TRANSCRIPTIONAL ANALYSIS OF RETINAL AND FOREBRAIN PROGENITOR CELLS DERIVED FROM HUMAN INDUCED PLURIPOTENT STEM CELLS

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Eye development has been extensively studied in traditional model systems but studies related to humans have been limited. The recent development of induced pluripotent stem cells (iPSCs) enabled the study of human development in culture at stages that would otherwise be inaccessible to investigation. By definition, Pluripotent stem cells are cells that have the capacity to generate any adult cell type, such as the muscle cell or the blood cell. A defined set of genes, known as eye field transcription factors (EFTFs) have proven to play an important role in eye development. Utilizing iPSCs as our model system, we sought to identify EFTFs that might play an essential role in the specification of the retina of the human eye.

iPSCs were directed to develop into retinal cells as previously established. Since these events occur early in the developmental process, samples were collected every two days over the first twenty days of differentiation. The development of retinal cells was determined by the characterization of gene expression patterns of six EFTFs over this timecourse in order to highlight important trends in retinal development.

Retinal populations were identified by the expression of numerous EFTFs which were absent from other non-retinal cell types. Our preliminary data utilizing iPSCs highlights similar trends in the expression of these EFTFs as anticipated. However, the expression patterns of two key EFTFs varied from the others in a manner which implicated them to be critical for retinal development from an unspecified stem cell source. Thus, these candidate EFTFs were investigated further to establish their specific roles in retinal development using a combination of genetic and molecular biology approaches.

The work presented in this study helps to elucidate the mechanisms by which retinal cells are specified and help establish iPSCs as a unique model system for studies of human development.

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