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Impact of improvements in breeding of laboratory rodents in ageing research

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Rodent models have long been a well-utilised tool in the study of ageing and the development of disease across the lifespan. The relatively short life-span of the Wistar rat allows for detailed study into the physiological and regulatory processes of ageing and chronic disease processes. Previous studies have demonstrated clear evidence of age-related disease at 18 months of age, with studies only continuing past this point if taking animals to natural death. Current work in our laboratory has highlighted a disparity between survivability and the progression of ageing in animals from the same outbred strain. Recently, it was found that aged rats (12–18 months) manifest less age-related morbidity and mortality than in previous work, despite being of the same breeding stock. This analysis compared the findings of a study of male rats aged to 18 months (HSD/Han Wistar rats, now sold as standard by Harlan UK; current cohort) with an earlier study of male Wistar rats supplied by the same company (historical cohort)^(1,2). The studies were run six years apart with animals housed in the same conditions.

Comparison of mortality indicated that currently available male Wistar rats were less prone to premature death (death < 18 months old) than the historical cohort (Table). Deaths of males were generally associated with cardiovascular and renal impairments, and this was apparent in histological evidence. Assessment of the total protein excretion of rats at 18 months indicated that this measure of renal function was significantly worse ($p < 0.05$) in the historical than in the current cohort.

Outcome measure	Historical Cohort (n = 10)		Current Cohort (n = 8)	
	Mean	SEM	Mean	SEM
Survival 9 months (%)	97	–	100	–
Survival 12 months (%)	82	–	100	–
Survival 15 months (%)	45§	–	100	–
Survival 18 months (%)	36**	–	100	–
Proteinuria (mg/24 hrs)	779.6	190.9*	112.1	14.7

Table: survival (%) and proteinuria (mg/24 hr) data from a historical (2005) and current (2011) cohort of male Wistar rats from ageing studies. § $P = 0.07$, * $P < 0.05$, ** $P < 0.01$ comparing historical and current cohorts.

These data suggest that changes in the quality of the Wistar strain provided to researchers by a commercial supplier have impacted substantially upon age-related outcomes.

With ageing research being of substantial importance for informing strategies for maintaining human health and well-being, animal models are an invaluable tool for assessing the progression of age-related disorders. Differences between past and current data suggest that rigorous breeding programmes may have altered the life trajectory of the Wistar rat. The reduced incidence of commonly observed markers of ageing in rodent models suggests a need for extension of age-related studies in these animals and questions the validity of using studies of lengths 12–18 months that were previously considered adequate for the induction of age-related decline.

1. Langley-Evans SC & Sculley DV (2006) The association between birthweight and longevity in the rat is complex and modulated by maternal protein intake during fetal life. *FEBS Lett* **17**, 4150–4153.
2. Joles JA, Sculley DV and Langley-Evans SC (2010) Proteinuria in aging rats due to low-protein diet during mid-gestation. *J Dev Orig Health Dis* **1**, 75–83.