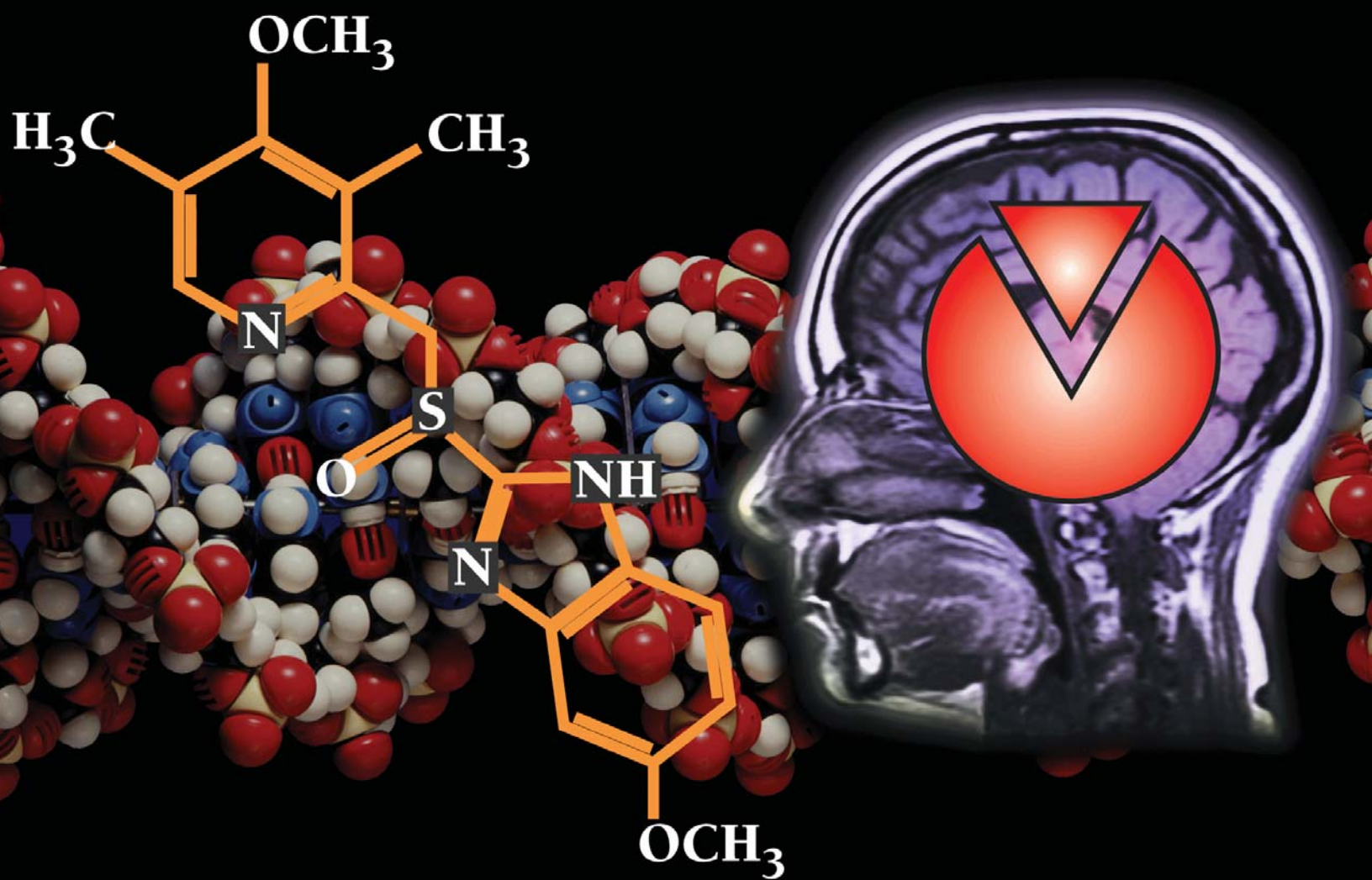


Explore Pharmacology

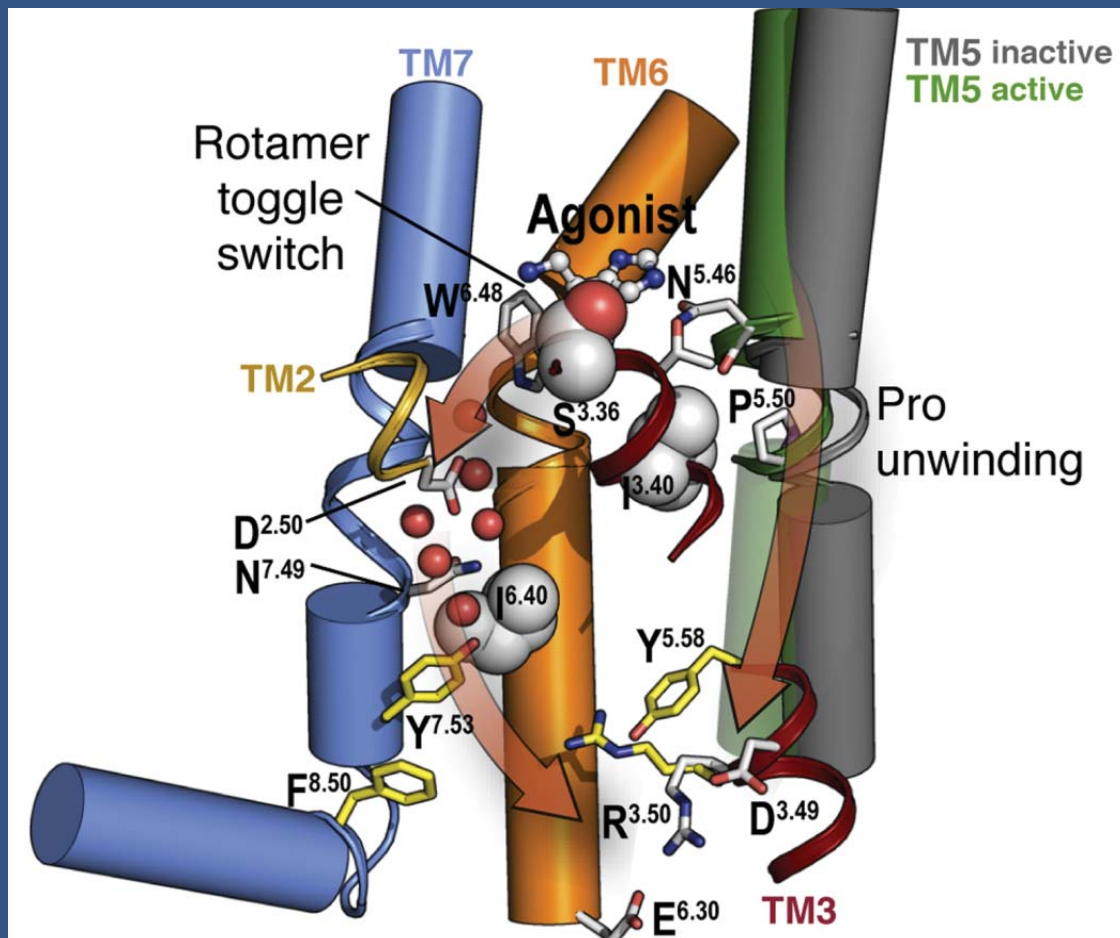
Graduate Studies in Pharmacology



American Society for Pharmacology
and Experimental Therapeutics

www.aspet.org





Model of G-Protein Coupled Receptors

Sansuk K et al. (2011) *Mol Pharmacol* 79: 262-269



Opportunities and Challenges in Pharmacology

If you are a highly motivated and inquisitive student who is seeking a career in the biomedical sciences and have a strong interest in making a major contribution to the understanding of both novel and current disease processes and the development of new therapies – then **Explore Pharmacology**.

In general terms, pharmacology is the science of how drugs interact with biological systems. It is a science that is basic not only to medicine but also to pharmacy, nursing, dentistry, and veterinary medicine. Pharmacological studies range from those that examine the effects of chemical agents on subcellular mechanisms, to those that deal with the potential hazards of pesticides and herbicides, to those that focus on treatment and prevention of major diseases.

