Program at UC San Diego School of Medicine

Kenneth Kaushansky, Co-Director
Chair, Department of Medicine

Rady Children's Hospital

Shiley Eye Center

UCSD Medical Center

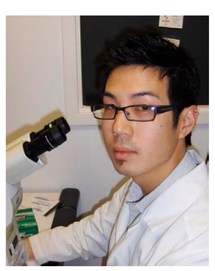
7. S/I reports emphasize learning and impact to attract new trainees

1. **Acquire a comprehensive clinical training experience illustrating the complexity of disease**. "Honestly there is too much to say to sum up this jam-packed 3 month experience. I was learning more and more the whole time and never got bored. I was able to indulge myself and learn more about those issues in the clinic that intrigued me. I would recommend this experience to anyone and hope that it teaches them as much as it has taught me. Without the fulltime immersion, the reality of disease and the behaviors/variables that affect life would still be foreign".

2. **Have increased motivation to cure disease because they have seen it firsthand**. "MIG exposed me to life threatening conditions associated with lupus such as nephritis, pneumonitis, cerebritis and vasculitis. I was astonished at how often these young patients were readmitted with these recurring conditions. I gained a new-found compassion toward sufferers of rheumatic diseases. MIG's invaluable training has put a face to my research, changed my perspective and focused my research goals on the development of new therapies".

3. **Understand current diagnostics and recognize the need to develop better diagnostics**. "**This program did a superb** job in training me in different diagnostics and therapeutics in cardiology. I saw state of the art procedures, including ablation for atrial fibrillation, stent procedures, pacemaker implants, coronary artery bypass, and pulmonary thromboendarterectomy. I was interested in Cardiac MRI and during an MRI reading I came up with a research idea for developing a novel method to treat aortic aneurysms".

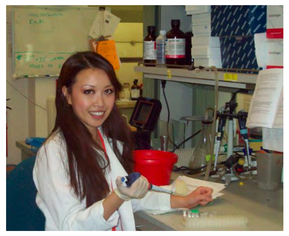
4. **Understand current therapeutics and recognize the need to improve disease treatments**. "My first rotation was a shocking introduction to the severity of cancer and brain tumors. I was given the opportunity to observe patients in both the clinic and operating room. Pharmacological remedies are limited for patients with brain tumors because they are commonly unable to cross the blood-brain barrier. This limitation remains a therapeutic challenge".



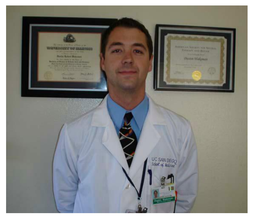
5. **Better appreciate their their molecular training because they will realize its vast potential to improve human health.** "I felt that one of the most important things to come out of this experience was a renewed sense of purpose for my research. I was reminded that although my research sometimes seems far from the clinic, it is nonetheless one piece of a complicated puzzle of developing highly cancer-specific therapeutics. I was able to observe first hand, how, although current standards of anti-cancer therapeutics can suppress disease progression or even achieve remission in some cancers, many times it comes with a heavy price. In CLL, many of these patients achieve slowed/arrested disease progression, but have little immune function during treatment and experience serious complications from infection. Current chemotherapeutics must be improved, and their target specificities must improve. We in the laboratories are the answer."

6. **Initiate new translational research collaborations between research and clinical faculty**. "MIG provided me a chance to combine my background with a clinical experience to pave the way to the development of novel therapeutics, devices, and diagnostics, and contribute to helping patients have a better quality of life. I am collaborating with UCSD physicians to improve devices I developed during MIG training, which are now under evaluation for patents."

6b. **Discover new collaborations in thesis research**: I work on malaria genomics and did not expect to see any cases of malaria in the San Diego area. I was pleasantly surprised, though, to see a presentation by a medical fellow from the US Navy detailing three cases of malaria that he had recently seen in San Diego. I plan to work with the US Navy to organize a protocol to obtain malaria samples first from those cases in San Diego, and utilize our whole-genome tiling microarray to analyze the samples to provide the US military an accurate picture of the specific threat in terms of resistant malaria strains that they face. Additionally, by amassing a library of genetic differences of field isolates, we can contribute substantially to the understanding of the genetics behind malaria drug resistance



7. **Use MIG training to refine/instruct your primary thesis research.** "I recognized the need to categorize genomic data based on the different phenotypes of autism seen in clinic"



