Paper of the Quarter

Outstanding 3R-Research from North Rhine-Westphalia
- 1st Quarter of 2025 -

The quarterly distinction 'Paper of the Quarter' of the 3R-Competence Network NRW recognizes outstanding contributions to the 3R principles. We are delighted to announce the winners for the first quarter of 2025.

Congratulations to

Daphne Bouwens & Nazanin Kabgani

RWTH Aachen University

for their publication

"A bioprinted and scalable model of human tubulo-interstitial kidney fibrosis"

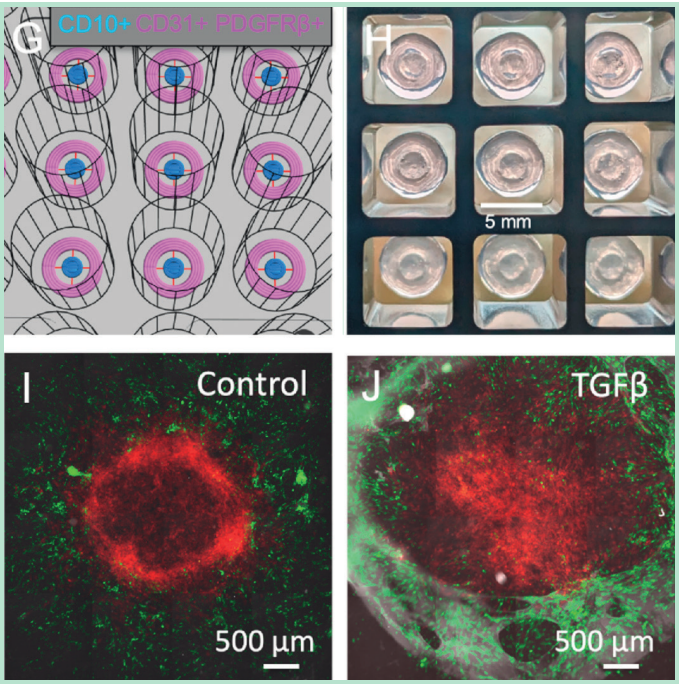
The "Paper of the Quarter" award was given to their publication because they strive in a special way to further develop the 3R principle—"Replace, Reduce, Refine"—which has been applied in laboratory animal science for more than 60 years.

The paper "A Bioprinted and Scalable Model of Human Tubulo-Interstitial Kidney Fibrosis" describes the development of an innovative bioprinted model for tubulo-interstitial kidney fibrosis that **uses human cell lines and thus actively replaces animal experiments**. The scalable 3D model shows the **potential for better understanding complex disease mechanisms and investigating new therapeutic approaches**.

By developing a system that mimics the complex cellular interactions in the human body, their research group is making a valuable contribution to **reducing animal testing in biomedical research**. The ability to obtain more accurate and relevant data will enable future studies to be designed more efficiently. **Their work is exemplary for responsible research and serves as inspiration for the sustainable use of modern technologies**.

▶ You can read the original article here

Bouwens, Daphne; Kabgani, Nazanin et al. "A bioprinted and scalable model of human tubulo-interstitial kidney fibrosis." Biomaterials vol. 316 (2025): 123009.



Bioprinted construct for fibrosis modeling. G: Printing template with CD10+ (blue) core and CD31+/PDGFRβ+ (pink) interstitium in 96-well format. H: Day 0 constructs with distinct compartments. I: Day 7 untreated constructs. J: IF of TGFβ/OTA-treated constructs: CD10+ (red) center, CD31+ (green) periphery, collagen (white), PDGFRβ+ not shown. The figure was adapted from the original article. © Bouwens, Daphne; Kabgani, Nazanin et al. "A bioprinted and scalable model of human tubulo-interstitial kidney fibrosis."

Q&A with the Winners
- 1st Quarter of 2025 -

How did this research come about?

Chronic kidney disease affects over 10% of the world's population, and fibrosis is a common hallmark across nearly all forms of kidney disease. Despite its prevalence, there are currently no approved antifibrotic therapies. Our research group focuses on uncovering the mechanisms underlying fibrosis development and identifying therapeutic strategies to halt, slow, or even reverse its progression. To this end, we are developing advanced in vitro kidney models that are suitable for high-throughput drug screening and more accurately reflect the human kidney environment. Traditional 2D monolayer cultures lack essential cell–cell and cell–matrix interactions that are critical in fibrotic disease. Therefore, our goal was to develop a reproducible, high-throughput 3D kidney model capable of mimicking human interstitial fibrosis. Using bioprinting technology, we can now spatially organize key human renal cell types into defined compartments within a fibrin-gelatin matrix, enabling the automated generation of physiologically relevant kidney constructs.

What is the contribution of this research to the 3Rs?

Our bioprinting approach uses fully characterized, biopsy-derived human immortalized renal cell lines and a fibrin-gelatin-based bioink to recreate the tubulo-interstitial microenvironment directly in 12- or 96-well plate formats. The automated printing process takes under one minute per construct, making it a fast and scalable platform for generating large numbers of physiologically relevant kidney models. We demonstrated functional cell–cell communication and relevant injury responses within these constructs. For example, stimulation with TGFβ led to a clear upregulation of extracellular matrix marker Collagen I at both gene and protein levels, confirming the model's responsiveness to fibrotic triggers. This in vitro system enables efficient pharmacological screening and has the potential to significantly reduce reliance on animal models in preclinical testing. By identifying the most promising therapeutic candidates in a human-relevant platform, we can both reduce the number of animals used and refine subsequent in vivo experiments for better translational value.

What is your next 3R research question that you would like to answer?

In addition to our bioprinted models, our group is developing kidney organoids derived from human induced pluripotent stem cells (iPSCs). These self-organizing "mini kidneys" differentiate into over 15 distinct human renal cell types, offering a highly representative in vitro system. Given the heterogeneity of kidney diseases, each with distinct triggers and progression patterns, we aim to develop tailored in vitro models that reflect specific pathological contexts. To achieve this, we expose our organoids to different types of injury and perform single-cell RNA sequencing to profile cellular responses. We then compare these transcriptional changes to those observed in patient samples, identifying which injury models best replicate specific human disease signatures. This precision modelling allows for more targeted therapeutic screening and prioritization, increasing the likelihood of translational success. By focusing on disease-relevant human systems, we anticipate further reductions in animal use, refinements in model predictiveness, and ultimately, better alignment with human disease biology.

What is "Paper of the Quarter"?

The quarterly distinction „Paper of the Quarter" serves to recognize outstanding publications in the field of 3R principle of the 3R Competence Network NRW. The aim is to recognize the diversity of research achievements and in particular those publications for which the extraordinary quality cannot be adequately reflected by quantitative evaluation criteria such as the Journal Impact Factor (JIF). A high JIF is not an exclusion criterion, but it is not a selection criterion either.

The award is presented as part of a quarterly open competition. The decision on the publication to be awarded is made by the network's Steering Committee which is formed by the representatives of the eight faculties of medicine in NRW. Each location represented on the Steering Committee has one vote, so that the winner is determined by a simple majority of votes. The selection can be made if at least 50% of the site representatives are present at the relevant meeting. The selected paper will be made visible as „Paper of the Quarter" by the network. The award is also recognized with a certificate.

For more information and submissions for the next round **until August 31st, 2025**, please visit

▶ **PAPER OF THE QUARTER**

3R-Kompetenznetzwerk NRW
Medical progress in line with best possible animal welfare

Website: www.3r-netzwerk.nrw
Email: 3r-netzwerk-nrw@ukbonn.de
LinkedIn: @3R-Kompetenznetzwerk NRW

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