



## From The Chairman's Desk

**Terence J. Irmen**

The Forbeck Foundation is now in our 24th year of operation. Many of the original volunteers assembled by *George and Jennifer Forbeck* in 1984 remain active with the Foundation, serving on the Board of Trustees and the Scientific Advisory Board. The magic of the Forbeck Foundation is the close working relationship between these two groups.

We will, however, greatly miss *Arnold Freeman, MD*, who is stepping down from the Scientific Advisory Board. Arnold has been with us from the beginning. We have Arnold's smiling face, beautiful words, and sincere passion for our mission archived on the Foundation's video. His contribution and friendship will be forever treasured.

The Board of Trustees has no personnel changes to report, however we continue to focus on succession planning by passing many key responsibilities onto the younger generation of trustees. It is critical that we ensure the long term viability of the Foundation.

The original mission developed during our first year continues as our beacon for growth, promoting advances in the field of oncology, particularly pediatric oncology. This past year's forum addressed the very important and current topic "*MicroRNA*" co-chaired by *Carlo Croce, MD*, Ohio State University and *Gregory Hannon, PhD*, Cold Springs Harbor Laboratories. The 2008 topic on "*Immunotherapy and Breaking Tolerance*" will be co-chaired by *James Allison, PhD*, Memorial Sloan Kettering, and *Stan Riddell, MD*, Fred Hutchinson. We plan to continue these forums as long as there is work to be done.

Our Scholar Board, led by *Jamie Collins*, organized the third Forbeck Scholar Retreat held in Lake Geneva, Wisconsin last September. The retreat was chaired by *Jean Wang, PhD*, a member of our Scientific Advisory Board. Participants in the retreat have indicated that this year's event was another overwhelming success. The Scholar Board held another great fundraising event following the retreat to help raise funds for next year's retreat.

We believe that we can make a difference and that a cure for cancer is immanent, however it is important to remain grounded enough to be prepared for a long battle. The continuation and improved quality of life for millions lies in the balance. We thank the many dedicated volunteers who have contributed so much to make the Forbeck Foundation the force that it is becoming in the fight against cancer.

**Terence J. Irmen**  
Chairman, Board of Trustees

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## SCIENTIFIC ADVISORY BOARD REPORT



**John T. Kemshead**

I have some news that saddens me considerably. I have to announce that *Arnold Freeman* has decided to retire from the Scientific Advisory Board (SAB). Arnold was the first Chairman of the SAB and he was instrumental in setting the direction of the Foundation, which has not changed over the years. I personally owe Arnold a great deal as he invited me to the first meeting of the Foundation, played a major part in asking me to join the Board and eventually to take over the Chair in mid 1990s.

Arnold spent his career in Paediatric Oncology in the USA and more recently in Israel; work that can be both extremely rewarding and draining. I know that he will be missed by both his work colleagues, patients and fellow members of the SAB. We all wish him well in his retirement and hope that if his plans permit he will visit the Foundation's meetings from time to time.

Even before Arnold's retirement from the SAB we were looking to the future and planning to bring a younger element into the group. In my opinion the most successful mix for the Foundation is to have Scientific Advisory Board members that can offer both experience and youth. However, without doubt the most critical aspect of being a member of the SAB is commitment. This is something that cannot be valued and it is truly offered

# 2007 Forbeck Forum: XXIII<sup>rd</sup> Annual Forum

November 1–3, 2007 Hilton Head Island, South Carolina

## Subject: MicroRNA and Cancer

- I: The Basics of MicroRNAs
- II: Altered MicroRNA Expression in Cancer
- III: MicroRNA Pathways
- IV: Moving MicroRNA Toward the Clinic

### Chairmen

Carlo M. Croce, MD	Ohio State University Cancer Center	Columbus, OH
Gregory Hannon, PhD	Cold Spring Harbor Laboratory	Cold Spring Harbor, NY

### Participants

Victor Ambros, PhD	Dartmouth Medical School	Hanover, NH
David Baltimore, PhD	California Institute of Technology	Pasadena, CA
Michele A. Cleary, PhD	Rosetta Impharmatics	Pasadena, CA
Anindya Dutta, MD, PhD	Univ Virginia School of Medicine	Charlottesville, VA
Scott M. Hammond, PhD	University of North Carolina	Chapel Hill, NC
Lin He, PhD	Cold Spring Harbor Laboratory	Cold Spring Harbor, NY
Tyler Jacks, PhD	MIT Center for Cancer Research	Cambridge, MA
Sakari Kauppinen, PhD	University of Copenhagen	Copenhagen, Denmark
Joshua Mendell, MD, PhD	Johns Hopkins University	Baltimore, MD
Amy Pasquinelli, PhD	University of California, San Diego	La Jolla, CA
Tariq Rana, PhD	University of Massachusetts Medical School	Worcester, MA
Martine Roussel, PhD	St. Jude Children's Research Hospital	Memphis, TN
Andrei Thomas-Tikhonenko, PhD	Univ Pennsylvania	Philadelphia, PA



*Carlo Croce*



*Gregory Hannon*

## 2007 Conference Report on “MicroRNA and Cancer”

by **Gregory Hannon**

The broad goal of the 2007 Forbeck Symposium was to examine the relationship between microRNAs and cancer. The past few years have seen a veritable revolution in biology, with the discovery that small RNAs act in a broad range of biological processes and pathways. In the expanding world of small RNAs, microRNAs hold a special place in that they are evolutionarily conserved regulators of gene expression networks. These ~18-22 nucleotide, single stranded RNAs are derived from fairly conventional genes, with the exception being that the end-product of the gene is a small, non-coding RNA rather than an encoded protein. Standard transcriptional regulatory circuits govern the synthesis of the primary microRNA transcript, which is then processed through two steps to yield a mature small RNA. These small RNAs join RISC, the core effector complex of the RNA

interference (RNAi) pathway, associating specifically with an Argonaute protein. The Argonaute protein uses the small RNA as a guide to select silencing targets based upon sequence complementarity between the small RNA and a target messenger RNA. Through such interactions, each microRNA can regulate the expression of potentially hundreds of genes. While the human genome harbors 20-30,000 protein-coding genes, microRNAs are numbered in the hundreds. However, this number, combined with broad target profiles, gives microRNAs potentially quite large roles in regulating the biology of an organism.

