not to go into great technical detail of existing approaches, but to allow new ideas to surface from general concepts. This opportunity is mostly lost if 40 slides are presented and the discussion drills down to the minutia of the presented data.”



Calvin Harley

Calvin B. Harley  
Chief Scientific Officer  
Geron Corporation  
Menlo Park, CA

The get together of a small number of people working on different experimental systems is an excellent opportunity to discuss various viewpoints on a common subject, and this was certainly so in this Forum. In addition to having discussions with people I had met before, it was also a pleasure to meet personally others whom I had only known from the literature. It was altogether a very stimulating occasion.”

Professor Leo Sachs  
Weizmann Institute of Science  
Rehovot, Israel

## 2001 SCHOLAR AWARD



David Tuveson

The Foundation received a number of very qualified applications for the 2001 Forbeck Scholar Award. The Scientific Advisory Board selected three outstanding young scientists to attend the 2001 Forum and receive this award. Unfortunately, two invitees declined due to travel restrictions following September 11th.

We were pleased to present this year's Scholar Award to *David Tuveson, MD, PhD*. He is currently an Instructor in Medicine at Harvard Medical School and is on the research and clinical staff of The Dana-Farber Cancer Institute in Boston. He received his BS at MIT and his MD, PhD at Johns Hopkins School of Medicine. David was nominated for the Foundation Scholar Award by James D. Griffin, MD who said "He is an expert in the therapy of human sarcomas, and has recently done an excellent job in providing the preclinical studies showing that the tyrosine kinase inhibitor, ST1571 or glivec, inhibits the proliferation of gastrointestinal sarcomas."

Forum participants have agreed these scholars add to the dynamic interaction of the Forum.

After attending the 2001 Forum David wrote "I agree that open communication between researchers (and industry) will facilitate progress greatly, and I'll try to do my small part in this agreement in the years to come."

*"The inadequacy of current treatments in the management of most oncology patients has persistently motivated me to pursue investigational studies aimed at improving therapies. I have been fortunate to conduct research in both basic science and clinical translational manner over the past several years."*

– David Tuveson, MD, PhD

## 2002 "FOCUS MEETING" GRANTS AWARDED

In this 4th year of the Focus program, the Foundation Scientific Advisory Board reviewed grant applications and selected two for funding.

### *Developing Bioradiomics for the Evaluation of Biologically Targeted Therapies.*

October, 2002

Michael V. Seiden, MD, PhD,  
Massachusetts General Hospital, Boston

Over the next several years there will be an increasing array of novel biologically targeted therapeutic agents that will be used to expand our treatment options in the battle against cancer. These agents, unlike classic chemotherapy, will be less likely to lead to measurable reduction in tumor volume and will most likely only demonstrate efficacy in individuals whose tumors express certain molecular markers.

There is a growing need for the development, validation, and use of imaging agents and technologies that can evaluate tumors for the expression of these key molecular structures. New technologies in the field of PET scanning, MRI technology as well as the development of a new collection of fluorescent probes offers exciting new research avenues within this field.

Experts in molecular imaging typically come from the field of physics, radiology, nuclear medicine and chemistry and are typically not in frequent communication with disease based experts or experts in experimental therapeutics. This conference looks to bring together leaders in the field of molecular imaging, image acquisition and novel therapeutics.

In order to focus on the meeting particular emphasis will be on tumors that involve the peritoneal cavity such as ovarian carcinoma, gastric carcinoma and pancreatic carcinoma. These tumors are typically all very difficult to image with standard technologies.

Introduction of these leaders to each other in the small meeting setting of the Forbeck conference will allow the development of important collaboration, synergy, and hopefully the foundation for planning informative clinical trials utilizing these novel technologies.

### *A New Tool in Cancer Medicine: Exploiting the Patient's Immunological Memory.*

April, 2002

Prof. Volker Schirmacher & Dr. Philipp Beckhove  
German Cancer Research Ctr, Heidelberg

We wish to introduce a new field of cancer immunology to an interdisciplinary group of outstanding experts, both basic scientists and clinicians. The meeting will focus on the interdisciplinary exchange of expertise to accelerate scientific progress and to draw up future clinical applications.

