

Behind the Scenes in Pharmacognosy

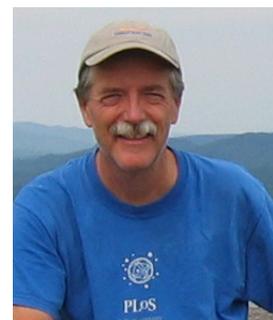
The Curious Quassinoids

by Ms. Amy Keller

In the March 2009 *Journal of Natural Products* honorary issue to Dr. David G. I. Kingston, the article entitled, "Quassinoid inhibition of AP-1 function does not correlate with cytotoxicity of protein synthesis inhibition" by John A. Beutler, Moon-Il Kang, Francis Robert, Jason A. Clement, Jerry Pelletier, Nancy H. Colburn, Tawnya C. McKee, Ekaterina Goncharova, James B. McMahon, and Curtis J. Henrich, was published. The *Newsletter* interviewed first author and ASP member Dr. John Beutler, who took time out his busy schedule to give us insight into those unique compounds, the quassinoids.

How did you become interested in the bioactivity of quassinoids?

We screened both pure compounds and plant extracts in an assay for inhibitors of function of the transcription factor AP-1. There were two pure quassinoids from the NCI repository which were active, and a bunch of plant extracts from the Simaroubaceae, the only family known to make this type of compound.



Dr. John Beutler

Who in your laboratory carried out the research?

Screening was done by a Johns Hopkins master's student, Ms. Katie Ruocco, who worked in Dr. Nancy Colburn's lab and then came upstairs to run the assay. A Korean postdoc, Dr. Moon-Il Kang, in Nancy's lab, did most of the detailed characterization of the compounds, quassinoids and otherwise. Dr. Jason Clement, a postdoc and former graduate student of Dr. David Kingston, both ASP members, did bioassay-guided fractionation of an extract under fellow member Dr. Tawnya McKee's guidance. When we realized that we needed backup in the area of protein synthesis, I contacted Dr. Jerry Pelletier at McGill, and his postdoc, Dr. Francois Robert, ran assays to investigate that aspect of things. I was the traffic cop, organizer, and manuscript drafter.

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?

A particular subset of quassinoids appeared to block the function of the transcription factor AP-1. The novelty was in identifying a few quassinoids that seem to have a different effect on cells than the very cytotoxic ones which went through clinical trials many years ago.

What impact does this research have from a health perspective?

It is hard to say at this time. Several well-known quassinoids failed in clinical trials years ago. It is not clear that protein synthesis inhibitors are going to be useful drugs for cancer. ASP member Dr. John Pezzuto's lab explored quassinoids a few years ago and found new biological activities. The basic point of the paper is that quassinoids probably do several things besides inhibiting protein synthesis in a nonspecific way. If we can tease those other mechanisms away from protein synthesis inhibition, we may have more useful drug candidates to test in cancer.

What is a favorite nonscientific activity of your lab?

Paintball, picnics, and the occasional hike on the Appalachian Trail.

What is your lab's motto?

A random saying that found its way onto the chalkboard in the lab was, "Once in a row isn't enough." Meaning, you have to repeat a result to have any confidence in it.

What is your greatest extravagance in the lab?

Government employees do not have extravagances!