The Symposium brought together leaders in the field of small RNA biology with leaders in cancer biology, who had a special interest in small RNAs. This group was charged with addressing three questions,

which can be broadly described as follows.

Cancer is fundamentally a genetic disease, with alterations in oncogenes and tumor suppressors driving tumor initiation and progression. Historically, only the role of protein encoding genes has been examined in depth; however, mounting evidence has suggested that microRNAs may contribute to cancer at a disproportionately high rate, considering that there are only about 1% as many microRNAs as protein coding genes. The first key question for Symposium participants was to examine the possibility that microRNAs play a special role in cancer, perhaps because of their ability to impact the expression of related networks of genes.

A significant percentage of metastatic tumors present without an obvious primary origin. Understanding the

tissue and cell type represented by these lesions is critical, as that information is used to guide therapeutic decisions. MicroRNA expression patterns can often serve as a signature of cell type, and several studies have indicated that determining microRNA profiles may serve as a more effective record of cell fate decisions than the expression patterns of protein coding genes. The Symposium was charged with discussing the issue of whether microRNA expression patterns may be used for diagnostic purposes, either to determine the cell of origin for a particular lesion or to reveal the underlying patterns of oncogenic mutations in a tumor.

The prospect that small RNAs can be used directly for therapy has generated an enormous amount of excitement. Engaging the RNAi pathway directly, by delivery of artificial microRNAs, may allow us to directly target the expression of even mutant forms of protein coding genes selectively. Moreover, given the emerging roles of microRNAs in cancer, these naturally occurring small RNAs may serve as therapeutics or targets for inhibition. The final goal of the symposium was to critically examine the promise and progress in targeting of the microRNA pathway for clinical benefit.

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The meeting began with a session devoted to the biology of microRNAs. **Greg Hannon** introduced the goals of the Symposium and provided an introduction to microRNA biogenesis and mechanisms of action. Key among the issues addressed was the lingering uncertainty over the precise manner through which microRNA repress the activity of protein coding mRNAs. Many hypotheses have been raised, each with some degree of supporting evidence. However, answers to such questions have stubbornly resisted being driven to the level of clarity that has been achieved for other small RNA-based regulatory events. Underlying mechanisms are critically relevant for two reasons. First, if one is to impact this pathway for therapeutic benefit, one must understand the mechanisms by which it acts. Second,

understanding the mechanisms of microRNA-mediated control may allow the field to improve the ways that it uses to discover microRNA-target mRNA relationships. Again, a confident sense of the regulatory networks that are touched by a given microRNA are critical for the use of these species for diagnosis or therapy. Greg presented data describing functional approaches to uncovering these regulatory networks. He also described emerging new classes of small RNAs, which are less conserved than microRNAs and whose biological roles are only now beginning to emerge.


**Victor Ambros**, who first discovered microRNAs, presented an overview of microRNAs in *C. elegans*. He pointed out that many microRNAs are deeply conserved through evolution and described an example regulatory network in which one of the first microRNAs to be discovered, let-7, acts. Victor again touched upon the issue of defining microRNA targets, describing improved computational methods that take into account the accessibility of the potential microRNA binding site for predicting a regulatory interaction. He also described procedures to complement the computational predictions of microRNA-target pairs with a direct, biochemical method for target identification. Finally, he described a new component of microRNA pathways in *C. elegans*, which might form a conserved part of this regulatory mechanism.



**Amy Pasquinelli** continued the *C. elegans* theme discussing one of the potential mechanisms through which microRNA might regulate their targets. She discussed a specific translational regulator, EIF-6, and how it might act to prevent proper assembly of the ribosome on microRNA-bound mRNAs. She also discussed physiological regulation of the microRNA pathway under different metabolic conditions. Her studies highlight an emerging theme in microRNA biology, that stressing cells can change the output of microRNA-

mediated control. This is likely to be highly relevant in cancer cells, which encounter stress in many forms, ranging from hypoxia to metabolic stress.

*"I am so impressed and inspired by the Foundation you have established and to feel your dedication to supporting scientific progress. Scientifically this ranks as one of the most informative and useful meetings I have ever attended and its prestige is well deserved."*



**Amy E. Pasquinelli, PhD**

**Michele Cleary** began the move from the basic biology of microRNA pathways to their biological roles in mammals with a discussion of her comprehensive efforts to identify the targets of many microRNAs. Her colleagues at Rosetta were among the first to report a robust method for understanding microRNA regulatory pathways. Michele hammered home the notion that if we are to consider microRNAs as therapeutics, we must understand the full spectrum of their targets, not just the one or two microRNA-target pairs that generally emerge in a typical academic report. She presented the roadmap that she and her colleagues are developing for that purpose and showed examples, such as miR-106b, where regulatory circuits could be uncovered and validated by this integrated approach.

