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An international collaboration led by Britain's Wellcome Trust Sanger Institute has published an almost complete sequence of the human X chromosome that offers, among many new insights, a better picture of how sex chromosomes evolved. A second paper in the same issue reveals some surprises about X inactivation of genes.

The Sanger Institute's Mark Ross and colleagues in the US and Germany determined 99.3% of the chromosome's euchromatic sequence and found 1,098 genes, including 399 "new" genes and 99 cancer-testis antigen genes.

But more than simply improving our understanding of individual genes, the sequence offers a powerful insight into the evolution of the chromosome itself, Ross told reporters at a press conference in London. "We can see the way evolution has shaped the chromosomes that determine our gender to give them their unique properties," he said. "The X chromosome is definitely the most extraordinary in the human genome."

Ross and colleagues offer some comparison of the sequence with that of the chicken to explore the development of the X chromosome from an autosome, which is thought to have occurred something like 300 million years ago. "Comparing the sequence of human X as it is with what is known about the sequences of other animal chromosomes allows you to tell where the X chromosome came from," said Robin Lovell-Badge from the National Institute for Medical Research, who wasn't involved in the study. "They've done some of that, but there's a lot more to be done."

Looking at more recent evolutionary history, the authors compared the human X chromosome with other mammalian sequences, finding nine major blocks of homology between human and mouse X chromosomes and 11 between human and rat. "The homology blocks occupy almost the entirety of each X chromosome, confirming the remarkable degree of conserved synteny of this chromosome within the eutherian mammalian lineage," they write.

The team's analysis revealed what coauthor Richard Gibbs from Baylor College of Medicine called "a lot of interesting local stories." "But maybe the message is not so much about surprise findings as the wealth of data," Gibbs told *The Scientist*. "It's mind-blowing the amount of biochemical data that has been generated."

The X chromosome has revealed itself to be quite different to autosomes, Lovell-Badge told *The Scientist*. "Compared with the autosomes that have been sequenced, it is relatively gene poor, which is interesting. It looks different to other chromosomes, so that's going to be interesting to study further."

One other difference is the relative density of disease related genes on the X, said Nature senior editor Chris Gunter, who wrote a News and Views article on the results. "It is the case that it is overrepresented with known disease genes," she told *The Scientist*. The sequence will be invaluable for identifying the genes for other known X-linked diseases, speakers at the press conference said.

The authors also note that LINE1 repeat elements cover a third of the X chromosome, "with a distribution that is consistent with their proposed role as way stations in the process of X-chromosome inactivation."

In the second paper, Laura Carrel from Pennsylvania State University College of Medicine, and Huntington Willard from Duke University, Durham, North Carolina, present a comprehensive profile of X-chromosome inactivation, the process by which genes on one X chromosome in female mammals are silenced in individual cells.

They found that about 75% of X-linked genes are permanently silent and about 15% permanently escape inactivation and are thus expressed at twice the level in women as in men. An additional 10% show variable patterns of inactivation, they write.

"This suggests a remarkable and previously unsuspected degree of expression heterogeneity among females," Carrel and Willard write, and could explain some sexually dimorphic traits.

This finding also points to the future direction genomics should take, said Steve Jones, professor of genetics at University College London, who was not involved in the research. "All the action in genetics in the future will not be in the anatomy of the genome, which this sequencing is, but in physiology."

"It's not the structure that's important," he told The Scientist. "It's the regulation and the function."

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