In the past, a number of tumor-associated-antigens (TAAs) have been characterised to be capable of initiating autologous and allogeneic T-lymphocyte responses against the respective tumors. Thus, TAA-reactive T cells may be potent agents for cancer treatment. Clinical usage of such cells is nevertheless hampered by their low frequency and often anergic status in the peripheral blood of patients. It is the aim of various approaches, such as dendritic cell vaccination, to increase the frequency of the patients TAA-specific effector cells. In contrast, we recently demonstrated that a majority of breast cancer patients are very well able to generate high frequencies of tumor-reactive T cells. These cells are not found in the peripheral blood, but stored as resting memory T cells in the bone marrow. Isolated and re-activated in vitro, these cells exert potent anti-tumor functions in vitro and in vivo. Thus, the bone marrow may be suitable as a therapeutic source of enriched TAA-specific lymphocytes for an autologous immunotherapy.

Other points of discussion will cover: the possible implication of B-cell immunity on cancer treatment, bone marrow as an exploitable compartment for B cell memory, the redistribution of applied cells within the lymphoid compartments and target tissues of the host, the use of dendritic cells for T- and B lymphocyte re-activation, immunological monitoring during immunotherapies and generation of clinically applicable immune cells under good manufacturing practice conditions.

## 2001 FOCUS MEETING SUMMARY REPORT

### **Significance of Blood Vessel Leakiness in Cancer**

Donald M. McDonald, MD, PhD  
University of California, San Francisco



Donald M. McDonald

Donald McDonald challenged the participants to consider the significance of the leakiness of blood vessels in tumors by addressing several questions: (1) Why are the blood vessels in tumors leaky and what are the consequences of the leakiness? (2) How can blood vessel leakiness be assessed in experimental tumors and in human cancer? (3) Would it be therapeutically beneficial to decrease the leak, and if so, how could this be achieved? (4) Would "normalization" of tumor blood vessel structure and function be beneficial in cancer therapy, and if so, how could this be done? (5) What strategies are available to target therapeutics to tumor vessels with the goal of normalizing or destroying the vessels?

At the end of the conference, all participants were asked to reflect on the presentations and discussions and summarize for this report some key questions to be addressed, experiments to be performed, and conclusions drawn about blood vessel leakiness in cancer.

#### Introduction:

- I. Endothelial barrier function of normal vessels
- II. Mediators of endothelial leakiness
- III. Leakiness of tumor vessels: Abnormalities in endothelial cell and pericyte structure, function, & basement membrane
- IV. Consequences of tumor vessel leakiness
- V. Genomic analysis of vascular targets
- VI. Targeting of drugs to tumor vessels
- VII. Therapeutic manipulation of tumor vessels
- VIII. Monitoring leakiness of tumor vessels

#### Summary

The 2001 William Guy Forbeck "Focus on the Future" Conference brought together experts in the fields of cancer biology and vascular biology to discuss the pathophysiological and therapeutic implications of blood vessel leakiness in cancer. This meeting, held October 4 to 7, 2001, in the Napa Valley of California, was the first of its kind focused

on the significance of blood vessel leakiness in tumors. Despite major advances in the field of tumor angiogenesis, relatively little attention has been paid to the permeability of blood vessels in tumors. The leakiness of tumor vessels is well documented in experimental tumor models and in human cancer, but the cellular mechanism of the leakiness is poorly understood, and importantly, the implications of the leakiness to rate of cancer growth, predisposition to metastasis, and delivery of macromolecular therapeutics to tumor cells are at an early stage of understanding.

Blood vessel leakiness not only influences the interstitial environment of tumors but also governs the access of therapeutic antibodies, gene therapy vectors, and liposomal drug delivery systems to tumor cells. Therefore, it is timely to determine the biological and clinical relevance of the leakiness of tumor vessels. This conference provided an opportunity for scientists who study blood vessel barrier function to join forces with scientists working on tumor angiogenesis and other areas of cancer biology to define the state-of-the-art in this field and to set out some directions for future research. The participants were charged with identifying what is known and what is not known about the field and to recommend experimental approaches that can help to reveal why

