

# The Crafoord Prize in Biosciences 2015

*The Crafoord Prize in Biosciences 2015 is awarded to the geneticists **Richard Lewontin**, USA, and **Tomoko Ohta**, Japan, for their contributions to knowledge of genetic variation. Thanks to Lewontin and Ohta, we know that the genetic variation within populations of plants and animals is many times greater than science once thought – and we understand why.*

The late twentieth century and early twenty-first century have seen a revolution in genetic research. New techniques for DNA sequencing have resulted in the rapid growth of knowledge in many areas of biology, including ecology, evolution and systematics. The influence of genetics can also be seen in popular culture, where TV series' crime scene investigators search for traces of DNA on a hunt for the killer. These traces are able to reveal who were at the scene of the crime because each person's genotype is as unique as his or her fingerprints. This doesn't only apply to humans, but to all animals and plants that reproduce sexually; there is considerable genetic variation between individuals of the same species and in the same population. This variation is so significant that we can be certain that two individuals do not have identical DNA even if they are closely related. The only exception to this is identical (monozygotic) siblings.

Knowledge of the great genetic variation found within populations and each individual's unique genotype is now a well-integrated element of our understanding of the world, as well as fundamental to science. But this has not always been the case – for most of the twentieth century, scientific theories about genetic variation were very different. It was only in the 1960s that the current ideas about genetic variation began to emerge, largely due to the Crafoord Laureates, Richard Lewontin and Tomoko Ohta.

## Previous theories

In order to understand how revolutionary Lewontin's and Ohta's discoveries were, it is necessary to understand the paradigms of biology up to the 1960s. A century earlier, Charles Darwin had written *The Origin of Species* (1859), which presented his theory of evolution by natural selection and laid the foundation for an evolutionary perspective on biology. Darwin stated that individuals with superior genetic variants will be more successful in survival and reproduction than those with less fit genotypes. This leads to a natural process that promotes organisms' improved adaptation to their habitats.

Until the 1960s, geneticists believed that every inherited mutation in nature was subject to this natural selection: either the mutation was harmful, and was then removed, or it was beneficial and thus every individual in the population would eventually carry it. One logical consequence of this idea was geneticists' assumption that all individuals in a population have more or less similar genetic variants. If all mutations are either beneficial and on their way to being spread through the entire population, or harmful and on the way to being removed, there is not a lot of allowance for genetic variation. A type of standard organism was described for both plants and animals, called a "wild type", which carried exactly the set of genes chosen by natural selection.

## The discovery

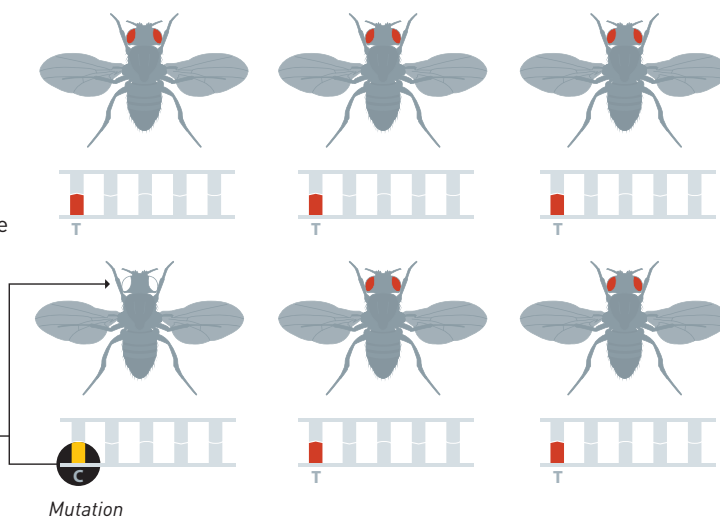
This was why **Richard Lewontin's** discovery of the actual situation, made when he was working at the University of Chicago in the 1960s, was so revolutionary. He has described how he long wondered how he would be able to analyse genetic variation in plants and animals in the wild, but had not found a solution to the problem. When Lewontin met his research colleague John Lee Hubby (1932–1996), who had developed a new method of separating proteins using an electric field, he realised that this was the tool he needed; the proteins' different electric charges were a direct reflection of their genetic differences. The two researchers started to collaborate and measure genetic diversity in plants and animals.