Additional specific examples of the biological impacts of microRNAs were provided by **Jun Lu**, one of the Forbeck Scholars. Jun Lu was among the first to show the value of microRNA expression profiles for diagnosis of human cancers. At the Symposium he showed a beautiful example of microRNAs acting in hematopoiesis, specifically with miR-150 acting at critical decision points in the erythrocyte differentiation pathway, probably through its regulation of a critical developmental transcription factor, c-myb. This provided an interesting example of a very linear microRNA-target interaction, as a contrast to the view that microRNAs exert their biological effects by regulating broad target networks.

**David Baltimore** continued the theme of microRNA biology with his description of the roles of microRNAs during inflammatory responses. Specifically, he discussed the response to LPS in macrophage, and the roles of microRNAs in regulating gene expression networks in this system. The focus was on miR-155, a known oncogenic microRNA and the product of the BIC non-coding RNA gene and on miR-146 family members.

The meeting continued to move toward a cancer focus with observations from **Anindya Dutta** on the role of let-7 in regulating the HMGA2 oncogene. Anindya also discussed the role of growth regulatory microRNAs in myogenic differentiation. He raised important concerns about methods for identifying new microRNAs and for quantifying changes in microRNA expression relevant to different physiological states. He noted potential anomalies in the output of microRNA profiling methods that could point to significant regulation of microRNA biogenesis or metabolism.



*"Thank you very much for your hospitality during the Forbeck Forum. It was one of the best meetings I attended in a long while, and a significant part of that was the easy ambience that was maintained by you and your family. I was very touched by your entire family's dedication to the cause of curing cancer."*

**Anindya Dutta, MD, PhD**

This theme was followed by **Scott Hammond** and **Carl Novina**. Scott had been among the first to report global changes in microRNA pathways in cancer, with the majority of microRNAs that were linked to differentiation decisions being expressed at lower levels in tumors and with microRNAs characteristic of stem/progenitor cells being expressed more prominently. Scott pursued the underlying mechanism that led to these observations and showed that microRNA biogenesis was regulated at the first processing step. He revealed that LIN-28 controlled the processing

of the let-7 family of microRNAs, and perhaps by extension differentiation-promoting microRNAs more broadly. This discovery may have fundamental implications for the adaptation of cancer cells to maintenance of a less differentiated state and for resistance to differentiation inducing signals. Carl Novina, another of the Forbeck Scholars, described the coordinate regulation of miR-211 and TRPM1 in melanoma. While TRPM1 is considered the host gene for miR-211, with the microRNA being processed from a TRPM1 intron, Carl noted a divergence in the expression of these genes in tumors. He proposed a complex relationship between splicing of the host intron and the microRNA machinery that may begin to reveal another underlying complexity in the pathways that lead to small RNA production.

**Andrei Thomas-Tikbonenko** discussed the roles of microRNA in B-cell lymphomas. He started with the curious observation that Pax-5 expression increased the levels of oncogenic transcription factors, Myb and Ets1 mRNAs, suggesting some form of post-transcriptional control. He found that Pax-5, itself a transcriptional regulator, acted by repressing the expression of miR-15 and miR-16, two known tumor suppressive microRNAs. These in turn normally repress Myb and Ets1 expression, allowing Pax-5 to drive the growth of CLL cells via its control of the mir-15-16 microRNA cluster.



Broad changes in the epigenetic state of the genome often accompany tumor formation. **Carlo Croce** highlighted a potential role for microRNAs in control of this process. He found that the miR-29 family of microRNAs controls DNA methylation patterns through its regulation of de-novo methyltransferases DNMT-3a and DNMT-3b. These microRNAs often show reduced expression in lung tumors, perhaps leading to de-regulation of DNA methyltransferases and aberrant tumor suppressor methylation. In fact, Carlo showed

that artificially increasing the expression of miR-29 in lung cancer cells restored methylation patterns to normal and allowed re-expression of tumor suppressor genes that had been silenced inappropriately by DNA methylation. This suggests that miR-29s may join the expanding family of tumor suppressive miRNAs.

**Tyler Jacks** continued the tumor suppressor theme with his discussion of the role of let-7 in a mouse model of lung cancer driven by k-ras activation. He showed that regulated expression of let-7 in this tumor type could potentially inhibit the growth of these tumors in animals. This correlated with the suppression of proposed let-7 targets including ras itself and HMGA2. Tyler had previously shown that partial loss of key components of the microRNA biogenesis pathway promoted tumor formation, indicating a broad impact of microRNAs on tumor suppression. His work with let-7 not only reinforced that notion but also provided one of the first examples of a tumor suppressive impact of a single microRNA an animal model of human cancer.



**Lin He** discussed the roles of microRNAs in known tumor suppressor networks, focusing on miR-34 as a known transcriptional target of p53. miR-34 can mediate the downstream effects of p53 activation on cell cycle arrest, senescence and growth arrest, depending upon the precise cellular context. While miR-34 likely forms a key component of a tumor suppressor pathway, it may also be a tumor suppressor in its own right. Studies presented by **Kristina Cole**, a Forbeck Scholar, focused on genomic rearrangements that might impact miR-34a. This gene is located on at 1p36, a region of common loss in many different tumor types. Kristina showed that 1p36 deletions in neuroblastoma often affect the miR-34 gene, and that these impacts often correlated with lowered miR34 expression.

