Welcome Message -- Charles Sawyers, Chair, Human Oncology and Pathogenesis Program--(Photo by Africa Fernandez)

Welcome Message -- Harold Varmus, President, Memorial Sloan Kettering Cancer Center--(Photo by Africa Fernandez)

Harold Varmus answering questions from the audience--(Photo by Nicole Kucine)

Session I, Tumor Invasion & Metastasis -- Robert Benezra, Cancer Biology and Genetics Program, presents Tumor Entrained Neutrophils Inhibit Seeding in the Pre-metastatic Niche--(Photo by Africa Fernandez)

Session I, Tumor Invasion & Metastasis -- Filippo Giancotti, Cell Biology Program, presents Suppression of Breast Tumorigenesis and Epithelial to Mesenchymal Transition by the Rho Family GTPase Rnd1--(Photo by Africa Fernandez)

Retreat attendees included senior scientists and physicians, as well as junior faculty, postdoctoral researchers, and graduate students--(Photo by Africa Fernandez)

Session II, Tumor Initiation by MicroRNAs -- Christine Mayr, Cancer Biology and Genetics Program, presents Control of 3'UTR Length by Alternative Cleavage and Polyadenylation -- A Mechanism for Regulation of Gene Expression--(Photo by Africa Fernandez)

Session II, Tumor Initiation by MicroRNAs -- Christopher Park, Human Oncology and Pathogenesis Program, Clinical Laboratories, and Pathology, presents Comparison of Leukemia Stem Cells to Their Normal Counterparts Reveals Widespread Dysregulated MicroRNA--(Photo by Africa Fernandez)

Session II, Tumor Initiation by MicroRNAs--Jason Huse, Human Oncology and Pathogenesis Program and Pathology, Surgical Neuropathology Diagnostic Services, presents An Analysis of the Role of MicroRNAs in the Phenotypic Expression of Oncogenic PDGF Signaling in Malignant Glioma
(Photo by Africa Fernandez)

Session II, Tumor Initiation by MicroRNAs -- Hans-Guido Wendel, Cancer Biology and Genetics Program, presents Genome-Wide RNAi Screen Identifies MiR-19 Targets in Notch-Induced Acute T Cell Leukemia (T-ALL)--(Photo by Africa Fernandez)

Recreation time -- (from left) Phillip Iaquinta, Vivek Arora, Sara Kubek--(Photo by Nicole Kucine)

Recreation time--(Photo by Africa Fernandez)

Recreation time--(Photo by Nicole Kucine)

Session III, A Focus on Research Funded by the Geoffrey Beene Cancer Research Center -- Moderator Ingo Mellinghoff, Human Oncology and Pathogenesis Program and Neurology Service--(Photo by Africa Fernandez)

Session III, A Focus on Research Funded by the Geoffrey Beene Cancer--Research Center -- Sindy Escobar Alvarez, Molecular Pharmacology and Chemistry Program, presents An Essential Mitochondrial DNA-Encoded Protein Processing Pathway Regulates Mitochondrial Function and Cell Metabolism in Human Cancer Cells
(Photo by Africa Fernandez)

Session III, A Focus on Research Funded by the Geoffrey Beene Cancer Research Center -- Vasilena Gocheva, Cancer Biology and Genetics Program, presents Roles of Cathepsin Proteases in Cancer Development and Progression--(Photo by Africa Fernandez)

