



具有皮肤抗衰老功能的新成分

A γ -glutamyl transpeptidase inhibitor (GGsTop™); a new stimulator for anti-aging of skin

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【研究的概要】

现在已经证明，作为 γ -谷氨酰转肽酶 (GGT) 的阻碍剂所开发出的新化合物 GGsTop™ 具有能使人体皮肤纤维芽细胞的弹性蛋白和胶原蛋白的产生能力亢进的功能，并进一步具有促进角质细胞游走的功能。其作为新功能的化妆品原料是很有价值的。

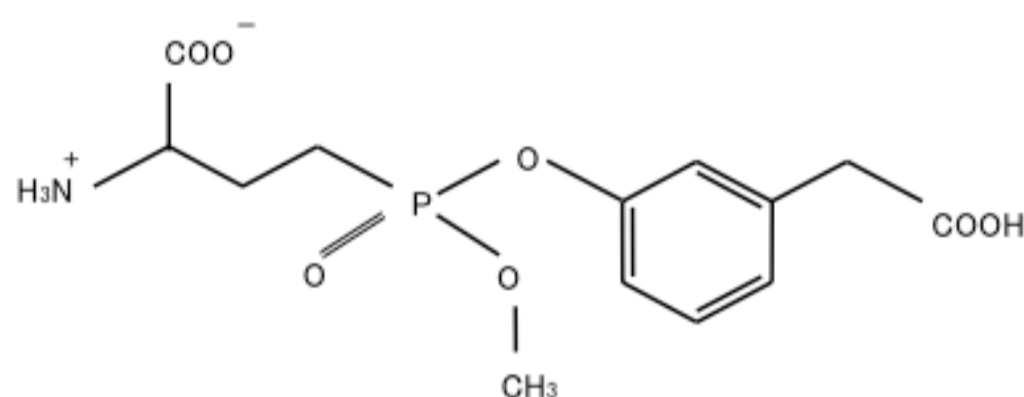
A decrease in the quantity and organization of connective tissue is associated with skin aging. Skin connective tissue is composed primarily of fibrillar collagen bundles and elastic fibers. An age-associated reduction in the expression of these dermal connective tissue elements is responsible for skin wrinkling. In this study, we investigated that the anti-aging effect and the mechanism of action for an inhibitor (GGsTop™) of γ -glutamyl transpeptidase, an important enzyme in glutathione degradation, using human skin fibroblasts and the keratinocyte cell line. A treatment of human skin fibroblasts with GGsTop™ induced collagen and elastin synthesis and increased the expression of α -smooth muscle actin (α -SMA). Additionally, GGsTop™ induced the expression of heat shock protein 47 (HSP47), a collagen-specific molecular chaperone. Furthermore, GGsTop™ treatment also enhanced the migration of keratinocytes. Collectively, these results provide new insights into the cosmetology of GGsTop™ in human skin fibroblasts and keratinocytes and suggest potential applications in the treatment of aging skin.