MicroRNAs were also placed in other well known oncogenic pathways by **Josh Mendell**. A surprisingly large number of

microRNAs are regulated by c-myc, with repression of microRNAs being a common consequence of c-myc binding at those sites. Indeed, Josh presented evidence that one of the c-myc repressed microRNAs, miR-195, could antagonize myc-mediated increases in cell proliferation, if the microRNA were released from c-myc control. Myc can also activate the expression of microRNAs, with the oncogenic mir-17-92 cluster being a classic example. **Andrea Ventura**, the fourth Forbeck Scholar, described his studies on this cluster and its relatives. Loss of function of these microRNAs, specifically in hematopoietic compartments, caused a defect in B-cell development, with prevalent death of B220-positive pre-B cells. This phenotype was entirely consistent with the demonstrated role of mir-17-92 in B-cell lymphoma, where inappropriate expression led to increased survival of pre-B cells, thus contributing to tumorigenesis.

**Martine Roussel** provided a paradigm for efforts to examine microRNA function in other tumor types, with her studies of medulloblastoma. This tumor, which likely arises as a result of a failure of granule neuron progenitor cells (GNPs) to differentiate, showed numerous alterations in microRNA expression. One hypothesis, based upon the general role of microRNAs in regulating cell fate decisions, is that restoring some element of the microRNA expression profile in these cells might induce differentiation even of the transformed derivatives of GNPs. Martine has developed powerful mouse models that not only permit her to address these hypotheses but that also allow the testing of other more conventional therapeutic strategies.



*“The meeting was truly electrifying for me and my first experience in such a forum. I met many scientists that I would not normally have a chance to talk to and besides making new friendships, I also made new colleagues, thanks to you.”*

**Martine Roussel, PhD**

The meeting concluded appropriately with two reports on the possible use of small RNAs as therapeutics. **Tariq Rana** discussed the use of nanoparticles to deliver both natural and artificial microRNAs to a variety of tissues. He also showed enticing data on the role of microRNAs in regulating the replication and spread of HIV. **Sakari Kauppinen** provided the flip-side of Tariq’s work, specifically the delivery of modified nucleic acids (LNAs) as specific inhibitors of microRNA function. He showed impressive data demonstrating inhibition of miR-122 in the liver in primates, which gave therapeutically relevant biological effects, in this case on serum cholesterol levels. Given the many demonstrations of the impact of microRNAs both as oncogenes and tumor suppressors during the Symposium, these final two talks sparked optimism that the biological insights that had been discussed over the preceding two days could ultimately lead to impacts on the lives of patients.

As with the best of meetings, perhaps the most significant outcomes were not the presentations themselves but were the informal interactions and discussions that arose from bringing together a group of leading investigators with diverse experience and expertise but with a common interest in this emerging and very important area of cancer biology. It is these interactions that will continue to resonate through the field in the form of new ideas and collaborations.

## Update: International Neuroblastoma Risk Groups (INRG)

Since 1986, The Foundation has sponsored and funded a series of conferences to standardize the international neuroblastoma criteria for diagnosis and response to treatment. Acceptance of these standards allows the principal neuroblastoma research groups around the world to compare results and compile large data bases used for improving diagnosis and treatments for this childhood cancer.

The rapid explosion of medical knowledge and technology has necessitated frequent updates to these standards.

In the fall of 2005, the Foundation funded the fourth such meeting chaired by **Drs. Susan Cohn and Andy Pearson**. Fifty-two delegates attended, representing the six major pediatric cancer study groups around the world.

This spring, Sue Cohn provided the Foundation with the following update.

*“We have submitted 4 papers to the Journal of Clinical Oncology discussing the new International Neuroblastoma Risk Group Classification Schema, the new INRG staging system, recommendations for evaluating of minimal residual disease, and standard operating procedures for examining tumor biology. We are hopeful that the JCO will agree with publish all 4 papers together. In addition, Kate Matthay is in the process of writing INRG recommendations for evaluating disease using MIBG.”*

*When I met with you a few years ago, I told you that I would make sure that we completed this project. While this project has been VERY challenging, it has also been VERY rewarding. At the neuroblastoma meeting in Japan, there are several papers that are going to be presented using the data we collected on over 8,000 children with neuroblastoma diagnosed around the world.*

*We are very excited that we have been able to come to international consensus on these important issues and we want to thank you again for your support for this project.”*

**Susan L. Cohn, MD**  
**University of Chicago**

### FOUNDATION DVD/VIDEO AVAILABLE

A DVD video presentation showing the history, purpose and activity of the Foundation is available by contacting the Foundation or on the website.

# Forum Planning

## 2008 Forum: Immunotherapy and Breaking Tolerance

The immune system in our bodies keeps us safe from our environment that is full of bacteria and viruses. When we catch a cold it is our immune system that fights the infection. When we cut ourselves our immune system ensures that foreign invaders do not take over our bodies.

For the last thirty years scientists and clinicians have tried to exploit the bodies immune system to treat patients with specific forms of cancer. Antibody therapy for diseases such as lymphoma and even breast cancer have been shown to be effective in many instances and these reagents are sold today for main line therapy. In academia efforts continue to exploit the cellular arm of the immune system and we are closer than ever to making an impact on specific cancers. Responses have been seen in patients but they remain unpredictable. Nevertheless the potential has been identified and the 2008 forum is intended to bring together a group of academics and clinicians to discuss manipulation of the immune system to assist in the treatment of cancer. This is the second time the Foundation has focused on this area of medicine indicating its importance in the development of new treatments for cancer and how quickly the field is moving. The formal title for the meeting is "Immunotherapy and breaking tolerance" and this will be chaired by *Drs. Dr James Allison and Dr. Stan Riddell*, both of whom are recognized as world leaders in this field.



