Biological Variability in Wistar-Kyoto and Spontaneously Hypertensive Rats

To the Editor:

Dr. Yukio Yamori has recently informed us (personal communication, 1987) that his commentary in our article, "Biological Variability in Wistar-Kyoto Rats: Implications for Research with the Spontaneously Hypertensive Rat," contains two errors in the dating of historical events in the development of spontaneously hypertensive rats (SHR) and Wistar-Kyoto rats (WKY). Unfortunately, these errors tend to further confuse the questions surrounding the genealogical background of SHR and WKY.

In taking exception to our statement that the National Institutes of Health (NIH) established an inbred strain of SHR in 1969, Dr. Yamori's commentary states that "the inbred strain was, in fact, first established in 1963" at Kyoto University. Dr. Yamori informs us that his reference to the year 1963 is incorrect and that the SHR was indeed established as an inbred strain in 1969. It should be noted that by 1969, investigators at both NIH and Kyoto University had achieved 20 generations of brother × sister mating of SHR. Hence, by this time, both had established inbred strains of SHR. We recognize that the NIH investigators began their breeding program with rats from Kyoto of the 13th generation, as noted by Dr. Yamori. Dr. Yamori also states that in 1977, he "donated the first WKY strain to NIH, in response to a request from NIH, after WKY had been selected for normotensive blood pressure by repeated sib mating for generations." Dr. Yamori informs us that the reference to the year 1971 is incorrect and that it should have been 1977 (as given in our paper). It would be of interest to know exactly how many generations of brother × sister mating occurred before these rats were sent to NIH.

Festing has recently noted that "any given inbred strain may be distributed internationally with some hope that all the colonies with the same name will be genetically identical." Yet, over 10 years ago, the Committee on Care and Use of Spontaneously Hypertensive Rats predicted that intercolony variation associated with the widespread distribution of SHR "ultimately could seriously compromise the strain's unique value." Unfortunately, little attention has been given to the Committee's recommendation that breeders of SHR "emphasize . . . periodic introduction of original stock from the SHR colony at the Veterinary Resources Branch, National Institutes of Health, in order to minimize genetic variables between laboratories." (Such a practice might also have been useful in the breeding of WKY.)

As emphasized by Dr. John Rapp, blood pressure can be influenced by many genetic loci and the genetic basis for high blood pressure may be different for different strains of hypertensive rats (e.g., SHR and SS/Jr). It appears that in rats of the so-called WKY strain, the set of alleles regulating blood pressure may differ from one colony to another. Given the presumed genetic heterogeneity in "SHR," 1-3 to what extent might the set of alleles causing hypertension in these rats also vary from one colony to another?

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