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THE CHALLENGE OF ACADEMIC PHARMACOLOGISTS: MEETING THE EDUCATIONAL NEEDS OF GRADUATE PROGRAMS AND THE HEALTH CARE PROFESSIONS

Edward D. French, Ph.D.[1]
Department of Pharmacology
University of Arizona
College of Medicine
Tucson, AZ 85724

Running Title: Challenges of academic pharmacology

Corresponding author: Edward D. French, Ph.D.
Department of Pharmacology
University of Arizona
College of Medicine
Tucson, AZ 85724

Tel. 520-626-4359
Fax. 520-626-2204
Email. efrench@u.arizona.edu

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Pharmacologists belong to a special fraternity, one whose members love to study drugs, even though we may have highly individualized viewpoints about what aspect of drug action delights our intellectual curiosities. Still it is this passion to understand everything about a drug that drives our need to uncover the essence of a chemical's effect on living cells and tissues, and ultimately how it exerts its therapeutic benefits. In this sense pharmacology is a discipline key to the health sciences in that it bridges basic and clinical endeavors, as well as between professional practices (Taylor, 2003). Over the past hundred years, pharmacologists have discovered breakthrough after breakthrough in the treatment and diagnosis of disease. Notwithstanding these accomplishments, there are still those who suggest that this rich scientific discipline may have seen its time. Some have opined that our discipline's very existence may be subsumed by newer more trendy scientific pursuits and that pharmacology will finally be viewed simply as just another amorphous biological science. Couched within this recurring discussion is also the notion that systems, integrative, or what some refer to as functional pharmacology has been victimized by the new "omic" boys on the block, and that what is fondly referred to as classical pharmacology may be an endangered species spiraling into its own ultimate demise. While I disagree with this general premise, there is some kernel of truth to it when one examines the present state of graduate training in pharmacology. The distinction between the research endeavors of faculty in our discipline and those in cancer biology, medicinal chemistry, molecular medicine and neuroscience often becomes ill-defined.

In fact there have been strong currents of change in our discipline. These changes that might be viewed as threatening, and the newer high-tech methodologies that are seen as encroaching, are in fact the sources of energy that will fuel the future needs and importance of pharmacology and the training of future pharmacologists. Ultimately, the success of every new lead candidate will depend upon its demonstrated safety and effectiveness in the clinic. Even though our continual pursuits for magic bullets will flourish and yield discoveries to satisfy our wildest expectations, we are also faced with a dichotomous challenge in our role as educators

and mentors of the next generation of pharmacologists and health care professionals. These two groups have vastly different needs in their pursuit of those skills necessary to achieve their goals, and oftentimes their potential employers have vastly different expectations. Will we be able to educate those wishing to carve out careers at the highest levels of research and development? Yet at the same time will we be able to recruit students for careers in academia and provide them with the tools needed to be successful researchers but also to mentor future pharmacologists and to educate the nation's future health care providers?

Like most of my baby boomer comrades, my introduction to pharmacology took place in an era where the discipline was principally oriented to the functional consequences of drug action. We were trained to become the specialists that would make the informed judgments as to the potential utility of a new chemical entity as a therapeutic agent: to understand and interpret system responses in disease and therapy. Thus, as a graduate student in pharmacology in the early 1970's much of what I learned about pharmacology in the basic and clinical arenas was centered on the *in vivo* approach to a research problem. Much of what we gleaned from the formal coursework in pharmacology was of a therapeutic nature, with a recital of the usual litany of indications for the use, mechanisms of action, ADME, side/adverse effects and contraindications. Fortunately, this experience prepared me and many of my contemporary academic pharmacologists well for a future life as a scholar and teacher in colleges of medicine, pharmacy and nursing. But what of today's aspirants to our discipline? What approach will be needed to prepare them? It is mind boggling to comprehend that current technology is capable of screening hundreds of thousands of compounds in a single run, and even more mind boggling as to how the new pharmacologists will need to not only master the molecular language of the cell but also to construct the model systems necessary to prove the safety and efficacy of thousands of new chemotypes. I have always believed that the younger generation seems more attuned to marketplace needs than we either recognize or admit to. These "kids" come to our programs having been schooled in reductionist biology, and they are keenly perceptive of the job opportunities available to those with a grasp of the essentials of this miniaturization. They are

aware that molecular biology and bioinformatics are adding new important dimensions to drug discovery, and as such they are demanding graduate training at a level that will provide them the knowledge base and technical armamentarium to be competitive in a pharmaceutical world that increasingly needs individuals who can interpret the complex data sets that are produced in profusion. In response to that demand, graduate programs, like ours, have adapted their curriculum to emphasize the importance of the "new" biology in drug discovery and development. If we did not, the viability of pharmacology graduate training programs would be at stake. However, if we are not careful our exuberance to embrace the new might cause us to either knowingly or unwittingly discard some important elements inherent to integrative or systems pharmacology.

