L. C. Dunn and Donald Charles on Quantitative Traits in the Mouse

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ORIGINAL CITATION

Studies on Spotting Patterns I. Analysis of Quantitative Variations in the Pied Spotting of the House Mouse
Leslie C. Dunn and Donald R. Charles
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DUNN and Charles (1937, p. 14) opens with an understated assessment on the state of developmental genetics at the time: “The processes which lead to the formation of patterns during ontogeny in animals are at present very imperfectly understood.” This was the first in a series of five articles that proposed that understanding the highly variable coat patterns of the mouse could provide a model for development, revealing “some of the steps by which one part or area of the body comes to differ from another.” The remarkable work that followed provides a window into the history of mouse genetics and quantitative trait studies at a time when little was known about the underlying mechanics.

Leslie Clarence Dunn was founder of the Genetics Society of America and was its President in 1932. Although he also worked on *Drosophila* and poultry, he is a legend in the mouse genetics community, spawning several generations of mouse geneticists through his research on coat color genetics and the *t* haplotypes.

Dunn became intrigued by the wide variation in mice homozygous for the “pied” or “piebald” phenotype (mutant gene *s*), which could range from almost completely white to almost completely pigmented. He noted the marked variation in spotting patterns in mice sold by “fanciers” and also found that inbreeding led to more consistent patterns. So, he set out to characterize the variability to determine whether it was genetic and/or stochastic, and how many genes might be involved.

The experiments that he undertook read remarkably like those conducted today, except of course that no genes were mapped. Dunn and his graduate student Donald Charles first

constructed new inbred strains selected for extreme phenotypes, developed a piebald grading scale for quantifying the trait, and then made F1 crosses and backcrosses. By applying the grading scale to these offspring, they were able to characterize the inheritance patterns of *s* modifier loci in terms of modes of transmission, numbers of modifier genes, and the contribution of these unlinked alleles to the trait. This and subsequent articles on the *W* (*Kit*) locus revealed the presence of modifiers of different strengths and, in the case of piebald, that some of these modifiers on their own could cause pigmentation abnormalities.

Today, *s* is known as *Ednrb*, for the endothelin receptor type B. The work of Dunn and his colleagues honed in on the genes influencing melanocyte development and pigmentation pathways, but without the tools needed to understand the molecular details that were still nearly a half century away.

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