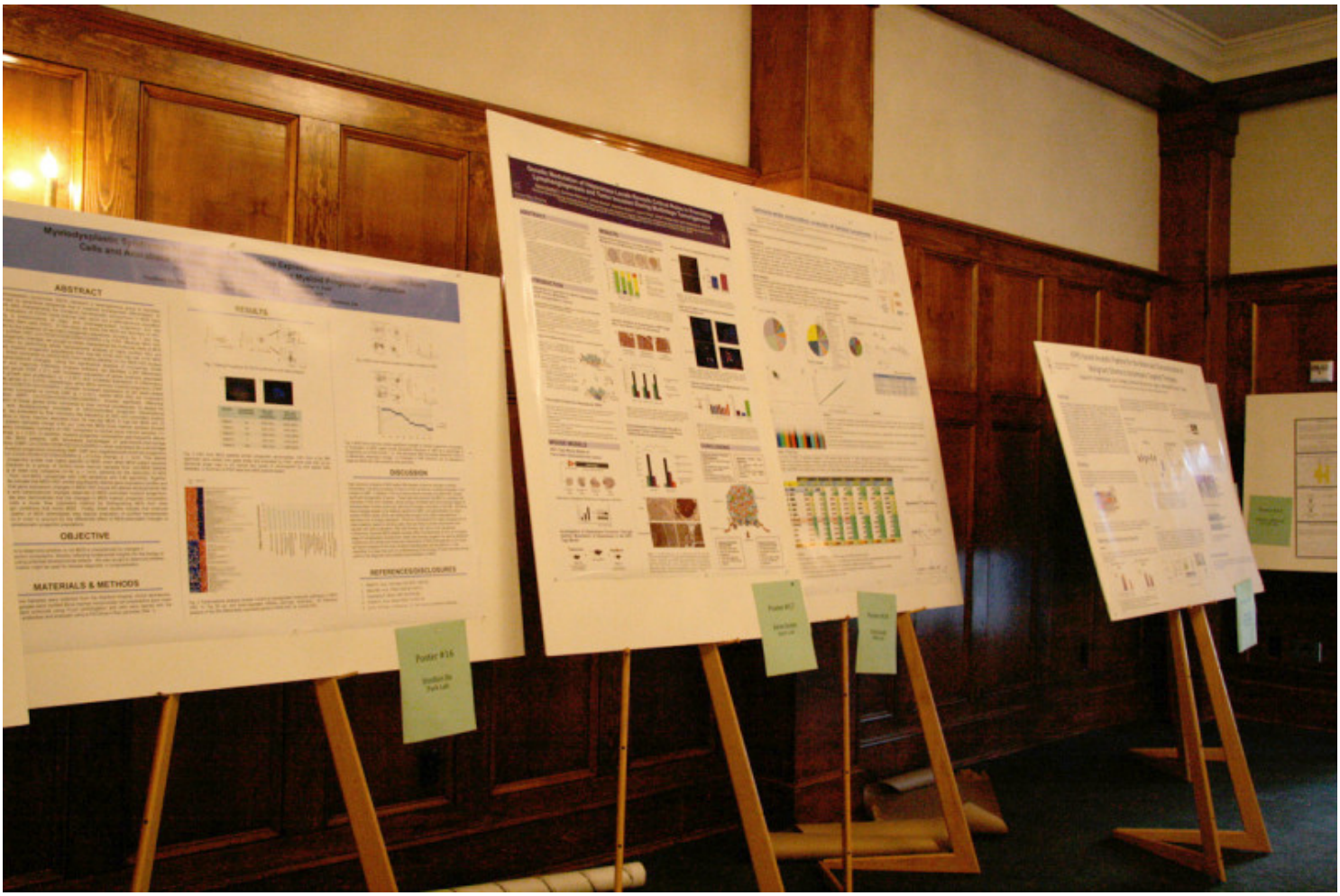
Ingo Mellinghoff and Vasilena Gocheva--(Photo by Nicole Kucine)

Session III, A Focus on Research Funded by the Geoffrey Beene Cancer Research Center -- Michael Overholtzer, Cell Biology Program, presents A Case for Murder: Entosis is a Cell Killing Mechanism Requiring Autophagy Proteins--(Photo by Africa Fernandez)

