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Fine-mapping of fearfulness

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Geneticists cut their teeth on conditions controlled by single loci. The harder task is to find the many loci that work together to control a single trait. In the 7 November Proceedings of the National Academy of Sciences Mott *et al*. demonstrate a new method for mapping these quantitative trait loci (QTL; *Proc Natl Acad Sci USA* 2000, published online before print). Previous methods all have their limits: family-based studies tend to be small and so can only do coarse mapping; population-based association studies give greater numbers (and thus potentially greater resolution) but are complicated by variable and unknown inheritance histories; and breeding studies in mice are plagued by a possible lack of segregating loci when two inbred mouse populations are used as founders. Mott *et al*. get around this last problem by using the progeny from an eight-way cross that was started 30 years ago and is now in its 60th generation. They use dynamic programming to calculate the probability that a given allele is descended from one of the eight progenitors. Use of single-marker association often fails because different QTL alleles occur on similar haplotypes, but multipoint analysis allows the authors to fine-map all five of the previously identified loci for fearfulness in mice. The authors propose that whole-genome fine mapping with this method would be cost-effective if 20 or more traits were mapped in parallel on the same set of mice.

References

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2. Searching for genetic determinants in the new millennium.