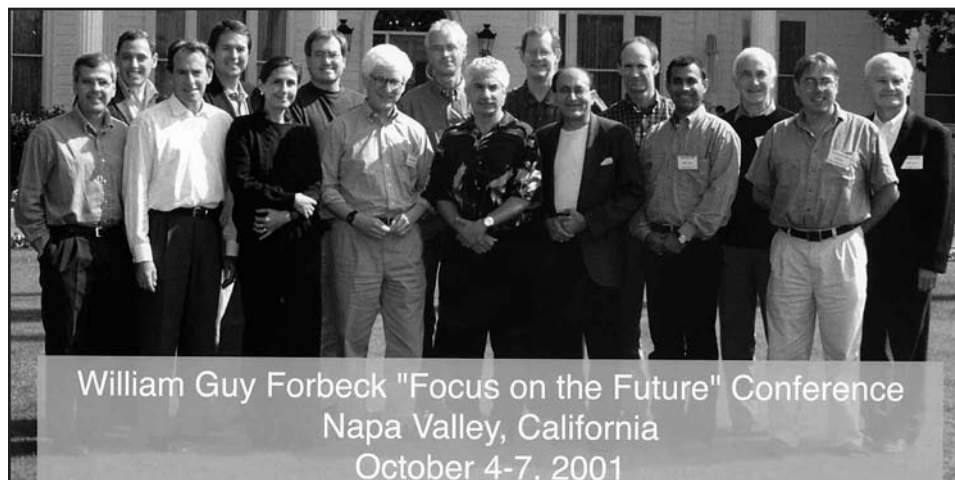
*"The conference was a great success. The topic was discussed from multiple points of view by selected experts over two entire days. Everyone felt they learned a lot and that the topic was timely, important, and exciting. The coffee breaks and meals provided additional opportunities for lively discussions and interactions. We appreciated the William Guy Forbeck Foundation providing support to make this exciting and stimulating meeting possible."*

— Donald McDonald

tumor vessels are leaky, the consequences of the leakage, whether the leakage is reversible, and how the reversal would impact tumor growth, metastasis, and drug delivery. The conference was energized by probing questions, lively discussion, and differing opinions. The participants discussed a broad range of issues, suggested many novel experiments, and drew insightful conclusions. At the end, many important areas for future research were in sharper focus.

Donald M. McDonald

*(For a complete summary, contact the Foundation or Dr. McDonald's office.)*



Front row from left: Neil Granger PhD, Louisiana Univ, Shreveport, LA, Robert Brasch, MD, Univ California, San Francisco, CA, Renata Pasqualini PhD, M.D. Anderson, Houston, TX, Donald McDonald MD PhD, Univ California, San Francisco, CA, David Cheresb PhD, Scripps Research Inst, La Jolla, CA, Rakesh Jain PhD, Mass General Hosp, Boston, MA, Raghu Kalluri PhD, Beth Israel Hospital, Boston, MA, Peter Baluk PhD, Univ California, San Francisco, CA

Rear row from left: Wadiah Arap MD PhD, M.D. Anderson, Houston, TX, Steven Metzger, AngelWorks Foundation, Dallas, TX, Richard Murray PhD, Eos Biotech Inc, San Francisco CA, Douglas Hanahan PhD, U/California, San Francisco, CA, Philip Thorpe PhD, U/Texas SW Medical Ctr, Dallas, TX, Gavin Thurston PhD, Regeneron Pharm, Tarrytown, NY, Fitz-Roy Curry PhD, Univ California, Davis, CA, Harold Dvorak MD, Beth Israel Hosp, Boston, MA.

## FOCUS MEETING GRANTS

The activities of the Foundation have been expanded by offering grants to support small "Focus Meetings" to be modeled on the annual Forum held in Hilton Head. The significant variation is that this forum is proposed and organized outside the Foundation and is based on a competitive application process.

We are interested in sponsoring small interactive meetings which focus on developing strategies which will improve our understanding of cancer and cancer therapeutics, and where there is a clear interchange of ideas between scientists and clinicians. Applicants identify a topic, venue, date, and take responsibility for organizing the meeting.

## THE FORBECK SCHOLAR AWARD

The Foundation looks for outstanding clinician or post-doctoral fellows with an interest in cancer research. Award recipients are invited to attend the Foundation Forum held in November in Hilton Head Island, South Carolina. A \$1,000 contribution is made to each award recipient's institution. Nominations are made by letter of recommendation from the applicant's director of studies, including a short synopsis of the applicant's research interest and a brief explanation of why this individual is recommended. Nominations are due in the spring of each year.

### Foundation Video Available

A video presentation outlining the history, purpose and activity of the Foundation was produced during the annual meetings and Forum. The trustees felt there was a need to be able to "show" what the Foundation does. Anyone desiring a copy of the video should contact the Foundation.

## Scientific Advisory Board Report 2001

...Continued from Page 1

that can be given to patients is determined. Phase II studies will subsequently be undertaken to determine how efficiently the drugs work in a larger group of patients. Finally, Phase III studies are designed to test the new drugs against the best known standard treatment available. These studies are normally undertaken in a blinded fashion to ensure that no bias is introduced into the trial as a result of the selection of patients into one particular arm of the study. The end result of this process is a very long-winded and extremely expensive process that has to be completed before drugs can be introduced into routine use. However, one must remember why this is the case; the whole procedure being designed to protect us against drugs that can have unpredictable catastrophic side effects.