**2008 Forum chairmen:**  
*Dr. James Allison & Dr. Stan Riddell*

## 2009 Forum: The Biology and Treatment of Primary Brain Tumors



**2009 Forum chairmen:**  
*Dr. Luis Parada & Dr. Tracy Batchelor*

Primary tumors of the central nervous system are the leading cause of cancer death in children, and a tumor of growing incidence in adults, in whom it is equally difficult to treat. Only recently have researchers begun to understand the basic genetic derangements that play a central role in the growth of these tumors.

In children, brain tumors are found in a variety of unusual types, some with unique and characteristic appearance on pathologic examination and in their clinical behavior. In adults, primary brain tumors usually arise in astrocytes, supporting cells of the nervous system, and, in their most common, and poorly differentiated form, these tumors, called gliomas, are exceedingly difficult to treat with any of the common approaches (surgery, chemotherapy, or radiation therapy).

Major efforts are now underway to elucidate the genetic changes in these tumors, the pathways and receptors activated by these changes, and the changes found in the tumor micro-environment. Animal models for some of these kinds of brain tumors have now been developed, and are providing information on tumor behavior and response to experimental treatment. New clinical trials are finding that these tumors are highly dependent on new blood vessels, and respond to treatments that destroy these

vessels. Abnormal receptors and activated growth pathways are found on the cell surface or inside these tumors and these may be the subject of new treatments as well. New information indicates that multiple aberrancies may exist in the signalling portfolio of these tumors, thus requiring multiple sites of attack.

In this rapidly evolving state of knowledge, the meeting, to be led by *Dr. Tracy Batchelor* of the Massachusetts General Hospital's Cancer Center, and *Dr. Luis Parada* of Univ Texas Southwestern Medical Center, should provide an exciting opportunity for bringing together leaders in the genetics, biology, and treatment of this important group of tumors.

### **WEB SITE - [www.wgfrf.org](http://www.wgfrf.org)**

The Foundation is in the process of updating the web site targeting completion by May. There will be new and updated information on the site. Features to be added include:

- A listing of papers our Scholars have published. We are extremely impressed to see all the great publications and work our Scholars have done just since the fall.
- The Newsletter will be available online.
- The updated video in a faster download.
- A cancer resource center- helpful links for people going through cancer or with friends going through cancer.
- Memorial Board

The Foundation web site already contains general information, summary articles on each of the Forums organized by the Foundation, information about the Scholar Board activities and donation information.

## Awards: “FOCUS on the FUTURE” Program

### The FORBECK SCHOLAR AWARD

The William Guy Forbeck Research Foundation is pleased to sponsor this program to further the advance of cancer research. The “Scholar Award” recognizes promising young scientists working in this field.

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. After receiving this award, scholars are invited to participate in the Scholar Retreat held in Lake Geneva, Wisconsin.

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.

### 2007 SCHOLAR AWARD

The Foundation received a number of very qualified applications for the 2007 Forbeck Scholar Award. The Scientific Advisory Board selected four outstanding young scientists to attend the 2007 Forum in Hilton Head and receive this award. The Foundation was pleased to present this year’s Scholar Award to Kristina Cole, Jun Lu, Carl Novina and Andrea Ventura.



2007 Scholars Andrea Ventura and Jun Lu talk with 2007 Forum participant and Nobel Laureate David Baltimore

### 2007 SCHOLARS

**Kristina Cole, MD, PhD** is a post-doctoral fellow in the lab of *John Maris, MD* at Children’s Hospital of Philadelphia. She is a pediatric clinician and an outstanding basic scientist.



Kristina’s research includes work on microRNAs in neuroblastoma that will hopefully lead to a drug target that can be pursued in the preclinical and translational research programs at CHOP. Dr. Maris said “Kristina’s work was completely designed and implemented on her own initiative. She conceived the idea, developed the experimental methods, and performed the research independently. This is truly extraordinary for a hematology/oncology fellow, and demonstrates her outstanding potential as a physician-scientist.”

*“It was a unique and incredible experience to hear from pioneers of this field who examine the topic from a diverse range of approaches. The discussions were thoughtful and lively, whether around the conference table or dinner table. I left with a refreshed enthusiasm to return to the laboratory and clinic, heartened by the idea that I will return to the Scholar Forum next fall.”*

**Kristina A. Cole, MD, PhD**

**Jun Lu, PhD** is a postdoctoral fellow in the laboratory of *Dr. Todd Golub* at the Broad Institute of MIT and Harvard, “and is the driver of all microRNA projects in my group.” Jun received his bachelor’s degree at Nanjing University in China, and his PhD degree in biochemistry at Boston University. Dr.

Golub notes “Jun published what is generally regarded as a landmark paper in microRNAs in *Nature* (2005), in which he discovered a new method for profiling microRNA activity, and demonstrated the ability of miRNAs to classify human cancers.”

**Carl Novina, MD, PhD** is an assistant professor at Harvard Medical School (Pathology) and Dana Farber Cancer Institute (cancer immunology and AIDS). Carl’s research program focuses on the basic biology of RNA interference by investigating mechanisms of microRNA-mediated silencing pathways, their regulation of normal lymphocyte functions, and how dysregulation of these pathways leads to leukemias. *Dr. Harvey Cantor* says “Carl has developed innovative approaches to investigate the biology of microRNAs in cancer. He is a rising star in cancer immunology.... The opportunity to interact and debate with international leaders in his field should have an enormous and positive impact on his career and research goals.”