①研究的背景

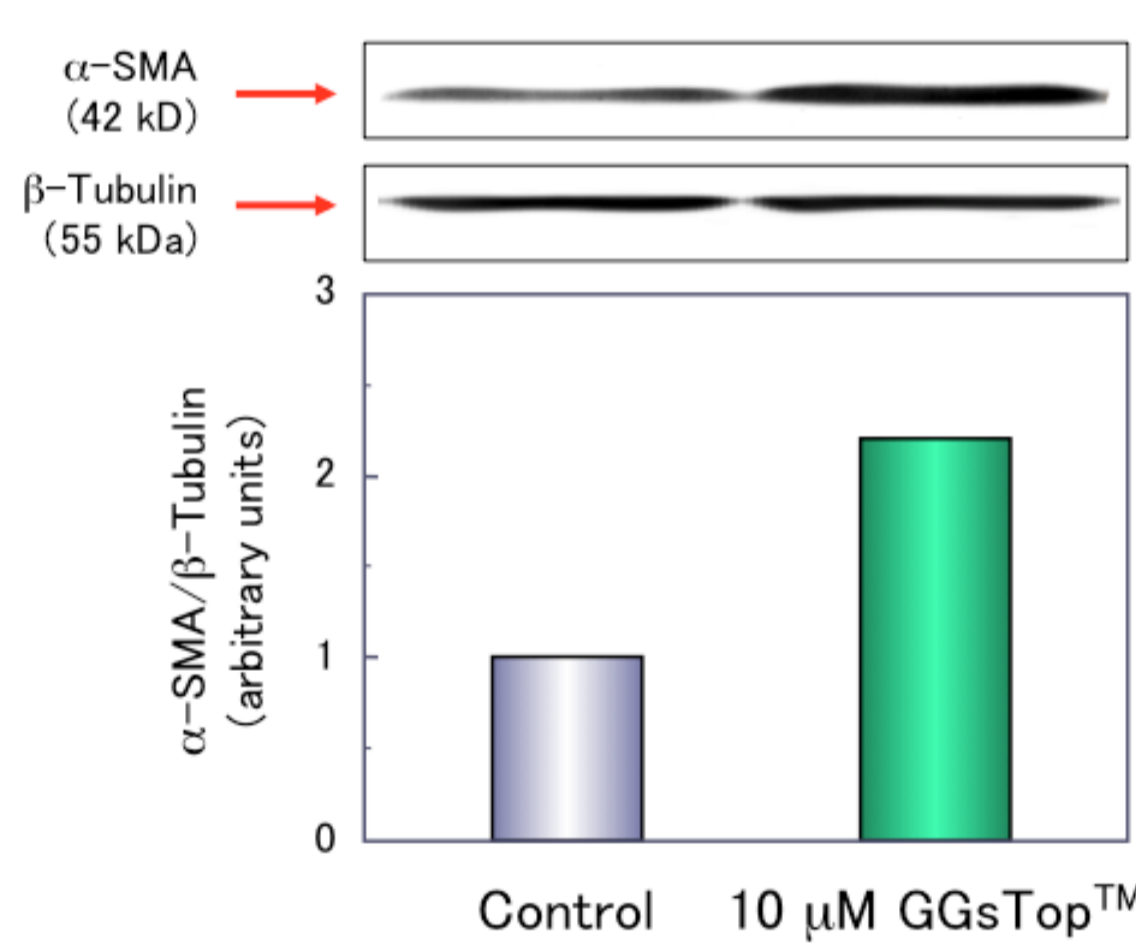
皮肤老化后，会影响到弹性蛋白和胶原蛋白的变性及减少，导致皮肤松弛和产生皱纹。肝的纤维化及肝硬化是由于肝脏中产生的弹性蛋白过剩而导致的。我们已经证明，在作为肝纤维化及肝硬化症的直接原因的肝星状细胞的弹性蛋白产生能力亢进的机理中，由于氧化酶的NADPH oxidase 活性的亢进导致的活性氧的急剧产生、和作为细胞内的氧化还原调节因素的谷胱甘肽量的一过性的减少，使得弹性蛋白的产生出现亢进的情况。本研究是根据这些研究结果，认为虽然在肝纤维化和肝硬化的进程中，弹性蛋白合成能力的亢进会使病态发展，但是对于维持人们的健康和年轻的某些部位和器官来说，丰富的弹性蛋白量是有益的，所以使这些部位及器官中存在的弹性蛋白产生细胞的弹性蛋白合成能力亢进也是有益的。我们是按照这样的逆向的设想来展开我们的研究的。

我们在研究中使用与谷胱甘肽的生物合成有关的 γ -谷氨酰转肽酶 (GGT) 的特异的阻碍剂GGsTop™、对人体皮肤成分的纤维芽细胞的弹性蛋白以及胶原蛋白产生能力亢进的效果及其机理进行分析，并进一步通过测定人体皮肤角质细胞的游走情况，研究了将GGsTop™作为新的功能性化妆品原料的有效性。

