The Collaborative Cross, a Community Resource for the Genetic Analysis of Complex Traits

Churchill, G., Airey, D.C., Allayee, H., Angel, J.M., Attie, A.D., …, **Page, G.P.**, et al. (2004). The Collaborative Cross, a community resource for the genetic analysis of complex traits. *Nature Genetics*, 36 (11):1133-1137.

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Many genomic insights happen only after researchers have developed the proper technology, models, and reagents. This paper, which has been cited 170 times, outlines the steps to develop the murine collaborative cross, often now called the advanced intercross. The Collaborative Cross will be a powerful tool for studying treatment, environmental, and genetic effects on organisms. Murine recombinant inbred (RI) strains are the daughter lines of two or more inbred lines that have been crossed and then bred to homozygosity (all loci are homozygous) through many generations of sibling mating. This process takes the original two genomes and shuffles them through the resulting generations, which then allows for study of different genetic combinations. Inbred and RI lines allow the same genetic background to be studied in a number of environmental and treatment regimens, which is not possible in out-bred strains.

The RI lines are powerful, but are expensive to develop and maintain. As a consequence, most strains have only 20–30 lines, which limit power and typically result from crossing only two parental lines. Crossing only two parental lines limits the genetic diversity of the resulting RI strains.

In this paper we proposed methods for developing 1,000 daughter RI lines from a cross of eight parental lines that include broad diversity, including most strains used in research.

Since the publication of this paper, the National Institutes of Health has allocated funding for the breeding of the Collaborative Cross, and the process has started. The full panel will be available in two to three years.

The Collaborative Cross will provide a common reference panel specifically designed for the integrative analysis of complex systems and will change the way we approach human health and disease.

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