So how can this process be changed? We now know the sequence of the human genome. This means that we know the code within our DNA that holds the information to produce every protein found within our cells. We are also making incredible progress on understanding more and more about how these proteins function and interact within the cell. Armed with this data we are on the verge of being able to produce "designer drugs" that can interfere with selective targets within the cell. Once we know the function of a protein it is possible to model its structure using powerful computers and subsequently design inhibitors that will block its function selectively. The whole activity can be undertaken on a computer before lead compounds are synthesised and tested both in the laboratory and in animals. Already there are two drugs that are used within cancer medicine that have been designed in this way. The first goes under the trade name of Gleevec, and is used in Chronic Myeloid Leukaemia. The other is called Iressa, and this is being tested in a variety of epithelial malignancies. Both of these drugs inhibit different tyrosine kinases within the cell; these being involved in the process of signalling and cell division.

In addition to designer drugs, we have

biological agents that are finally beginning to make an impact on cancer. For example, a monoclonal antibody called Rituximab is being used to treat patients with certain forms of lymphoma. These agents as well as therapies based on the use of cells of the immune system will almost certainly be used in a more routine fashion in the future.

We also have to become far more sophisticated as to how we judge the activity of the drugs we are developing. If we can define biological readouts of response rather than undertaking classical Phase I – III tests it will shorten the time to bringing new compounds to the marketplace. The development of these tests partially depends on the information we can glean from understanding, in more detail, how the cell functions.

However, we must not forget that nature can be very clever. Designer drugs may be designed to hit very specific targets in the cell but they may have a multitude of effects upon the cell that we did not anticipate. From a positive standpoint these effects may enhance the drugs toxicity but alternatively they may contribute to toxicity. It will be some time before classical drug therapy is replaced by the designer type drugs that I refer to but we truly stand at the crossroads of a new era that beckons with the hope that the new drugs will be so much more effective and less toxic than those we have today.

There is a great deal for our colleagues in industry and academia to do in the coming years. Our meetings in Hilton Head have focussed on many of the issues that I raise above. We have our part to play in shortening the time needed to bring effective cancer therapies into routine use and on behalf of the rest of the Scientific Advisory Board and the Trustees I would like to thank you for your continual support.



**John T. Kemshead, PhD**  
Chairman, Scientific Advisory Board

# Forum Planning

## 2002 FORUM: Cellular Senescence and Cancer

The Forbeck Foundation Forum in the year 2002 will be co-chaired by *Ronald DePinho, MD* from the Dana Farber Cancer Institute in Boston and *Charles Sherr, MD, PhD* from St. Jude Children's Research Hospital in Memphis. The topic for the forum will be 'Cellular Senescence and Cancer'. This topic pertains to the growth abnormalities that are characteristic of all types of tumors. Normal cells have limited lifespans while tumor cells acquire genetic changes that result in immortalization and infinite growth capacity. Studies in the past decade have begun to unravel the molecular mechanisms responsible for this uncontrolled growth. These studies have provided many insights into how cancers start since the genes that cause this unrestricted growth are so commonly mutated in human cancers. In addition, since normal cells in the body are not immortalized, blocking these immortalizing steps could be selectively toxic to tumor cells. Thus, identification of proteins in cells responsible for keeping tumor cells growing indefinitely also provides potential novel targets for the design of new therapeutic agents in the treatment of cancer. Such agents might be broadly useful in a wide range of cancers. The discussions at this forum will focus on what is known about the molecular mechanisms of cellular immortalization that leads to the development of tumor cells and will extend to concepts of how this information can be used to prevent or better treat cancers.

### Web Site [www.wgfrf.org](http://www.wgfrf.org)

The Foundation web site contains General Informational, a summary article on each of the Forums organized by the Foundation, information about "Focus on the Future" awards and grants, and several web site "pointers" for more information on cancer.