Pharmacologists also use molecular modeling and computerized design as drug discovery tools to understand cell function. Pharmacology can be studied at all levels, from the molecule to the cell to the organ to the whole animal. New pharmacological areas include

genomic and proteomic approaches to treatment, which together with emerging knowledge of genetic variability will aid in developing personalized medicine. Regenerative pharmacology will accelerate and optimize the development, maturation, and function of bioengineered and regenerating tissues. Computational and modeling approaches have opened whole new ways to study biological systems and the effect that drugs have on them.

In general terms, pharmacology is the science of how drugs interact with biological systems.

Pharmacology integrates the knowledge of many scientific disciplines and thus has a unique perspective for solving drug-, hormone-, and chemical-related problems as they impinge on human health. As it unlocks the mysteries of drug actions, discovers new therapies, and develops new medicinal products, pharmacology inevitably touches all our lives.

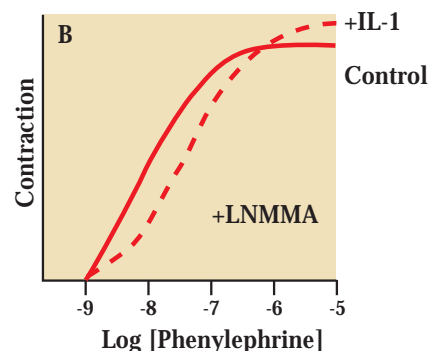
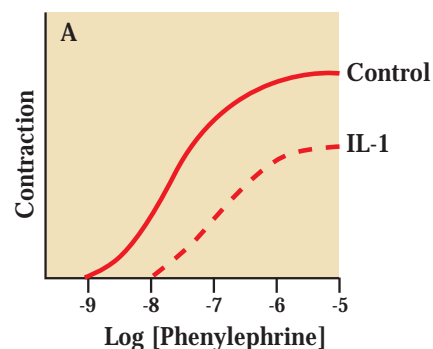


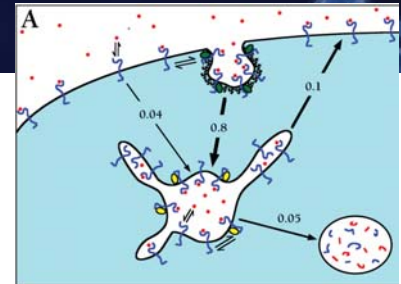
While remarkable progress has been made in developing new drugs and in understanding how they act, the challenges that remain are endless. Ongoing discoveries regarding fundamental life processes will continue to raise new and intriguing questions that stimulate further research and evoke the need for fresh scientific insight.

This booklet provides you with a broad overview of the discipline of pharmacology. It describes the many employment opportunities that await graduate pharmacologists and outlines the academic path that they are advised to follow. If you enjoy problem solving and feel a sense of excitement and enthusiasm for understanding both drug action and the potential of drugs to offer new insights into disease mechanisms, then you have little choice but to...

Explore Pharmacology

This will be the first step into an absorbing, challenging, productive, and rewarding scientific career.





Pharmacology: Its Scope

Pharmacology is the study of the therapeutic value and potential toxicity of chemical agents on biological systems. It targets every aspect of the mechanisms for the chemical actions of both traditional and novel therapeutic agents. Two important and interrelated areas are pharmacodynamics and pharmacokinetics. Pharmacodynamics is the study of the molecular, biochemical, and physiological effects of drugs on cellular systems and their mechanisms of action. Pharmacokinetics deals with the absorption, distribution, and excretion of drugs. More simply stated, pharmacodynamics is the study of how drugs act on the body while pharmacokinetics is the study of how the body acts on drugs. Pharmacodynamic and pharmacokinetic aspects of the action of chemical agents are applicable to all related areas of study, including toxicology and therapeutics. Toxicology is the study of the adverse, or toxic, effects of drugs and other chemical agents. It is concerned both with drugs used in the treatment of disease and with chemicals that may be present in the household, environment, or industrial hazards. Therapeutics focuses on the actions and effects of drugs and other chemical agents with physiological, biochemical, microbiological, immunological, or behavioral factors influencing disease. It also considers how the pharmacokinetics of a drug can change with disease states, where the disease may modify the absorption of a drug into the systemic circulation and/or its tissue disposition. Each of these areas is closely interwoven with the subject matter and experimental techniques of physiology, biochemistry, cellular and

molecular biology, microbiology, immunology, genetics, neuroscience, and pathology. Modern pharmacology goes by many names – chemical biology, drug discovery science, molecular medicine - but regardless of what you call it, research involving the study of drugs is pharmacology.

Modern Pharmacology goes by many names, but regardless of what you call it, research involving the study of drugs is pharmacology.



oral pharmacology ... gene therapy ...
integrated biology ... macromolecular
nistry ... behavioral pharmacology ...
... systems and integrated biology ...
biology ... biochemistry ... behavioral
veterinary medicine ... systems and
physiology ... molecular biology ...
ology ... chemotherapy ... veterinary
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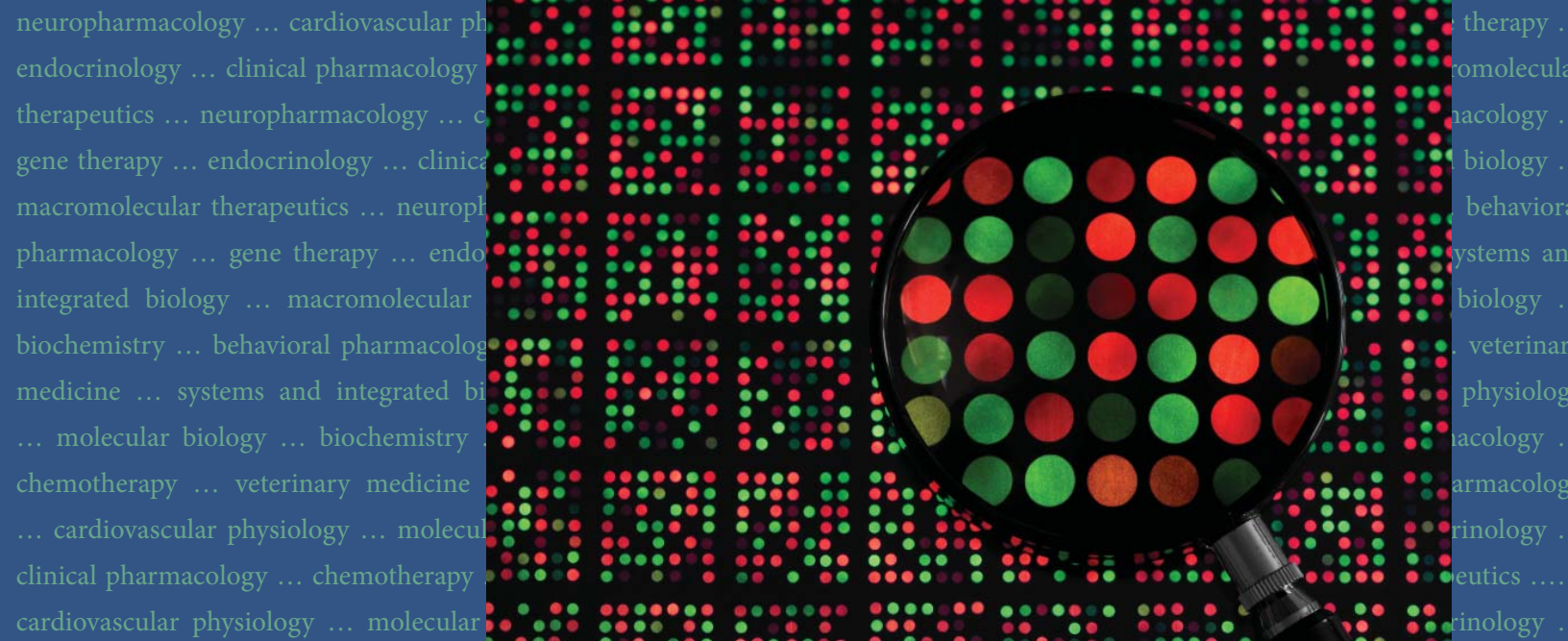
Pharmacology can be further subdivided:

Neuropharmacology is the study of drugs on components of the nervous system, including the brain, spinal cord, and the nerves that communicate with all parts of the body. Neuropharmacologists study drug actions from a number of differing viewpoints. They may probe new ways to use drugs in the treatment of specific disease states of the nervous system. Alternatively, they may study drugs already in use to determine more precisely the neurophysiological or neurobiochemical functions of the nervous system that are modified by drug action. Neuropharmacologists also use drugs as tools to elucidate basic mechanisms of neural function and to provide clues to the underlying neurobiological nature of disease processes.