8. **Recognize the benefits as well as the limitations of animal models for disease**. "One of the most important moments in my MIG experience occurred in the basement of the VA Hospital with Drs. Mark Tuszynski MD and Harry Powell MD, discussing the relative distances a dopaminergic neural precursor would have to correctly extend projections from the midbrain substantia nigra to the striatum in order to correctly reconstruct and re-innervate the mesostriatal system with regulated dopaminergic tone in a typical Parkinson's disease patient. It immediately became clear why the plethora of positive data obtained in rodent and non-human primate models for fetal DAergic transplants failed to predict gross adverse effects in human PD patients. The unequivocal differences in anatomical organization and cortical mass that humans exhibit are easily overshadowing when modeling complex human disease in simpler organisms. MIG provided the necessary exposure to fine tailor my current work to ensure accurate preclinical testing of stem cell therapy."

9. **Recognize the most important and relevant research questions**. "After completing MIG training, I feel much more comfortable with my judgment towards deciding what specific questions to address at the "bench". I have a stronger understanding of some of the most important needs towards cancer biology and I feel it will have a long-term impact as I progress through my doctoral research and beyond.

10. **Change focus for post-doctoral studies**: "I was interested in Med-into-Grad because I wanted to study infectious diseases in my postdoctoral work, and I wanted to do work that was clinically relevant. Most of my training occurred in Peru, where I focused on malaria and tuberculosis in a remote lab in rural Iquitos. The education I got in Peru really does inform my thinking on TB in important ways. I am so grateful that Med Into Grad exists and that I had the opportunity to participate, because it already is having a meaningful impact on my career. My post-doctoral work at Harvard will focus on tuberculosis in a manner that I hope will contribute to improvements in managing tuberculosis in poor countries, where it poses the greatest public health problem."

8. Additional training outcomes

Outcomes
Encourage Collaborations

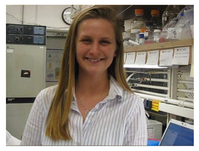
Are non-human sugars enriched in atherosclerotic lesions?
Can nanoparticle technology be used to detection ocular degeneration?
Could calcification in breast cancer be associated with over-expression of BMP7?
Does human CLL have dysfunction in cell cycle control by ATR/ATM?
Can new proteomes predict intervention points of current therapeutics?
Can one develop a better drug-eluting stent using new bioengineered materials?

Outcomes
Capture new knowledge

Make this an experiment in education:
Do molecular minds recognize new feasible projects in the clinical arena?
Assess using required "Proposal"
- New Diagnostic
- New Therapeutics
- New Research Project/Molecular Mechanism

Thesis PI and clinical director read proposal and discuss feasibility
Student proposals are in Booklet

Outcomes
Improved graduate student recruitment



See 2 minute talk on computer

Outcomes
Disease-oriented Post-doc studies

Student	Graduate Work	MIG area	Post-doctoral work
D. Cecil	Inflammation/osteoarthritus	Rheumatology	Tumor vaccine group, UW
S. Shell	DNA mismatch repair	Tropical Disease	Tuberculosis pathology
E. Lau	Cdc6 in S phase regulation	Cancer	ATF2 in melanoma/squamous cancer
A. Kapasi	CMV transcription by host	Infectious Dis.	CDC tropical public health
Y. Shrager	Memory mechanisms	Alzheimer's Dis.	Memory storage in Alzhiemers
J. Hagopian	SR protein phosphorylation	Cancer	Cancer Therapeutics, RNAi

9. Recognize the many logistics! (Make survival manual - see Booklet)

Malpractice insurance, Approval by your committee of education policy
Immunizations, Security clearance and obtaining badges for state/federal facilities
Medical school histology - Purchase microscopes, slides, lockers, keys
Contact to make travel arrangements for clinical conferences
Contact for expense recharge
Minority scholarship application through Office of Graduate Studies

10. Our current challenges

Some mentors say there is no good time to take Med-into-Grad. Interferes with research.
Didactic courses in translations research. This year electives are
- Biostatistics (clinical research masters program)
- Patient-oriented research (clinical research masters program)

Institutionalization
- T32 Training grants, which would also fund that quarter. Currently: Cancer, Pulmonary
- Molecular Medicine T32. Problem, only 3 slots in first 4 years
- For credit only, paid for by PI's who value the experience

Community-building experiences--not desired by students.
- They are plugged into their own graduate program and don't have more time
- They retain contact with their specific clinical group, when desired