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Mouse model of a human neurological disorder

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Neurofibromatosis type 1 (NF1) is an inherited neurological disorder that affects 1 in 3,500 people worldwide. It is caused by mutations in the *NF1* gene, which encodes neurofibromin, a protein involved in the Ras signalling pathway. Patients have tumours of neural origin and many have learning difficulties.

Previous attempts to knock out the *NF1* gene have been unsuccessful because the mutant mice die as embryos. Now, a team of researchers led by Luis Parada of the University of Texas Southwestern Medical Center have generated mice in which an *NF1* gene mutation is triggered only in neuronal cells. Reporting in the 1 April Genes and Development, Zhu *et al* inserted *loxP* sites flanking exons 31 and 32 of the mouse *NF1* gene. By crossing these mice with a transgenic mouse strain that expresses Cre recombinase under the control of a neuronal-specific gene (Synapsin I), exons 31 and 32 of the *NF1* gene were deleted in most differentiated neuronal populations (*Genes Dev* 2001, **15**).

The *NF1* mutant mice had severe learning defects but did not develop tumours. This suggests that the loss of *NF1* in mature, differentiated neurons might not be sufficient to induce tumour development. The cerebral cortex of mutant mice was 20% smaller than in their wild-type counterparts, and there were increased numbers of astrocytes in the cortex, hippocampus and brain stem. The hyperproliferation of astrocytes, a condition known as astrogliosis, has been seen in a number of *NF1* patients at post-mortem but was thought to be the result of chemotherapy. This conclusion may therefore need to be reassessed given that *NF1* mutant mice also display astrogliosis.

References

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