Cardiovascular pharmacology concerns the effects of drugs on the heart, the vascular system, and those parts of the nervous and endocrine systems that participate in regulating cardiovascular function. Researchers observe the effects of drugs on arterial pressure, blood flow in specific vascular beds, release of physiological mediators, and neural activity arising from central nervous system structures.

Molecular pharmacology deals with the biochemical and biophysical characteristics of interactions between drug molecules and those of the cell. It is molecular biology applied to pharmacological and toxicological questions. The methods of molecular pharmacology include precise mathematical, physical, chemical, and molecular biological techniques to understand how cells respond to hormones or pharmacologic agents, and how chemical structure correlates with biological activity

Biochemical pharmacology uses the methods of biochemistry, cell biology, and cell physiology to determine how drugs interact with, and influence, the chemical “machinery” of the organism. The biochemical pharmacologist uses drugs as probes to discover new information about biosynthetic pathways and their kinetics and investigates how drugs can correct the biochemical abnormalities that are responsible for human illness.



Behavioral pharmacology studies the effects of drugs on behavior and of how behaviors can influence drug effects. Research includes topics such as the effects of psychoactive drugs on learning, memory, wakefulness, sleep, and drug addiction. Research may also study the behavioral consequences of experimental intervention on enzyme activity or brain neurotransmitters and metabolism. Conversely, behavioral pharmacologists also study how various behaviors influence drug-taking.

Endocrine pharmacology is the study of drugs that are either hormones, hormone derivatives, or drugs that may modify the actions of hormones normally secreted by the body. Endocrine pharmacologists are involved in solving mysteries concerning the nature and control of diseases of metabolic origin.

Clinical pharmacology is the application of pharmacodynamics and pharmacokinetics to patients with diseases. This discipline now has a significant pharmacogenetic component. Clinical pharmacologists study how drugs work, how they interact with the genome and with other drugs, how their effects can alter disease processes, and how disease can alter the effects of drugs. Clinical trial design, the prevention of medication errors, and the optimization of rational prescribing have become critical components of the work of clinical pharmacologists.

Chemotherapy is the area of pharmacology that deals with drugs used for treatment of microbial infections and malignancies. Pharmacologists work to develop chemotherapeutic drugs that will selectively inhibit the growth of, or kill, the infectious agent or cancer cell without seriously impairing the normal functions of the host.

Systems and integrated pharmacology is the study of complex systems and whole animal model approaches to best predict the efficacy and usefulness of new treatment modalities in human experiments. Results obtained at the molecular, cellular, or organ system levels are studied for their relevance to human disease through translation into research in whole animal systems.

Toxicology is the study of the toxic effects of drugs and other chemicals. In the context of pharmacology, toxicology involves studying the adverse, or toxic, effects of drugs on development, organ systems, and molecular and cellular processes.

Drug Metabolism is the study of how drugs are changed by the body to make them easier to be excreted, although in many cases, drugs are also changed by the body to be more active or more toxic. Pharmacologists who study drug metabolism look for ways to control how drugs are altered by the body in order to maximize their therapeutic effects and minimize their undesirable side effects.

Pharmacogenetics is the study of how a person's genetic makeup affects their response to drugs such that the drugs might be more or less effective and have diminished or intensified side effects. Drug treatment can then be tailored to each patient using the individual's pharmacogenetic data.

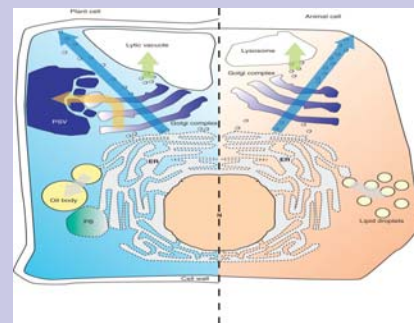
Veterinary pharmacology concerns the use of drugs for diseases and health problems unique to animals.

Often confused with pharmacology, **pharmacy** is a separate discipline in the health sciences. **Pharmacy** uses the knowledge derived from pharmacology to achieve optimal therapeutic outcomes through the appropriate preparation and dispensing of medicines.

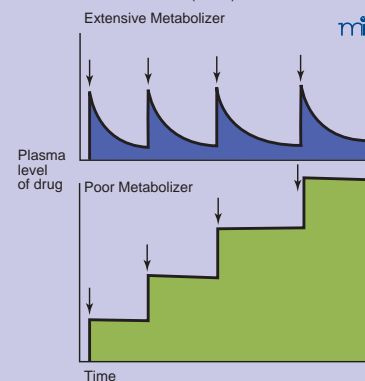
WHAT WILL PHARMACOLOGISTS BE STUDYING IN THE FUTURE?

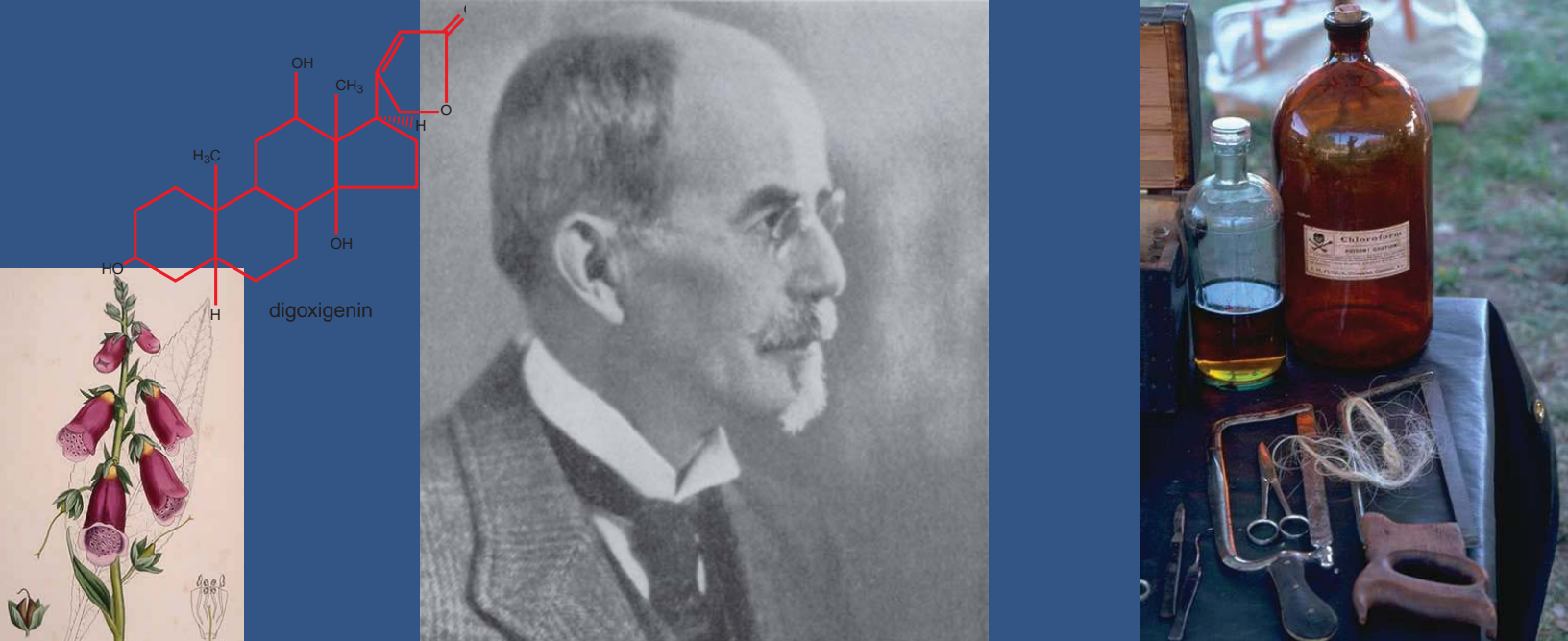
Adverse Drug Reactions
Anticancer & Antiviral Agents
Biological Networks
Combinatorial Chemistry
Developmental Pharmacology
Drug Policy & Regulation
Environmental Pharmacology
Gene Therapies
Immunopharmacology
Individualized Medicine &
Pharmacogenomics

Nanotechnology
New Drug Design & Development
Novel Drug Delivery Systems
Pharmacogenetics
Pharmacology of Aging
Proteomics
Recombinant-DNA Derived Drugs
Regenerative Pharmacology &
Medicine
Traditional and Herbal Medicines



Vitale A and Pedrazzini E (2005) *Mol Interv* 5: 216-225





Pharmacology: Past and Present

Although drugs have been a subject of interest since ancient times, pharmacology is a relatively new discipline in the life sciences.

