

Indiana University Cancer Center Newsletter

A National Cancer Institute-
Designated Cancer Center

March 2000

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In the spotlight.....

Jian-Ting Zhang, Ph.D.

I would like to take this spotlight opportunity to thank all my teachers and mentors who have helped shape my career path and carried me to each and every stage of my life. They are my *Gui-Ren* (Chinese: important person who has mysterious power for helping others) and if it were not for them, I would not have been here writing this article.

Unlike many scientists who had dreams and love for science, I never thought I would ever become one of the Hollywood's "weirdoes". As a high school teen, I was very much involved in sports. I wanted to be an athlete, a professional one. My first passion was basketball that began in grade school. This devotion lasted until college. Although playing basketball never became my career, basketball nevertheless became part of my life until too much science took it away.

It was during the high school years that my dream of becoming a professional basketball player was shattered. My genetic materials apparently were not allowing me to reach that 6-foot size. I was then recruited to the team for target shooting for which I was told I had the build. After a year of hard working and a summer of intensive training in the provincial shooting school, the door once again shut on me. At the time, I was desperate to make a decision for I had only one year left in high school. What do I want for my life?

At this time, one of my *Gui-Ren* appeared. It was my high school literature teacher, Mr. Ge Zhai. Mr. Zhai, over my whole high school years, never got tired of trying to persuade me to reshape my career goal and had always encouraged me to go to college. He would not miss any opportunity, even in the men's room, to talk me into preparation for college. I stubbornly refused to listen to him and kept on playing my basketball and shooting my guns. He stubbornly would not stop trying to convince me either and kept on talking and talking. When I ended up with no where else to turn after the athletic doors had closed on me, Mr. Zhai welcomed me and kindly guided me to prepare for college. "This is it" he said to me. "You have to operate at a top speed to catch up" and knock open college doors in 1979.

If Mr. Zhai helped steer my wheel at college doors, Mr. Bencai Wang, my high school chemistry teacher, had to be the *Gui-Ren* who helped step on my gas pedal. Mr. Wang was the one who helped me catch up and make constant progress. It was also Mr. Wang who had vision and encouraged me to chose a Biochemistry major once I was ready for Nanjing University.

Four years of college were fast. Before I knew it, I had to face choices again. I knew at the time that I was not ready for government-assigned jobs and thus decided to have a graduate education. This time, it was another *Gui-Ren*, Professor Dexu Zhu, in Nanjing University who accepted me into his laboratory and then provided me an opportunity to compete for a

CUSBEA fellowship. For better or worse, I became one of the 55 students who were chosen in 1983 to study for Ph.Ds. in the USA.

Once in Buffalo, New York, my whole life had changed. I could not express what I wanted to say and could not understand what I heard. I had to take basketball completely out of the picture. Fortunately, God sent me another *Gui-Ren*, Dr. Bruce J. Nicholason. Bruce just got his first faculty appointment in SUNY, Buffalo, when I needed a Ph.D. thesis supervisor. At the time, I did not know what I was interested in and only felt that I wanted to clone some genes. Bruce did not like the idea and also did not want me to risk my graduate years on a potential fruitless cloning process. But, we finally agreed that I would risk a year to clone a gap junction gene and change direction if necessary. Luckily with Bruce's help, I was able to clone the mouse liver gap junction protein, connexin 26. Gap junctions are channels linking two neighboring cells and providing the two cells with electrical and metabolic coupling by allowing a free passage of small molecules and ions. Connexin 26 is one of the hepatic gap junction proteins that can form such a channel.

Believe it or not, five years of graduate study in a country so foreign to me were also fast. Before I was ready, it was time to make new decisions again. I had wondered during my graduate studies what my research was for. With a shallow mind, I could not see how what I did would benefit mankind. I knew that anything I did as a postdoc might end up to be a major part of my life and I had better do something that could offer me a better drive for my shallow mind. I thought that cancer research might be a good candidate for a lifetime endeavor and whatever I did with cancer might directly benefit fighting against the devastating disease.