## 2003 Forum: DNA Damage and Cancer Susceptibility Syndromes

The Forbeck Foundation Forum in 2003 will be chaired by Dr. Alan D'Andrea of the Dana Farber Cancer Institute in Boston and Dr. Jan Hoeijmakers of the Erasmus University in Rotterdam. The topic for the forum will be "DNA Damage and Cancer Susceptibility Syndromes". The important role that DNA damage plays in cancer development is illustrated by the clear connections between exposures to certain types of DNA damaging agents in the environment and the development of cancer, such as the links between cigarette smoking and lung cancer or sunlight exposure and skin cancer. In addition, the majority of inherited syndromes characterized to date that lead to increased cancer development in families result from inherited mutations in genes that are important for DNA damage responses. For example, inherited mutations in either the *Brc1* or *p53* genes results in a very high risk of developing breast cancer and both of these gene products are important for helping cells respond to various types of DNA damage. The genes mutated in certain rare diseases that affect children, such as Fanconi's Anemia, Ataxia-telangiectasia, and Xeroderma Pigmentosum, all play roles in cellular responses to DNA damage and children with these diseases have very high incidences of certain cancers. Studies of the genes mutated in these diseases have led to a much better understanding of how all cells respond to DNA damage and even more importantly to insights about how cancers develop. In addition, since radiation therapy and most chemotherapies used to treat cancer cause DNA damage, understanding how these gene products operate provides new ways to approach the treatment of cancer. The discussions at the forum will focus on how these gene products function, how they contribute to cancer development, and how they can be manipulated to improve cancer therapies.

## 2001 Financial Report

The accounting firm of Cherry, Bekaert and Holland audits the Foundation's financial records annually.

The Foundation has established a very sound financial position. Steady growth in income has allowed the Foundation to expand its program, primarily through the funding of "Focus" grants. The Trustees continue to aim at a very high mark - that 90% of the total expense goes directly to support scientific programs.

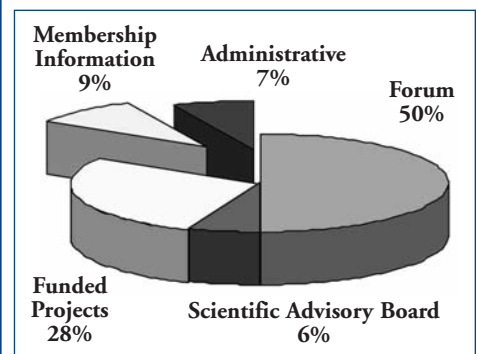
### BASIS OF SUPPORT

The William Guy Forbeck Research Foundation desires and has a broad base of support. Of major significance to the Foundation are the contributions from many individuals and their families. Many people have chosen to use the Foundation as a fitting memorial gift. A number of corporations and other foundations have also supported the Foundation with contributions, some having very rigorous qualifications for grants.

A significant increase in income beginning in 1997 is due to the support of the Homefront Bike Tour.

### EXPENSES

Historically, 85%-90% of the total expenses go directly to supporting the annual Forum and Foundation projects. Membership information costs include the annual newsletter, member mailings, and the video.



The Foundation has no paid employees, and the trustees participate at their own expense. Administration expenses include auditing costs, as well as printing and postage expense.

Members of the Scientific Advisory Board attend the Forum meeting in Hilton Head and hold their annual meeting at that time. The SAB provides the technical direction for the Forum and the Foundation.

Projects funded during 2001 include the Scholar Award and funding one Focus meeting grant.

# Home Front Bike Tour Donors

Mr. Alan D. Aaskov  
 Ms. Alexandra G. Abbott  
 Mr. and Mrs. Christopher C. Abbott  
 Mr. and Mrs. Gordon Abbott  
 Mr. and Mrs. John H. Abbott  
 Mr. and Mrs. Daniel H. Abram  
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# HOME FRONT TOUR

August 18, 2001

## 140-mile Bike Ride Benefits Foundation

Six years ago, Jim and Jennifer Buchanan astonished the Foundation Board of Trustees with their proposal – to organize a Bike Tour from Massachusetts to Maine, covering a distance of 140 miles in one day. They set a goal to raise \$250,000 over a five-year period, with the proceeds going to the William Guy Forbeck Research Foundation to help find a cure for pediatric cancer.



*Riders at a rest stop along the way*

At sunrise on August 18, 2001 Jim, Jennifer and nineteen others set out on the 5th Home Front Tour. The Buchanans with the help of their many friends exceeded their goals and have raised over \$335,000.