So, is there any wonder then that, contrary to economic principles, training in "classical" pharmacology became scarce both in supply and demand? Might we even see a time when genomics, proteomics, metabolomics, micoarrays, and informatics supplant classical pharmacology? I doubt it. In fact, I suspect the opposite. Recent trends, again driven primarily by the private sector indicate otherwise (Koppel, 2003). A quick perusal of the employment advertisements in scientific journals and the comments I have heard made by speakers from industry suggests an increasing need for those who not only understand the newer technologies, but who also have the skills to guide a molecule through the intricate network of assays and biological test systems to its ultimate use as a pharmacotherapeutic (Preutsch, 2002; Cockett, 2003). Moreover, it is industry that has raised its voice to the academic community to emphasize the need for pharmacology graduates who can think critically about the relevance of animal models to the human clinical situation rather than have a mastery of technical skills in a particular experimental model (Kling, 1999; Preutsch, 2002). Still, it remains to be seen whether industry will also dedicate more resources to address this need especially in light of the huge financial commitments that they need to make for state of the art robotics and computational methodologies. Nevertheless, we can hope that the following question posed in a recent big Pharma ad is a harbinger of positive changes in this regard: "In vivo pharmacologists–looking

for a challenge?" A speaker from a large multinational consumer products/pharmaceutical company made the point in no uncertain terms at a past graduate student seminar that knowledge of whole animal systems pharmacology will be an essential element to their success in the industry. A report out of a meeting sponsored by the National Institute of General Medical Sciences on training programs in pharmacological sciences further emphasized the importance of assuring scientific diversity in pharmacological research training (Preutsch, 2002). Thus, as there is resurgence in the demand for the functionalist, the marketplace is poised to once more exert its influence on graduate student behavior. The students will certainly take notice and in response our training programs will need to re-adapt and incorporate more integrative-systems scenarios into the curriculum. In fact, it is in our best interests to begin now to revamp our educational goals in anticipation of this future demand. One simple approach may be to have incoming students rotate through at least one laboratory which utilizes integrative/systems methodologies. Another approach might be akin to a cafeteria whereby a minimum number of laboratory exercises using *in vitro*, *in situ*, *in vivo* and several newer technological test systems are made available to the student for their choosing. Although there are students who come to the discipline with a focused agenda and well-delineated career goals, such diverse experiences would at least give them a glimpse of the importance of other techniques in the process of drug identification and development. However, we should not hesitate where appropriate to convey to our students what we have learned through our own experiences that more often than not trendy research activities may not reflect medical needs. Moreover, we will also need to foster in our students a recognition of the growing importance of working in a team, developing time management skills, and the necessity of mastering the skills required for effective written and verbal communication.

By adequately preparing our graduate students for success in the practice of the art and science of pharmacology, we may have inadvertently failed, however, to identify the next cadre of pharmacology faculty who will be needed to educate our future health professionals. This is a challenge that we currently face, but one which may not be met so easily. As the chairperson of

a large graduate program it has become evident to me that fewer and fewer applicants show any inclination for careers in academia. My colleagues in other graduate programs have made similar observations (FASEB, 2003). The current cohort of pharmacology graduate students seem to have an expert's understanding of the limitations of becoming an academic professional, and they would rather see themselves in other venues where the perceived demand and rewards for their scientific prowess is escalating rapidly. Once into their graduate studies, many openly profess the myopic view that they have no interest in the therapeutic aspects of drugs, and furthermore that they cannot understand what relevance courses in medical pharmacology and systems physiology have to their future career goals. Some of these students are so strident in their quest for the reductionist view of drug action that they see only the proverbial trees but not the forest. They know the myriad details of receptor activation and downstream transduction processes, but do not know, and have little interest in learning, what the consequences of receptor activation are for cardiac contractility or systemic vascular resistance, for example. There seems to be little realization that molecular reductionist studies in isolated tissues cannot predict the integrated response in the whole animal. Somewhere in the evolution of how we teach our discipline there has been an erosion in our conveyance of the belief that it is the *in vivo* studies that will show how medications work in patients. Thus, all too often we graduate students with an advanced biomedical degree, but without that global view of pharmacology that would be requisite for them to serve as educators of future doctors, pharmacists or nurses. How can you teach therapeutics in the absence of knowledge about disease states, or at least a solid grounding in physiological systems? Traditionally, pharmacology-trained faculty have long been the purveyors of the essential knowledge of therapeutics that needs to be taught in schools of medicine, pharmacy and nursing. However, if for the lack of the essential element, the motivated faculty instructor with a clear vision of the forest, we will be hard put to accomplish this educational mission. Current economic pressures exerted on clinical faculty, both MDs and PharmDs, have also led to a reduction of their participation, or at least a desire to be integral players, in basic biomedical science curriculums. Still, it is imperative that students in the

