

【Noteworthy Patent Introduction #6】

Hepatocyte Induction Method

Abstract

A method for producing hepatocytes by culturing AFP positive hepatoblasts in a medium containing pregnenolone or an adrenergic agonist.*

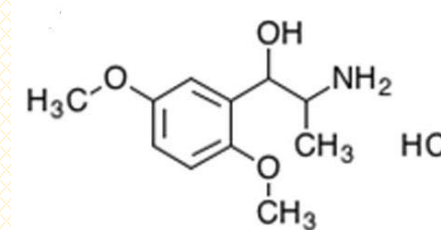
In the above, the AFP positive hepatoblasts may be obtained by culturing SOX17 positive endodermal cells in a medium containing DMSO, and the endodermal cells may be obtained by culturing iPSCs in a medium containing Activin A and a GSK-3 β inhibitor.

Advantage

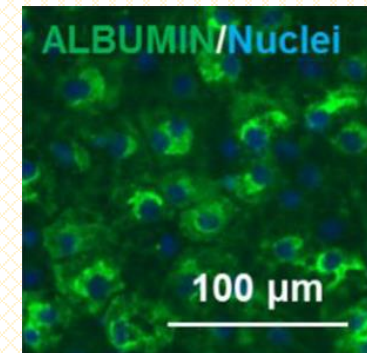
- Hepatocytes induced from hiPSC-derived hepatoblasts using low-molecular compound, i. e. pregnenolone or an adrenergic agonist are equivalent to those induced from hepatoblasts by a conventional method using growth factors (HGF and OsM), in the following points.
 - Molecular species and expression levels of drug metabolizing enzymes
 - Hepatocytes specific gene expression profile
- The relevance of adrenergic α 1 receptor subtype is suggested for the mechanism of increased efficiency of inducing hepatocyte from hiPSCs-derived hepatoblasts using adrenergic drugs.

Background

It is desirable if hepatocytes can be obtained from hiPSCs or the like instead of from human body for use in regenerative medicine and drug development for the therapy of liver diseases and in the evaluation of hepatotoxicity of drugs. However, since growth factors used as inducers are costly, alternative methods of producing hepatocytes at a lower cost have been studied.



*The chemical structure of methoxamine hydrochloride used in the embodiments of the invention



Immunostaining image of hepatocytes differentiation-induced by methoxamine hydrochloride

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