

Commentary

ACCELERATED BONE AGING IN THE TRICHOThIODYSTROPHY MOUSE MODEL

In the paper by de Boer and colleagues (1), we described mice carrying an engineered mutation in the XPD gene, which encodes a DNA helicase involved in both DNA repair and transcription. The point mutation mimicked the causative allele of a patient suffering from the rare repair-transcription syndrome trichothiodystrophy (TTD). We reported the identification of many symptoms of premature aging, including osteoporosis and kyphosis, osteosclerosis, early greying, cachexia, infertility, and reduced life span.

In the commentary by Gerhard and Kasales (2), it is noted that, while both the kyphosis and osteoporosis are well documented, the linkage between the two was not discussed. In addition, other mechanisms that can cause kyphosis, for example, growth plate abnormalities, osteosclerosis, and muscular dystrophy, were mentioned.

The initial description of the aging phenotype of TTD mice lacked a detailed account of the underlying molecular and cell biological parameters. We are currently in the stage of further exploring the link between different aging endpoints, among which is the presumed relationship between osteoporosis and kyphosis. On the basis of ongoing detailed analysis of bone of aging wild-type and TTD mice (to be published elsewhere in detail), we conclude at this point that the bone phenotype observed in long bones of

aging TTD mice displays features of bona fide aging-related osteoporosis. With respect to the aspect of kyphosis, we failed to detect a causative trabecular bone loss, but other possible mechanisms have not yet been investigated. Thus, we observe bone features that resemble age-related changes found in mice and humans as well as bone parameters that behave differently in TTD mice and need further investigation concerning the mechanism.

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