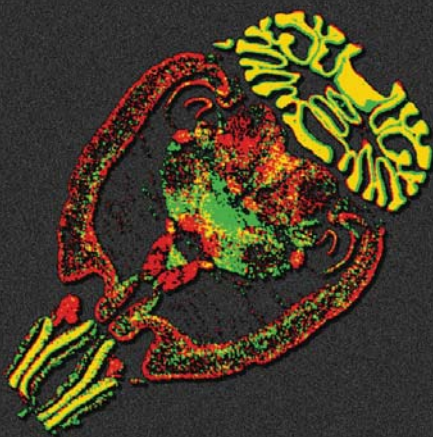
Distinctions between the useful actions of drugs and their toxic effects were recognized thousands of years ago. As people tried plant, animal, and mineral materials for possible use as foods, they noted both the toxic and the therapeutic actions of some of these materials.

The term pharmacology comes from the Greek words pharmakon, meaning a drug or medicine, and logos, meaning the truth about or a rational discussion.

Past civilizations contributed to our present knowledge of drugs and drug preparations. Ancient Chinese writings and Egyptian medical papyri represent the earliest compilations of pharmacological knowledge. They included rough classifications of diseases to be treated and recommended prescriptions for such diseases. While other civilizations made their own discoveries of the medicinal value of some plants, progress in drug discovery and therapeutics was minimal until after the Dark Ages.

The introduction of many drugs from the New World in the 17th century stimulated experimentation on crude preparations. These experiments were conducted chiefly to get some ideas about the possible toxic dosage for such drugs as tobacco, nux vomica, ipecac, cinchona bark, and coca leaves. By the 18th century, many such descriptive studies were being conducted. How drugs produced their effects was, however, still a mystery.

The birth of experimental pharmacology is generally associated with the work of the French physiologist Francois Magendie in the early 19th century. Magendie's research on strychnine-



containing plants clearly established the site of action of these substances as being the spinal cord and provided evidence for the view that drugs and poisons must be absorbed into the bloodstream and carried to the site of action before producing their effects. The work of Magendie and his pupil, Claude Bernard, on curare-induced muscle relaxation and carbon monoxide poisoning helped to establish some of the techniques and principles of the science of pharmacology.

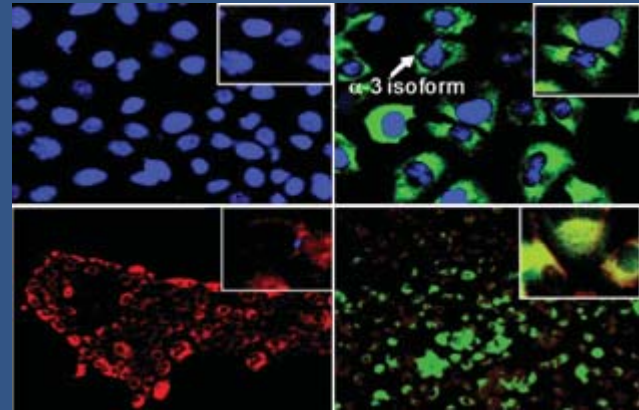
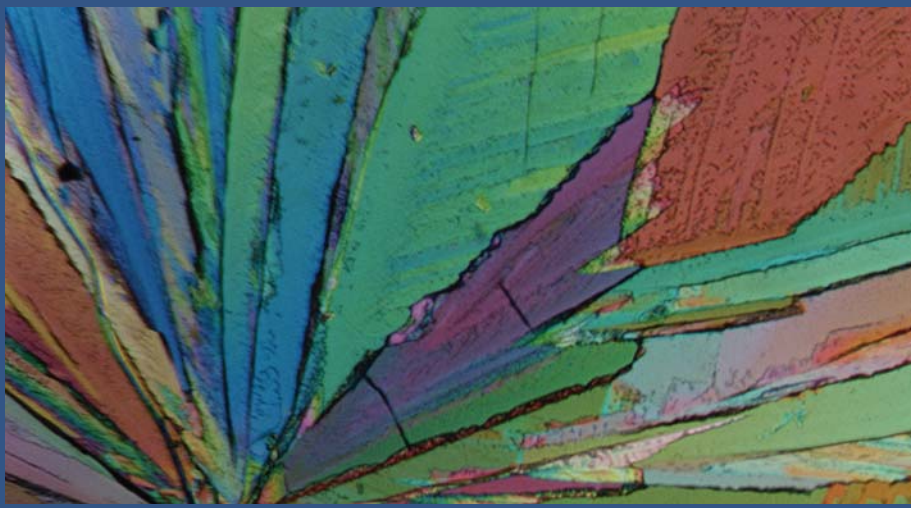
It was in the German-speaking universities during the second half of the 19th century that pharmacology really began to emerge as a well defined discipline. This process began with the appointment of Rudolf Buchheim to teach **material medica** at the University of Dorpat in Estonia. Long taught in medical schools, material medica was concerned largely with questions

about the origins, constituents, preparation, and traditional therapeutic uses of agents used in healing. Buchheim, however, called for an independent experimental science of pharmacology, involving the study of the physiological action of drugs. He established the first institute of pharmacology at the University of Dorpat in 1847.

Among the students who received research training in Buchheim's laboratory was Oswald Schmiedeberg. In 1872, Schmiedeberg became professor of pharmacology at Strasbourg, and over a number of years some 120 students from all over the world worked in his pharmacological institute. His students later occupied 40 academic chairs in pharmacology departments throughout the world.

One of the most eminent of his many distinguished pupils was John Jacob Abel, who brought the new science of experimental pharmacology from Germany to the USA.

In the beginning of the 20th century, Paul Ehrlich conceived the idea of specifically seeking



Newman RA et al. (2008) *Mol Interv* 8:28-35

special chemical agents with which to treat infections selectively and is thus considered the “Father of Chemotherapy.” His work on the concept of the “magic bullet” treatment of infections paved the way for the triumphs of modern-day chemotherapy.

The progress and contribution of 20th century pharmacology were immense, with over twenty pharmacologists having received Nobel prizes. Their contributions include discoveries of many important drugs, neurotransmitters, and second messengers, as well as an understanding of a number of physiological and biochemical processes.

The field of pharmacology in general and the development of highly effective new drugs in particular burgeoned during the last half of the 20th century. This unprecedented progress paralleled similar progress in related disciplines upon which pharmacology builds: molecular biology, biochemistry, physiology, pathology, anatomy, and the development of new analytical and experimental techniques and instruments.

Pharmacology in the 21st century continues to build on the discoveries of the previous century. Obtaining the sequence of the human genome allowed scientists to see where changes might occur in the genome that would affect how an individual responds to drugs. Now it is up to pharmacologists to figure out how to identify those changes in specific individuals to allow the dosage regimen or selection of drugs to be customized to the genetics. Nanotechnology approaches to drug delivery open the door for site-selective delivery and more accurate dosing. As civilization encroaches on the oceans and the rain forests, there are ever more urgent opportunities to identify drugs that derive from those sources. There are still many diseases that we do not know how to treat adequately – cancer, autism, depression, and drug abuse, to name just a few.

