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Letter to the Editor

Mouse Strain Backgrounds: More Than Black and White

A recent Viewpoint in *Neuron*, which arose from a Banbury Conference (Silva et al., 1997), provided a series of recommendations on genetic backgrounds of mutant mice used in neuroscience research. Three principles emerged: (1) that the background be described in sufficient detail, so as to be reproducible; (2) that the background be sufficiently simple, so as to be reproducible; and (3) that a common genetic background be used, so that results from several laboratories may be compared directly. The strong, specific recommendations were for the use of C57BL/6 and 129 × C57BL/6 F1 hybrids as standard strain backgrounds.

The first two principles are sound, but in the context of "recommendations" for a broad neuroscience community, the third should have been accompanied by a more balanced discussion of its chief limitation—namely, the missed opportunity to observe potentially critical effects of a mutation. Given the surprising diversity of neurological characteristics exhibited among existing inbred strains, it seems unnecessarily rigid to recommend two genetic backgrounds so strongly, reserving others as alternatives for exceptional situations.

Readers should examine a recent article by Crawley and colleagues (1997), which was cited but not sufficiently explored in the Banbury Viewpoint. Crawley et al. discussed the functional diversity in various behavior-related phenotypes of an extended panel of common mouse strains to determine which may be the best choices for particular experiments. The authors sampled the extensive "neurodiversity" that exists among common strains for a few key traits, including learning, aggression, anxiety, and reproduction. Crawley et al. also aired the concept of achieving a balance between the "most appropriate" control strain and the need for more stringent statistical considerations when less appropriate genetic controls are practical. The authors concluded:

> "There is no 'best' strain that can be recommended across all behavioral paradigms for all null mutations. Rather the strain is chosen for its predicted sensitivity... The present authors hope that this article will serve to guide investigators to the wealth of available knowledge in behavioral genetics, to make an informed choice of the best inbred strain for the development of a new null mutation."

That is, for many traits no one strain or hybrid has a patent on "wild type." Moreover, in contrast to the heavyhandedness of the Banbury message, the Crawley et al. article exemplifies a style of scientific enterprise and communication in which a body of literature is distilled so that researchers can make their own informed choices, while bearing in mind the issues of appropriate controls. Many other neurological phenotypes would also suffer from restricting background strains to the two suggested, among them neuronal excitability and degeneration (Messer et al., 1992; Schauwecker and Steward, 1997; Cox et al., 1997; Hamilton et al., 1997) and hearing loss (Erway et al., 1993).

An extended panel of readily available common inbred strains that would serve neuroscientists well, based on existing literature, include A, BALB/c, CAST, CBA, C3H, C57BL/6, FVB, DBA/2, NZB, SJL, and 129 (substrain designations omitted but not ignored). Although it is prohibitive for many researchers to do test crosses of their targeted mutation with more than a few of these strains, critical opportunities for discovery will nevertheless be missed by limiting studies to any one pair. Indeed, the plot will thicken as mutagenesis allows researchers to go beyond knockouts to more subtle mutations, the effects of which are likely to be even more strongly influenced by genetic background. The surprising (yet undeniable) neurodiversity represented in a full-color strain panel is merely nature's way of supplying many more mutations (and consequential biological effects) than could be easily put together by hand. It would be a shame to miss the opportunity for new discovery. Being mindful of the appropriate genetic and experimental controls is important whether we work in black and white or in color.

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