

INDIANA UNIVERSITY CANCER CENTER NEWSLETTER

January 2001

Special points of interest:

- *In the Spotlight*–
John Foley, Ph.D
- Kelley Named Simmons Professor of Pediatrics
- Nakshatri Receives DOD Grant
- Comprehensiveness
- ACS Grant Funds Awarded
- Honors - David Williams, M.D

In the spotlight.....

John Foley, Ph.D

I was born in Kenosha, Wisconsin to an urban Irish father and a Norwegian/Yankee mother from farm country. My father spent his entire career working for public school systems. My mother did the work at home, but developed a strong scientific interest in nutrition, particularly the interface of diet and cancer. My siblings and I grew up taking a vast array of dietary supplements (antioxidants) before we left for school each morning

Like many children born in the 60's, I developed an intense interest in dinosaurs and archeology. As a result, I began collecting rocks, arrowheads and fossils by age 3, and this remains an avocation I pursue to this day. Throughout grade and high school I excelled in two apparently opposing fields; the hard sciences and the social sciences. By the time high school graduation approached, I had decided I would pursue a law degree because it appeared that lawyers had far greater incomes and status as compared to scientists. My mother has never been much of a fan of lawyers, so she stepped in and arranged for me to talk with an old college friend of hers. This turned out to be Vitamin K and blood clotting researcher John Suttie of the University of Wisconsin Biochemistry Department. While he was not too enthusiastic about careers in biochemistry, he thought a biochemistry undergraduate degree might be a good background for law school. So I took his advice and enrolled in the University of Wisconsin, majoring in biochemistry

Like many preprofessional students, I attempted to learn as little as possible from my undergraduate classes at the University of Wisconsin while maintaining a high GPA. For the most part, my undergraduate course work failed to interest me, primarily because the focus was on basic concepts that seemed out of date. Fortunately, I had an outstanding teaching assistant for my biochemistry lab course. Greg Miggelita performed research at McArdel Cancer Research Laboratory and played semi-pro hockey. After final exams, Greg invited us over to a neighboring tavern for beers on him. As the beer flowed, Greg's conversation turned towards recent paradigm-shattering discoveries in the field of cancer research. The Harold Varmus lab had just recently reported how endogenous oncogenes could become activated through insertion of retrovirus sequences into the genome. I was so impressed with this finding that the next day I went to the library and read the article (Payne et al. Nature, 295: 209-14, 1982) despite having a hangover (one of the perils of a UW education). This research allowed me to begin explaining to my mother how the many disparate causes of cancer might share a single mechanism, namely activation of oncogenes. Even after this "light bulb" type of experience, I finished my degree with the intention of going to law school

I had self-financed my undergraduate education by working part time as a butcher and a shoe salesman, and now I was broke. Paying my own way through school probably taught the importance of perseverance and provided me with a real appreciation of the opportunities education provided. I decided to take some time off and work full time to save some money for law school tuition. For a year and a half after college I hustled, unloading trucks at JC Penney, fitting skis and boots at a ski hill and managing a local punk rock band. During this time my bank account balance did not grow, and I decided to put my biochemistry degree to work for me. I got a job working for Bibhuti DasGupta at the University of Wisconsin Food Research Institute purifying Botulinum neurotoxin. My intention was to work a year and one half and get that money for law school. It turned out that I enjoyed the hands-on learning of basic protein biochemistry and didn't mind the smell of the 40-liter botulism cultures. During this time, I met an outstanding Ph.D. student named Anne Herian who also enjoyed fossil collecting. Of course, we would later get married. I stayed on the job three years, and a post-doc in the lab, Bal Ram Singh, convinced me that I didn't want to be a lawyer. Instead, I enrolled in the Anatomy and Cell Biology graduate program at the University of Cincinnati

At Cincinnati, I joined Linda Parysek's laboratory principally to learn how to apply molecular biology techniques to questions in cell biology. Linda had isolated and cloned a novel neuronal intermediate filament protein that was eventually named peripherin. Linda permitted me to have a free hand in designing my thesis project and I was able to develop a research direction related to cancer. This involved cloning the human peripherin gene, studying its regulation in neuroblastoma cell lines and using peripherin antibodies as tumor markers for neuroblastomas. Shortly after I started my Ph.D. program, Anne and I were married. To my delight, she got a job as a microbiologist for a local microbrewery. For a Wisconsin native, free beer is almost as good as free cheese. When it came time to leave Cincinnati, it was Anne's turn to pick the place we would go. She chose to work on infant formula at the Nestle research and development center in New Milford, Connecticut, an hour and twenty minute drive from Yale

Yale University offered many postdoctoral opportunities, but I was very fortunate that my c.v. came to the attention of Arthur Broadus, chief of the endocrine section. Arthur's lab had recently cloned the humoral hypercalcemia of malignancy factor, PTHrP, and was now entering an exciting phase where important basic questions about the molecule were being asked. These were: 1) what was the physiological role of the molecule? 2) how was its expression regulated in tumor cells? I began studying regulation of PTHrP gene expression in squamous cell carcinoma cell lines and exploring a potential relationship to p53 status. After a fast start, the work bogged down mainly because our *in vitro* assays could not recapitulate the complexity of the regulation of the endogenous PTHrP gene within a cell or tumor. As part of this work, I began evaluating PTHrP gene expression after sunburn-mediated induction of p53 activity in mouse skin. I found the biology of sunburn to be fascinating and began probing the field of dermatology to understand this system better. At this time, Arthur's lab began producing several transgenic and knockout mice to evaluate PTHrP function, and I was given the responsibility of evaluating the skin phenotypes. These mice turned out to be a treasure trove of information, shedding insight into skin patterning, hair follicle growth and skin aging. During my postdoctoral years, Anne quit her job with Nestle so she could work full time taking care of our daughters Sarah and Cecilia, born in 1993 and 1996 respectively