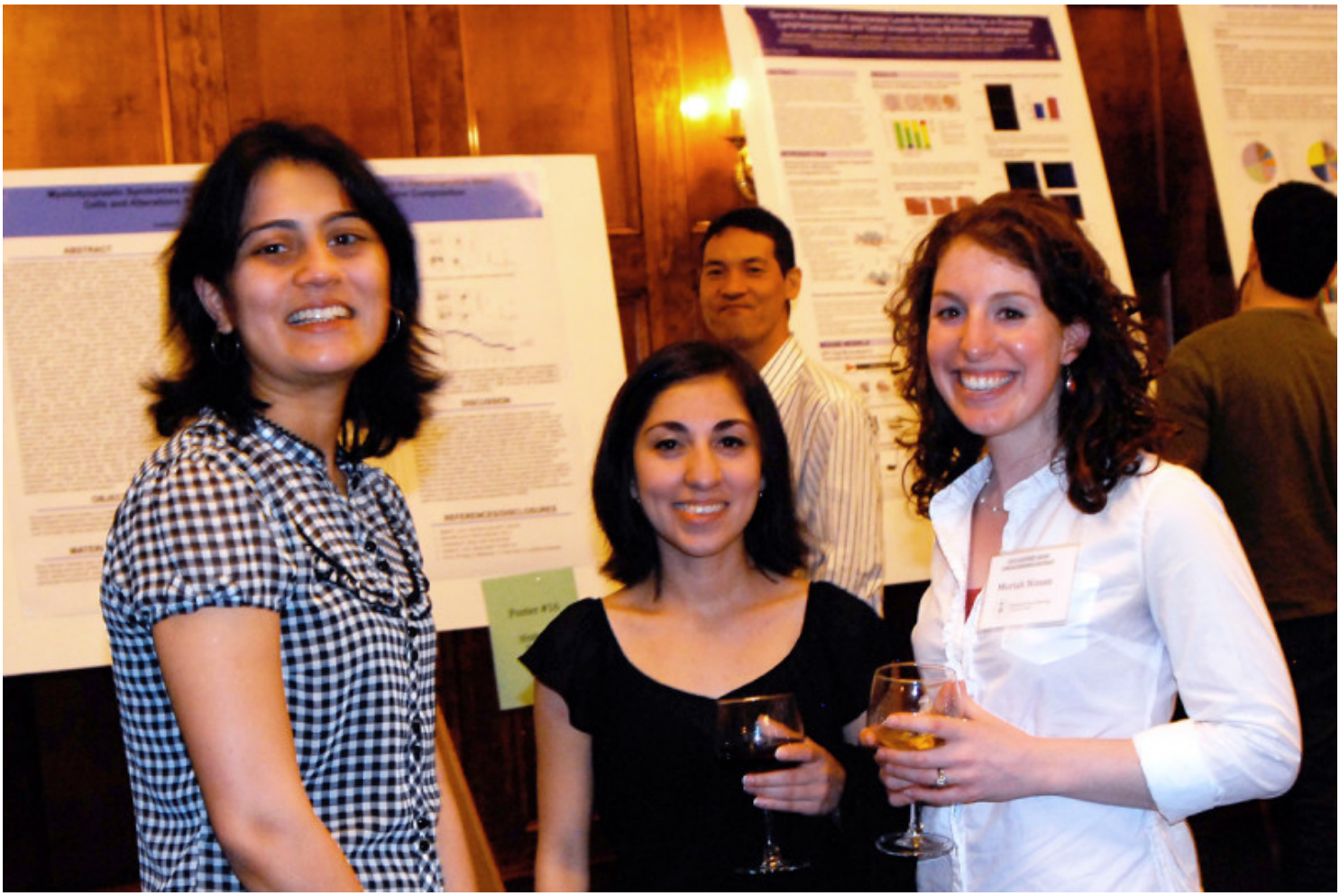
Mrs. Mara Hutton and Mr. G. Thompson Hutton from the Geoffrey Beene Foundation and Geoffrey Beene, LLC--(Photo by Daniel Danila)

Guest speaker Lou Staudt, Center for Cancer Research, National Cancer Institute, presents RNAi Screening & Cancer Gene Resequencing for the Achilles Heel of Cancer--(Photo by Africa Fernandez)

Lou Staudt--(Photo by Africa Fernandez)



Hemlock Ballroom, setup for the poster session--(Photo by Nicole Kucine)



Poster session - (from left) Neha Bhagwat, Berenice Ortiz, and Moriah Nissan--(Photo by Africa Fernandez)

Poster session--(Photo by Africa Fernandez)

Cancer Biology and Genetics Program attendees at the poster session--(Photo by Africa Fernandez)

Chris Sander, Chair, Computational Biology Program, at the retreat dinner--(Photo Daniel Danila)

Session IV, Cancer Genetics & Genomics -- Tari King, Surgical Breast Service, presents Gene Expression Profiling Demonstrates Two Stable Clusters of Lobular Carcinoma in Situ--(Photo by Nicole Kucine)

Session IV, Cancer Genetics & Genomics -- Cameron Brennan, Human Oncology and Pathogenesis Program and Department of Neurosurgery, presents Molecular Subclasses of Glioblastoma and Implications for Therapy--(Photo by Nicole Kucine)

Session IV, Cancer Genetics & Genomics -- Robert Klein, Cancer Biology and Genetics Program, presents Prostate and Gastric Cancer Susceptibility SNP in the Promoter of MSMB--(Photo by Nicole Kucine)

