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Opinion Article

Advancements in 3D Culture Techniques for HepaRG Cells

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DESCRIPTION

HepaRG cells, derived from a human hepatocellular carcinoma, exhibit a remarkable blend of characteristics that bridge the gap between traditional hepatoma cell lines and primary human hepatocytes. They maintain liver-specific functions, including drug metabolism, and possess the ability to differentiate into both hepatocyte- and biliary-like cells. This versatility positions HepaRG cells as an attractive model for studying liver physiology, drug toxicity, and disease mechanisms. In cell culture methodologies, the shift toward Three-Dimensional (3D) culture systems has revolutionized our ability to mimic *in vivo* conditions. This is particularly noteworthy in the case of HepaRG cells, a human hepatic cell line with a unique combination of features that make it a valuable model for liver research. This article explores the significance of 3D culture techniques in cultivating HepaRG cells and their potential implications for liver-related studies.

Advanced cell cultures

Traditional 2D culture: Traditional Two-Dimensional (2D) cell culture, while convenient, has limitations in recapitulating the complex microenvironment of the liver. Hepatocytes, including HepaRG cells, cultured in 2D conditions often experience phenotypic drift and may not fully express the diverse functions observed *in vivo*. Additionally, drug metabolism and response to stimuli can differ significantly from what is observed in the human liver.

3D culture techniques: To address the shortcomings of 2D culture, researchers have turned to 3D culture techniques. These methods aim to create an environment that better mirrors the *in vivo* conditions, allowing cells to interact more naturally with their surroundings. In the context of HepaRG cells, 3D culture offers a platform for enhanced differentiation, increased functionality, and improved recapitulation of liver-specific responses.

Advantages of 3D culture for HepaRG cells

Enhanced hepatocyte differentiation: 3D culture systems promote a more liver-like differentiation of HepaRG cells, leading to the development of mature hepatocytes with improved functionality. This is crucial for studies involving drug metabolism and liver-specific functions.

Physiological relevance: Mimicking the 3D architecture of the liver allows for better replication of physiological conditions. This includes cell-cell interactions, nutrient gradients, and extracellular matrix interactions, which collectively contribute to a more realistic representation of hepatic biology.

Improved drug metabolism studies: HepaRG cells in 3D culture exhibit enhanced drug metabolism capabilities, making them more suitable for pharmacological studies. This is particularly important for assessing the potential toxicity and efficacy of drugs, as the 3D environment better mirrors the *in vivo* response.

Long-term stability: Unlike traditional 2D cultures, which may experience dedifferentiation over time, HepaRG cells in 3D culture systems demonstrate greater stability in maintaining their differentiated state over extended periods.

Applications in liver research: The adoption of 3D culture techniques for HepaRG cells has broad implications for liver-related research. These include studies on drug metabolism, hepatotoxicity assessment, infectious disease modeling, and investigations into liver development and regeneration.

CONCLUSION

The evolution from 2D to 3D culture techniques represents a paradigm shift in the way we approach cell culture, particularly in the context of HepaRG cells and liver research. As we continue to refine and expand these 3D culture methodologies, the potential for more accurate and clinically relevant findings in drug development and liver-related studies. The ability to recreate a liver microenvironment *in vitro* not only advances our understanding of liver biology but also holds great potential for improving the safety and efficacy assessment of pharmaceutical compounds.

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