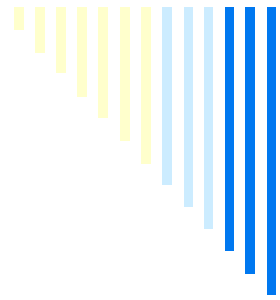




# Gerstner Sloan-Kettering

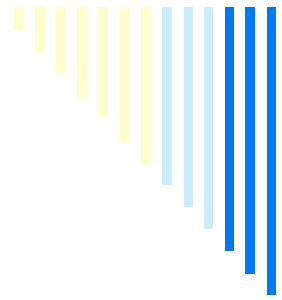
Graduate School of Biomedical Sciences



# Memorial Sloan-Kettering Cancer Center (MSK)

- Oldest free-standing cancer center
  
- Four entities that work closely together for the benefit of each other
  - Memorial Hospital—Robert Wittes, MD, Physician-in-Chief
  - Sloan-Kettering Institute—Thomas Kelly, MD/PhD, Director
  - Gerstner Sloan-Kettering Graduate School—Ken Mariani, PhD, Dean
  - Memorial Sloan-Kettering Cancer Center—Harold Varmus, MD, President and CEO (until July 7<sup>th</sup>)

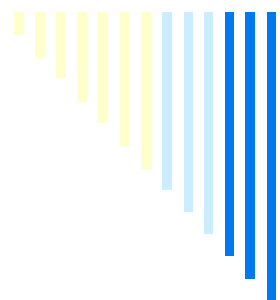




# Louis V. Gerstner, Jr. Graduate School of Biomedical Sciences

- Chartered September 10, 2004
- First class matriculated August, 2006
- Accredited May 20, 2008

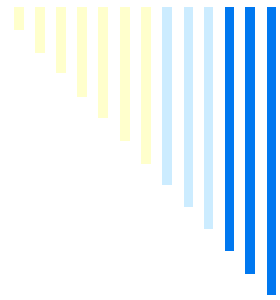




# First Year

- GSK Core Course
- Logic & Critical Analysis
- President's Research Seminar JC
- Graduate Student Seminar
- Responsible Conduct of Research
- Observing in the clinic**
- Meet the research and clinical faculty
- Laboratory rotations
- Selection of the research mentor





# First Year

- GSK Core Course
  - Genome Biology
  - Proteins and Gene Expression
  - Cells and Regulation of the Cell Cycle
  
  - Signaling and Development
  - Cancer Immunology
  - Cancer Biology





# GSK Core Course

## Gene Expression

### *Errors in protein folding and cancer*—1 unit, Neal Rosen

The protein-folding problem—Spontaneous versus chaperone regulated folding  
Folding and chaperone machinery

Biologic function

Chaperones as regulators of the proteome

Role of folding apparatus/Hsp90 in evolution

Role of chaperone system in the cellular response to stress

Chaperones and cancer

Protein unfolding and cellular stress: roles of Hsp90 and the upr

Hsp90 as permissive for transformation: folding of mutated oncoproteins

Chaperone regulation of activating signaling pathways

Therapeutic manipulation of protein unfolding

Hsp90 inhibitors—Induction of target degradation

Proteasome inhibitors—Increasing protein unfolding

Peptide chaperonemimetics

Inhibitors of upr transduction

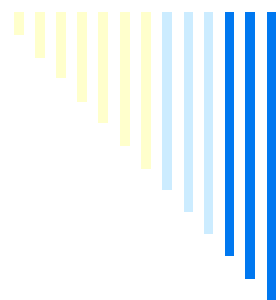
Preclinical hypotheses and clinical studies

### Papers

Isaacs, J. S., et al. (2003). Heat shock protein 90 as a molecular target for cancer therapeutics. *Cancer Cell* 3: 213-217.

Solit et al. (2003) Inhibition of heat shock protein 90 function down-regulates AKT kinase and sensitizes tumors to Taxol. *Cancer Res.* 63: 2139-2144.

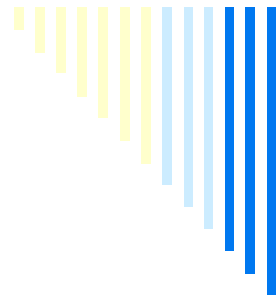




# GSK Faculty

- GSK faculty are drawn from both the basic science and clinical arms of MSK
  - Sloan-Kettering Institute (SKI) 60%
  - Memorial Hospital (MH) 17%
  - SKI and MH 23%





# Clinics visited by first year students

- Brain cancers
- Breast cancers
- Gastrointestinal cancers
- Gynecologic cancers
- Leukemias
- Lung cancers
- Lymphomas
- Myelomas
- Sarcomas



