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Letter to the Editor

Retinoic Acid Receptor Beta in Pathophysiology of Age-Related Macular Degeneration

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Dear Editor-in-Chief

At present, the effect of retinoic acid as an angiogenesis inhibitor in the treatment of cancer cells has been demonstrated (1, 2). These cells may lose their sensitivity to the drug after a while and 13-cis retinoic acid fails to exert its anti-angiogenic effect (1). The cancer cells are resistant to the effects of 13-cis retinoic acid can be re-sensitive to this drug through increased expression of Retinoic Acid Receptor beta (RAR-beta), one of the six receptors of retinoic acid (1). Furthermore, retinoic acid exerts anti-angiogenic effects on Retinal Pigmented Epithelium (RPE) cells (3), the major cell type involved in age related macular degeneration (4).

There are a few points that have been linked to these findings and age-related macular degeneration (AMD). First, the RPE cells express only one of the six-retinoic acid receptors, which is precisely RAR-beta (5). Second, the main chromophore of lipofuscin particles, that the degree of their participation is an important criterion in evaluating AMD progression, namely A2E for the formation is dependent to retinoic acid existence (6). Third, excess retinoic acid in patients with AMD accelerate formation and development of lipofuscin particles and can worsen AMD (7, 8). So we can say that RPE cells resistance to retinoic acid, which can occur due to decreased expression of RAR-beta, lead to the development and progression of AMD via two pathways.

In the first pathway with reduced expression of RAR-beta, retinoic acid cannot be able to impose its anti-angiogenic effects on RPE cells and thus production of angiogenic factors such as VEGF are increased by these cells that can cause wet AMD. In the second pathway decreased expression of RAR-beta, a nuclear retinoic acid receptor, can leads to the accumulation of retinoic acid in high concentrations in the cell cytoplasm resulting in the formation of greater amounts of A2E in the cytoplasm. The increased levels of A2E in the cytoplasm in addition to can be associated with several undesirable consequences (9, 10), also have the phototoxicity properties, as it have been shown the accumulation of such large amounts of the chromophore in human RPE cells receiving blue light lead to apoptosis (11).

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