health professions need to pass their board certification exams, advance through their clinical years, and become competent practitioners. If they fail along the way for a perceived lack of adequate training in their basic science subjects, it will only be a matter of time that the relevance of that faculty member's department to the institution will be questioned.

Unfortunately, it is difficult to see a quick fix to solving this dilemma. As one of my colleagues noted: The importance of what we do derives from its relevance to the development of rational therapies for human disease. Thus, for those graduate students already in our programs we should cajole them to form an appreciation for the clinical condition for which drugs are used and that their life's scientific endeavors will be directed toward developing therapies to correct physical and psychic maladies. We can encourage the faculty who teach our graduate courses to incorporate a more systems and integrative view of drug action, even when conveying the complexities of second messenger systems, apoptosis, nuclear receptors, growth factors, etc. For some faculty this will require teaming with a colleague who has the more global view of systems pharmacology; an approach that gives a strong message to the student. We can also emphasize to our students the importance of seeing the big picture in their own scientific pursuits. How much they take the message to heart still ultimately rests in their hands. Although our graduate programs are always searching for the best and the brightest, we should actively recruit those students who express an interest in becoming system/integrative academic pharmacologists. As our institutions are attempting to become more diverse so should our graduate training programs. It will be imperative that department heads and review committees have to be convinced that those faculty with a zeal for teaching basic sciences should be given incentives for honing those skills and be rewarded for their educational accomplishments, especially in decisions of tenure and promotion. The chatter about and movement toward mission-based budgeting in many schools will provide a mechanism whereby hard monetary support will be given to faculty whose principal activity is serving the institution's educational needs. These efforts, if successful, will likely convince more pharmacologists to embrace the broader, but historical, view that pharmacology is still a critical link between the basic and

clinical sciences. Hopefully, there will be sufficient opportunities in graduate programs to meet the demand.

While risking to be labeled a Pollyanna, I expect the next 100 years of pharmacology will produce unimaginable accomplishments in drug development and therapeutics. In large part because of the avalanche in the terrain of molecular biology, there will be a resurgent demand for pharmacologists to move the indefinite new discoveries to clinical applications. The resulting increased pervasiveness of pharmacotherapies in our society will also generate vast opportunities for pharmacologists in other arenas such as the print and electronic media, think tanks, government agencies, and public relations. In particular, our educational enterprise, from secondary to post-secondary institutions, will be a major beneficiary of the pharmacologists who can effectively articulate the intricacies of therapeutics and health. The combination of these forces will drive us to the next level of scientific discovery and lead to a renewed interest by students and graduate programs in the integrative or the 'classical' approach to the understanding of drug action. It is going to be an exciting time for our science and its practitioners if we can meet the challenges.

REFERENCES

Anonymous (2003) Keeping the identity of pharmacology strong for the future. Mol Interv 3: 6-10.

Cockett M (210 10 003) The systems biology challenge. Drug Discovery and Development 6: 13.

FASEB News (2003) 36: 11.

Kling J (1999) Calling all pharmacologists. Industry seeks the classically trained. The Scientist , 13: 7-8.

Koppel T (2003) Pharmacology's Resurrection. Drug Discovery and Development 6: 28-32.

Preusch PC (2002) What is training in the pharmacological sciences? Molecular Interventions 2: 270-275.

FOOTNOTES

[1]Dr. French is a Professor in the Department of Pharmacology, University of Arizona, College of Medicine. He directs the second year medical course, The Pharmacological Basis of Therapeutics. He served for 8 years as Chairman of the Interdisciplinary Graduate Program in Pharmacology & Toxicology and is presently the Director of the Graduate Program in Medical Pharmacology.