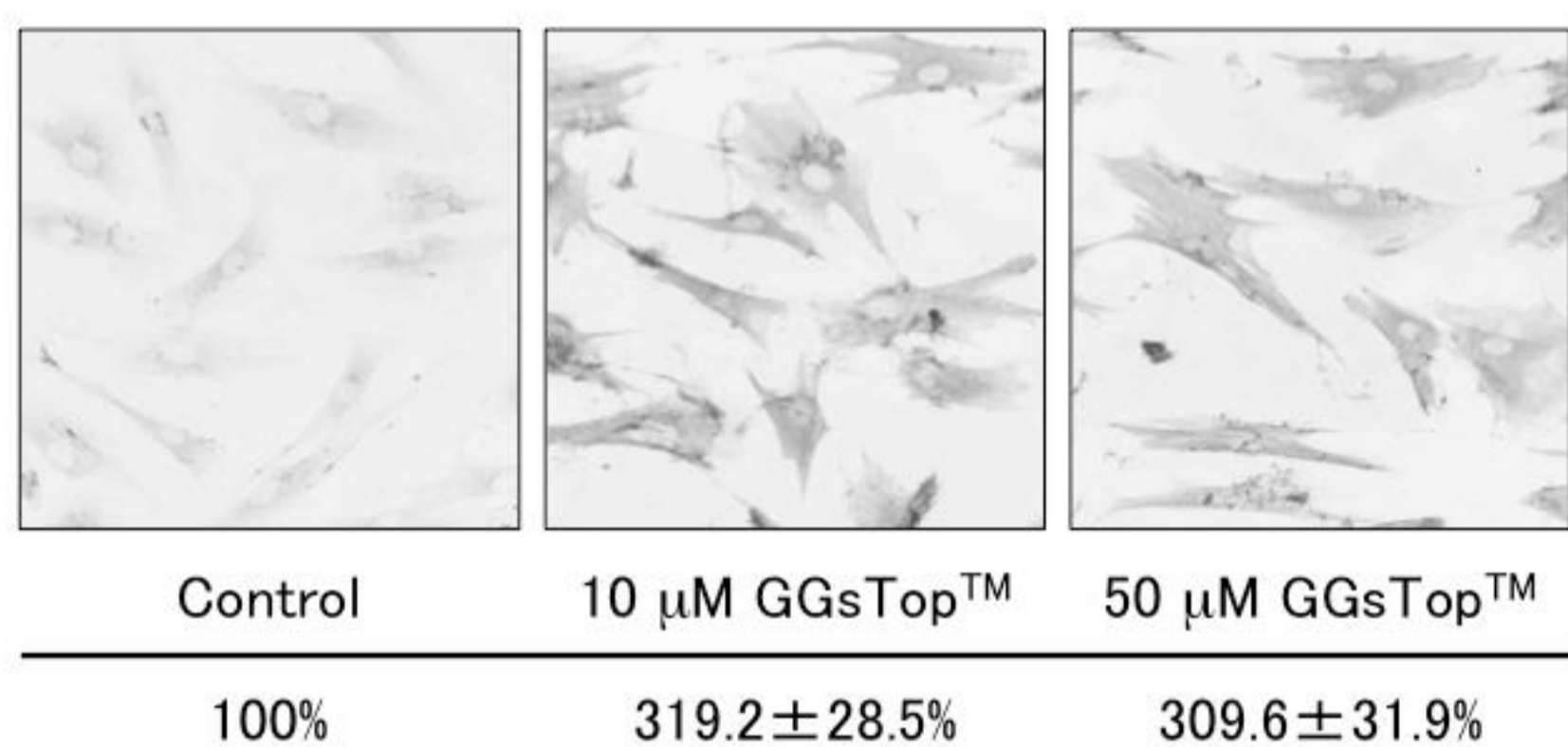
②研究的内容



Chemical structure of GGsTop™.

