Mislabelling of Donryu Rats

To the Editor:

Between 1992 and 2000, 21 papers1-21 were published that used rats from inbred colonies in Melbourne and Tokyo that were believed to be of the Donryu (DRY) strain. These rats were thought to have been the same strain as DRY used by Dr Tanase in early breeding experiments in relation to blood pressure in spontaneously hypertensive rats (SHR).22,23 The original DRY strain had been held at the Sankyo Co. Ltd. in Japan. At some time before 1991, however, it appears that in the company’s laboratories there had been an unrecognised substitution of Fisher 344 (F344) for DRY (see below) and that authentic DRY were culled and no longer exist.

In 1991, the company supplied 5 brother-sister breeding pairs to the Melbourne Biological Research Facility at the Austin Hospital. Accompanying documentation attributed specific genetic biochemical profiles of the DRY strain to these animals and differentiated them from the F344, BUF (Buffalo), and LEW (Lewis) strains. A separate colony was also established in Tokyo in the same manner.

The subsequent generations of these animals were used predominantly in cross-breeding studies of blood pressure, cardiac size, and intracellular calcium. These studies included genome-wide mapping in which the purported DRY strain from the Melbourne colony was genotyped for polymorphic markers. These data were subsequently made available on the Internet (www.genome.wi.mit.edu/rat/public/).

Recently, Dr Tanase indicated that the animals supplied to Melbourne and Tokyo that had been labeled as DRY were instead likely to be F344 rats. The company believed that before transfer to Melbourne and Tokyo, the labeling of authentic DRY animals and F344 had been unknowingly and accidentally swapped, and the authentic DRY were culled as supposed F344 in excess to needs.

These revelations prompted a comparison of the public polymorphic markers for the purported DRY (from Melbourne) and the F344, which revealed a genotypic difference of only 7%. Further biochemical polymorphic analysis revealed no differences between the profiles of the purported DRY from Melbourne and reference F344. Other studies in Japan by Dr Tanase confirmed that the polymorphism profiles of 43 markers from chromosomes 1, 2, 4, 5, 6, 7, 8, 9, 10, 12, 14, 16, 17, 18, 19, 20, and X were completely consistent between the purported Donryu animals from Tokyo and known authentic F344 rats from Sankyo.

In addition, the DNA polymorphic profile of a previous cross derived from SHR and authentic DRY animals was compared against the profile of the purported DRY from Tokyo. Of the 43 markers tested, the comparisons were informative for 17 loci, for which the cross (derived from authentic DRY) and the purported DRY animals were identical at 7 and nonidentical at 10.

Therefore, based on the available evidence that the purported DRY showed only minor differences from F344 and significant differences from authentic DRY, we conclude that the animals described as DRY in the listed publications1-21 were in fact inbred F344. In itself, this does not have implications for the results of the individual studies. The purported DRY were never intended to represent genetically appropriate controls for any strain, in particular SHR. Instead, they were intended simply as inbred normotensive controls, unrelated to SHR and used to maximize the informativeness of the linkage analyses. In fact, it is fortuitous that the control strain for crossbreeding studies of cardiac size should transpire to be the F344, which has one of the smallest hearts among normotensive rats.24 All subsequent publications that refer to these animals will use their correct designation of F344.

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