Enhancing The Specification Of Retinal Neurons From Human Induced Pluripotent Stem Cells

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A variety of retinal degenerative diseases, including retinitis pigmentosa and age-related macular degeneration, result in the loss of retinal neurons leading to a gradual loss of vision. An *in vitro* model to study the development of human retinal cells would provide a better understanding of the structure and functionality of the retina, eventually leading to new therapeutic approaches to blinding disorders that could involve replacing cells that had been lost to disease. Following previously established protocols, two types of populations of cells are observed early in the differentiation process, those that lead to retinal cells and those that lead to other anterior phenotypes of the central nervous system. These cells arise from a common progenitor population derived from induced pluripotent stem cells, yet the mechanism underlying the differentiation of these two different types of cells remains elusive. To further study the specification of retinal cells from this common progenitor population, a more efficient method to produce these cells needs to be developed. The purpose of this experiment is to test several candidate growth factors and observe their effect on the production of retinal cells. This study tests five different growth conditions using insulin-like growth factor-1, fibroblast growth factor-2, the sonic hedgehog agonist purmorphamine, retinoic acid and an untreated control. Treatment was carried out from Day 7 until Day 20, a period during which previous studies have demonstrated an ability to influence the decision of these cells to become retinal non-retinal. Immunocytochemistry (ICC) and RT-PCR analysis was used to monitor the expression of proteins characteristic of retinal and non-retinal cells. These results can be used to devise a more efficient protocol for retinal specification from human induced pluripotent stem cells and in turn, will further our understanding of the development of the retina.

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