Eric Holland, Cancer Biology and Genetics Program; Vice Chair, Translational Research, Department of Neurosurgery; Director, Brain Tumor Center; and Mark Frattini, Leukemia Service, enjoy a brief discussion during a break between sessions--(Photo by Africa Fernandez)

Session V, Targeting Aberrant Signal Transduction -- Michael Glickman, Immunology Program and Infectious Diseases Service, presents A Critical Role for the PTEN-PI3K-Akt Pathway in Susceptibility of Bladder Cancer Cells to BCG Infection--(Photo by Nicole Kucine)

Session V, Targeting Aberrant Signal Transduction -- James Fagin, Human Oncology and Pathogenesis Program and Chief, Endocrinology Service, presents TshR Signaling-dependence for Braf-induced Thyroid Tumor Initiation in Mice--(Photo by Africa Fernandez)

Session V, Targeting Aberrant Signal Transduction -- Charles Sawyers presents Overcoming Resistance to Anti-Androgen Therapy--(Photo by Africa Fernandez)

A view of the audience during the session--(Photo by Nicole Kucine)

Closing Message -- Joan Massagué, Chair, Cancer Biology and Genetics Program

A view of the Evergreen Ballroom--(Photo by Africa Fernandez)

Skytop grounds and gardens--(Photo by Nicole Kucine)

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On April 8 and 9, 2010, the Geoffrey Beene Cancer Research Center held its third annual retreat at Skytop Lodge in Pennsylvania. The agenda focused on a wide range of topics related to translational research in oncology, a field that is at the core of the Beene Center's mission. Attendees included lab members in the Cancer Biology and Genetics Program (CBG) within the Sloan Kettering Institute and the Human Oncology and Pathogenesis Program (HOPP) within Memorial Hospital, as well as senior faculty within the Memorial Sloan Kettering.

Then Memorial Sloan Kettering Cancer Center President Harold Varmus kicked off the retreat on Thursday with opening remarks. He recognized G. Thompson Hutton, Trustee of the Geoffrey Beene Foundation, for his vital role in the creation and continued support of the Beene Center at Memorial Sloan Kettering. His introduction was followed by presentations from Beene grant recipients Cameron Brennan, James Fagin, Filippo Giancotti, Michael Glickman, Tari King, Robert Klein, and Michael Overholtzer. For the first time, this year's retreat also featured lectures by two Beene graduate-student fellowship awardees, Sindy Escobar-Alvarez and Vasilena Gocheva.

HOPP and CBG faculty members Robert Benezra, Jason Huse, Joan Massagué, Christine Mayr, Christopher Park, Charles Sawyers, and Hans Guido Wendel also presented on the topics of tumor invasion and metastasis, tumor initiation by microRNAs, and approaches to targeting aberrant signal transduction. Lou Staudt gave a feature talk titled “RNAi Screening and Cancer Gene Resequencing for the Achilles Heel of Cancer.” Dr. Staudt is Deputy Chief of the Metabolism Branch at the National Cancer Institute, and he also co-directs the Lymphoma/Leukemia Molecular Profiling Project (LLMPP), a multi-institutional consortium that aims to develop a new molecular framework for the diagnosis of all lymphoid malignancies.

The cocktail hour/poster session included 41 poster presentations by trainees. This year, research fellows/scholars and faculty members judged the posters and presented awards to the top five posters. Awardees included Nikki Charles from Eric Holland’s lab, Semanti Mukherjee and Jason Willis from Robert Klein’s lab, Praveen Raju from Beene grant recipient Alexandra Joyner’s lab, and Tanya Shree from Johanna Joyce’s lab. See a complete list of poster awardees and abstracts below.

The annual retreat continues to be the Beene Center’s most successful event due to the enthusiastic participation of the various departments throughout Memorial Sloan Kettering, emphasizing the importance of translational research in both the clinical and lab environments. The Beene Center has new initiatives underway to encourage interactions among clinicians and basic scientists and plans to continue its endeavors to strengthen the translational programs at Memorial Sloan Kettering.