## Clinical Visit Survey

### •**Briefly describe your experiences for the clinic visits**

*The clinic gave me a first-hand look of why I'm doing cancer research. It put a perspective on how badly new treatments are needed for cancer patients. It also put a face on "cancer," as I engaged in conversation with many of the patients and learned about their struggles and needs.*

### •**Did the experience complement something that you learned in the classroom?**

X Yes, please explain

No, please explain and include opportunities you think can be extended on

*We need better treatment, and we need to work out mechanism of resistance.*

### •**Did the experience change/complement your views?**

X Yes, please explain

No, please explain

*Current chemos suck.*

### •**Is there something you observed that you can bring back to the laboratory?**

X Yes, please explain

No, please explain and include opportunities you think can be extended on

*It doesn't matter if you have a great drug that inhibits the target you want in a cell-culture dish, if it is uncomfortable or inconvenient to have administered to people, patients won't take it. i.e. if you have a treatment that could cure cancer but needed to be taken by I.V. 2x daily, people wouldn't take it. Clinic taught me you need to think past "does it work" and think about if it helps the patient as a person and not as just a tumor.*

### •**In the overall, what were your expectations and do you feel they were met?**

X Yes, please explain

No, please explain

The only thing that surprised me was how un-melancholy the clinic was. I expected the clinic to be gloomy, but people were cheerful, and not everyone was dying (bonus!).

### •**In the overall, how would you characterize your experience in the clinics with respect to your graduate training?**

X Very valuable

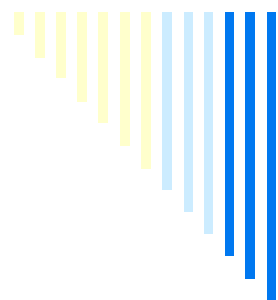
Valuable

Somewhat valuable

Not valuable

### **General Comments:**

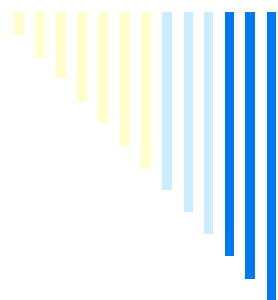
*It will keep my research focused on the true goal at hand.*



# Clinic Visit Evaluations (Students)

- Opportunity to see how lab findings are translated
- Gained insight to clinical challenges
- Opportunity to establish a dialog with clinicians
- Realized different constraints and priorities that clinicians have
- Revealed the overlap between the basic science sections of the course and the clinic
- Helped integrate basic biology studies and their implications in the clinic
- Valuable to discuss what new drug targets might exist and be most promising
- Helped to realize how important translational research is to curing disease
- One of the best aspects of the first year

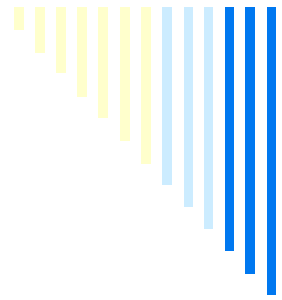




# Clinic Visit Evaluations (Sponsors)

- The experience from my standpoint was excellent. This is a great opportunity to see how complementary the lab and bed side are, and may help the students shape their future research projects. It is also a good opportunity for the students and faculty to build ties for collaborative work.
- Excellent program which I would be glad to continue supporting.
- Thanks for the opportunity to interact with the GSK students. I will be happy to speak about lung cancer and clinical research in either a seminar or lecture format. I also will welcome GSK students to my outpatient office to meet patients and see firsthand the clinical issues that can help focus basic research.





# Second Year and Beyond

- Selection of the clinical mentor (end Yr 2/begin Yr 3)
- Current Topics JC
- Graduate Student Seminar
- Thesis Proposal Examination (March, Yr 2)
  - Advancement to Candidacy
- Dissertation Research





# Clinical Apprenticeship

- To inspire and promote students to think about addressing clinical problems through the basic sciences
- Learn the lexicon, be able to have a scientific exchange
- Informal meetings with Clinical Mentor, directed readings, identify issues and pressing challenges
- Grand rounds, resident's reports, SPORE and Program Project meetings, DMT conferences
- Involve clinical fellows
- Round with the CM and fellows
- Collaborate (already happening)
- CM attends student seminar, committee meetings
- Report on a significant clinical challenge and the potential for a basic science approach



***Third Year Student: Karen Hunter***

***Thesis Mentor: Johanna Joyce (Cancer Biology & Genetics)***

***Clinical Mentor: Diane Reidy (Medicine)***

My clinical mentor is Dr. Diane Reidy who is on the GI service, with a focus on neuroendocrine tumors. As the RIP1-Tag2 mouse I work on is a neuroendocrine tumor model, we have been working in collaboration with Dr. Reidy and a pathologist, Dr. Laura Tang, to validate our findings in human samples. Dr. Reidy and I have had several useful discussions on my findings in the mouse model and how this relates to patients and directions to take in my research. As neuroendocrine tumors are a rare tumor type, much more research is needed to understand this tumor type and develop better treatments. To work towards better understanding of these tumors, Dr. Reidy and Dr. Tang are creating a registry of patients and samples that we have gotten samples from and will be able to work with in the future. Additionally, in collaboration with the Moore lab we will be working to derive and characterize additional neuroendocrine cell lines derived from patients that are seen in the clinic. In addition to these collaborations, Dr. Reidy and I have set up a schedule where I will attend the GI tumor board meetings where patient cases are discussed every other week and come spend the morning in the clinic once a month. Visiting the clinic has been very beneficial to see how patients with neuroendocrine tumors are treated and also to sit in on enrolling patients in the registry and to speak to them about how we hope to use their information and samples to better understand their disease.

