# Research finds X doesn't always mark the spot

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Research from the University of Bath has found a greater number of 'escaping genes' on the X chromosome than have been previously detected, with implications for the understanding of mental impairment in humans.

Human females, unlike males, have two copies of the X chromosome. This double dose of the X chromosome presents an interesting genetic conundrum, namely what happens to the genes on this extra chromosome? If all of the genes were to be expressed then females would have twice the dose of the genes' products compared with males.

To compensate for this extra set of genes in females, a process called X-Chromosome Inactivation switches off one entire X chromosome and its complement of genes, shriveling it up like a raisin so that the genes can't be expressed.

However, this process is not perfect, and some genes are able to escape this 'silencing'. These escaping genes are of interest as in about one in a thousand births of girls where the newborn inherits a further copy of the X chromosome, making them XXX rather than simply XX. The very high level of expression of the genes that have escaped X-chromosome inactivation can have serious consequences including growth abnormalities and mental impairment.

Professor Laurence Hurst, from the University of Bath's Department of Biology & Biochemistry, in collaboration with colleagues from Shanghai Institute for Biological Sciences, in China, has carried out a unique study which has built on previous understanding in this area. Unlike previous research that compared X-chromosome inactivation between mice and humans, this study looked within the human species at two different groups, Europeans and Yorubans from Africa, with interesting results.

The study found that 114 genes on the X chromosome had escaped X-chromosome inactivation, including 76 that had not been previously identified.

Professor Hurst said: "The genes we have identified are located in areas of the X chromosome where we expected to find escaping genes. We have now found that there are also great variations between the two populations we studied, and between individuals within these populations. This level of variation matches what we see in women with three X chromosomes – some appear normal but some are profoundly affected."

In some individuals, up to 80 genes were shown to escape. The genes that were most variable in escape were also shown to be the fastest evolving. Previous research has found that escaping genes undergo stronger purification selection - the process of selective removal of genes that are deleterious or harmful, but the current evidence didn't confirm this.

The work has implications for understanding genetic diseases. Professor Hurst commented that "importantly, our research could tie in the sorts of genes that escape X-chromosome inactivation with the symptoms of having too many X chromosomes, in that the genes we found were commonly those previously associated with mental impairment, the most common symptom of XXX syndrome.

"We have found 22 genes of interest that both escape X inactivation and that are associated with mental functioning. We hope that this research will enable the pinpointing of exactly which of these genes are associated with XXX syndrome and in turn, in the future, to better management of the condition."

**More information:**
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