P-55

Enhanced radical-scavenging activities and cell growth inhibitions of planar catechin analogues having alkyl side chains

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The protective role of flavonoids against free-radical induced diseases, such as cancer and heart disease, has been widely studied, and this has prompted the development of new types of antioxidants to remove reactive oxygen species. Recently, we reported that a planar catechin analogue (PC1), in which catechol and chroman moieties in natural (+)-catechin structure are constrained to be planar, showed higher antioxidative ability compared with (+)-catechin. Here we describe the practical method for a preparation of planar catechin analogues (PCn), which is capable to introduce various types of side chain. Thus synthesized planar catechin analogues (PC2 ~ 8) having various length of alkyl side chains showed potent radical-scavenging ability and effective protection towards oxidative DNA damage induced by the Fenton reaction, especially the larger the number of the carbon in the alkyl chains is, the stronger their antioxidative abilities become. In addition to the potent antioxidative ability, PCn showed cell growth inhibition through induction of apoptosis in cancer cell lines, as well as stillbene resveratrol that was a typical cancer chemopreventive agent present in grape. We then considered that PCn might be used as a lead compound for the development of antimutagen.

脂溶性平面型カテキンの抗酸化作用と生物作用
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P-56

Mutational property of 8-hydroxy-dGTP during DNA replication by cellular extract lacking DNA polymerase eta

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Oxidative nucleotide lesions as well as oxidative DNA lesions appear to contribute to mutagenesis induced by reactive oxygen species. We have studied roles of Y-family DNA polymerases, which are involved in translesional synthesis, in mutations induced by oxidative nucleotide lesions. In this study, we compared mutational property of 8-hydroxy-dGTP (8-OH-dGTP) during DNA replication by cellular extracts lacking DNA polymerase (pol) eta. Plasmid DNA containing the SV40 ori and the supF gene, the unmodified dNTPs, the SV40 large T antigen, and extracts of XP-V cells lacking DNA pol eta were incubated with and without 8-OH-dGTP. Replicated DNA was then transfected into an indicator E. coli strain KS40/pOF105, and the supF mutant frequency was measured. Extracts of HeLa cells were used as controls. Although the supF mutant frequency was increased by addition of 8-OH-dGTP, the frequency of mutation induced by 8-OH-dGTP was similar for XP-V and HeLa cell extracts. Thus, DNA pol eta is not major DNA pol which promotes incorporation of 8-OH-dGTP.

DNAポリメラーゼη欠損細胞抽出液によるDNA複製における8-hydroxy-dGTPの誘発変異
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