***Fourth Year Student: Dimiter Tassev***

***Thesis Mentor: Nai-Kong Cheung (Pediatrics)***

***Clinical Mentor: Ron DeMatteo (Surgery and Immunology)***

My clinical mentor is Dr. Ron DeMatteo. Initially, we began discussing our work and interests. Dr DeMatteo mentioned that some of his work involves the use of Gleevac in the adjuvant setting for gastrointestinal stromal tumor (GIST) and that he was working with Novartis on starting a randomized 5-year trial. I then mentioned to him that I have a strong interest in clinical investigation and he allowed me to sit in on his meetings with Novartis. This was extremely helpful to me since I want to pursue a career in this area. The MSK team and the company's team came to an agreement about how the trial should be managed but we haven't had subsequent talks about that subject. **Our focus then shifted to monoclonal antibodies, since he was interested in using antibodies along with Gleevac for the treatment of GIST-bearing transgenic mice. We came up with several experiments that our lab and his lab could do together to carry out his goals.** Currently, we are still in discussions with respect to the experimental design. In conclusion, lately our relationship has been more of a collaborative one in which I try and offer assistance to his lab.

***Fourth Year Student: Jim Dowdle***

***Thesis Mentor: Scott Keeney (Molecular Biology)***

***Clinical Mentor: Jason Konner (Medicine)***

So far my clinical mentorship has involved shadowing Dr. Konner in his clinic and regular meetings over lunch. Although I find the shadowing a valuable and informative experience, I do not see the value of continuing this exercise on a regular schedule as subsequent visits have not proved much different from the first. That being said, I can see visiting the clinic 3 or 4 times a year as the perspective gained is fleeting. Lunch-time discussions have mostly revolved around what we think the clinical mentorship relationship should be, our focus and goals in our respective fields and as of late Jason has acted more as a first year mentor than a clinical mentor. Jason has attended my GSS and I keep him up-to-date with my project in the lab but beyond a superficial interest in my project and my parallel level of interest in his clinical duties we have not progressed beyond this. For my project specifically, there is no clear tie between my research and Jason's disease specialty, the disconnect being the reason for our mutual lack of interest. Ultimately, as we are both quite busy, not having a clear idea of what either of us stands to gain from the mentor relationship has left things stagnant.

**Third Year Student: Semanti Mukherjee**

**Thesis Mentor: Robert Klein (Cancer Biology & Genetics)**

**Clinical Mentor: Zsofia Stadler (Medicine)**

Dr. Zsofia Stadler is a medical oncologist who specializes in the treatment of gastrointestinal malignancies. Her interest in population genetic studies and the clinical translation of genomic based cancer risk assessment inspired me to choose her as my clinical mentor. She was excited to learn about my thesis project that is focused on identifying genetic predisposition to cancer. We decided to schedule clinical observations and case study meetings twice a month. To start with, she suggested I shadow her in the genetics clinic where she provides clinical counseling for individuals who may have an inherited predisposition to gastrointestinal cancers or other cancer syndromes. This is scheduled every Wednesdays from 9:30am- 1:30pm. I shadowed her on my first visit in January. During my second visit, she introduced me to genetic counselor Sherry R. Boyar. I shadowed Ms. Boyar with her case. Depending on family history and pedigree analysis, the patients and their relatives at high risk are assessed and tested for known mutation offered by MSKCC. Some of the genetic tests are *p53* gene (Li-Fraumeni syndrome), *STK11* gene (Peutz-Jeghers syndrome), *MEN1* gene (multiple endocrine neoplasia type 1), *MLH1*, *MSH2*, and *APC* genes (hereditary colon cancer syndromes) and *BRCA1* and *BRCA2* (breast cancer cases). I have also attended two case study/diagnosis meetings with Dr. Stadler (scheduled every Friday 10am - 1pm). This was an opportunity for me to learn how genetic counselors and oncologists discuss their patients' case history / diagnosis and the pedigree analysis. Overall the experience has been fruitful. Dr. Stadler has agreed to join me in my thesis committee meetings and also advice me on how to analyze the clinical data. I am looking forward to working more closely with her in the future.