California Institute for Regenerative Medicine

Differentiation of human pluripotent stem cells to retinal pigmented epithelium in defined conditions using purified extracellular matrix proteins.

Journal: J Tissue Eng Regen Med
Publication Year: 2012
Authors: T J Rowland, A J Blaschke, D E Buchholz, S T Hikita, L V Johnson, D O Clegg
PubMed link: 22514096
Funding Grants: Training Program in Stem Cell Biology and Engineering, UCSB Stem Cell Biology Training Program

Public Summary:
A potential application of human embryonic stem cells (hESCs) and induced pluripotent stem cells (iPSCs) is the generation of retinal pigmented epithelium (RPE) to treat age-related macular degeneration (AMD), a common but incurable retinal disease. RPE cells derived from hESCs (hESC-RPEs) and iPSCs (iPSC-RPEs) express essential RPE markers and can rescue visual function in animal models. However, standard differentiation protocols yield RPE cells at low frequency, especially from iPSC lines, and the common use of Matrigel and xenogeneic feeder cells is not compatible with clinical applications. The extracellular matrix (ECM) can affect differentiation, and therefore changes in ECM composition may improve the frequency of stem cell-RPE differentiation. We selected several purified ECM proteins and substrates, based on the in vivo RPE ECM environment, and tested their ability to support iPSC-RPE differentiation and maintenance. iPSCs differentiated on nearly all tested substrates developed pigmented regions, with Matrigel and mouse laminin-111 supporting the highest pigmentation frequencies. Although iPSC-RPEs cultured on the majority of the tested substrates expressed key RPE genes, only six substrates supported development of confluent monolayers with normal RPE morphology, including Matrigel and mouse laminin-111. iPSCs differentiated on mouse laminin-111 produced iPSC-RPEs expressing RPE proteins, and hESCs differentiated on mouse laminin-111 resulted in high yields of functional hESC-RPEs. This identification of key ECM proteins may assist with future scaffold designs and provide peptide sequences for use in synthetic, xeno-free, GMP-compliant generation of RPE from human pluripotent stem cells relevant to clinical translation. Copyright © 2012 John Wiley & Sons, Ltd.

Scientific Abstract:
A potential application of human embryonic stem cells (hESCs) and induced pluripotent stem cells (iPSCs) is the generation of retinal pigmented epithelium (RPE) to treat age-related macular degeneration (AMD), a common but incurable retinal disease. RPE cells derived from hESCs (hESC-RPEs) and iPSCs (iPSC-RPEs) express essential RPE markers and can rescue visual function in animal models. However, standard differentiation protocols yield RPE cells at low frequency, especially from iPSC lines, and the common use of Matrigel and xenogeneic feeder cells is not compatible with clinical applications. The extracellular matrix (ECM) can affect differentiation, and therefore changes in ECM composition may improve the frequency of stem cell-RPE differentiation. We selected several purified ECM proteins and substrates, based on the in vivo RPE ECM environment, and tested their ability to support iPSC-RPE differentiation and maintenance. iPSCs differentiated on nearly all tested substrates developed pigmented regions, with Matrigel and mouse laminin-111 supporting the highest pigmentation frequencies. Although iPSC-RPEs cultured on the majority of the tested substrates expressed key RPE genes, only six substrates supported development of confluent monolayers with normal RPE morphology, including Matrigel and mouse laminin-111. iPSCs differentiated on mouse laminin-111 produced iPSC-RPEs expressing RPE proteins, and hESCs differentiated on mouse laminin-111 resulted in high yields of functional hESC-RPEs. This identification of key ECM proteins may assist with future scaffold designs and provide peptide sequences for use in synthetic, xeno-free, GMP-compliant generation of RPE from human pluripotent stem cells relevant to clinical translation. Copyright © 2012 John Wiley & Sons, Ltd.

Source URL: https://www.cirm.ca.gov/about-cirm/publications/differentiation-human-pluripotent-stem-cells-retinal-pigmented-epithelium