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〈Regular Article〉

Plasmin Derived from Senescent Fibroblasts Is Induced by Prostaglandin E_2 and Increases the Degradation of Collagen

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Abstract

Photoaging and intrinsic aging of the skin results from collagen degradation in the dermis by matrix metalloproteinases (MMPs), but photoaging differs from intrinsic aging due to the obvious emergence of skin wrinkles. It could be thought that photoaging is increased by intrinsic aging because its signs are expressed suddenly in the dermis of advanced intrinsically aged skin. In this study, we constructed a 3D photoaged model of the dermis using collagen-embedded senescent fibroblasts and analyzed collagen degradation and plasmin activity, because we had found that plasmin derived from fibroblasts activates MMP-1. Senescent fibroblasts had increased levels of plasmin activity in a non-irradiated 3D model and had increased degradation of collagen following exposure of the 3D model to ultraviolet (UV)-A radiation. Moreover, it was found that prostaglandin E_2 (PGE_2) increased plasmin levels in normal fibroblasts and the increase of plasmin in senescent fibroblasts was reduced by treatment with the PGE_2 inhibitor NS398. Treatment with tranexamic acid, plasmin or NS398 reduced collagen degradation in the 3D photoaged model. These results suggest that the increased level of plasmin in the 3D senescent fibroblast model depends on the expression of PGE_2. Our study suggests that intrinsic aging increases photoaging in a plasmin- and PGE_2-dependent manner and that tranexamic acid prevents photoaging especially in aged dermis.

Key words: plasmin, prostaglandin E_2, MMP-1, 3D collagen model, senescent fibroblast.