This Week's Citation Classic®

CC/NUMBER 30
JULY 29, 1985

Bailey D W. Recombinant-inbred strains. An aid to finding identity, linkage, and function of histocompatibility and other genes. *Transplantation* **11**:325-7, 1971.
[Jackson Laboratory, Bar Harbor, ME]

A set of seven mouse strains was constructed from a cross of two existing inbred strains Each new strain then was independently inbred by a regimen of over 20 generations of full-sib matings The set has advantages for testing genetic linkages of polymorphic genes [The *SCI*® indicates that this paper has been cited in over 260 publications since 1971]

Donald W. Bailey
Jackson Laboratory
Bar Harbor, ME 04609

June 25, 1985

In 1959, while at the NIH, I became interested in histocompatibility (H) genes, which code for antigens causing rejection of grafted tissues. Because H genes are so plentiful and have the single phenotype of eliciting graft rejection, the only currently known way to identify each gene is to genetically isolate it in a congenic strain and then find its location on a chromosome. This procedure was successfully shown to work in the pioneering studies by George Snell in the preceding decade.[1] Snell concentrated on studying many alleles at a few loci; I wanted to concentrate on few alleles at many loci. This meant that after I eventually completed the arduous task of constructing the contemplated 100 congenic strains I would need to do many linkage tests.

It occurred to me that a set of inbred strains constructed from a cross of the same two inbred progenitor strains that were used to construct the congenic strains would provide a genetically segregated, yet genetically fixed, set of genotypes. These genotypes would be useful for sorting out linkage relationships of the H genes that were to be isolated in my congenic strains. I therefore began constructing a set of 12 (later reduced to 7) "recombinant-inbred" (RI) mouse strains.

When I accepted a new position at the University of California Medical Center in San Francisco, I took all my incipient congenic and RI mouse strains across the continent with me. I continued with the construction of these strains for six more years, whereupon I accepted a position at the Jackson Laboratory in Maine. I once again brought my mouse strains across the continent. I must admit that I was tempted to desert my RI strains at this time, for I had not yet used them and I wasn't sure the skin-graft tests on them would be sufficiently decisive for their intended purpose. Moreover, the number of strains I held had increased significantly from my other research projects, and I was looking for ways to reduce the number of mice to be shipped.

This publication has been frequently cited probably because at the time of its appearance, a raft of polymorphic loci determining such traits as antigens, allozymes, serum proteins, and immune responses, among others, were being discovered in the mouse. Although the RI-strain methodology was originally planned for the linkage analysis of the set of H genes, it would work as well with any other polymorphic loci at which the two progenitor strains differ.[2,3] A shortcut method of determining genetic linkage was appealing. It saved time, effort, and research funds.

1 **Snell G D.** Methods for the study of histocompatibility genes *J Genetics* **49** 87-108, 1948 (Cited 195 times since 1955)

2 **Bailey D W.** Recombinant inbred strains and bilineal congenic strains (Foster H L, Small J D & Fox J G, eds) *The mouse in biomedical research* New York Academic Press, 1981 Vol 1 p 223-39

3 ----------. Strategic uses of recombinant inbred and congenic strains in behavior genetics research (Gershon E S, Matthysse S, Breadefield X O & Ciaranello R D, eds) *Genetic research strategies for psychobiology and psychiatry* Pacific Grove Boxwood Press, 1981 p 189-98