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Brains may be genetic mosaics

Nerve cells mysteriously mislay chromosomes.
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Losing genes change what a cell can do.
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Many cells in the average brain may be missing huge chunks of genome, scientists revealed at a San Francisco meeting yesterday. The puzzling omissions might decide our risk of disease.

Cells are generally assumed to need a full set of DNA to run without major flaws. In fact, a third of dividing cells in one region of the adult mouse brain have gained or lost at least one chromosome - the same goes for up to 15% of the adult neurons these cells produce, biologists have discovered.

This hints that every person's brain may be a mosaic of cells with different genetic make-ups. "We were stunned," said Dhruv Kaushal of the University of California at San Diego at the American Society for Cell Biology conference. "We want to know what this means for the brain."

Cells that gain or lose chromosomes could predispose or protect from certain diseases, speculates Kaushal. Down syndrome symptoms, for example, might be lessened in patients who have frequently lost the extra copy of chromosome 21 that is responsible for the disorder.

Cells lacking chromosomes might also be prone to form tumours. And some scientists speculate that an increased risk of developing Alzheimer's disease might arise in otherwise healthy people who carry a subset of brain cells with an extra copy of chromosome 21.

Last year, the same San Diego team showed that cells elsewhere in the embryonic and adult mouse brain often lack a chromosome[1]. The group added weight to their argument by counting chromosomes in a region of the cortex that produces new nerves throughout life.

Team member Mike McConnell argues that the cellular

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phenomenon - thought to arise when chromosomes are divvied up inaccurately at cell division - must serve some biological purpose in the brain. Immune cells and blood cells they have examined appear not to show the same effect, so "It doesn't seem to be a mistake".

Losing genes "changes what a [nerve] cell can do," says McConnell, perhaps slowing the speed that they communicate. Some bacteria, for example, shuffle their genomes when they are in uncomfortable conditions, to create a new mutant that can survive.

By contrast, cells lacking the correct number of chromosomes in the growing embryo are carefully eliminated from the body's tissues, reveals Gillian MacKay who studies chimeras at the MRC Reproductive Biology Unit in Edinburgh, UK.

Embryo and placenta start from the same ball of cells. Yet according to prenatal diagnostic testing, around 2% of placentae - but not the embryos they nurture - contain a mix of chromosomally normal and abnormal cells.

MacKay used a fluorescent protein to track the fate of cells carrying double the normal number of chromosomes in chimeric mice embryos.

At first normal and aberrant cells are mixed, she found. By a third of the way through gestation they are ousted from the embryo. The anomalous cells "must be selected against," says MacKay. They may commit suicide or be sorted into the placenta.

References

1. Rehen, S. K. *et al*. Chromosomal variation in neurons of the developing and adult mammalian nervous system. *Proceedings of the Naional Academy of Sciences*, **98,** 13361 - 13366, (2001). **|Article|**