

Abstract

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Age-dependent telomere-shortening is repressed by phosphorylated alpha-tocopherol together with cellular longevity and intracellular oxidative-stress reduction in human brain microvascular endotheliocytes.

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OBJECTIVE AND METHODS: Cellular life-span of neonatal human brain microvascular endotheliocytes (HBME) was estimated by population doubling levels (PDLs) for serial subcultivations until spontaneous proliferation stoppage, and was 2.4-fold longer for continuous administration with the 6-O-phosphorylated derivative (TocP) of alpha-tocopherol (Toc), being bio-available owing to its water-solubility, or TocP plus 2-O-phosphorylated ascorbate (Asc2P), and 1.3-fold longer with Asc2P, at a dose of 150 microM, than for the non-administered control. Enlarged cell diameters indicative of cellular aging were repressed for TocP-administered cells as analyzed with a channelizer.

RESULTS: Age-dependent shortening of telomeric DNA length (291 bp/PDL) was slowed markedly for TocP (165 bp/PDL) or TocP plus Asc2P, but slightly for Asc2P. Telomerase activity as assessed by the PCR-based TRAP method was detectable slightly at younger ages but no longer at middle ages for the non-administered cells, but, for TocP-administered cells, was intensely detected at younger ages and appreciably until middle ages. Intracellular TocP amounts were not changed age-dependently in contrast to a marked decrease in Toc which accrued from TocP esterolysis. This may be partly attributed to age-dependent changes in the lipid peroxidation product acrolein (ACR), which was abundant at older ages in non-administered cells, but scarcely in TocP-administered cells. Furthermore, intracellular reactive oxygen species (ROS) such as H₂O₂ and hydroperoxides as detected using the redox indicator CDCFH-DA was less abundant in TocP-administered cells than in non-administered cells.

CONCLUSION: Thus the telomeric-DNA retention, concurrently with retained telomerase activity, was shown to be correlated with cellular longevity, and may be supported by diminished oxidative stress, in hydrophobic microenvironment, which can be achieved by TocP rather than AscP.

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