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КОМБИНИРОВАННАЯ СВЕРХЭКСПРЕССИЯ *Foxa3* и *Hnf4a* УСИЛИВАЕТ ПРОЛИФЕРАЦИЮ И ПРОДЛЕВАЕТ ФУНКЦИОНАЛЬНУЮ СОХРАННОСТЬ ПЕРВИЧНЫХ ГЕПАТОЦИТОВ[1]

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В системе культивирования *in vitro* пролиферативная активность первичных гепатоцитов обычно низкая и сопровождается снижением жизнеспособности и потерей специфических для гепатоцитов функций. Ранее показано, что комбинированное введение определенных гепатоцитспецифических факторов транскрипции приводит к конвертированию фибробластов в функциональные гепатоцитоподобные клетки. Однако комбинированное использование факторов транскрипции в первичной культуре гепатоцитов еще недостаточно изучено. Белки FoxA3 (forkhead box protein A3) и Hnf4α (forkhead box protein A3 hepatocyte nuclear factor 4α) представляют собой факторы транскрипции, которыми обогащена печень, и играют жизненно важную роль в дифференцировке и поддержании гепатоцитов. В представленном исследовании в гепатоцитах крысы получили одновременную избыточную экспрессию двух генов: *Foxa3* и *Hnf4a*. Показано, что комбинированное усиление экспрессии двух транскрипционных факторов: FoxA3 и Hnf4α – приводит к повышенной скорости пролиферации и стабилизации специфических функций первичных гепатоцитов в течение длительного периода культивирования.

Ключевые слова: гепатоциты, пролиферация, печень, FoxA3, Hnf4α

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Combinational Overexpression of *Foxa3* and *Hnf4a* Enhance the Proliferation and Prolong the Functional Maintenance of Primary Hepatocytes

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In an *in vitro* culture system, primary hepatocytes usually display a low proliferation capacity, accompanied with a decrease of viability and a loss of hepatocyte-specific functions. Previous studies have demonstrated that the combination introductions of certain hepatocyte-specific transcription factors are able to convert fibroblasts into functional hepatocyte-like cells. However, such combinational usage of transcription factors in primary hepatocytes culture has not yet sufficiently studied. The forkhead box protein A3 (FoxA3) and hepatocyte nuclear factor 4α (Hnf4α) are liver-enriched transcription factors that play vital roles in the differentiation, and maintenance of hepatocytes. Thus, we simultaneously overexpressed the two genes, *Foxa3* and *Hnf4a*, in rat hepatocytes and observed that the combinational augmentation of these two transcription factors have enhanced the proliferation and stabilized the hepatocyte-specific functions of primary hepatocytes over a long-term culture period.

Keywords: hepatocytes, proliferation, liver, FoxA3, Hnf4α