Philip Hieter: 2018 George W. Beadle Award

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The Genetics Society of America's (GSA) George W. Beadle Award honors individuals who have made outstanding contributions to the community of genetics researchers and who exemplify the qualities of its namesake. For his work fostering communication and collaboration among members of the many subfields of genetics, Philip Hieter of the University of British Columbia has been named 2018's recipient of the award. Among his contributions are many initiatives that aim to better link human and model organism geneticists, including the Canadian Rare Diseases Models and Mechanisms Network—a consortium that connects investigators who identify rare disease genes in humans to basic scientists who can study the genes in model organisms.

SCIENTIFIC research is a social enterprise. When researchers share knowledge and resources, they accelerate discovery; when they collaborate across disciplines, they broaden their impact. But it is often difficult for individual scientists to predict how their expertise and research could make a difference outside their field. Phil Hieter has dedicated much of his career to systematic efforts to link scientists and foster collaboration, making it easier for researchers to cross the boundaries of their disciplines and work together. In recognition of these valuable contributions, Hieter is the 2018 recipient of the Genetics Society of America's George W. Beadle Award.

Many of Hieter's efforts have focused on linking researchers working on humans with those who use model organisms. As the 2012 GSA President, he made it his mission to establish a close relationship between GSA and the American Society of Human Genetics—groups that had historically not interacted much. But his dedication to bringing geneticists together was evident long before he became GSA President. In the early 1990s, Hieter recognized that the new flood of expressed sequence tags (ESTs) being produced could be used to rapidly functionally annotate the human genome. Hieter's group computationally identified ESTs with homology to yeast proteins and used the corresponding cDNA to map the human gene. This provided medical geneticists, who were using the locations of disease gene mutations placed on the human genetic map to identify the corresponding human disease genes by positional cloning, with new candidate genes, often with functions already known from previous yeast research (Tugendreich *et al.* 1993). Many collaborations grew from such links. Hieter also became well known as one of the creators of XREFdb, a searchable database that allowed researchers to draw connections between known functions of genes in nonmammalian model organisms and phenotypes associated with gene mutations that had been genetically mapped in humans and mice (Bassett *et al.* 1997).

More recently, Hieter cofounded the Canadian Rare Diseases Models and Mechanisms Network (RDMM)—a consortium that connects researchers in ways that directly benefit patients with rare diseases (Foley 2015). Specifically, the network links the people who are discovering new disease-linked mutations and genes with basic scientists who study those or similar genes in model organisms (Wangler *et al.* 2017). He and his cofounders created the RDMM in 2014 in response to the rapid pace at which rare disease genes were being identified with next-generation sequencing—particularly after the cost of whole-exome sequencing dropped dramatically. Despite the ever-growing number of rare disease genes identified, there remains a dearth of functional data to help reveal underlying mechanisms and aid in the development of cures.

The existence of collaborations like the ones the RDMM fosters is not new—combining data on human diseases with information from model organism research has well-recognized value. What makes the RDMM unique, however, is that it acts as a matchmaker, bringing together researchers who otherwise may never have found each other. "Just by looking and trying to search the literature, you're going to miss a lot of connections," Hieter says. This is in part because researchers have such extensive unpublished knowledge of the genes they study. Through the RDMM, participating model organism researchers state how well-situated they are to begin functional studies on their genes of interest, allowing them to be matched with human geneticists. "It's a numbers game," Hieter says. "If you do 10 of these, there will certainly be increased productivity. If you do hundreds of them, some people are going to win the lottery. There are going to be chance interactions that really have a huge impact."

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The influence of circumstance and chance is a motif that features prominently in Hieter's career. He hadn't always expected to be a scientist; though he was a good student in high school—and particularly excelled in math—he entered college without a clear plan for the future. It wasn't until he took on a work-study job in a biology lab that he discovered his love for research and began to seriously consider a career in science.

Still, he remained undecided about his future plans after completing his bachelor's degree, and worked as a lab technician as he considered whether to go to graduate school or medical school. His uncertainty dissolved when he attended a lecture by Philip Leder, then director of the Laboratory of Molecular Genetics at the National Institutes of Health. Leder's talk on the genetics of antibody diversity was so captivating that even now, decades later, Hieter describes it as a "mind-blowing experience". Hieter called Leder the very next day, and the pair worked out a plan for Hieter to enroll in a doctoral program at Johns Hopkins University and take 2 years of graduate courses there before completing his thesis research in Leder's lab.

Hieter's thesis research on human antibody genes, which involved cloning the constant regions of the kappa and lambda light-chain genes and investigating their rearrangement in B-cell leukemia, was extraordinarily successful. When Hieter arrived at Ronald Davis's lab at Stanford University as a postdoctoral researcher, Jasper Rine—then also a postdoc in Davis's lab—says he viewed Hieter as an "experimental genius." Rine, who served as GSA President in 2015, says of Hieter's doctoral research: "It was really, really impressive work."

Hieter says it was Rine and Mark Johnston, another postdoc in Davis' lab at the time (and current Editor in Chief of this journal), who taught him genetics. "I had never learned genetics before that, but people would now call me a geneticist," Hieter says. "I realized that I should have been a geneticist all along."

Learning yeast genetics with no background in the subject was evidently worth the risk—Hieter conducted his research just as yeast was coming to the fore as a model eukaryote. Medical schools were showing interest in hiring model organism researchers when Hieter was completing his postdoctoral work, and he set up his own yeast lab at Johns Hopkins University in 1985.

In his lab at Hopkins, and later at the University of British Columbia, where he moved in 1997, Hieter made many major contributions to our understanding of chromosome biology, including the dissection of yeast centromeres and kinetochores and the identification and characterization of many genes involved in genome stability. His work has been instrumental in establishing yeast as a useful model organism for cancer research.

But, although Hieter's work on chromosome biology constitutes a major contribution to the field, the Beadle Award honors his impact on the genetics research community as a whole. For example, during his research he established a tradition of community building by openly sharing his group's developments, including yeast host strains and vectors and techniques like physical mapping and synthetic lethality screening methods. In fact, almost 30 years after Hieter's group developed the pRS series of vectors, these tools remain in ubiquitous use in yeast labs; the paper describing them is the most cited article ever published in *GENETICS* (Sikorski and Hieter 1989).

Hieter has also had an impact by designing ways to unite distinct research communities at conferences. He conceived of and organized two "Yeast Genetics and Human Disease" meetings (in 1996 and 1999) that cemented the role of yeast as a model for human biology. "People who attended those meetings still talk about them!" says Johnston. The meetings became the model for GSA's "Model Organisms to Human Biology" conferences, the first of which Hieter helped organize. He went on to become a driving force behind GSA's The Allied Genetics Conference (TAGC) in 2016, which brought together many normally siloed model organism groups under one umbrella to encourage new collaborations and synergism. Hieter's vision of encouraging collaboration by bringing together diverse groups has been an enormous success and will continue in 2020 at the next TAGC.

Hieter's generous contributions to the genetics research community exemplify the spirit recognized by the George W. Beadle Award. "He never needed acknowledgement, never wanted to be a coauthor just for sharing something," Rine says. "He's just everyone's idea of a perfect colleague."

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