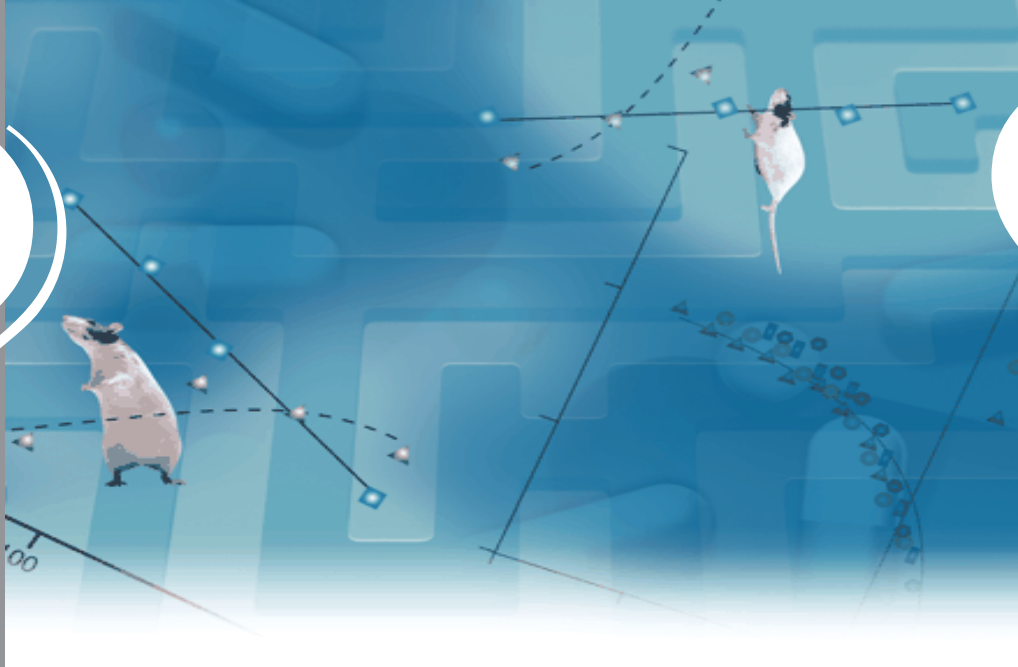




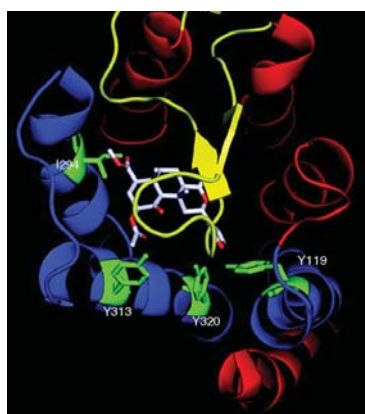
Examples of Questions that Pharmacologists Ask:

- How do drugs act at cell surfaces to alter processes inside cells?
- What points in biochemical pathways are rate limiting and thus potential sites at which drugs act to alter pathways?
- How well do the traditional mechanisms of action for a given drug truly correlate with its biological effects, and do these mechanisms explain all the effects of a drug?
- How can drugs be used to unravel details of biochemical and physiological processes?
- What changes in the brain are responsible for schizophrenia, depression, and autism, and what agents will be most effective in treating these conditions?

Pharmacology encompasses all fields of biomedicine.



- How can drugs with known mechanisms of action be used to learn more about the diseases that they treat?
- How can knowing the structure of a biological molecule be used to design new drugs that will bind to and change the activity of that molecule (e.g., receptor, protein)?
- How do organisms, organs, and individual cells become more or less sensitive to drugs?
- Why do people respond differently to the same drug?
- How does the body terminate the actions of drugs?
- Can effective drugs be made that don't have any side effects?
- What causes Alzheimer's disease and other forms of dementia and can those problems be prevented, halted, or reversed by drugs?



Vortherms TA and Roth BL (2006) *Mol Interv* 6: 257-265



Olivera BM and Teichert RW (2007) *Mol Interv* 7: 251-260



Why Choose Pharmacology?

Ask some students who have!

Comments from students enrolled in graduate programs in pharmacology indicate that they pursue careers in pharmacology primarily because of its biomedical interdisciplinary character and the range of possibilities for conducting interesting research.

- “Pharmacology is everywhere.”
- “Pharmacology is helping to create some of the fastest paced medical advances today. It is exciting to be at the heart of this research.”
- “Pharmacology rocks. Others need to know that.”
- “It gives me a lot of fulfillment to know that the science I am studying is helping to generate significant improvements in medical treatments.”

Many students perceive the flexibility and diversity of pharmacology programs as a key advantage:

- “It allows me to diversify, go into different areas of research, which gives me a job advantage over, say graduates in biochemistry, physiology, or molecular biology.”
- “Pharmacology incorporates so many disciplines – biology, chemistry, genomics, physiology – it was a natural choice after finishing a liberal arts based undergraduate training.”
- “So many fields to choose from.”

When asked if pharmacology differs from other life sciences, most students answered affirmatively. Those who considered pharmacology to be different generally pointed to its integration of other fields, its potential for practical application, and its emphasis on human biomedical advances.

- “Pharmacology has a greater emphasis than other life sciences on eventually finding a practical application for research results.”
- “Not only do we learn pharmacology, we must be proficient in many related fields – biochemistry, physiology, molecular, and cellular biology.”
- “One of the strengths of pharmacology is that it is ‘integrative.’”

Pharmacology has a greater emphasis than other life sciences on eventually finding practical applications for research results.

Career Opportunities

The breadth of pharmacological training opens a wide range of employment opportunities in academic, governmental, and industrial organizations. The increasing need for expertise in studying drugs in living systems indicates that graduates will find employment that allows them to use their own special skills and pursue their areas of special interest.

Pharmacologists who wish to pursue joint teaching and research careers in academic institutions can join university faculties in all areas of the health sciences, including medicine, pharmacology, dentistry, osteopathy, veterinary medicine, pharmacy, pharmaceutical sciences, and nursing. Universities also offer research opportunities in virtually every pharmacology specialty.

Government institutions employ pharmacologists in research centers such as the National Institutes of Health, the Environmental Protection Agency, the Food and Drug Administration, and the Centers for Disease Control. Government laboratories engage in basic research to study the actions and effects of pharmacological agents. The Food and Drug Administration assumes drug safety and regulatory responsibilities.

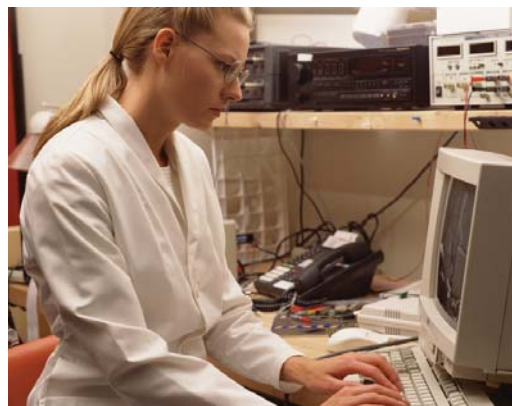
The applications of pharmacology to health and to agriculture have resulted in phenomenal growth of the drug manufacturing industry. Multinational pharmaceutical corporations employ a large staff of pharmacologists to develop products and to determine molecular or biochemical actions of various chemicals; toxicologists determine the safety of drugs with therapeutic potential.