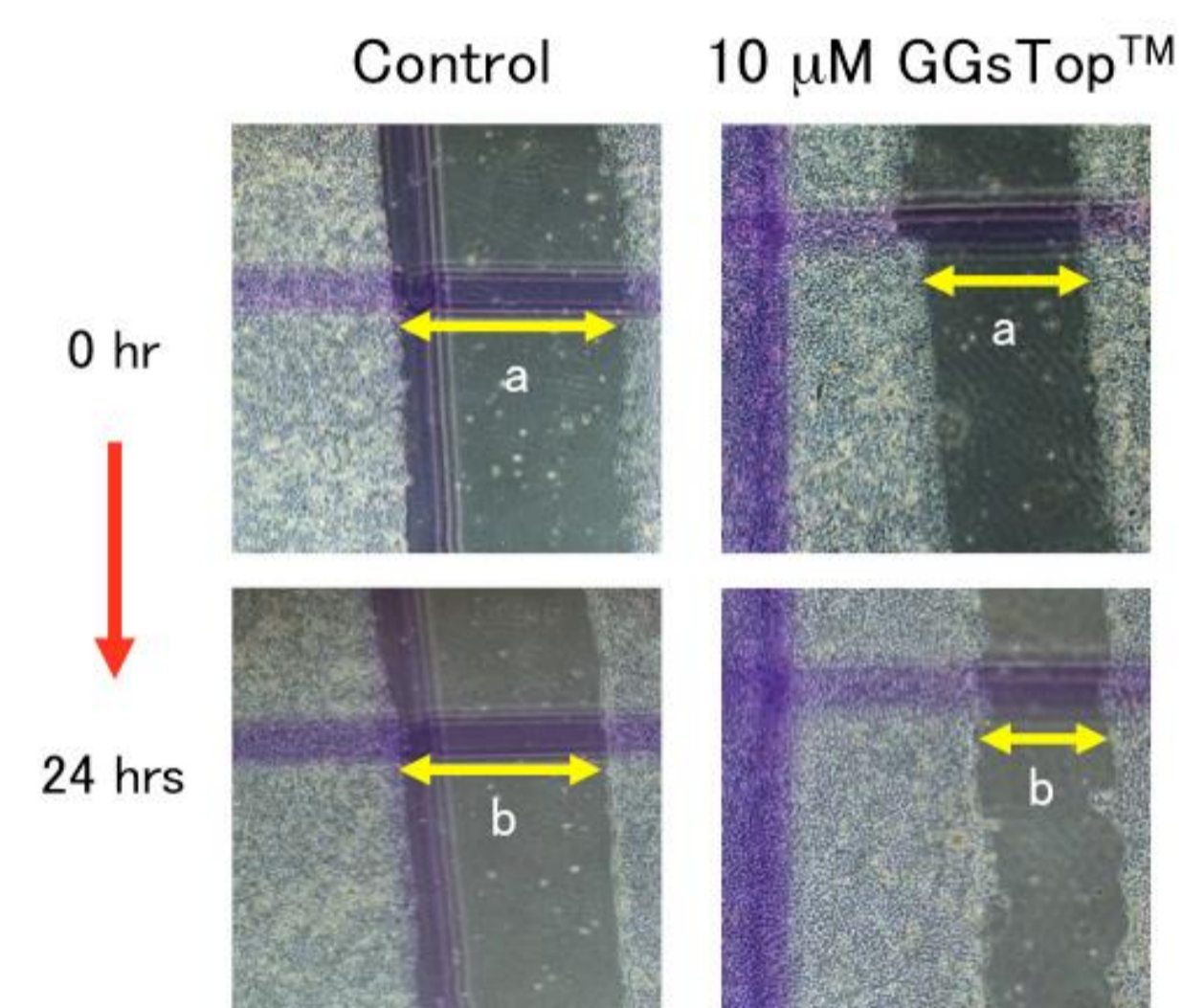


Effect of GGsTop™ on expression of α -SMA in human skin fibroblasts.