Their experiments had surprising results: the genetic variation between individuals in a population was many times greater than Lewontin and others had expected. These results were published in *Genetics* in 1966 and aroused a great deal of attention. The first analysis was of fruit flies, but the pattern was repeated in every species examined by the researchers. Most species demonstrated a significant and unexpected genetic variation that appeared to contradict the principles of natural selection.

### The theory before the 1960s

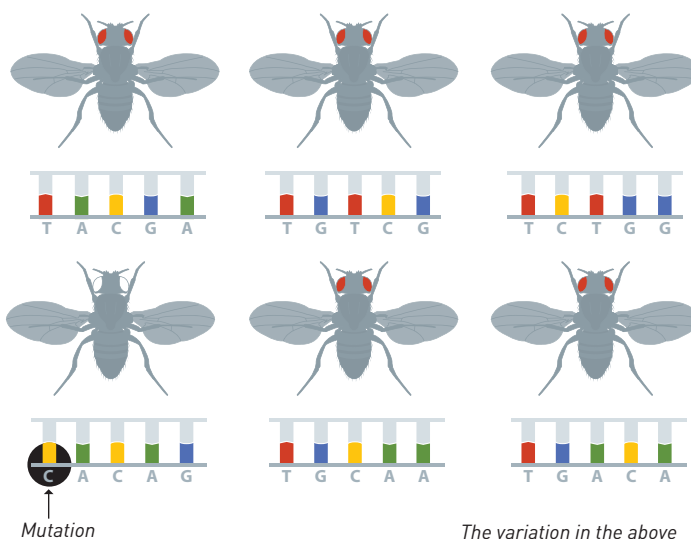
Before it was possible to analyse DNA, it was thought that all individuals in a population had the same sequence in the gene for a particular trait. In rare cases, individuals displayed a mutation.

*In this case the mutation has replaced T with C, which gives the individual white eyes instead of red eyes.*



### The new theory

When DNA was analysed, it became apparent that there is significantly greater variation in genes – almost all individuals had different sequences, despite having the same traits. This is explained by the theory of neutral and nearly-neutral mutations.



*The variation in the above example is exaggerated for educational reasons.*

Could there be neutral mutations – gene variants that are neither advantageous nor harmful for the individual, and which are therefore not affected by natural selection? One theory – the neutral theory – was proposed by Motoo Kimura (1924–1994) at National Institute for Genetics in Japan. The theory eventually found support as it appeared to provide a good explanation for the great genetic variation discovered by the researchers.

**Tomoko Ohta**, also from the National Institute for Genetics, believed that such a simple division into three types of mutations – good, neutral and harmful – did not reflect reality's true complexity. In actual fact, almost all mutations in genes that affect the encoded proteins are somewhat harmful, but the effect of this is so insignificant that these gene variants can remain in the population, Ohta explained. Moreover, chance means that even less-than-optimal variants can spread in the population. Ohta also showed that the size of a population is decisive in the effectiveness of natural selection: the smaller the population, the greater the effect of chance, and natural selection will function more poorly.

Tomoko Ohta continued to develop this nearly-neutral theory after presenting it in *Nature* in 1973. In an article in *Proceedings of the National Academy of Sciences (PNAS)* in 1974, Tomoko Ohta and Motoo Kimura proposed five general principles for molecular evolution. These included rates of evolution and in which parts of the gene it could be assumed to go faster or slower. At that time, access to empirical data was very limited, but the enormous amount of genetic information generated in recent decades has shown that Ohta's predictions were accurate.