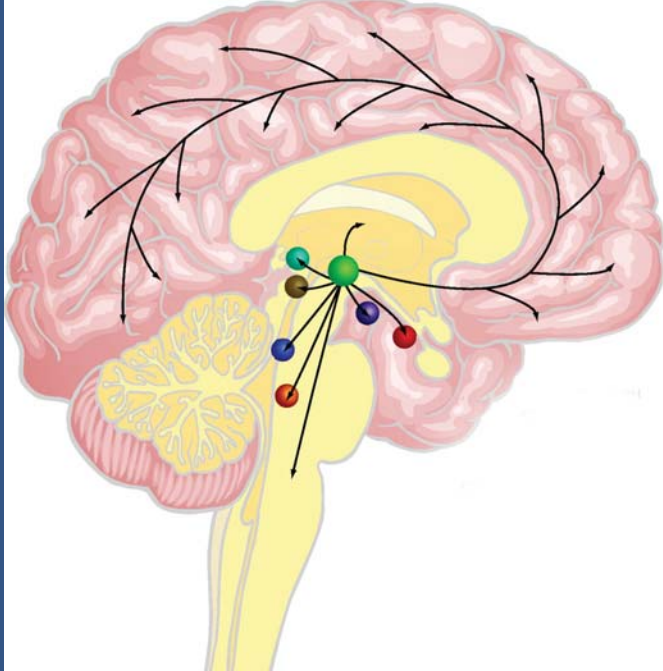
Private research foundations involved in addressing vital questions in health and disease also draw from the research expertise of pharmacologists. Such foundations offer exciting opportunities for pharmacologists in a variety of specialty fields.

Some pharmacologists hold administrative positions in government or private industry. Working in this capacity, they may direct or oversee research programs or administer drug-related programs.

Pharmacologists often work as members of multidisciplinary research groups.

Regardless of the setting, pharmacologists often work as members of multidisciplinary research groups. Collaborating with scientists from many backgrounds contributes to the thrill of entering unexplored realms and participating in discoveries that have an impact on life and health.





Preparing for a Career in Pharmacology

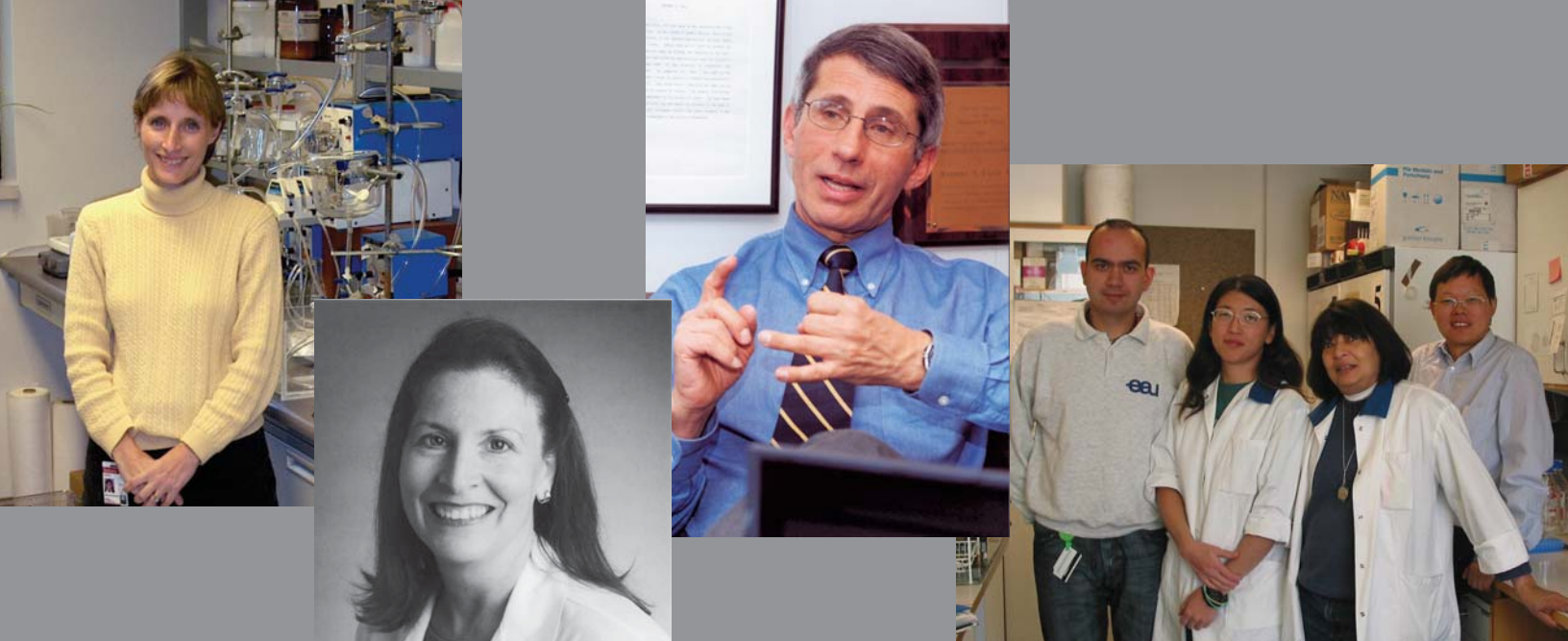
College Years

Since pharmacology is not offered in most undergraduate programs, students are advised to earn a bachelor of science degree in chemistry, one of the biological sciences, or in pharmacy.

Because success in science depends on the ability to communicate clearly and think systematically and creatively, courses in writing, literature, and liberal arts are invaluable. Other undergraduate courses that help in preparing for pharmacology include physics, biology, molecular biology, biochemistry, organic and physical chemistry, mathematics (including differential and integral calculus), and statistics. If your college is among the increasing number of schools offering an undergraduate course in pharmacology, you should also take advantage of this special training opportunity.



Hands-on experience to see how scientists tackle problems is helpful. If you are interested in pursuing a career in biomedical science, get acquainted with professors who have active research programs and inquire about working as a laboratory assistant, either during the academic year or during the summer. Information about summer job opportunities in a laboratory can be obtained by contacting student placement services, work-study programs, or student research programs. Also, the American Society for Pharmacology and Experimental Therapeutics has a summer fellowship program for undergraduate research opportunities in pharmacology departments. Information on this program can be obtained from the Society office.



Graduate Study

To become a pharmacologist, a PhD degree or other doctoral degree is required. PhD programs in pharmacology are located in medical schools, pharmacy schools, schools of veterinary medicine, schools of osteopathy, and graduate schools of biomedical sciences. If you would like to obtain a medical degree as well, inquiries should be made about combined MD/PhD programs. Earning a PhD degree generally requires four to five years. Earning an MD/PhD degree takes about two years longer.

In addition to having course work prerequisites, each program requires that certain performance standards be met with regard to grade-point average and scores on the Graduate Record Examination. Assistantships and fellowships including stipends and tuition fees are generally offered. Highly qualified students, including women and minorities, are actively recruited.

While programs vary substantially, the PhD curriculum typically includes both didactic courses and research-based studies. Courses in cellular and molecular biology, biochemistry, physiology, neurosciences, statistics, and research design are intended to broaden and deepen scientific backgrounds. In addition, a solid foundation in the pharmacological sciences is provided. This may include basic pharmacology, molecular pharmacology, chemotherapy, and toxicology, as well as specific discipline and organ-system based courses such as cardiovascular pharmacology, renal pharmacology, and neuropharmacology. The major portion of the graduate degree program is, however, devoted to laboratory research. The primary goal is to complete an original and creative research study that yields new information and withstands peer review.

Because each program has different areas of emphasis, it is important to investigate several programs, keeping in mind how they relate to your own areas of interest.

