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Genomes carry a heavy burden

Most people's DNA contains genetic mutations that are potentially lethal to offspring.

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Members of the Hutterite ethno-religious group are descended from a small group of founding individuals.

Most people carry one or two genetic mutations that can cause early death or infertility in their offspring, researchers report in a study published on 8 April in *Genetics*[1].

That estimate puts humans on a par with animals such as fruit flies[2] and zebrafish[3], which have smaller genomes. But it is probably a conservative figure, says lead author Ziyue Gao, a geneticist at the University of Chicago in Illinois.

Gao's team examined recessive mutations that cause lethal disease in people who inherit two copies of the flawed gene — one from each parent. People with one copy do not show symptoms, but can pass the mutation on to their children. The researchers' findings account for only mutations that would prevent a person from reproducing in the absence of modern medical care — excluding recessive conditions that do not always result in early death or infertility.

Scientists have tried to estimate the average number of lethal recessive mutations in an average person by comparing the genes of children from unrelated parents to those from parents who are first cousins or other blood relatives[4, 5]. But people who marry relatives tend to differ in other ways from people who do not, making it hard to separate genetic and environmental factors.

To avoid this problem, Gao's team chose to study a US ethno-religious group called the Hutterites. Members of the group have a communal lifestyle, with shared property and equal access to modern medical care. They keep detailed genealogical records and traditionally marry within the group. These characteristics minimize variations in environmental influences that could skew the researchers' analysis, Gao says.

Follow a family tree

The analysis involved 1,642 Hutterites living in South Dakota. The study group stretches back 13 generations and is descended from just 64 founders.

Gao's team used computer simulations to determine the likelihood that a recessive mutation in a founder would show up as a genetic

disease in a Hutterite child born after 1950. The team compared this result with the number of present-day Hutterites who have severe genetic diseases to infer that each founder carried about 0.58 recessive lethal mutations.

The team then adjusted this number because research in mice suggests that about half of offspring who inherit recessive lethal diseases die before birth[6, 7]. From this, they concluded that each Hutterite founder carried one or two recessive lethal mutations.

The results suggest that, on average, two first-cousins are 1.8% more likely than unrelated parents to produce a child with a serious genetic disease — a relatively small effect, says Gao.

Alan Bittles, a geneticist at the Murdoch University in Perth, Australia, says that the work adds to a growing body of research suggesting that concerns about marriage between relatives are overblown. “It’s one more study that tends to show, and show quite clearly, that our previous ideas of the ill effects of first-cousin marriage have been grossly exaggerated,” he says.

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References

1. Gao, Z., Waggoner, D., Stephens, M., Ober, C. & Przeworski, M. *Genetics* **199**, 1243–1254 (2015).
2. Simmons, M. J. & Crow, J. F. *Annu. Rev. Genet.* **11**, 49–78 (1977).
3. McCune, A. R. *et al*. *Science* **296**, 2398–2401 (2002).
4. Morton, N. E., Crow, J. F. & Muller, H. J. *Proc. Natl. Acad. Sci. USA* **42**, 855 (1956).
5. Bittles, A. H. & Black, M. L. *Early Human Development* **86**, 737–741 (2010).
6. Mitchell, K. J. *et al*. *Nature Genet.* **28**, 241–249 (2001).
7. White, J. K. *et al*. *Cell* **154**, 452–464 (2013).