**Andrea Ventura, MD, PhD** received his MD and PhD in Italy before joining the laboratory of *Dr. Tyler Jacks* at the MIT Center for Cancer Research in Boston as a post-doctoral fellow. Dr. Jacks describes Andrea’s work saying he “has performed important research in a range of areas, including the development of vectors for the controlled expression of RNAi molecules and the analysis of the effects of reactivation of the p53 tumor suppressor gene in established cancers in the mouse. Both of these projects resulted in first-author publication in top journals. Recently, Andrea has focused on the question of the developmental and oncogenic functions of miRNAs... generating novel mouse strains with constitutive and conditional loss-of-function mutations in the mi17~92 cluster and its paralogs.”

*“The quality of the meeting greatly exceeded my highest expectations. Its format is also particularly suited to encourage junior investigators such as myself to actively participate to the discussion. I look forward to attend the Scholar retreats in the years to come.”* **Andrea Ventura, MD, PhD**

# Foundation Scholar Board



**Jamie Collins**

Many thanks for everyone's support of the Scholar Retreat. I am always impressed by the support that the Lake Geneva community gives the Foundation. Together we have created a forum that is unique and builds super highways of communication through out the scientific community.

## The Scholar Retreat

Every year enthusiasm for the Scholar Retreat keeps growing. It is exciting to get e-mails or calls from scientists asking how they can apply for the Scholar program because they have heard great things. I guess that means we are doing something right.

We said goodbye to four more of our "graduating" Scholars,

*"This is a great forum. I think you will enjoy seeing it evolve over the years. I will miss it."*

**Elsa R. Flores, PhD**



but hope to see them at future forums and in publications for doing great things. We wish the best to *Jim Amatruda, Elsa Flores, Chris Bakkenist and Ned Sharpless.*

Past Scholar *Jan Karlseder* was invited back as a mentor for the 2007 Scholar Retreat. He opened the Retreat at the Thursday night keynote address discussing aging and cancer and the effect of dysfunctional Telomeres.

We appreciate Jan's constant enthusiasm and are excited that he has joined the Foundation Scientific Advisory Board. Jan makes the second Forbeck Scholar to serve on the SAB, along with 1991 Scholar *David Fischer*. Jan has also agreed to organize the 2009 Scholar Retreat and is already working on an impressive mentor group.

*David Fischer* will lead the Scholar Retreat again this coming September. He has lined up a great mentor group, including 2007 graduating scholar *Ned Sharpless*, two participants from the 2007 Forum on MicroRNA, *Martine Roussel* of St. Jude and *Anindya Dutta* of the University of Virginia and returning mentor *Chuck Sherr*.

We appreciate the time these doctors give to the Foundation and have even

more gratitude for the time they put towards defeating cancer.

## The Blue Jean Ball

The Blue Jean Ball was a great success. *Chandler Dimberg* and *Galen Eckland* chaired the fundraising committee this year. They added a crucial asset - *Gretchen Eckland Oettinger* who works for Culture 22, an event coordinating and marketing group. With the help of her husband, Christopher they set up the event and added many creative touches.

Our fundraising goal each year is to net enough from the event to fund the Scholar Retreat and we accomplished that goal again in 2007! Our other goal is to stay in line with the Foundation's spending policies, and ensure that your donations are maximized for the Scholar Retreat and cancer research.

We will be hosting the Blue Jean Ball again this year since the casual theme was quite popular. We will again have an award for Best Dressed in Denims. Join us at the George Williams Campus, Lake Geneva on the evening of September 13th. If you did not receive an invitation last year but want to make sure you are on the list this year contact us or visit the web site after mid-May for event details and to purchase tickets.

## The Scholar Board

Many loyal board members work very hard on the event. *John Lehman, Nancy Paulin, Mollie Ring, Jeannie Gallucci* and *Bridgid Kyle* were integral in setting up. *Dick Payne* organized and set up the bar. *Nicole and Bryant Rowean* and *Diane Dimberg* managed the front desk. *Aaron Jesser* maintained the web site.

Retreat attendees are always impressed to be met at the airport by Scholar Board members. Participants also enjoy the boat ride to dinner, no matter how cold it is. *Glenn & Katie Pankau, Tricia Forbeck* and *Ben Collins* provided and captained the boats.

My thanks to all,

Jamie Forbeck Collins



**Chandler Dimberg and Galen Eckland chaired the "Blue Jean Ball" committee**

## MEMBERS OF THE SCHOLAR BOARD

Brendan Cashman	Chicago, IL
Benjamin Collins	Lake Geneva, WI
Jamie Forbeck Collins	Lake Geneva, WI
Renee Dahlstrom	Chicago, IL
Chandler Dimberg	Chicago, IL
Galen Eckland	Oregon, WI
Brian Fanning	Lake Geneva, WI
Liz Fanning	Lake Geneva, WI
Jeannie Gallucci	Chicago, IL
Lisa Hoffman Garrison	Chicago, IL
Michael Goetsch	Chicago, IL
Nicole Mazzei Goetsch	Chicago, IL
Aaron H. Jesser	Chicago, IL
Bridgid Reed Kyle	Chicago, IL
John E. Lehman, III	Chicago, IL
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Dick Payne	Lake Geneva, WI
Mollie Ring	Chicago, IL
Bryant Rowean	Chicago, IL
Nicole Vaughan Rowean	Chicago, IL
Aaron Taylor	Chicago, IL
Chrissie Taylor	Chicago, IL

## HOW YOU CAN HELP

- Mark your calendars for the Blue Jean Ball! September 13th.
- Donate auction items.
- Help find sponsors.