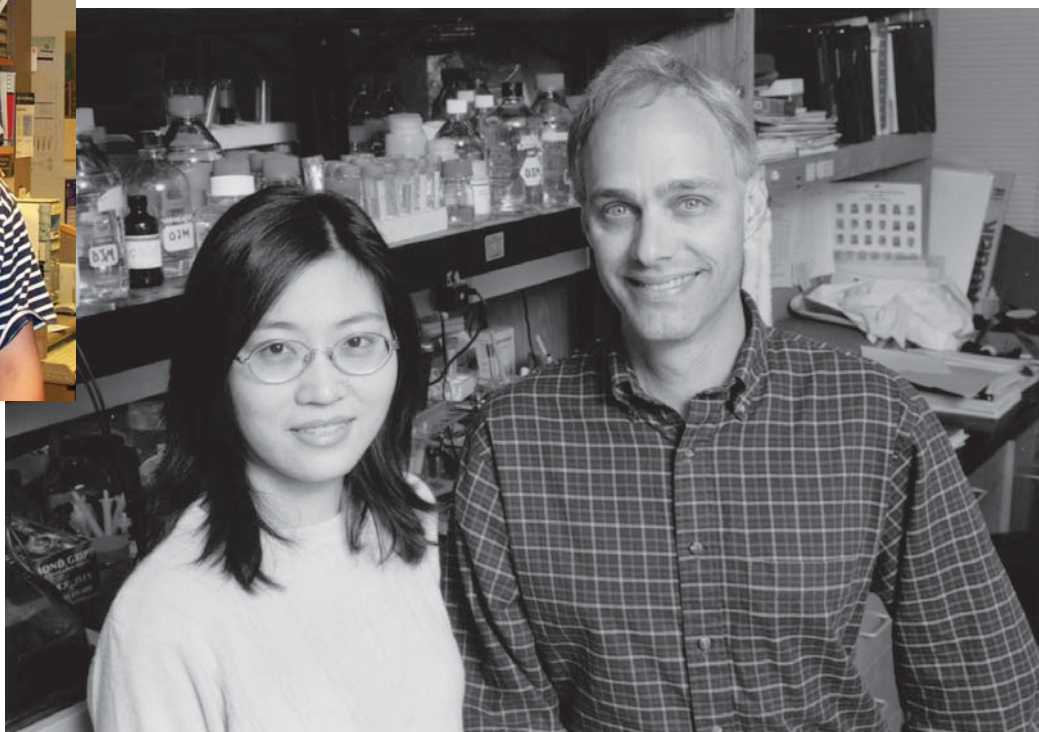
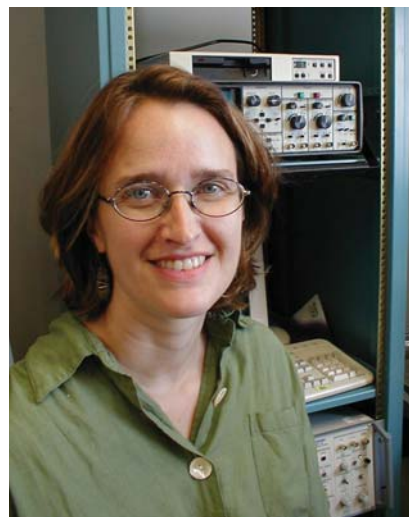
Thorough inquiries should be made into the following:

- Areas of research expertise among faculty
- Publications of faculty
- Research funding of faculty
- Student flexibility in choosing research projects
- Availability of training grants and stipends designated for graduate student support
- Extent to which research efforts are independent or linked by interdisciplinary team approaches
- Positions held by previous graduates.



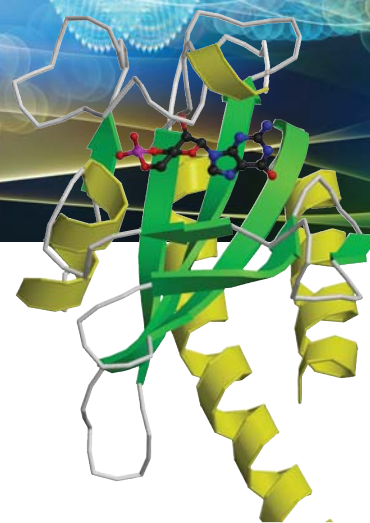
Postdoctoral Research

Before taking permanent positions, most PhD graduates complete two to four years of further research training. This provides the opportunity to work on a second high-level research project with an established scientist, to expand research skills and experience, and to mature as a scientist. The combination of graduate and postdoctoral experiences enables young investigators to contribute new perspectives on unique areas of research. Salaries and fellowships for postdoctoral scientists reflect research experiences and expectations of the studies to be conducted.





Achievements and New Frontiers

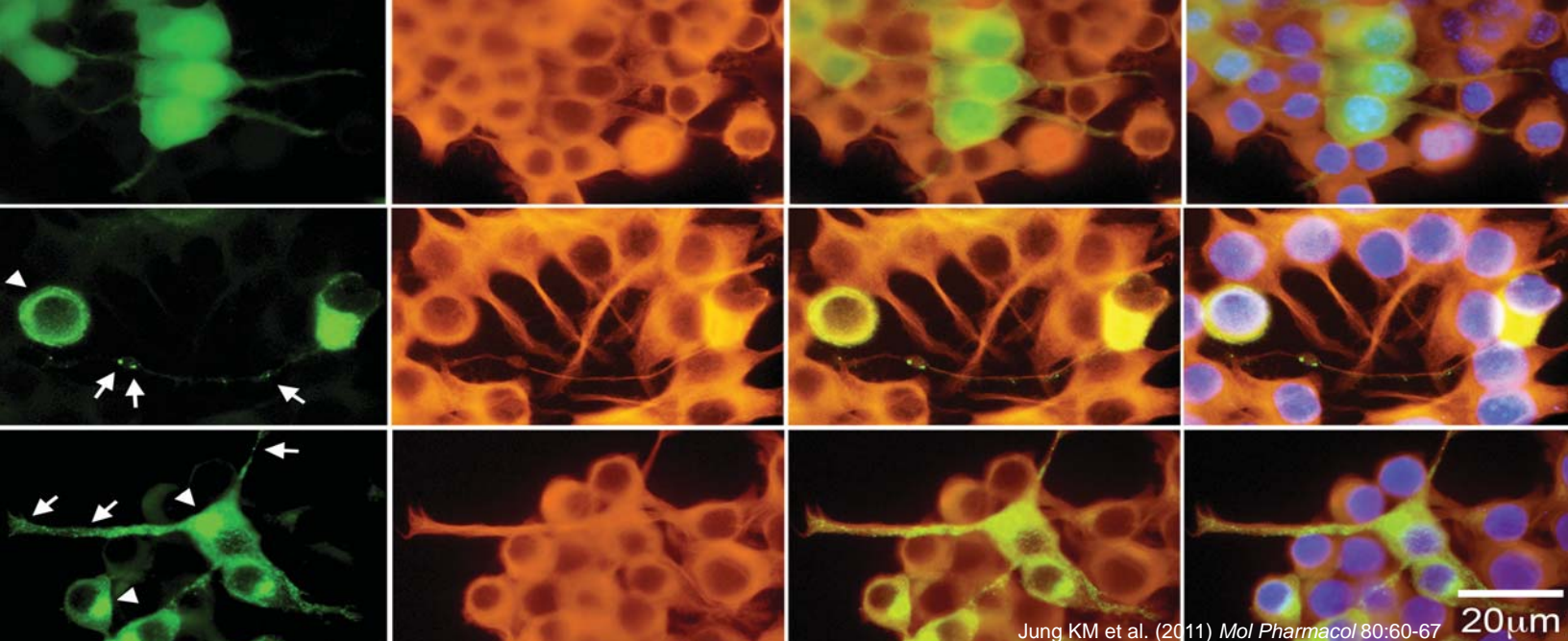


Research in pharmacology extends across a wide frontier that includes developing new drugs, learning more about the properties of drugs already in use, investigating the effects of environmental pollutants, using drugs as probes to discover new facts about the functions of cells and organ systems, and exploring how genetic variation impacts drug disposition and efficacy.

A major contribution of pharmacology has been the advancement of knowledge about cellular receptors with which hormones and chemical agents interact. Through this research an understanding of the process of activation of cell surface receptors and the coupling of this response to intracellular events has been made possible. New drug development has focused on steps in this process that are sensitive to modulation. Identifying the structure of receptors will allow scientists to develop highly selective drugs with fewer undesirable side effects.

Out of this research has come a multitude of discoveries and achievements: advances in antibacterial and anticancer chemotherapy that have played a major role in reducing infectious diseases and producing cures for certain types of cancers; development of drugs for the treatment of hypertension, congestive heart failure, and cardiac arrhythmias; effective treatments for asthma; and development of drugs that control pain, anxiety, and chronic psychiatric disorders with far fewer unpleasant side effects.

