Jennifer Graves

Jennifer Graves is an evolutionary geneticist who works on Australian animals, including kangaroos, platypus, Tasmanian devils, emus and dragon lizards. Her group uses their distant relationship to humans to discover how genes, chromosomes and regulatory systems evolved and how they work in all animals, including humans. Jenny received her B Sc and M Sc degrees from Adelaide University, Australia and completed her Ph D in molecular biology at the University of California, Berkeley, USA. She joined La Trobe University, Melbourne, Australia in 1971 and worked there for 30 years before moving to Australian National University (ANU) Canberra in 2001, where she founded the Comparative Genomics Department and directed the ARC Centre of Excellence in Kangaroo Genomics. She returned to La Trobe as Distinguished Professor in 2011 and at present is also Professor Emeritus at ANU, Thinker-in-Residence at Canberra University and Professorial Fellow at the University of Melbourne. Graves has written three books and more than 400 research articles. She has also received many honours and awards, including the Macfarlane Burnet Medal of the Australian Academy of Science in 2006 and was appointed Officer of the Order of Australia (AO) in 2010. She is a Fellow of the Australian Academy of Science and was on the Executive for 8 years, first as Foreign Secretary, and later as Education Secretary with responsibility for the Academy's science education projects. She is a 2006 L'Oreal–UNESCO Laureate for Women in Science and recently received the Australian Prime Minister's Prize for Science.

Graves delivered a public lecture on vertebrate sex determination by genes, chromosomes and the environment at the Indian Institute of Science, Bengaluru on 13 March 2018. Excerpts from her lecture on sex chromosomes and their evolution are given below.

Sex chromosomes X and Y: The human X chromosome contains many genes with a wide range of functions, but those involved in reproduction and intelligence are over-represented, and are thought to play a major role in human evolution. The tiny Y chromosome is a genetic wasteland bearing only 45 genes. Many of the 27 that are on the male-specific region of the Y chromosome are active only in the testis. The sex-determining gene on the mammal Y chromosome is *SRY*. There are several problems posed by sex chromosomes. The X and Y chromosomes do not pair very well at male meiosis (causing infertility), the dosage difference of the X chromosome between the sexes requires compensation, its monosomic state in males causes sex-linked diseases, and translocations of the terminal *SRY* leads to sex reversal.

XY evolution: To trace the evolution of the human X and Y chromosomes, the chromosomes, genes and DNA in distantly related mammals, and even birds and reptiles were compared. Kangaroo sex chromosomes reveal the original mammal sex chromosomes, to which a region of an autosome was added in placental mammals. The platypus sex chromosomes, more related to those of birds, indicate that human sex chromosomes are relatively young. The human X and Y chromosomes evolved from an ordinary autosome pair only about 166 million years ago and the Y chromosome then degraded progressively. It started out with 1669 genes and today has only 45 genes. At this rate the Y chromosome will disappear in about 4.6 million years. If humans do not become extinct, new sex-determining genes and chromosomes will evolve, maybe leading to the evolution of new hominid species.

Sex without sex chromosomes: There are many reptiles and some fish that have no sex chromosomes. Sex is determined by environmental factors such as temperature (temperature sex determination (TSD)), through epigenetic changes. The Australian dragon lizard has a ZW system driven by a different sex-determining gene. However, when eggs are incubated at higher temperature, all of them hatch as females. The ZZ sex-reversed females are fertile, and when mated with ZZ males produce all ZZ offspring, whose sex depends entirely on temperature. In a single generation, the sex-determining system was changed from genetic sex determination (GSD) to TSD. Transcriptome analysis of ZZ sex-reversed females suggests that temperature acts, via the stress pathway, to activate epigenetic modifications involved in male determination.

In a one-on-one interview, Graves addressed the following questions:

What motivated you to take up science, in particular genetics?

When I was in primary school, people would ask me what I wanted to be when I grew up. When I asked my parents this question, they suggested that I could take up architecture since I was good at art and maths. (I did design our house in Melbourne.) It wasn't until my last year of high school that I recognized that I was quite good at science. Initially I didn't like biology very much because I thought it was full of random facts and I didn't see a pattern to it. Then I learnt about genetics and Mendel's laws. What got me interested was the idea that there were rules and laws that gave a basis for all this variation. Of course, much later I learnt all about evolution, the grand law that unites everything.

Can you talk about some of the work you carried out?

I started out with X chromosome inactivation and epigenetics for my MSc, and returned again and again to this fascinating system, showing that genes on the inactive X chromosome were not transcribed into RNA, and that activity was repressed by DNA methylation. When I went to Berkeley to pursue my Ph D, I became interested in cell fusion, because I was trying to fuse two X chromosome-active and single X chromosome-active cells. I then became interested in the biology of interspecies cell hybrids, looking at what their chromosomes and genes did. Later I came back to La Trobe and started seriously working on gene mapping with the idea to explore the evolution of the X chromosome. Later, our finding that the candidate

sex-determining gene *ZFY* is the wrong one got me interested in the Y chromosome and sex determination.

You were the Secretary of Education and Public Awareness at the Australian Academy of Science and involved in administering the Academy's highly successful new science education programmes. Can you briefly talk about these programmes?

I was pleased to hold that position because I always wanted to be involved in science education in Australia, which is absolutely critical in making it a more science literate society. The Academy came up with good programmes that aimed to excite young children. There were two programmes that I championed. The first was for primary school students – kindergarten to year 7, which is all of elementary school. This programme was aimed as much at the teachers as the students. It contained a series of units that were carefully developed to actually involve children in a way that is not fact-oriented. The idea was for children to explore a topic, make hypotheses, and carry out experiments to validate them. This was done to engage both the teacher and the student. The programme also emphasized writing about science. It has been implemented in 74% of all primary schools in Australia. We have another programme directed at junior high school. Its aim is to connect the teachers and help them develop a programme for the students. It is a web-based programme for science teachers to communicate and help each other. After my term, the Academy developed a senior science programme and is developing an inquiry maths programme. Hence the Academy has been a big player in science education in Australia.

You were the first to introduce measures to remove gender bias in the Academy, from election to fellowships. In what other initiatives were/are you involved?

When I was elected to the Academy, I was only the 13th woman out of some hundreds of elected fellows. Over the years I made suggestions as to how we could look for women candidates. When I became a member of the Executive, I suggested that the committees that assess the nominations put forward at least one woman among the three shortlisted candidates. People hated this rule and watered it down by amendments. The best thing that happened was a year in which no woman was elected. This gained a lot negative publicity and completely changed the pressures on the Council. A new (male) member of the Council put forward a similar suggestion and it was then accepted. This has worked well as the number of women doubled in just a few years. The Academy now spearheads a new programme (Science in Australia Gender Equity (SAGE)), which engages institutions in changing policy and making practical improvements to retain women in science.

What areas of research will you focus on in future?

I am interested in temperature-dependent sex determination. With the work on dragon lizards progressing in the University of Canberra, we have a very good chance of using that system to ask how temperature sex works, and how it evolved and how it can change. We haven't yet seen a change from temperature back to chromosomes, but we can devise ways of looking for that or maybe even manipulating the sex.

I no longer have a lab of my own, and I work with groups all over the world. I am currently collaborating with a group in China that studies falcon genomes; working with a group in New Zealand on fish that change sex, as well as with a group in Australia on the koala genome, and continuing my interest in the platypus in Adelaide. I can't complain about lack of variety.

S. Priya (*S. Ramaseshan Fellow*), Current Science Association, Bengaluru 560 080, India.
e-mail: priya@ias.ac.in