*Lindsay Buchanan*

Like Billy Forbeck who was diagnosed with neuroblastoma in 1983, the Buchanan's daughter *Lindsay* was stricken with this rare and deadly disease in 1995. With advances made in diagnosing and treating neuroblastoma, doctors were able to put Lindsay in remission (free of disease). However, a year and a half ago Lindsay relapsed. In Jim Buchanan's words, *"The 4th annual Home Front Tour was more difficult than we could have imagined. A week prior to the ride and almost five years to the day, our daughter Lindsay relapsed. We were stunned. Words can't describe the feeling. We thought about canceling but felt it was necessary to stay with our commitment to help battle cancer, cancer that attacks kids. After all, a commitment is what changes a promise to reality."*

Since then, Lindsay has undergone a marathon of treatment. This has included all the traditional methods as well as leading edge therapies. It is Lindsay's strength, will and determination in battling this disease that has inspired her parents to get involved and to try to make a truly meaningful difference.

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*In grateful acknowledgement of our donors...*

*(from January, 2001 thru February, 2002)*

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*Frequently, we are asked for advice from people who are faced with dealing with cancer for the first time. Although each situation is unique, there is the common urgent need for specific information. Because of the nature of the disease, it is necessary to make decisions quickly and move rapidly to a treatment program. This can be a terrifying time, and the pressure of gaining sufficient knowledge to make these important decisions under stress is overwhelming. From our experiences, we recommend the following*

### Move quickly.

This is a disease that does not wait. If not treated quickly it will metastasize (spread to other areas of the body). The earlier the treatment, the better the prognosis (chance of recovery).

### Keep a notebook.

Start making notes immediately. If a question comes to mind, write it down. If you have a peculiar symptom, write it down - it may be significant. When you meet with your doctor, it is important to

be able to give information and to get answers. Don't ever be afraid to ask a question. Your doctor will appreciate it if you have your questions ready, and it will maximize the time you have with your doctor.

### Gather information and take charge.

Ask for and read any information your doctor has available. Take advantage of the NCI Cancer Information Service (see below) as well as other sources of information. A second opinion is never out of order, do not be bashful (remember to take copies of all your records).

### Go to an NCI designated Cancer Center.

These centers are designated by the National Cancer Institute as having the medical staff, equipment and facilities for comprehensive and multidisciplinary diagnosis and treatment of cancer as well as a strong program of cancer research. There is a concentration of doctors who are specialists in specific cancers as well as specialists in the various aspects of treating cancer such as radiation therapy

and surgery. They may also have staff members specializing in peripheral cancer care disciplines such as dentistry, physiotherapy, family counseling and even tutors for school-age children. If appropriate, they will work with your local doctor to set up a treatment program closer to your home.

It would be our greatest hope that no one would ever need this information. It is our experience that at some time, most everyone will.

George and Jennifer Forbeck

*Reprint from SPRING, 1998 newsletter*

### FOR ADDITIONAL INFORMATION

The National Cancer Center  
web site: [www.nci.nih.gov](http://www.nci.nih.gov)

NCI Cancer Information Service:  
(800) 4-CANCER (800-422-6237)  
Monday through Friday,  
9am to 4:30pm, all local times

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## In Appreciation



Our heartfelt thanks go to all the people who have worked to make the activities of the Foundation a success.

We are grateful to the Scientific Advisory Board and the Forum participants, the scientists and clinicians whose leadership and effort are the front line in the war against Cancer.

Our special appreciation goes to the Foundation trustees and volunteers whose thoughtfulness, time and energy have done so much for the success of the Foundation and the Forums.

Most importantly, our thanks go to the hundreds of donors, individuals, businesses and foundations, whose financial support assures our continued work in Cancer research.

Sincere Thanks,

George and Jennifer Forbeck

## Objectives

- The objective of the William Guy Forbeck Research Foundation is to promote advances in the field of oncology, particularly pediatric oncology.
- While the foundation may provide grants for pilot research studies and educational efforts, its centerpiece activity will be an annual scientific roundtable held at Hilton Head Island, South Carolina.
- Attending each year will be up to twelve physicians and scientists who will meet in a completely private "think tank" environment, where they can exchange ideas freely in the hope of building on each other's ideas, knowledge, and experience.
- The objective is not to discuss published research, but rather to provide a forum for the cross fertilization of ideas, concepts, and observations. The hope is to shorten the cancer research timetable.
- Participants will be invited on the recommendation of the Foundation's Scientific Advisory Board, a distinguished panel of medical scientists.

*It is through your generous support that continuing research in the field of childhood cancer can be ensured. Contributions are tax deductible for federal IRS purposes. The IRS file number is 580063499. For additional information please write: William Guy Forbeck Research Foundation, 23 Peninsula Drive, Hilton Head Island, South Carolina 29926 or fax: (843) 837-3088 or visit our web site <[www.wgfrf.org](http://www.wgfrf.org)>*