

Behind The Scenes: A Fruitful Collaboration

by Dr. Amy Keller

In the January of this year, *Biochemical Pharmacology* published the paper, "Opioidergic mechanisms underlying the actions of *Vitex agnus-castus* L." in which last author and ASP member Dr. Jim Wang collaborated with Dr. Norm Farnsworth, among others. The Newsletter interviewed Dr. Wang about this exciting research; he graciously gave us insight into this interesting investigation and tells us what it was like to work with the late, great Dr. Farnsworth.

How did you and Dr. Farnsworth end up collaborating on *V. agnus-castus*, phytochemicals with opioidergic activity, and perhaps other projects?

The collaboration was initiated at the suggestion of Dr. Harry Fong, then head of the Department of Pharmacognosy and Medical Chemistry at the University of Illinois, Chicago (UIC). At that time, UIC/ National Institutes of Health (NIH) Botanical Center, which was founded and directed by Dr. Farnsworth, was looking for ways to determine the pharmacological activity of *V. agnus-castus*. As fate would have it, my laboratory has been running some central nervous system (CNS) and receptor-based assays for years. When we started to test extracts and compounds from *Vitex*, we hit the jackpot. The collaboration was quickly expanded to a number of other plants such as other species of *Vitex*, *Viburnum prunifolium* and related species, *Cimicifuga racemosa*, *Angelica sinensis*, and *Trifolium pratense*. It was one of the most productive and joyful collaborations that I could have possibly formed professionally and personally.

Who in your laboratory carried out the research?

Two former graduate students were instrumental in carrying out the *Vitex* study. Dr. Jian Lu, who is now a senior scientist with GlaxoSmithKline, started the project. Dr. Donna Webster, who works at Herbalife as a Manager of Scientific Affairs, then took over and really made a significant contribution to the understanding of *Vitex* pharmacology. This publication represents a part of her dissertation entitled "Botanical, chemical, genetic, and pharmacological studies of *Vitex agnus-castus* L." On the photochemistry side, Dr. Farnsworth's colleagues Drs. Shao-Nong Chen and Guido Pauli prepared and chemically characterized extracts and compounds that were used in the study.

Could you provide a brief explanation of the work and results in your own words? In what way are the data in your paper new?

In this study, we first confirmed the affinity of *Vitex* extracts to certain opioid receptors, namely the mu and delta opioid receptors. We have reported affinity previously; however, it is not known what kind of functional activity they exhibited. In the study, we demonstrated that some of fractions and compounds activate these two opioid receptors. As discussed in the paper, agonistic activity can be beneficial in certain medical conditions.



DR. SHIXIN DENG

Dr. Farnsworth and Dr. Wang, right after Dr. Farnsworth's acceptance speech for the ASP Research Achievement Award in 2005.

What impact does this research have on natural product science?

Probably not too significant by this one publication alone, unless somebody is interested in *Vitex*. However, my approach to the natural product pharmacology is less on high-throughput screening, but focuses more on activity-based pharmacology that addresses each ethnomedical claim from different angles. Each plant is going to have thousands of constituents. There will be some hits and misses in many assays if conditions are not controlled. However, if one can design pharmacological studies from different levels and even different receptor systems, and when net outcomes start to corroborate with each other, the effect becomes more reliable and worthy of additional studies. With *Vitex agnus-castus*, we have studies ranging from genetic and epigenetics, to receptor pharmacology, and in vivo studies. We can start to put pieces of this puzzle together.

Is there a notable story or interaction with Dr. Farnsworth that occurred during this work? In general, how did working together on this research help further your own work in natural products?

Let me start with my first meeting with Dr. Farnsworth. I joined the faculty of UIC College of Pharmacy in 2001, but it took almost two

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DR. NORMAN FARNSWORTH

Dr. Wang group photo in the Atkins Garden at UIC.
Front, From left: Cheng Yang, Pradeep Shukla, Yingjian Li, Lei Tang, Terry Chen, Z. Jim Wang.
Back: Jian Lu, Peter Nissan, Donna Webster, Mee-Ra Rhyu, Divya Iyer.

years before I finally talked to him. He had this “bigger than life” fame topped off with his trademark Marsh-Wheeling cigars, which can really scare a new assistant professor! One day, I was talking with Dr. Harry Fong about our opioid research and Harry immediately suggested that we should meet Norm. My first reaction was how to make an appointment. To that, Harry laughed aloud and led me straight into Norm’s office without checking with his assistant or even knocking on the door. Quickly, I learned how easily approachable this scientific giant was.

I was given a key to his office for my involvement with *Phytomedicine* and NAPRALERT. However, the key was essentially useless, as his door was almost always left unlocked. In fact, he preferred people come into his office without knocking as it would be too much distraction (and indeed a big effort walking across from his large office to answer the door). Those who did knock were often met by his answering “go away.” But even the first year graduate students quickly figured out it really meant, “come in.” For those who noticed the Chinese characters on his business card, his three-word Chinese name literally meant “sick

and tired of being bothered.” However, behind his serious look and tough critiques, he had a warm heart that was always there for everybody who came to seek support, consultation, collaboration, or a \$1 bet on any current affairs big or small. While going into his office was effortless, getting out might not be so easy, especially if the purpose was to discuss some data, manuscript, or grant applications. Norm was critical on even the best results or writing, which really made one think and work harder.

What is your lab’s motto?

I have not thought much about a motto, and it is certainly not something that we hang on the lab door. (Thinking about it, we probably should). But one thing I learned when I was a student at University of California, San Francisco, was the brave attitude of “capable of doing,” no matter how difficult the task may be. This is one teaching I hope every graduate and postdoc will carry away when they leave my laboratory. It is especially useful in dealing with natural products since they are so complicated. But if one is careful and clever, there are always some methods that we can design to study them. ■