A second major contribution that is currently receiving renewed attention is the area of pharmacogenetics/pharmacogenomics, i.e., how variation in genetic information impacts

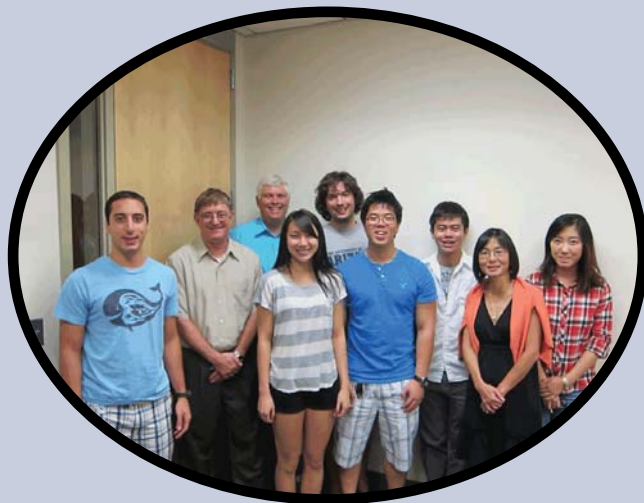
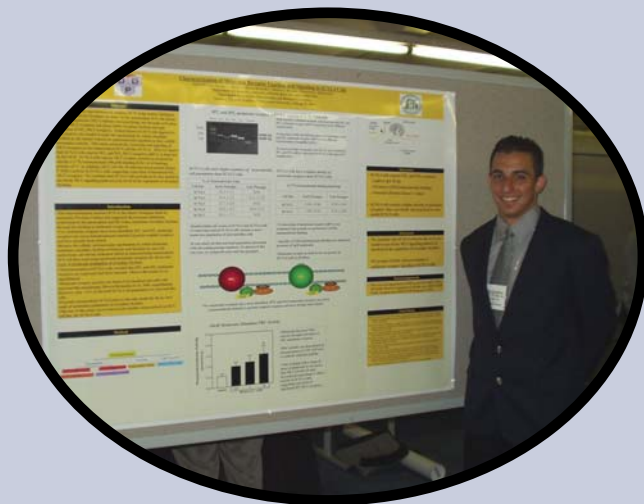


how a particular drug is adsorbed, metabolized, and/or eliminated, as well as how the particular drug interacts with its cellular targets. This field, which has experienced a major boost since completion of the human genome project, offers considerable promise for the development of novel therapeutics, optimized drug trials, and medicine tailored to each person's response.

Over the next several decades, the knowledge emerging from pharmacological studies will have an immeasurable impact on society. There are still many diseases that we do not know how to treat adequately – cancer, autism, depression, drug abuse, to name just a few. Major challenges include developing better drugs for treating AIDS and other viral diseases, cancer, drug-resistant bacteria, and preventing rejection of organ transplants. A better understanding of the potential toxic effects of abused substances on the fetus and on the heart, brain, and other organ systems will evolve. Research on drug addiction holds the promise of developing new treatments for drug dependence and withdrawal as well as identifying individual differences that may influence a person's susceptibility to drug abuse. Gene therapy is another new focus of pharmacological research. The possibility of developing gene products that could alter the course of a disease will open new horizons in the effectiveness and the selectivity of therapeutic agents. The effect of chemical substances in the environment and their possible relationship to cancers or birth defects will be an area of great social concern and one with which pharmacologists will be confronted. The emergence of tissue engineering to treat failing organs demands drugs that can facilitate the process. Finally, discoveries in the area of pharmacogenetics will allow for a better understanding and avoidance of adverse drug reactions, as well as development of individualized therapeutic regimens.

Pharmacology is such an integral part of our lives that we often are not even aware of it. Aspirin, antibiotics, acne medicine, and antiseptics are so common in our lives that we forget there was a time when they did not exist. As a pharmacologist, you can help improve human health by being part of a profession whose work is woven into the fabric of our daily lives. It is, indeed, an exciting and challenging time to **Explore Pharmacology!**

Young Pharmacologists in Training



**This Could Be You...if you
*Explore Pharmacology!***

This brochure was prepared with the assistance of the Graduate Recruitment and Education Committee of the American Society for Pharmacology and Experimental Therapeutics, September 2003, updated June 2006 and June 2012.

Chairs: Barbara S. Beckman (2002-2005), Stephanie W. Watts (2005-2007), Joey Barnett (2007-2013).

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Editor: Christine K. Carrico, PhD

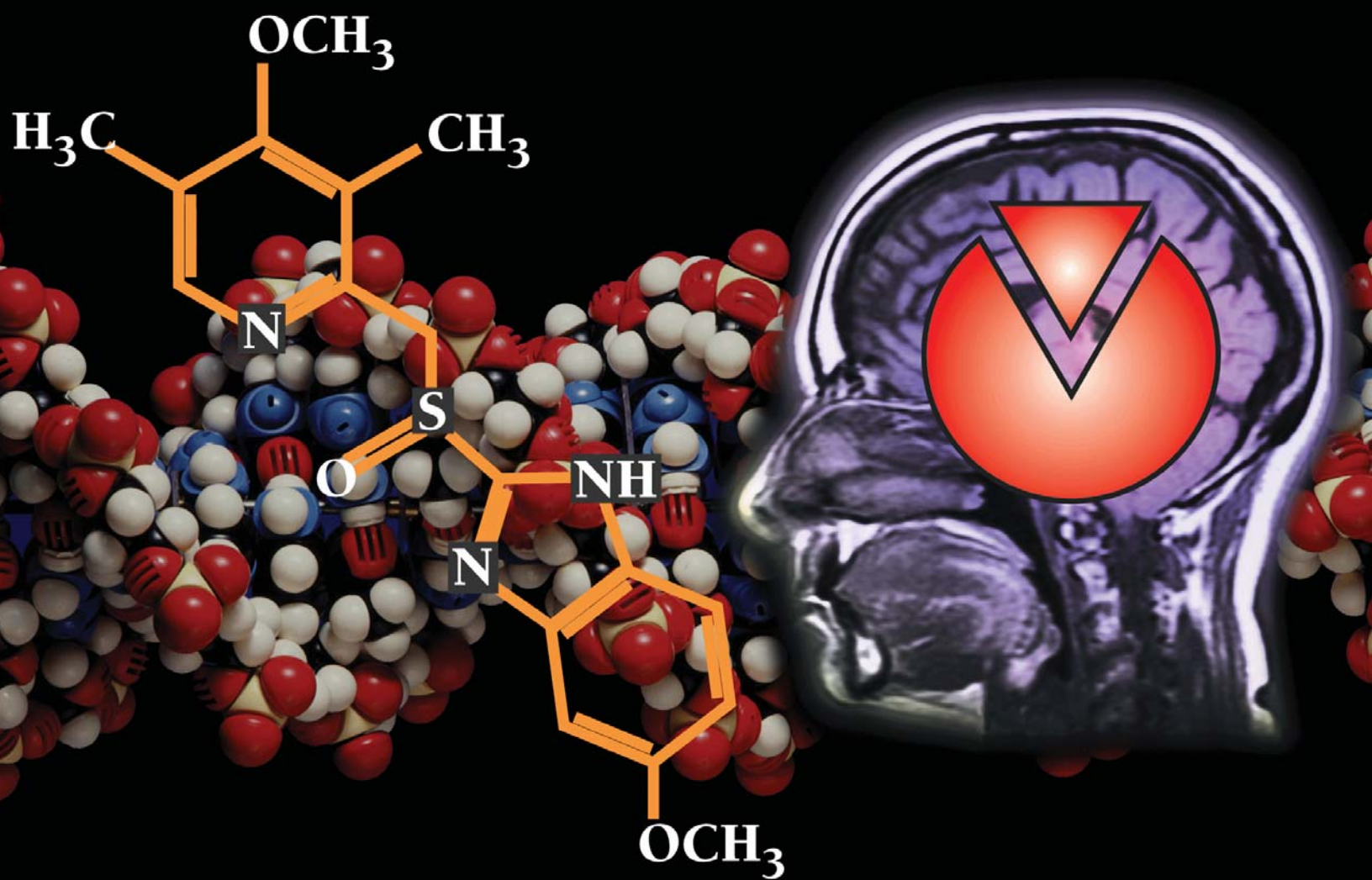
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