## HOW TO CONTACT the SCHOLAR BOARD

- Scholar Board page on web site [www.wgfrf.org](http://www.wgfrf.org)
- Email: [jrboard@wgfrf.org](mailto:jrboard@wgfrf.org)
- Contact any Scholar Board member

*The Retreat "is one of a kind, I gained from this meeting much more than I gain from any other meeting. Every year it's the one meeting I'm looking forward to. I can definitely say that most of the people I met during the Forbeck meetings became friends and I hope that at least some of them will become colleagues."*

**Michal Safran, PhD**

**SCHOLAR BOARD CONTRIBUTORS**

*SPONSORS: Each year, our sponsors pledge a generous contribution, allowing the Scholar Board to cover all initial expenses. We are grateful for the support of:*

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*Many people help make the Scholar Board fund raising project a success, through general contributions or through donation of event supplies and auction items. Many thanks to the following:*

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**3RD SCHOLAR RETREAT**

*September 13-16, 2007 - Lake Geneva, WI*

For the third year the Forbeck Foundation's Scholar Board organized a superb meeting for the Forbeck Scholar awardees at George Williams College in Lake Geneva, Wisconsin. Members of the Scholar Board worked tirelessly to ensure that the participants had everything they needed for a successful meeting. The efforts of the Scholar Board were matched by the enthusiasm of both senior scientists and scholars attending the Retreat.

The concept behind these meetings is to provide a basis for scientific collaboration and the exchange of ideas to further the field of cancer research. To attend, candidates have to be selected initially to receive the prestigious Foundation's Scholar Award at the Forum in Hilton Head. The caliber of the scholars that apply for this recognition is beyond reproach and each year it becomes more difficult for the Foundation's Scientific Advisory Board to select four scholars out of the applicants.

The two day meeting is split into four sessions, each mentored by a senior scientists presenting on their area of expertise. The remainder of each session is devoted to talks from the scholars and discussion. Scholars are invited to come to four Scholar Retreats, held on an annual basis.

The Scholar Retreat builds a base for the best up and coming scientists to get to know each other and form relationships and collaborations that likely would never occur without their attending the forum. As in many areas of science, cancer research has become highly specialized and researchers tend to remain focused in their particular areas of interest. Breakthroughs often occur when ideas in one field are applied to another. A

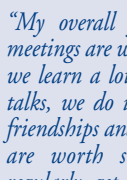
further benefit is that the scholars interact with today's senior scientists who have built considerable reputations in the field of cancer research. This is again a wonderful opportunity for the scholars to discuss their work outside of their institution and to gain insights into new ideas to progress their studies.

The Trustees and Scientific Advisory Board have endorsed this activity as extremely worthwhile for the Foundation, both in the short and long term. This type of investment in future leaders in cancer research is something that can only bring benefits in fighting this group of diseases.

**COMMENTS FROM SCHOLAR RETREAT**



*The Scholar Retreat "is a truly wonderful experience for the beginning investigator. It forces me to take stock of my progress annually, to re-focus our efforts to maximize our productivity, and realize how much improvement we've made in a year or more. I really like the opportunity to keep presenting my work to a familiar audience who are more than willing to stop and criticize without feeling at all worried about being perceived as overly aggressive."* **Kim Rathmell, MD, PhD**



*"My overall feeling is that the meetings are working! Not only do we learn a lot from hearing great talks, we do in fact make lasting friendships and collaborations that are worth so much to us. I regularly get emails or speak to other Forbeck scholars, and really benefit from sharing information. I think the format fully succeeds in its goals."* **Nabeel Bardeesy, PhD**

**2007 ATTENDEES**

SENIOR INVESTIGATORS

- Guillermina Lozano
- William G. Kaelin, Jr. MD
- Jan Karlseder, PhD
- John Kemshead, PhD
- Jean Wang, PhD

2003 SCHOLARS

- James F Amatruada, MD, PhD
- Christopher Bakkenist, PhD
- Elsa Flores, PhD
- Norman Sharpless, MD

2004 SCHOLARS

- Edward Attiyeh, MD
- Nabeel Bardeesy, PhD
- Anthony G. Letai, MD, PhD
- W. Kimryn Rathmell, MD, PhD

2005 SCHOLARS

- Kimberly Kelly, PhD
- Ingo K. Mellinshoff, MD
- Michal Safran, PhD
- Benjamin B. Williams, PhD

2006 SCHOLARS

- Benjamin L. Ebert, MD, PhD
- Carla F. Bender Kim, PhD

- |                                     |                  |
|-------------------------------------|------------------|
| M.D. Anderson Cancer Center         | Houston, TX      |
| Dana- Farber Cancer Institute       | Boston, MA       |
| The Salk Institute                  | La Jolla, CA     |
| Baxter Cellular Therapies           | Manchester, UK   |
| University of California            | San Diego, CA    |
| Univ Texas SW Medical               | Dallas, TX       |
| University of Pittsburgh            | Pittsburgh, PA   |
| M.D. Anderson Cancer Center         | Houston, TX      |
| Univ. North Carolina                | Chapel Hill, NC  |
| Children's Hospital of Philadelphia | Philadelphia, PA |
| Dana Farber Cancer Institute        | Boston, MA       |
| Dana Farber Cancer Institute        | Boston, MA       |
| Univ. of North Carolina             | Chapel Hill, NC  |
| Massachusetts General Hospital      | Charlestown, MA  |
| University of California            | Los Angeles, CA  |
| Dana Farber Cancer Institute        | Boston, MA       |
| Dartmouth Medical School            | Hanover, NH      |
| Broad Institute of Harvard & MIT    | Boston, MA       |
| Children's Hospital                 | Boston, MA       |

