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Survival of the thriftiest: restricted nurture reveals the thrifty nature of a growth gene in *Bos indicus*

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ABSTRACT. Growth hormone (GH) is a part of the somatotropic axis that controls metabolism, growth, development and aging in a wide range of animals. Mutations that reduce GH signaling have been associated with extended life spans and increased longevity in ways similar to what is observed in dietary restriction (DR) models. However, the mechanism by which DR works is not well understood. Here, we show that DR works as a factor in the evolution of the genetic make-up of domestic cattle. In a series of 6864 bovines of seven *Bos indicus* and tropically adapted *Bos taurus* breeds, the frequency of a short, wild-type allele of the promoter region of the bovine *GH* gene, *G1* allele, varied from 2.7 to 17.7%. The frequency of the long, domestic *G2* allele increased from 88 to 95% along 20 calf crops of commercial *Bos indicus* cattle of the Nelore breed undergoing selection for increasing

post-weaning weight gain with *ad libitum* nutrient intake. Under DR, however, the *G1* allele sustained growth better than the *G2* allele, as observed in a series of feeding tests. The *G2* allele was even detrimental or abiotropic, as it caused rapid body decay under DR. We observed a reflection symmetry of *GH* allele substitution effects on body weight under different dietary schemes. The *G2* allele is featured as the "demanding allele", because it is optimally fitted to *ad libitum* nutrient intake. The *G1* allele is featured as the "thrifty allele" because it is optimally fitted to DR. Our results show that dietary regimens need not extend lifespan or increase longevity in the sense of age-specific fitness. Instead, adaptation to any particular dietary regimen is just as much a consequence of selection as its cause; dietary regimens work as do any selection force, optimizing genotypic fitness to nutritional conditions.

Key words: Growth hormone; *Bos indicus*; Dietary restriction; Thrifty gene; Longevity; Marker-assisted selection

