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, pomegraniin A, and eucarpanin T_1). Among them, pomegraniin 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 pomegraniin A. Furthermore, this effect of pomegraniin 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 μmol) of pomegraniin A. Thus, daily intake of pomegraniin 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 urorithin A can be used as a therapeutic agent for reducing the risk of skin damage after chronic UVB exposure.