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Special Issue: Human Genetics

On the shoulders of worms

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Newton famously wrote in a letter to a colleague 'If I have seen further it is by standing on the shoulders of Giants.' He was referring to work that had been done earlier by Descartes that his own work built upon. So much of what we do in science owes a great debt to the work that was done before us that it is difficult to know where a discovery starts. I would wager, however, that a great many of the discoveries about human health started from work in model organisms.

The Nobel Prize in Medicine and Physiology, for example, has often been awarded for discoveries made in model organisms and, indeed, seeks to highlight findings from basic science as well as traditional clinical breakthroughs. Numerous advances in genetics have been honored with the Nobel Prize (Table 1), from Thomas Hunt Morgan, whose work established *Drosophila* as a model organism, to Andrew Fire and Craig Mello, for their discovery of RNAi in *Caenorhabditis elegans*. Even what is arguably the highest prize in the field of human genetics recognizes how much we can learn from bacteria, plants, and flies.

In this era of the $1000 human genome, however, the study of human genetics is becoming much more direct. Efforts are underway to identify the genetic etiology of all Mendelian diseases (http://mendelian.org/), genome-wide association studies (GWASs) continue to uncover variants linked to complex diseases, and large-scale population genetics studies are impacting our understanding of the natural spectrum of variation in the human population (http://www.1000genomes.org/about). Other large-scale sequencing efforts are tackling the influence of epigenetics and the environment on human phenotypes. Despite these impressive undertakings, however, the 'grand' human genome leaves much unexplained. We still struggle to definitively identify causal variants from the mass of data and many studies end with lists of candidate genes.

Model organisms remain the place where candidate genes make history. Basic science in tractable genetic organisms is more important today than ever before, not only as a proving ground for variants identified in genomic studies, but also as a means of answering compelling questions about the fundamentals of evolution, epigenetics, and environmental effects. This Special Issue on human genetics is devoid of any direct work on humans and yet each piece addresses a question relevant to human health and disease and highlights the power of basic research to illuminate human genetics. If physicists stand on the shoulders of giants, geneticists stand on the shoulders of yeast, and, flies, and worms, and plants.

We thank all of the authors and reviewers for their contributions to this issue and we thank you for reading it. Your comments and ideas are always welcome; you can contact us with feedback or questions at tig@cell.com.

Table 1. The Nobel Prize in Physiology and Medicine is often awarded for basic research conducted in model organisms. A selection of some of the prizes related to genetics is listed below.

Year	Awardee	Rationale[a]	Model organism
1933	Thomas Hunt Morgan	'for his discoveries concerning the role played by the chromosome in heredity'	*Drosophila melanogaster*
1935	Hans Spemann	'for his discovery of the organizer effect in embryonic development'	Amphibians
1946	Hermann Joseph Muller	'for the discovery of the production of mutations by means of X-ray irradiation'	*D. melanogaster*
1958	George Wells Beadle and Edward Lawrie Tatum	'for their discovery that genes act by regulating definite chemical events'	*Neurospora crassa*
	Joshua Lederberg	'for his discoveries concerning genetic recombination and the organization of the genetic material of bacteria'	*Escherichia coli*
1959	Severo Ochoa and Arthur Kornberg	'for their discovery of the mechanisms in the biological synthesis of ribonucleic acid and deoxyribonucleic acid'	*E. coli*
1965	François Jacob, André Lwoff, and Jacques Monod	'for their discoveries concerning genetic control of enzyme and virus synthesis'	*E. coli*/phage
1968	Robert W. Holley, Har Gobind Khorana, and Marshall W. Nirenberg	'for their interpretation of the genetic code and its function in protein synthesis'	*E. coli*/*Saccharomyces cerevisiae*
1969	Max Delbrück, Alfred D. Hershey, and Salvador E. Luria	'for their discoveries concerning the replication mechanism and the genetic structure of viruses'	Bacteriophage
1983	Barbara McClintock	'for her discovery of mobile genetic elements'	*Zea mays*
1995	Edward B. Lewis, Christiane Nüsslein-Volhard, and Eric F. Wieschaus	'for their discoveries concerning the genetic control of early embryonic development'	*D. melanogaster*
2001	Leland H. Hartwell, Tim Hunt, and Sir Paul M. Nurse	'for their discoveries of key regulators of the cell cycle'	*S. cerevisiae*/sea urchin
2002	Sydney Brenner, H. Robert Horvitz, and John E. Sulston	'for their discoveries concerning genetic regulation of organ development and programmed cell death'	*Caenorhabditis elegans*
2006	Andrew Z. Fire and Craig C. Mello	'for their discovery of RNA interference – gene silencing by double-stranded RNA'	*C. elegans*
2009	Elizabeth H. Blackburn, Carol W. Greider, and Jack W. Szostak	'for the discovery of how chromosomes are protected by telomeres and the enzyme telomerase'	*Tetrahymena*/*S. cerevisiae*
2013	James E. Rothman, Randy W. Schekman, and Thomas C. Südhof	'for their discoveries of machinery regulating vesicle traffic, a major transport system in our cells'	*S. cerevisiae*/mice

[a]As stated by the Nobel Prize Organization (http://www.nobelprize.org/nobel_prizes/medicine/laureates/).

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