Lewontin has also continued to make considerable contributions to the knowledge of genetic variation, both theoretically and experimentally. One example is his work on genetic variation among humans. In 1972, in a renowned article in *Evolutionary Biology*, Lewontin demonstrated that the majority (80–85 per cent) of the genetic variation in humans is found within each population, and that genetic differences between peoples are thus marginal. These results have been vital to the abolition of the concept of race biology in humans.

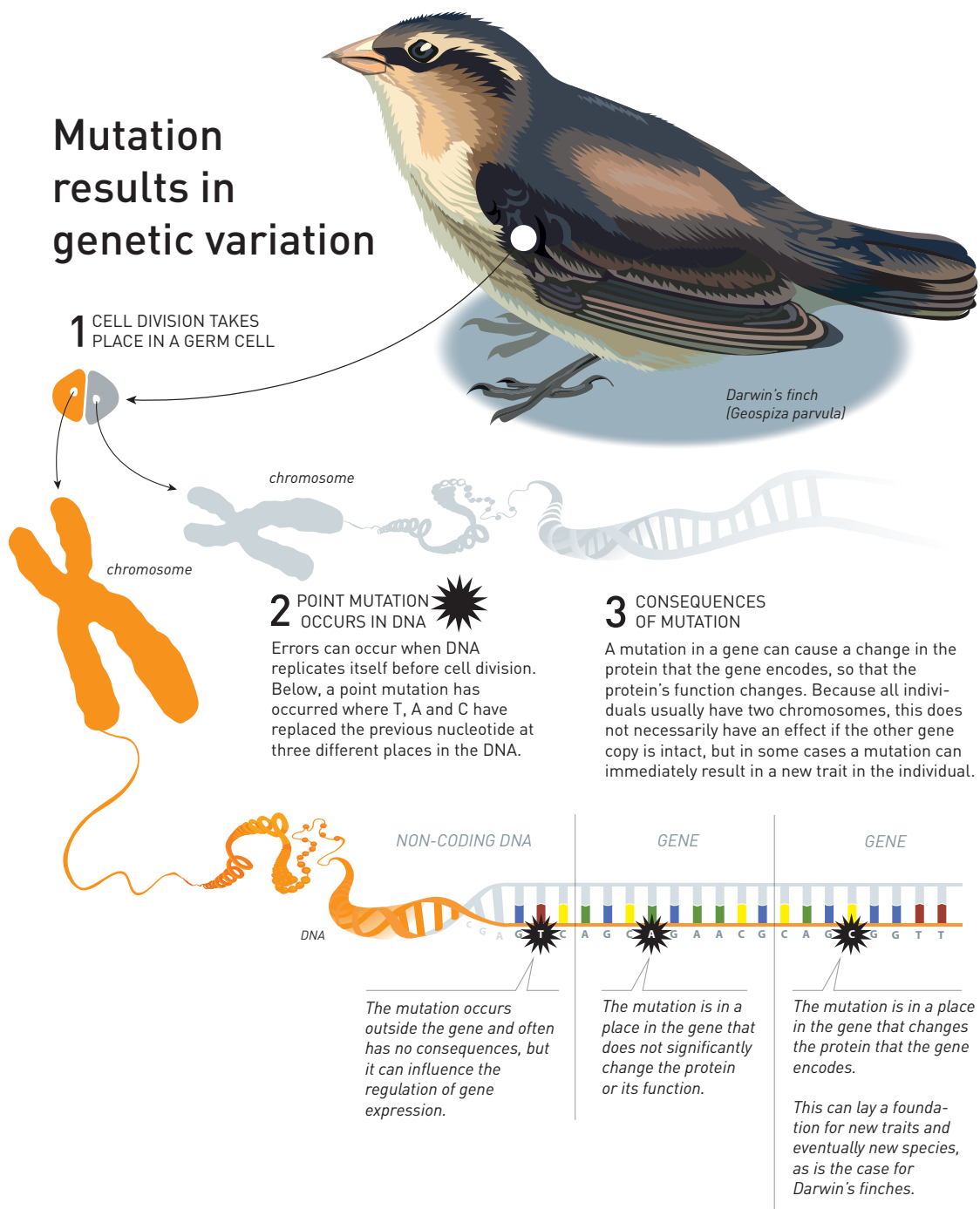
## Significance

Tomoko Ohta and Richard Lewontin are awarded the Crafoord Prize for basic research of great general significance. The prize-winners have provided science with a more accurate image of how natural selection works at a molecular level, how populations evolve and the amount of genetic variation between species and populations of both plants and animals. This knowledge is now a fundamental element of genetics and the natural starting point for all future genetic research.

