

HGF influences the RPE proliferation by ZO-1 disassembly and nucleus CSDA accumulation

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Abstract

Retinal pigment epithelium (RPE) is a single cell layer protecting photoreceptors from damage, also playing critical role in visual cycle and retinal homeostasis. Any structural or functional disorders ceases visual disabilities, even blindness. Therefore, some growing studies have focused on differentiation of human embryonic stem cells towards RPE, also stimulation of in vivo RPE proliferation. Our previous study reported the proliferative activity of hepatocyte growth factor (HGF) on hESC derived RPE and ex vivo rabbit RPE sheet. Now, we focused on molecular mechanism of proliferative effect of HGF on non-proliferative rabbit RPE sheets. Our results showed that HGF treatment of rabbit RPE sheets increase the BrdU+ cells when the marks were compared to control group. By administrating HGF, the sequestered CSDA were released from ZO-1, then localized to the nucleus which is confirmed with DAPI counterstain. The pigmentation rate of RPE revealed that mature RPE contain a lot of melanin pigments. Although, when the cells were treated with HGF, they were quitted from G0 phase and re-entered to cell cycle. Therefore, their pigments were decreased and the cells consumed their energy for proliferation. It was concluded that the high pigmentation and normal morphology of RPE as an epithelial cells has been kept by ZO-1 proteins in plasma membrane which is followed by CSDA sequestration in cell membrane. When the cells were treated by proliferative factors like HGF, the ZO-1 was disorganized, the cells have become recognized by mesenchymal morphology and the CSDA was entered to the nucleus. Therefore, the HGF could be used in future clinical studies for in vivo delivery in order to stimulate in situ RPE proliferation for treatment of visual disorders such as AMD.

Biography

Fereshteh Karamali currently works Department of Cellular Biotechnology, Cell Science Research Center, Royan Institute for Biotechnology where she is an integral part of it. M.S. developmental biology, Tehran University, Tehran, Iran. 2004-2006. B.S. Zoology, Tehran University, Tehran, Iran. 1999-2003. She has done her M.Sc. Thesis Effects of gamma radiation on different strains of mESCs.



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