Survival of the Fittest Tools

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THE Genetics Society of America's 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 as a respected academic, administrator, and public servant. The 2014 recipient, Hugo Bellen, has made seminal contributions to the fields of genetics, developmental biology, and neuroscience. In parallel with his landmark science, he has worked to expand the toolbox available to *Drosophila* geneticists. He has helped develop technologies now used by the majority of *Drosophila* labs, advancing almost all fields of biology.

CONTRIBUTING to the genetics community has always been one of my primary scientific goals. While my lab has focused on the molecular mechanisms of synaptic transmission, neural development, Notch signaling, and most recently neurodegeneration, many of our efforts relate to developing technologies, generating useful *Drosophila* stocks, and disseminating genome-wide libraries for a wide range of *in vivo* analyses. I truly enjoy creating tools and reagents that impact research in many fields and promote the use of our favorite model organism. And so I am very honored to receive this award because it is intended to recognize individuals "who have made outstanding contributions to the community of genetics researchers."

It is fair to state that, currently, no other multicellular organism allows more sophisticated and elegant manipulations *in vivo* than the fruit fly, thanks to the efforts of many geneticists and molecular biologists over the past century. Indeed, almost half of the recipients of the Beadle award since its initiation in 1999 are *Drosophila* geneticists, including Michael Ashburner, Allan Spradling, Gerry Rubin, Norbert Perrimon, Thomas Kaufman, William Gelbart, and Scott Hawley. These individuals and many others in the fly community have developed new methods or tools and helped propagate their use. This spirit of sharing tools and reagents has driven many discoveries in *Drosophila* and will continue to advance our research.

Continued tool and reagent development is critical for the survival, expansion, and evolution of the *Drosophila* field.

—H.J.B.

My lab has focused on methodologies and tools that can be applied to many genes or to the entire genome. They include the enhancer detector transposable elements that have permitted the cloning of hundreds of genes and have also led to the development of other technologies, such as the UAS/GAL4 system (Bellen *et al.* 1989; Wilson *et al.* 1989; Brand and Perrimon 1994). In collaboration with Roger Hoskins and Allan Spradling, we generated a library of >15,000 publicly available insertion strains by tagging genes with transposable elements, allowing mutational analysis of nearly 10,000 genes (Bellen *et al.* 2004, 2011; Venken *et al.* 2011a). My lab also developed a method to rapidly map chemically induced lethal mutations based on *P* elements (Zhai *et al.* 2003). In addition, we constructed an improved transformation vector named P[acman] that permits cloning and elegant genetic manipulations using recombineering in bacteria followed by site-specific integration of transgenes up to 250 kb in length (Venken *et al.* 2006). In collaboration with Roger Hoskins and Pieter De Jong (Venken *et al.* 2009), this vector has been used to produce two BAC libraries (20 and 80 kb) of >100,000 transformation-ready P[acman] clones that cover 98% of the whole genome. In collaboration with Thom Kaufman, we used a collection of >400 80-kb BACs to create an X-chromosome duplication set (Venken

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et al. 2010), which allows the mapping and analysis of X-linked mutations. Most recently, we developed a new transposable element named MiMIC that facilitates genomic tagging of proteins (Venken *et al.* 2011a). We are using MiMICs to tag thousands of genes that allow elegant and specific genetic manipulations in cell culture (Neumüller *et al.* 2012) and *in vivo* (S. Nagarkar-Jaiswal and P.-T. Lee, personal communication).

Many adaptations of these methods/tools have been implemented in other model organisms and hence impact other fields. Obviously, this cross-fertilization works both ways. We regularly borrow from other geneticists: *P*-element enhancer detection was inspired by *Bacillus subtilis* experiments (O'Kane *et al.* 1986; O'Kane and Gehring 1987), the GAL4/UAS system was based on elegant experiments developed in yeast (Fischer *et al.* 1988; Brand and Perrimon 1994), and P[acman] recombineering was based on research on phages and bacteria (Yu *et al.* 2000; Venken *et al.* 2006). Numerous other examples of borrowing across species exist (Venken *et al.* 2011b), and this underscores the need for continued support for genetically tractable organisms such as yeast, bacteria, and viruses.

Hugo has been one of the most selfless contributors to the general good of the *Drosophila* community over the past two decades. I doubt there is anyone in this field that has not benefited directly from his generosity.

—Ethan Bier, University of California, San Diego

Continued tool and reagent development is critical for the survival, expansion, and evolution of the *Drosophila* field. In a sense, it is a process of Darwinian selection in the struggle for survival of the fittest organism to perform biological experiments. As long as *Drosophila* is fit, the field will continue to attract some of the brightest and best biologists. These tools also allow us to assess the function of many genes *in vivo*, which is needed now more than ever as human geneticists discover disease-causing genes at an unprecedented pace, while <30% of the fly's genes are functionally annotated *in vivo* (St Pierre *et al.* 2014). Because the fly homologs of thousands of human genes are still poorly annotated, detailed functional studies of these genes will contribute to the annotation of vertebrate genomes, improve our understanding of evolutionarily conserved pathways/processes, and reveal the underlying mechanisms of many diseases. While the past two decades have found detailed descriptive information about sequences, types of transcripts, regulatory elements, tissue expression, and protein–protein interactions (Boley *et al.* 2014), functional information on genes/proteins is necessary if we are to translate this valuable information into biological and pathological insight. *Drosophila* is perfectly situated for the pursuit of these avenues of research and will continue to provide important biological insights at the cellular and organismal level. Continued technological developments and genome-wide reagents will drive the success of *Drosophila*, and sharing will dramatically accelerate the process. I see many more Beadle Awards for *Drosophila* geneticists in the future.

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