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MAMMALIAN D-ASPARTYL ENDOPEPTIDASE: A SCAVENGER FOR NOXIOUS RACEMIZED PROTEINS IN AGING

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The accumulation of D-isomers of aspartic acid (D-Asp) in proteins during aging has been implicated in the pathogenesis of Alzheimer's disease, cataracts and arteriosclerosis. Here, we identified a specific lactacystin-sensitive endopeptidase that cleaves the D-Asp-containing protein and named it D-aspartyl endopeptidase (DAEP). DAEP has a multi-complex structure (MW: 600 kDa) and is localized in the inner mitochondrial membrane of mouse and rabbit, but DAEP activity was not detected in *E. coli*, *S. cerevisiae*, and *C. elegans*. A specific inhibitor for DAEP was newly synthesized and inhibited DAEP activity (IC_{50}, 3 μM), a factor of ten greater than lactacystin on DAEP. On the other hand, the inhibitor did not inhibit either the 20S or 26S proteasome.