However, even if this fundamental understanding must be regarded as having the most important value of that generated by Ohta's and Lewontin's research, it is also possible to provide a number of examples of how the knowledge of genetic variation is put to use.

- In ecology and conservation it has led to a better understanding of population structure and genetic vulnerability among threatened populations. Another result has been new methods for estimating the size of natural populations using the DNA analysis of animal spoor, such as scat.
- In systematic biology, knowledge of genetic variation has resulted in new opportunities for understanding relationships between and within species.

- Thanks to knowledge of genetic variation, it is now possible to determine close relationships between individuals using DNA analysis. This has had a great impact on evolutionary ecology, such as its use in paternity analyses. It has been shown that in many species the females mate with more than one male, so that the offspring in a litter are often half-siblings.
- Additionally, knowledge of genetic variation has naturally been very important in the field of medicine. It lays the foundation for the extensive research being conducted into genetic risk factors for various diseases, but also for the increased focus on individually-adapted treatments on the basis on the patient's genetics.



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## THE LAUREATES

### **RICHARD LEWONTIN**

US citizen. Born 1929 in New York, USA. Ph.D. 1954 from Columbia University, NY, USA.  
Emeritus Professor at Harvard University, MA, USA.  
[www.mcz.harvard.edu/Departments/PopGenetics/lewontin\\_r.html](http://www.mcz.harvard.edu/Departments/PopGenetics/lewontin_r.html)

### **TOMOKO OHTA**

Japanese citizen. Born 1933 in Miyoshi, Japan. Ph.D. 1967 from North Carolina State University, NC, USA.  
Emeritus Professor at the National Institute of Genetics, Mishima, Japan.  
[www.nig.ac.jp/english/section/ijin/ijin-1.html](http://www.nig.ac.jp/english/section/ijin/ijin-1.html)

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## LINKS AND FURTHER READING

More information about this year's prize is available at [www.crafoordprize.se](http://www.crafoordprize.se) and the Royal Swedish Academy of Sciences' website, <http://kva.se/crafoordprize>

### **Richard Lewontin**

#### **Lectures**

The concept of race: The confusion of social and biological reality, University of California Television  
[www.youtube.com/watch?v=JvG1ylKhzoo](http://www.youtube.com/watch?v=JvG1ylKhzoo)

Gene, organism and environment: Bad metaphors and good biology, University of California Television  
[www.youtube.com/watch?v=we4ZzjKxFHM](http://www.youtube.com/watch?v=we4ZzjKxFHM)

#### **Scientific publication**

Lewontin, R. C., Hubby, J. L. 1966. A molecular approach to the study of genic heterozygosity in natural populations. II. Amount of variation and degree of heterozygosity in natural populations of *Drosophila pseudoobscura*. *Genetics* 54: 595–609  
[www.ncbi.nlm.nih.gov/pmc/articles/PMC1211186](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1211186)

### **Tomoto Ohta**

#### **Interview**

*Current Biology*, 22, 16: R618–R619  
[www.sciencedirect.com/science/article/pii/S0960982212007075](http://www.sciencedirect.com/science/article/pii/S0960982212007075)

#### **Scientific publication**

Ohta, T. 1973. Slightly deleterious mutant substitutions in evolution. *Nature* 246, 96–98  
Abstract: [www.nature.com/nature/journal/v246/n5428/abs/246096a0.html](http://www.nature.com/nature/journal/v246/n5428/abs/246096a0.html)

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