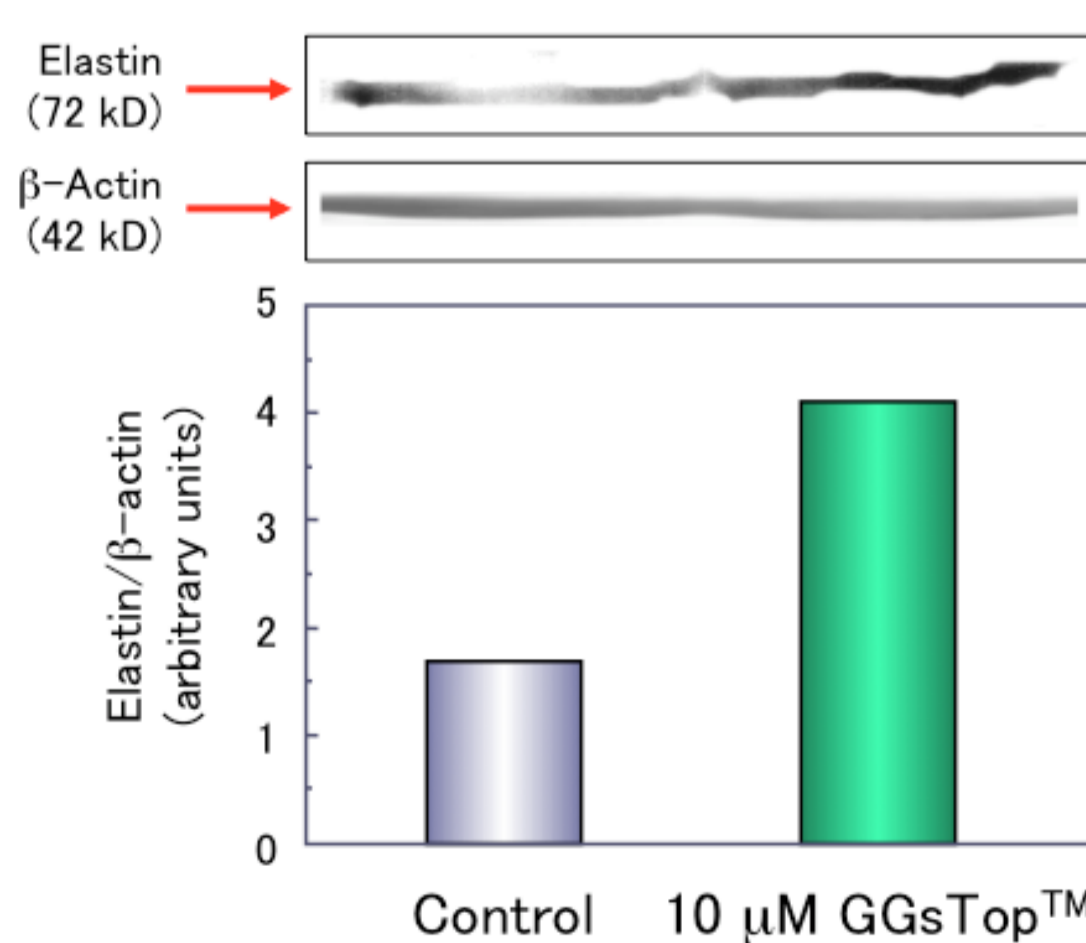


Effect of GGsTop™ on expression of type I collagen in human skin fibroblasts.

