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Unlimited source of human kidney cells: Applications include in vitro toxicology, disease models, regenerative medicine

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Researchers at the Institute of Bioengineering and Nanotechnology (IBN) have successfully generated human kidney cells from human embryonic stem cells in vitro. Specifically, they produced the renal cells under artificial conditions in the lab without using animals or organs. This has not been possible until now.

According to IBN Executive Director, Professor Jackie Y. Ying, "This discovery has wide-reaching implications for in vitro toxicology, drug screening, disease models and regenerative medicine. In particular, we are interested in applying our technology to develop predictive in vitro drug testing and renal toxicity models as alternatives to animal testing."

IBN Team Leader and Principal Research Scientist Dr Daniele Zink elaborated, "The kidney is a major target organ for drug-induced toxic effects. Therefore, it is important for pharmaceutical companies to find out early in the development phase whether their drugs would cause nephrotoxicity in humans. However, animal models are of limited predictability, and there is currently no regulatory accepted in vitro assay based on renal cells to predict nephrotoxic effects. A major problem is the lack of suitable renal cells, which may now be resolved through our discovery."

At present, human kidney cells are extracted directly from human kidney samples. However, this method is not efficient because such

samples are limited, and the extracted cells die after a few cell divisions in the petri dish. Also, cells obtained from different samples would display variable features, depending on age, gender, health status and other conditions of the donor. Therefore, cells that have been isolated from human samples are of limited suitability for research and applications in industry and translational medicine, which require large cell numbers.

An alternative approach is to use human renal cell lines that have been rendered immortal, i.e. they can be reproduced indefinitely in the lab. However, such cells may not be used in many applications due to safety issues, and their functional features have usually been changed so profoundly that they may no longer be useful toward predicting cell behavior in the human body.

IBN's technique, on the other hand, enables human embryonic stem cells to differentiate into renal proximal tubular-like cells. This particular kidney cell type plays an important role in kidney disease-related processes and drug clearance. Results showed that the renal proximal tubular-like cells generated by IBN were similar to the renal proximal tubular cells isolated from fresh human kidney samples. For example, they displayed very similar gene and protein expression patterns. Also, since human embryonic stem cells may grow indefinitely in cell culture, the IBN researchers have discovered a potentially unlimited source of human kidney cells.

"We are currently adapting our approach to use induced pluripotent stem cells as the source," shared Dr Karthikeyan Narayanan, IBN Senior Research Scientist. "We are also planning to modify our protocol in order to generate other renal cell types from stem cells."

The IBN researchers have tested the renal cells they generated in in vitro nephrotoxicology models developed by the Institute, and have obtained

very promising test results. They welcome industry partners to collaborate with IBN on commercializing this technology.

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