

Molecular basis for anti-aging effects of pomegranate-derived polyphenols

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論 文 名 : Molecular basis for anti-aging effects of pomegranate-derived polyphenols
(ザクロ由来ポリフェノールの抗老化機能とその分子基盤に関する研究)

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論 文 内 容 の 要 旨

Pomegranate-derived polyphenols are expected to prevent life-style related diseases. In this study, I evaluated the ability of eight pomegranate-derived polyphenols, along with other polyphenols, to augment *SIRT3*, a mammalian *SIR2* homolog localized in mitochondria. I established a system for screening foods/food ingredients that augment the *SIRT3* promoter in Caco-2 cells and identified three *SIRT3*-augmenting pomegranate-derived polyphenols (eucalbanin B, pomegranin A, and eucarpanin T₁). Among them, pomegranin A activated superoxide dismutase 2 (SOD2) through *SIRT3*-mediated deacetylation, thereby reducing intracellular reactive oxygen species. The other *SIRT3*-augmenting polyphenols tested also activated SOD2, suggesting antioxidant activity. My findings clarify the underlying mechanisms involved in the antioxidant activity of pomegranin A. Furthermore, this effect of pomegranin A on intestinal cells might lead to the activation of interorgan interaction and prevention of age-related disorders, the possibility of which must be evaluated in the future study. However, the homogenate of fresh arils (2 kg) of pomegranate contains only 11mg (3.5 μ mol) of pomegranin A. Thus, daily intake of pomegranin A as a supplement is thought to be more desirable.

Ultraviolet (UV)-B is an established etiological cause of skin damage. *SIRT1*, a mammalian *SIR2* homolog localized in nuclear and cytosol, plays a protective role in the UVB-induced DNA damage. Although many kinds of polyphenols have been studied to elicit effects on prevention of sunburn, the repair function of *SIRT1*-activating foods in UVB-induced cell damage is sparse. Previously I established a system for screening foods/food ingredients that augment the *SIRT1* promoter in HaCaT cells and identified four *SIRT1*-augmenting pomegranate-derived polyphenols (ellagic acid, punicalin, punicalagin, urolithin A). In this study, I found that all of these *SIRT1*-augmenting polyphenols contributed to cell proliferation in UVB-irradiated HaCaT cells. Among them, punicalagin and urolithin A showed abilities to remove UVB-induced CPD through activating nucleotide excision repair (NER) system. Both punicalagin and urolithin A up-regulated NER-related XPC expression and XPA deacetylation level depending on *SIRT1*. In the present study, I tried to clarify the underlying mechanisms involved in the repair activity of pomegranate-derived polyphenols in UVB-damaged HaCaT cells. The interesting point of this study is that I treated the HaCaT cells with polyphenols after UVB irradiation instead of pre-UVB treatment, expecting that these polyphenols could repair UVB-damage skin cells by uptake or external use. It remains to be determined whether topically applied punicalagin and urolithin A can be used as a therapeutic agent for reducing the risk of skin damage after chronic UVB exposure.