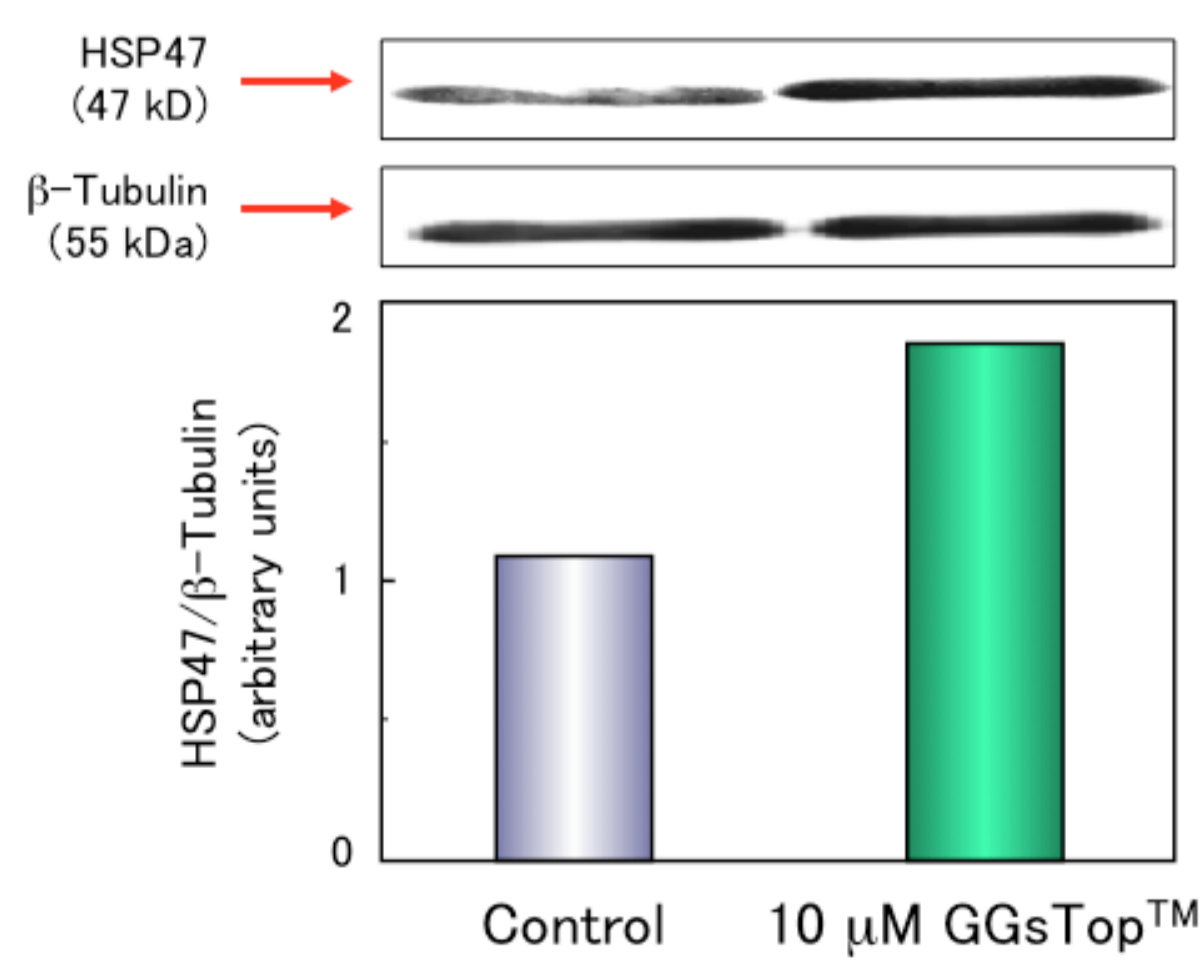
The staining intensity of type I collagen expression (% of control) are presented as the means \pm S.D.



