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## Dr. David Graves: Exploring the Chemistry of Nucleic Acids

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## faculty interview: chemistry

### Dr. David Graves: Exploring the Chemistry of Nucleic Acids

Chemistry, Drew Buie



*Dr. David Graves has spent 25 years investigating the interactions of small molecules with nucleic acids and trying to answer the basic questions -- what, why, how, and what of it. As chair of the department of chemistry, Dr. Graves has worked hard to facilitate an increase in research as well as increasing undergraduate research experience.*

**Q** How did you become interested in research?

**A**) I was an undergraduate chemistry major and found that working in a research laboratory was both interesting and an excellent way to earn extra money. I worked part-time in the UAB Department of Obstetrics and Gynecology (OBGYN) in the endocrine research laboratory. I became interested in research by working on projects determining steroid hormone levels in two types of patients: women trying to become pregnant or women who were pregnant and having various health problems with their pregnancies. My job was to determine the concentrations of different types of estrogens (E1, E2, E3, E4) and monitoring how the concentration levels of these estrogens change over gestational periods. One can use these estrogen levels to monitor the well being of both the mother and fetus. As an undergraduate, I found it intriguing that such a small molecule like estradiol could have such a profound impact on so many organ systems in the body. The steroid binds to a protein called an estrogen receptor. The estrogen receptor protein then directs the expression of discrete genes ensembles throughout the body. It was the initial concept that something as small as a particular estrogen molecule could cause vast changes in the numerous

organ systems through its controlled interactions with nucleic acids. What was most intriguing was that the estrogen receptor protein was highly selective in selecting its DNA target(s). The selectivity at the molecular level and the forces driving these interactions formed the foundation of the next four decades of my scientific interests.

For my graduate studies, I was admitted to the Ph.D. program in the UAB Department of Biochemistry research, and worked in the Laboratory of Molecular Biology under the direction of Drs. Lee and Dr. Lemone Yielding. In my Ph.D. research, I was able to extend my research interests in targeting nucleic acids in a variety of ways. My Ph.D. research was more focused toward the biochemistry of cancer and effects of DNA damage and repair on cancer. My graduate research consisted of development of novel compounds that would selectively target nucleic acids, and, through my research under their direction, I became more and more entrenched in studying the molecular interactions of the small molecules with nucleic acids. For this reason, I chose to do my postdoctoral work at the University of Rochester working with Professor Thomas Krugh in the Department of Chemistry in the area of biophysical chemistry of

nucleic acids. While at the University of Rochester, my research focused on the structure, stability, and sequence-selective nature of the interactions of numerous anticancer agents with their target DNAs. After four years at the University of Rochester in the Krugh Laboratory, I joined the faculty in the Department of Chemistry at the University of Mississippi. As a new tenure track assistant professor, I continued to examine the interactions of anticancer agents with nucleic acids.

have had considerable success in promoting extensive collaborative research ties between the Department of Chemistry and numerous departments and research centers within the UAB biomedical research community.

**Q)** What advice would you give to undergraduates who are considering research activities both now and later as a career?

*As an undergraduate researcher, you will gain valuable experience in what science is all about: how it is conducted from the lab bench to the actual publication of manuscripts and dissemination of knowledge to the rest of the scientific community. In reference to career goals, it provides you with a unique experience to enhance your resume for any field you wish to pursue, including medicine, dentistry, optometry, and any other health profession.*

Of the vast number of drugs that are currently in use as chemotherapeutic agents in the treatment of cancer, roughly 50% have DNA as their biological target. We need to gain a basic understanding of how these agents exert their biological activity if we are to improve their activity in their evolution to the next generation of drugs - the discovery of new compounds that will target nucleic acids. Our research focuses primarily on the biophysical characterization of the interactions of parent compounds that are currently used to treat cancer to discern why and how selected anticancer agents targeted DNA and triggered apoptosis in cancer cells. Research efforts focused on the structural and thermodynamic origins of sequence selectivity. The rational design of new DNA targeted drugs requires a thorough understanding of the binding mechanisms of existing compounds that bind to DNA with unique types of specificity.

**Q)** How long have you been at UAB and what persuaded you to come here?

**A)** After 20 years in the Department of Chemistry at the University of Mississippi, I returned to UAB in 2003 as the Chair of the Department of Chemistry. I feel that one of the primary reasons for my selection for this position at UAB was due to my strong background in biomedically related research in drug discovery. Since my arrival at UAB, my goal has been to enhance the Department of Chemistry's research efforts in areas of drug discovery, biophysical chemistry, structural biology, and computational chemistry. We have had significant successes in hiring outstanding new faculty and building state-of-the-art infrastructure in these areas. Through these enhancements, we

**A)** One of the most enjoyable and beneficial experiences you will ever have as an undergraduate is that of getting involved in a research laboratory. In reality, this is why you are at UAB, to take advantage of its world-class research environment. It is the perfect opportunity for you to grow both in your academic and career goals. As an undergraduate, you will have very strong research mentoring, and we want you to succeed; we are going to be putting you on projects that will be exciting, productive, and significant. As an undergraduate researcher, you will gain valuable experience in what science is all about: how it is conducted from the lab bench to the actual publication of manuscripts and dissemination of knowledge to the rest of the scientific community. In reference to career goals, it provides you with a unique experience to enhance your resume for any field you wish to pursue, including medicine, dentistry, optometry, and any other health profession. Students wishing to continue postgraduate degrees in research will go on to graduate schools. Undergraduate research will help you to select and make you highly competitive for top research institutions for your advanced degrees. Having a research experience on your resume allows you to stand out in a crowd. In my experience here at UAB, I have found the undergraduate chemistry majors at UAB to be highly motivated, focused, and very successful in achieving their goals upon graduation. Those students who take advantage of the research opportunities are very successful in their future careers in their postgraduate studies in medical and graduate schools.