One summer day in 1989, I was reading *Scientific American* and the cover story was on P-glycoprotein written by Dr. Victor Ling from Canada. P-glycoprotein is a membrane protein which acts as a drug pump on cell surface and prevents accumulation of anticancer agents in cancer cells. It is the first defense system that cancer cells use to fight against anticancer drugs. Thus, cancer cells that over-express this protein can survive drug treatment and will become drug resistant. The pretty cover picture of P-glycoprotein and the well-written story attracted my attention and I decided immediately that I wanted to study this protein. So, I headed north to Canada to meet my next *Gui-Ren*, Dr. Victor Ling.

The training in Vic's lab was very fruitful. He helped me write successfully a fellowship from NCI of Canada and helped me develop an in vitro system to study the folding of P-glycoprotein. Using this system, I found that P-glycoprotein can form more than one topological structure which may be responsible for its multiple functions. A series of publications on this topic resulted in an offer for a tenure-track position from University of Texas Medical Branch at Galveston.

With a trembling heart to set up a new lab from scratch, I had a different game to play. Fortunately, Dr. Luis Reuss, my Chairman, offered all his help and support. Luis was like a fatherly *Gui-Ren* to me. He provided me with a very nourishing environment. You would respect him for his warm heart and his willingness to help and support. Yet, you would be scared and afraid of him criticizing you for what you have done or will do wrong. He read and criticized every grant application I wrote and nourished my growth. With his help and support, my FIRST award application received a score of 3.4 percentile in the first round competition during the dry season of NIH in 1994. During my stay at Galveston, I continued the study on topological folding of P-glycoprotein and found that it was regulated co-translationally by cytoplasmic factors such as ribosome. I also found that P-glycoprotein has dramatic conformational changes during its catalytic cycle that may involve topological conversion.

After five years in the Gulf of Mexico with hot and humid climate, I decided that it was time to move again to meet my future *Gui-Rens*. I arrived at IUSM on May 1, 1998 with appointments in the Experimental Therapeutics Program in IUCC, Walther Oncology Center, and Department of Pharmacology/Toxicology. I am very glad to be in such an interdisciplinary environment here at IUCC and I have to thank Dr. Len Erickson for his trust and effort in recruiting me. My appreciation also extends to Dr. Henry Besch, Dr. Hal Broxmeyer, and Dr. Steve Williams for their support and their role in my recruiting process. I am now continuing the study on structure-function relationship of P-glycoprotein and I am developing chemosensitizing agents to overcome drug resistance in cancers. My laboratory is also involved in studying translation initiation factors and their role in controlling cell growth. The current family members of my lab include postdoctoral fellows: Qun Chen, Zizheng Dong, Baoguang Han, Yang Liu, and Youyun Yang and graduate students: Zhisheng Huang, Lisa Liu, and Roxana Pincheira. I am sure that the above bosses and lab members are my current *Gui-Rens* and they will help carry me successfully to the next stage of my life.

In conclusion, life has taken care of me very well, although I appear to have been on the run. I have to thank the Lord, my biggest *GUI-REN* for each and every piece of success and honor I

received. I also have to thank my parents and grandparents who always loved and supported me over the long march of my academic career. I appreciate very much for the help, advice, and support from those who played a part in my life one way or another. One last note, after moving to Indianapolis, I met Jingyuan Liu, now my wife, and we were married last Thanksgiving. I now have a real life and a *Gui-Ren* who will travel with me for the rest of my life and the rest of my scientific career.

Flow Cytometry Shared Facility Upgrades & Pricing

The Flow Cytometry shared facility was recently upgraded by the purchase of a new sorter and analyzer. The analyzer (FACScalibur) has been in use for few weeks and the sorter (FACS Vantage SE) should be operational before the end of this month. We are also working on adding two work stations in the computer room to accommodate a heavier demand for off-line data analysis.