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*In the early years of the Foundation, each of the Founding Sponsors made a commitment for \$5,000 per year for five years. These pledges provided a stable financial basis for the Foundation and allowed efforts to be concentrated on establishing the Foundation and organizing programs.*

***In grateful acknowledgement of our donors... (from January, 2007 thru March, 2008)***

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Jennifer and George Forbeck	Cindy and Kevin Forbeck	Jo and Tony Terlato	Pat Wheeler
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William Guy Forbeck	Thomas G. Heyward	William Marscher	Howard R Wright
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William H. Frackelton, MD	Heidi Jacobson	John J. O'Doherty	
Frank Gallucci, Sr.	Clara Jacobson	Elizabeth "Bettie" Ogden	

## 2007 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 in additional funded projects and now through the efforts of the Scholar Board, the "Scholar Retreat." The Trustees continue to aim at a very high mark - that 90% of the total expense goes directly to support scientific programs. In 2007, 84.6% of all expenses funded scientific activities.

### 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.

In 2007, the Junior Board raised funds through their Fallfest fund raising event and contributions. They met their goal in funding most of the costs of the Scholar Retreat.

### EXPENSES

Historically, 85%-90% of the total expenses go directly to supporting the annual Forum and Foundation projects.

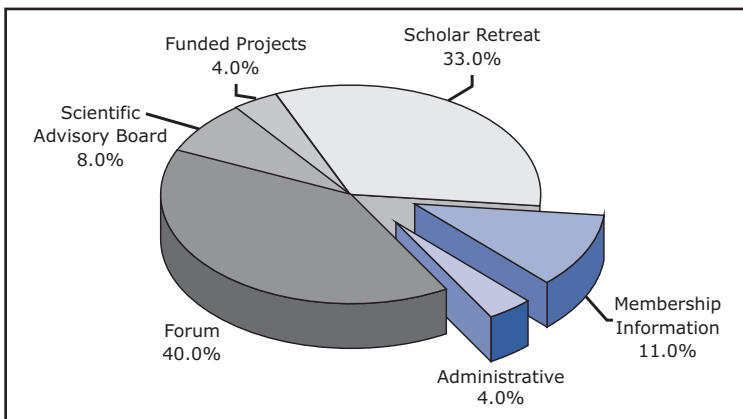
Membership information costs include the annual newsletter, member mailings, the video and the web page.

In 2007, an unusual expense was funding significant upgrade to the Foundation 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 2007 included four Scholar Awards.



### Scientific Advisory Board Report

Continued from Page 1

by all of our Board members today.

Currently, our SAB has a Broad spread of age and expertise. We range from individuals whose skills sets are basic science, to those who have worked in medical and paediatric oncology. In addition, the board members cover a wide geographical spread from Boston, Massachusetts (*Bruce Chabner*) to Dallas, Texas (*John Minna*) and San Diego, California (*Jean Wang*). I remain the lone voice representing Europe, living in the UK but working for an American Company in Chicago, Illinois. It is a good mix and the Board is about the right size but when the opportunity arises I am hoping that we can continue to recruit members that bring new and different viewpoints to the team. It is a focus on planning for the future that will ensure that the Foundation will flourish in years to come.

Picking new members of the SAB is a joint effort as each board member has a say and can make recommendations. In addition, the Board of Trustees has to approve the choice of the SAB in electing new members to the group. Luckily, we have a fountain of talent to draw upon with respect to finding new SAB members through both the main Forum meeting and the scholar programs we run.

*David Fisher*, from Dana Farber in Boston joined the SAB after first attending the Foundation's Forum as a scholar in 1991. Last year *Jan Karlseder* from the Salk Institute in California also joined the Board, first attending the Foundation as a scholar in 2002. Both David and Jan have been involved in the Scholar Retreat Program and the different expertise they bring to the Foundation is welcomed.



*These meetings are terrific, and I will do my best to help keeping it that way.*  
**Jan Karlseder**

For the future I have no doubt that we will have absolutely no problems in identifying candidates as potential SAB members. We are very lucky and can stick to the philosophy of selecting members from individuals who have attended a meeting run by the Foundation. In this way people join the team knowing our philosophy and what is expected from them.

Tenure on the SAB is for a minimum period of five years, this being one of the rules we stipulate on electing a member. Whilst some of our team, including myself, have tenures that stretch way beyond this time, it is the mix of experience, commitment and youth the makes the board successful in driving the scientific direction of the Foundation.

I remain indebted to my fellow Board members for their devotion to the Foundation and to the Trustees for their support.

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

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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

## Mission

The mission of the William Guy Forbeck Research Foundation is to promote advances in the field of oncology, particularly pediatric oncology, by shortening the cancer research timetable.

## Strategies

While the Foundation may provide grants for pilot research studies and educational efforts, its centerpiece activity will be an annual Forum, a scientific roundtable held at Hilton Head Island, South Carolina.

Attending the Forum each year will be twelve to fifteen 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.

Participants will be invited to the Forum based on the recommendation of the Foundation's Scientific Advisory Board, a distinguished panel of physicians and scientists.

We fully support the activities of the William Guy Forbeck Research Foundation Junior Board, particularly the Scholar Retreat.

*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 fax: (843) 837-3088, visit our web site [www.wgfrf.org](http://www.wgfrf.org) or write: William Guy Forbeck Research Foundation, 23 Peninsula Drive, Hilton Head Island, South Carolina 29926*