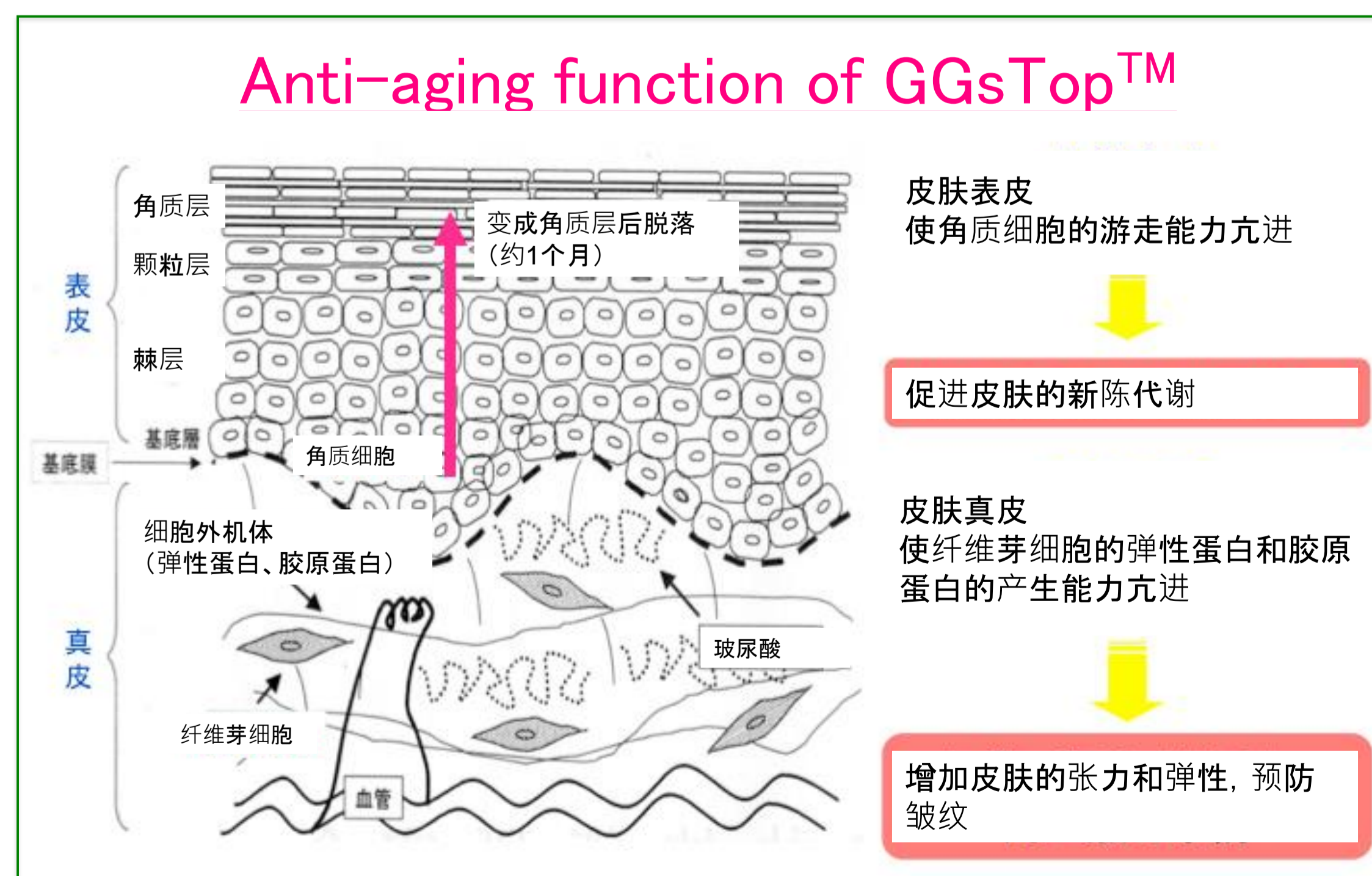
Effect of GGsTop™ on scratch wound healing of HaCaT cell confluent monolayers. Cells cultured in 35 mm dishes were mechanically scratched with a sterile 200-1000 μ l pipette tip, and cultured again with or without 10 μ M GGsTop™ for 24 hrs.



Effect of GGsTop™ on expression of elastin in human skin fibroblasts.



Effect of GGsTop™ on expression of HSP47 in human skin fibroblasts.



③对研究的评价

被独立行政法人科学技术振兴机构采纳为A-STEP (研究成果最佳展开支援项目) 创业挑战型项目 (2009~2011年度)。已经在学术杂志上发表了论文。

④研究内容的成果、技术转移的方向

GGsTop™已经以Narusgen的名称正在作为防老化的化妆品原料被使用，由株式会社NAHLS, CO. LTD销售。