The new instruments will allow you to do new things which were not previously available in the lab. Most notably are two added functions. First, the analyzer allows you to use 488nm and 625nm light simultaneously while measuring 6 independent parameters. So it is now possible to read up to 3 colors off the blue line and to add APC for a fourth color from the red line. Second, the sorter is equipped with 3 lasers allowing us to run blue (488nm), red (625nm) and UV light simultaneously and it is possible to collect up to 8 signals (6 colors and light scatter properties) at the same time.

Scheduling of time in the lab is going to change due to the demands of operating, maintaining and assisting users on four instruments at once. When all instruments are up and running, the lab will be open from 9 am till 6 pm. One of the sorters will be available from 9 to 4:30 and the other will be available from 10 to 6. Both analyzers will be available all the time, and provided certain conditions can be met and responsibility accepted by individual users, the analyzers may be available beyond 6 pm.

The most important change which will affect every user is that the lab will now operate with a chargeback mechanism which will be strictly enforced. No one will be allowed to use any instrument if he/she cannot provide the lab with an active account number that can cover the ensuing charges. The chargeback schedule is as follows:

Analysis:

Cancer Center members: \$35/hr

Non Cancer Center members: \$75/hr

Cell Sorting:

Cancer Center members: \$60/hr

Non Cancer Center members: \$100/hr

Chargeback fees will be effective as of July 1, 2000 for Cancer Center members and as of March 1, 2000 for non members. If you have any questions or concerns, please do not hesitate to contact Edward Srour, Ph.D. at 274-0343 or Ms. Sue Rice at 274-7587. Once again, we urge you all to include flow cytometry charges in the budget of all your grant applications if you anticipate the use of flow cytometry for the conduct of your research.

Suk-Hee Lee, Ph. D. , Receives DOD Grant

Suk-Hee Lee, Ph.D., Associate Professor, Biochemistry and Molecular Biology has received a three year DOD Grant for his project entitled **“Role of DNA-Dependent Protein Kinase in Breast Cancer Development/Progression”**.

The overall goal of this proposal is to explore the role of damage signaling & DNA repair factor, DNA-Dependent Protein Kinase (DNA-PK), in the development and progression of breast cancer. The study will test whether DNA-PK activity and its function is altered in breast cancer, which can be used as a prognostic measure of various stages of breast cancer. Also, the study will examine the role of DNA-PK in drug resistance and in damaged DNA repair associated with breast cancer progression.

Christopher Fausel , PharmD, Receives Highest Credentials

Christopher Fausel, PharmD, recently earned the designation of Board Certified Oncology Pharmacist (BCOP) from the Board of Pharmaceutical Specialists (BPS). This is pharmacy's highest credential in the practice of oncology pharmacy. Through board certification, oncology pharmacists demonstrate a defined level of education and training, as well as mastery of the knowledge and skills necessary to meet the public's demand for expert pharmaceutical care.

Dr. Fausel met all the eligibility requirements for certification, including advanced training and/or work experience in oncology pharmacy and passing the 200-item specialty examination. Dr. Fausel was one of 66 individuals granted certification in oncology pharmacy. Congratulations on your achievement.

Lawrence Einhorn, M.D. , Receives Teaching Honor

Distinguished Professor of Medicine Lawrence Einhorn, M.D., will be among the honored at the Founders Day Ceremony on March 5, 2000. Dr. Einhorn will receive the Frederic Bachman Lieber Memorial Award. This is the oldest of Indiana University teaching honors. Dr. Einhorn has been an IU faculty member since 1973 and is being recognized for his dedication and commitment to the education of medical students and residents.

Seminars/Conferences/Meetings

Important message to Cancer Center Members.

Beginning March 1, 2000 the Combined Seminar Series and the Indiana University Cancer Center Grand Rounds schedules will no longer be mailed out to Cancer Center Members. We will continue to send hard copies to the main departmental offices for posting. Instead, the schedules will be made available via the IUCC web page under seminars and conferences and electronic emails will be sent out on a weekly basis as reminders.

Web Page Address

www.iupui.edu/~iucc/

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

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