Poster Awardees and Abstracts

Perivascular Nitric Oxide Activates Notch Signaling and Promotes Stem-Like Character in PDGF-induced Glioma Cells

Nikki Charles

Nikki Charles, Tatsuya Ozawa, Massimo Squatrito, Anne-Marie Bleau, Cameron W. Brennan, Dolores Hambardzumyan, and Eric C. Holland

eNOS expression is elevated in human glioblastomas and correlated with increased tumor growth and aggressive character. We have identified a novel role for nitric oxide (NO), which is produced from eNOS in the tumor vasculature and promotes stem-cell-like characteristics in glioblastomas. By activating the Notch signaling pathway in a population of stem-like cells residing in the microvascular environment of a subset of gliomas, we demonstrate that nitric oxide accelerates glioma progression and shortens the survival of mice.

Evaluating Statistical Power of Shared Controls in Genome-Wide Association Studies

Semanti Mukherjee and Robert J. Klein

Semanti Mukherjee

Genome-wide association (GWA) studies have become the method of choice for identifying genetic variants associated with specific diseases. In shared control study design, a common group of healthy individuals are used as controls for multiple diseases. We evaluated the idea of using genotype data of controls from publicly available sources as shared controls in our GWA study. We observed that the analytical power of a GWA study increases with increasing number of cases, genotype relative risk, disease allele frequency, and case:control ratio. The maximum power reaches at 1:10 ratio of cases and controls. We analyzed pancreatic cancer cases genotyped in-house with shared controls from publicly available sources. To correct for population stratification resulting from combining data, we used principal component analysis (PCA). Our simulated studies demonstrate that the PCA-corrected method significantly lowers the false-positive rate. We found that in real datasets, PCA can reduce the inflation of test statistics effectively. The performance of four known disease loci associated with pancreatic cancer improved in our dataset as we increased case:control ratio by adding shared controls. Thus, we reported a systematic method for using shared controls that will substantially lower time and cost of GWA studies.

Genetic Inducible Mosaic Analysis (GIMA): A Novel Genetic Method for Modeling and Characterizing Sporadic Tumorigenesis in the Mouse

Praveen Raju

Praveen Raju, Zhimin Lao, Luis Barraza, Brian Bai, and Alexandra L. Joyner

Cancer arises sporadically from one or a few cells within a tissue that acquire a number of critical genetic changes. However, current animal models of cancer do not accurately model sporadic tumor formation. Using sophisticated mouse genetics, we are developing a novel approach to study the natural progression of sporadic tumors and test cancer treatments.

Inhibition of Cysteine Cathepsin Proteases Enhances Effects of Chemotherapy in Reducing Primary and Metastatic Breast Cancer Progression

Tanaya Shree

Tanaya Shree, Benelita T. Elie, Alfred Garfall, Katherine Bell-McGuinn, Kenishana Simpson, Violetta Barbashina, and Johanna A. Joyce

The tissue environment in which tumors arise and grow can profoundly influence the trajectory of those tumors; namely, how aggressive they can become and even whether or not they metastasize. Recent studies suggest that a tumor's environment can also influence how it responds to treatment. In our studies of breast cancer, we have found that enzymes called cathepsins are increased when tumors are treated with chemotherapy, and that inhibiting these enzymes while giving chemotherapy greatly enhances antitumor effects of the chemotherapy. Thus, these enzymes may be involved in helping tumors recover from chemotherapy and regrow, and inhibiting them allows us to impair this process. Taking this strategy further, a triple-drug therapy we designed — targeting tumor blood vessels in addition to cathepsins while administering standard chemotherapy — was highly effective at reducing tumor growth in an animal model, and also significantly reduced lung metastases. Thus, we believe that targeting "normal" cells in the microenvironment of tumors in addition to our standard treatments targeting tumor cells will help us achieve maximum therapeutic benefit.

Excess Germline Copy Number Variation Is Associated with Pancreatic Cancer Risk

Jason A. Willis, Sarah H. Olson, Robert C. Kurtz, and Robert J. Klein

Jason A. Willis

The goal of our project is to locate inherited mutations in DNA that predispose some individuals to pancreatic cancer and influence their overall prognosis. The research is a collaborative effort between geneticists, statisticians, and physicians at Memorial Sloan Kettering Cancer Center. We hope that this project will lead to a better understanding of how pancreatic cancer arises and to the development of new therapies. The poster describes some of our preliminary findings. First, a certain type of inherited mutation (called copy number variation) is more common in patients who have multiple family members affected by pancreatic cancer. We are currently investigating how and why this type of mutation may lead to increased risk of cancer. Second, at least one previously undiscovered mutation seems to correlate with very poor survival from pancreatic cancer. We are confirming this result in a much larger study.