

## Meet Kathleen Grant, Ph.D



**Kathleen Grant, Ph.D.** is a senior scientist, and chief of the neuroscience division at the Oregon National Primate Research Center (ONPRC), as well as a professor in the department of behavioral neurosciences at Oregon Health & Science University (OHSU).

Dr. Grant recently won the RSA Begleiter Excellence in Research Award at the Research Society on Alcoholism's annual meeting in June 2013 in Orlando, Florida.

*Writer Sherry Wasilow interviewed Dr. Grant from her office at OHSU.*

### **SW: How did you begin your work in the field of alcohol studies?**

**KG:** I have had a fairly straightforward path. As a science major in college, I was interested in a wide range of sciences, but biochemistry, organic chemistry, and biopsychology were my favorite subjects. I volunteered at the only biopsychology lab on campus and got my introduction into animal models of alcohol abuse and alcoholism.

For graduate studies, I chose to get a degree in physiological psychology, which at the time was a precursor of today's behavioral neuroscience. I subsequently received a postdoctoral award from the National Institute on Alcohol Abuse and Alcoholism (NIAAA) to study monkey models of addiction in the department of psychiatry at the University of Chicago. Here I was given the opportunity to learn about integrating human and non-human primate studies on the etiology of drug addiction.

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After my postdoctoral training, I join the NIAAA intramural laboratories at the National Institutes of Health (NIH) and became versed in the cellular pharmacology of alcohol tolerance and dependence. This is when I began collaborating with electrophysiologists to link how alcohol alters brain synaptic communication with alcohol's ability to capture and control behavior among individuals with alcohol use disorders (AUDs).

From the NIH, I joined the faculty in the department of physiology and pharmacology at Wake Forest University School of Medicine where I again had the opportunity to study monkey models of drug self-administration, and expand these studies to in vivo imaging. With the help of great colleagues, we built a large monkey program in behavioral pharmacology. Looking to go back to the west coast, I accepted my current position at OHSU and ONPRC where there are large, multidisciplinary and translational efforts in understanding alcohol addiction.

**SW: How would you describe your current research focus?**

**KG:** I use two main approaches to understand how alcohol addiction manifests in individuals. These approaches, drug discrimination and self-administration, provide complimentary information to better understand the risk for and consequences of heavy drinking.

With the drug discrimination procedure, we can characterize how alcohol interacts with drug receptors in the brain to control behavior. Since alcohol is a simple organic compound that can reach every cell in the body, untangling its effects throughout the brain is a challenge. Drug discrimination allows us to understand the mechanisms of how alcohol is perceived by the individual, essentially breaking down the component parts of alcohol's simultaneous activity at multiple receptors while observing behavioral action. This has led to discoveries that some neurotransmitter systems, for example the gamma-aminobutyric acid receptor system, most likely underlie the low dose, rising phase of alcohol's actions like feeling energetic, while other neurotransmitter systems, such as the glutamatergic system, may underlie higher dose effects like memory loss.

The self-administration procedure is a direct model of alcohol drinking, allowing us to understand factors that contribute to individual differences in the propensity to drink to the point of alcohol dependence. In this procedure, we allow each monkey to choose its own pattern of alcohol consumption, or water and food. Patterns of drinking displayed by the monkeys reveal aspects of human alcohol consumption such as sipping through drinks and thereby avoiding intoxication, or gulping down drinks that results in rapid intoxication. We also see occasional three- or four-day sprees of very heavy drinking, voluntary periods of abstinence, morning tremors, and relapses to heavy drinking after imposed periods of abstinence. The self-administration procedure allows for sophisticated analysis of time course and threshold changes in how genes are modified with continued drinking and in vivo imaging of brain adaptations to chronic alcohol consumption.

**SW: What day-to-day applications do you think your research has for both clinicians and non-clinicians?**

**KG:** For the non-clinician, the monkey model of individual risk in developing excessive drinking should help dispel popular explanations that AUDs are solely the result of a lack of will or restricted to families of alcoholics. Rather, there are large influences both external - such as the restrictions placed by society - and internal - such as how alcohol makes you feel in the moment - superimposed on a background of personal history, that interplay to result in alcohol addiction.

For the clinician, we have found that in vivo brain imaging can show cortical brain shrinkage, similar to alcoholics, but with the added information of the threshold dose of effect and an estimation of cortical loss per additional daily drink. We are exploring brain areas, and genes within those brain areas, that are particularly vulnerable to long-term adaptations and damage due to alcohol in order to help tailor pharmacotherapies. Finally, we have evidence for specific brain circuitry involved in the brain mechanisms that are predominant in propagating the ability to repeatedly drink 12-24 drinks per day; intakes that are equal to double or triple the lethal dose in a naive individual. Being able to understand how the already intoxicated individual can continue to drink is a basic scientific question that should provide important insight into how to control or eliminate the process of drinking to alcohol dependence.

**SW: What does your recent award – the Begleiter Excellence in Research Award – mean to you on a personal level?**

**KG:** It is a privilege to be recognized by my mentors and peers in the RSA and to be included in this distinction with the past recipients who have all been leaders in the field. Because the award is meant to acknowledge a lifetime of achievements in translational science, I am particularly honored because my career has been devoted to using animal models of alcohol addiction to improve our public health.

**SW: What would you like to see happen in the addiction-research field?**

**KG:** We have all the pieces to understand and change the course of alcohol addiction. Our diagnostics are based on solid epidemiological, cognitive, and cellular science data, our genetics research is highly sophisticated and at the cutting edge of applications in complex disorders, our understanding of dose thresholds for adverse biomedical outcomes and the capacity for organ systems to recover is progressing at a rapid pace, and our understanding of vulnerable stages in life, such as fetal development, adolescence, and the senior years, have provided important prevention strategies. I think we will soon have sensitive, reliable, and accurate biomarker information based in multiple parameters of blood proteins and ribonucleic acid (RNA) that will be easily assessed and available in clinical centers. Perhaps the biggest barrier will be to develop individualized therapeutics for patients presenting with AUDs, because the data show that different populations – like adolescents, women, ethnic minorities, etc. – have different responses to current behavioral and drug therapies.

**SW: What advice do you have for people now entering addiction research?**

**KG:** Addiction is the result of multifaceted factors, and so my advice to early-stage scientists is to push themselves to understand not only their main area of interest, such as genetics, but also other aspects at the level of another scientific discipline, such as cognitive function. Addiction is an area of research that crosses all scientific boundaries and extends beyond clinical medicine into social norms, so curiosity will be their best partner in sustaining a fruitful career.

**SW: Any last words for the ATTC audience?**

**KG:** My commitment to alcohol research evolved through my desire to understand behavior. Alcohol holds an incredibly important place in the course of human history, politics, economics, agriculture, community health, family medicine and personal health. To be a part of the scientific discoveries of how this simple 2-carbon molecule can become such a powerful force in human behavior is a privilege and a great opportunity.

**Additional website:**

<http://www.ohsu.edu/xd/research/centers-institutes/onprc/scientificdiscovery/scientists/kathleen-a-grant.cfm>