

## Press Information

2024年10月3日

### **World's first, Nikkiso and Kanazawa University Confirm Nephrotoxicity of Puberulic Acid in a Human Cell Experiments ~The nephrotoxicity of a compound contained in food and pharmaceutical products is efficiently evaluated in cell experiments~**

Nikkiso Co., Ltd. and the research group led by Hiroshi Arakawa, who is an associate professor in Faculty of Pharmacy, Institute of Medical, Pharmaceutical and Health Sciences of Kanazawa University, confirm that puberulic acid which is a concomitant compound in Beni-koji (Red Yeast Rice) supplements is directly toxic to human renal proximal tubular epithelial cells. This identification was conducted for the first time in the world in a human cell experiment. The result is expected to help elucidate the causal relationship between puberulic acid and the health hazard. In addition, the nephrotoxicity evaluation method with the cell culture experiments, which is adopted in this time, is also expected to be a powerful tool for appropriately and efficiently evaluating nephrotoxicity of various compounds contained in foods and pharmaceuticals.

#### ■Background and significance of the research

Puberulic acid is a natural compound from blue-green mold and is a chemical identified as one of the causes of health hazards with foods contained red yeast.

Japanese Society of Nephrology reported in interim report that renal dysfunctions including tubulointerstitial nephritis as its health hazards. Degeneration and necrosis of the proximal tubules have also been observed in animal experiment conducted by the National Institute of Health Sciences. However, direct effects on human renal cells have not been verified to date.

3D-RPTEC, human renal cell for drug discovery research made by Nikkiso, was adopted in this research and we verified impacts of puberulic acid to renal cells by the nephrotoxicity evaluation method established in the collaborative research. As a result, it was found that puberulic acid above a certain concentration causes toxicity in proximal tubular epithelial cells and is the cause of renal dysfunction.

#### ■Details of the research results

Used Cell : 3D-RPTEC, human renal cell for drug discovery research made by Nikkiso

Evaluation Method : Method described in the following article

[Hiroshi Arakawa et al., Three-dimensional Culture of Human Proximal Tubular Epithelial Cells for an in vitro Evaluation of Drug-induced Kidney Injury. Journal of Pharmaceutical Sciences. August 15, 2024](#)

Main Discoveries : It was confirmed that puberulic acid above a certain concentration leads cell

death of proximal tubular epithelial cells. Although the blood concentration of puberulic acid whose use is suffered from health hazard by foods contained red yeast is unidentified, the result showed that puberulic acid has cytotoxicity comparable to that of cisplatin, an anticancer drug that causes multiple kidney damage. In addition, it was suggested that an organic anion transporter, a type of drug transporter\*, is involved in the pathway by which puberulic acid is taken up by proximal tubular epithelial cells.

#### ■ Future development

We believe that results of the research help to reveal the nephrotoxicity and the mechanism of puberulic acid.

Moreover, although toxicity and safety evaluations of chemical substances, including pharmaceuticals, have relied heavily on animal experiments in general, we showed that cellular experiments can evaluate properly, and it will promote to cellular experiments.

Nikkiso and Kanazawa University will continue to conduct further collaborative research to establish an appropriate and efficient evaluation method for nephrotoxicity of compounds in general by cellular experiments.

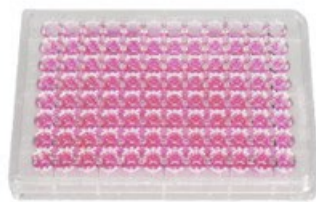
#### 【About 3D-RPTEC】

“3D-RPTEC” is a research cell that expresses a drug transporter\* similar to the human renal cortex by culturing primary human proximal tubular epithelial cells (RPTEC; Renal Proximal Tubule Epithelial Cells) in three dimensions.

Traditionally, cell-based toxicological and pharmacological evaluations have used renal lineage and primary cells, which are not fully responsive to drugs.

The 3D-RPTEC provides improved drug responsiveness and more sensitive evaluation than conventional renal cells.

The product is manufactured and marketed by Nikkiso since July 2023. (At present, sales only in Japan)



【3D-RPTEC (Cell)】



【3D-RPTEC culture medium】

\*Drug transporter: A protein that exists in the cell membrane. It has the role of a device that allows endogenous/exogenous hypomineralized substances, including drugs, to enter or leave the cell. In renal cells, the existence of numerous transporters involved in drug transport is known.

#### About Nikkiso

Since its establishment in 1953, Nikkiso has contributed to solving social issues by anticipating the changing times with world-first and Japan-first technologies and products. In the industrial business, Nikkiso has created new markets by developing products in the energy field, hemodialysis-related products in the medical business, and CFRP (carbon fiber reinforced plastic) aerostructures in the aerospace business.

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NIKKISO CO., LTD.

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Date of Establishment: 6022, Japan  
December 26, 1953  
President & CEO: Toshihiko Kai  
Business Overview: Nikkiso provides specialized pumps and systems in the Industrial Business, CFRP (carbon fiber reinforced plastic) aircraft parts in the Aerospace Business and hemodialysis related products in the Medical Business.  
URL: <https://www.nikkiso.com/>

### **About Kanazawa University**

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