After completing my postdoc, Anne and I decided we would like to return to the Midwest so we could be closer to our families. In 1998, Indiana University Medical Sciences Program offered a very unique opportunity for us. Here was a job in a wonderful small town, close to excellent fossil hunting, and within 50 miles of an outstanding dermatology department at the IU Medical Center. With the help of Dan Spandau and Jeff Travers of the Dermatology Department, I have established a research program centered on exploring PTHrP function in skin. With the collaboration of Zhor Bouizar from Paris, I have turned my interest in PTHrP gene expression into a program evaluating the expression and function of the peptide in metastatic breast cancer

Recently, in collaboration with Steve Williams of the IU Cancer Center and Ken Nephew of the Medical Sciences Program, I am using my background in regulation of gene expression to help develop an ovarian cancer-specific promoter to drive novel therapeutic agents in advanced ovarian cancer patients. I have been very impressed with the collaborative spirit at the IU School of Medicine, and I look forward to future research work or fossil hunting with my fellow faculty members

Kelley Named Simmons Professor of Pediatrics

Mark Kelley, Ph.D., Professor of Pediatrics and of Biochemistry and Molecular Biology, was named the Jonathon and Jennifer Simmons Professor of Pediatrics by the I.U. Board of Trustees. This endowment was established by the Riley Memorial Association and the Simmons family to support translational cancer research to hasten the development of innovative therapies for pediatric cancer. Dr. Kelley is recognized nationally and internationally for his research in DNA repair. He received his Ph.D. in genetics from Louisiana State University. After six years of faculty position at Loyola University Medical School, he joined the faculty at Indiana University in 1993. Dr. Kelley serves as the Associate Director of the Herman B. Wells Center for Pediatric Research. Dr. Kelly's research is in targeting DNA repair enzymes to cells, either to make them more sensitive, or less sensitive, to chemotherapy. This has the potential to dramatically alter how many cancers are treated. This novel approach has been pioneered by Dr. Kelley and he is considered the world's leader in this area. Congratulations to Dr. Kelley

Harikrishna Nakshatri Receives DOD Grant

Harikrishna Nakshatri Ph.D., Assistant Professor, Department of Surgery, has received a three year Department of Defense grant for his proposal entitled "**NF-kappaB Mediated Repression of GADD153/CHOP: A Role in Breast Cancer Initiation**"

In this proposal, Dr. Nakshatri will explore the nexus between NF-kB and GADD153 in breast cancer initiation. He will also determine whether NF-kB plays an active role in survival and cancerous growth of normal breast cells that are damaged by environmental toxicants. Furthermore, Dr. Nakshatri will investigate whether NF-kB alters the normal pathway of growth, division and death of breast cells. Several laboratories including Dr. Nakshatri's are currently measuring the effect of inhibitors of NF-kB on the response of breast cancer to chemotherapy. This proposed study is the first step in developing similar drugs that can prevent breast cancer initiation

"Comprehensiveness"

There is some misunderstanding about the designation received by the IU Cancer Center in the fall of 1999. IUCC is a clinical cancer center and was not given the designation of "comprehensive." The cancer center review process is complex. The first stage of the review is submission of the core grant application and a site visit. In the case of IUCC, this review was favorable, and the subsequent review by the parent committee and the NCI Executive Committee was equally favorable. This review resulted in the funding of our core grant (for five years with minimal budget reduction) and IUCC became an "NCI-designated clinical cancer center"

The review for comprehensiveness is a two step process. The first step occurred at the time of the review of the core grant application but is a separate process. To be a comprehensive cancer center, the institution must be deemed to demonstrate strong interactions among basic, clinical, and cancer control investigators. This decision is made by the site visit team and the parent committee. In the case of IUCC, the recommendation for comprehensiveness was not made because there were an insufficient number of interactions among cancer control scientists and basic and clinical investigators. While there are many on-going collaborations, they were not thought to be sufficiently mature as judged by the number of co-publications or grants. The second step is a review by the Executive Committee of our community outreach and education program. It is still a priority of the IUCC to attain comprehensive status. A number of steps are underway to do so and we are confident that this will occur either before or at the time of our

competing renewal. However, the lack of this designation does not alter the fact that we are indeed an NCI-designated cancer center nor does it alter our funding

American Cancer Society Grant Funds

It is a pleasure to announce the recipients of the American Cancer Society Grant Funds. The following applicants and projects have been named to receive this grant

- Edward Chan, M.D., Dept. of Medicine, “**Genetic Alterations in Leukemia**”
- Pierre C. Dagner, M.D., Dept. of Nephrology, “**On the Mechanism of Action of Guanine Bases and Nucleosides as Anti-Cancer Drugs**”
- Victor Fomin, Ph.D., Dept. of OB/GYN, “**The Expression of Protein Kinase C (PKC) in Human Leiomyoma**”
- Martin Kaefer, M.D., Dept. of Pediatrics, “**Bladder Cancer: A Novel Molecular Approach to the Treatment of Localized and Metastatic Disease**”
- Qi-Huang Zheng, Ph.D., Dept. of Radiology, “**New Radiotracers for PET Imaging Breast Cancer**”

Honors

David A. Williams, MD, has been awarded the William Dameshek Prize for his pioneering contributions to the field of retroviral-mediated gene transfer and human gene therapy. The prize was presented Dec. 5 at the meeting of the editor of *Blood*

Schedules are available via the IUCC web page under seminars and conferences.
Web Page Address

[Http://iucc.iu.edu/](http://iucc.iu.edu/)

If you have a conference, seminar or meeting that you would like posted please contact:

Chasity Miller (chasmill@iupui.edu)
phone 278-4717 or fax 278-0074