



# Paper of the Quarter

Outstanding 3R-Research from North Rhine-Westphalia  
- 3<sup>rd</sup> 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 third quarter of 2025.

Congratulations to

## Bettina Budeus & Diana Klein

University of Duisburg-Essen



for their publication

### ***“Matrix-free human lung organoids derived from induced pluripotent stem cells to model lung injury”***

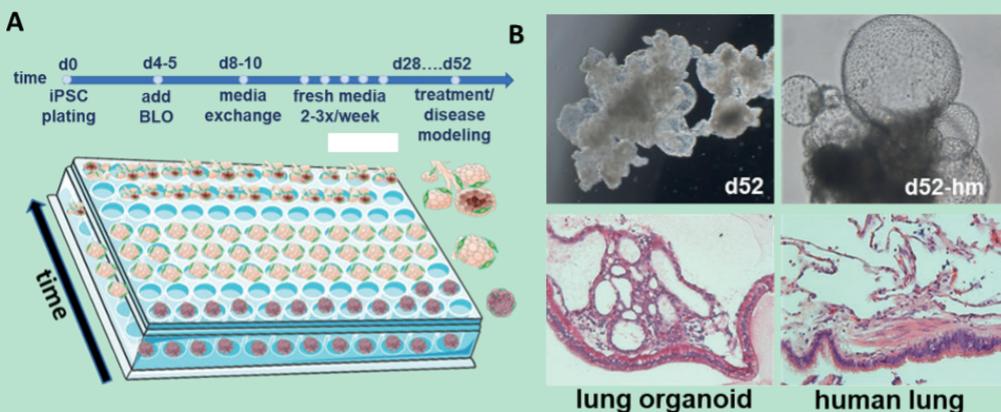
The “Paper of the Quarter” award was given to their publication because they strive in a special way to further develop the 3R principle—“Replace, Reduce, Refine”—which has been applied in laboratory animal science for more than 60 years.

The paper “Matrix-free human lung organoids derived from induced pluripotent stem cells to model lung injury” stands out for its scientific excellence, high relevance to the 3R principle, and an innovative model that sets new standards in preclinical research. In their paper, the authors present a **matrix-free, iPSC-based human lung organoid model** that does not require animal components and yet achieves a high degree

of structural and functional similarity to the human lung. The model enables the **investigation of radiation-induced lung damage in a manner relevant to humans** and accurately maps cell type-specific radiation responses. Your work impressively demonstrates that certain complex pathophysiological issues can be addressed **without the use of laboratory animals, thus making an important contribution to replacement.**

► You can read the original article here

[Budeus B, Kroepel C, Stasch LM, Klein D. Matrix-free human lung organoids derived from induced pluripotent stem cells to model lung injury. Stem Cell Res Ther. 2024;15\(1\):468.](#)



**(A) Scheme for the experimental design including the time line.** iPSCs were cultured as embryoid bodies in in ultra-low attachment plates for 4-5 days prior BLOB medium addition. After another 4-5 days, regular media exchanges were performed. **(B) Representative bright-field images of LuOrgs** generated matrix-free from human iPSCs plates at indicated time point using the 5x and 20x objective of an inverted microscope (upper panels). Histology staining of paraffin-embedded sections of the lung-like regions of LuOrgs using hematoxylin and eosin staining. Normal human lung tissue was included as positive control. Magnification: 5x.

# Q&A with the Winners

## - 3<sup>rd</sup> Quarter of 2025 -

### How did this research come about?

Thematically, the research of the AG Klein is situated in experimental radiation oncology. We aim to understand the molecular mechanisms of radiation-induced cell death processes in tumor and normal tissues in order to develop new strategies for the biological optimization of chemo- and radio-sensitivity modulation, which can then serve as a basis for optimizing cancer therapy. This is a field of research in which preclinical animal experiments – at least until a few years ago – played a central role. Increasing ethical concerns, high time and financial costs, but above all limitations in the transferability of the results have led to a shift in focus towards more complex in vitro systems that are expected to represent a more physiologically relevant human model. And so, within the framework of alternative methods to animal testing, funded by the Federal Ministry of Research, Technology and Space, we are now investigating whether and to what extent lung organoids can serve as a suitable normal tissue toxicity model.

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

The establishment of the described lung organoids for studies on radiation-induced normal tissue toxicity, taking into account the corresponding tumor response, could not achieve a reduction in the number of experimental animals; furthermore, it can be determined whether certain animal experiments can be adequately and meaningfully replaced. While the analyses of DNA damage/repair and their kinetics involved rather short time points after irradiation (30 minutes to a maximum of 48 hours), differentiation studies require longer time periods (up to approximately 4 weeks). This means that for the common mouse model of radiation-induced pneumopathy, an approach with at least 4-6 mice per group (in practice, for statistical reliability, it would be more likely to be 6-9 mice per group) requires at least 5 (average number of mice) x 4 (0, 5,

10, and 15 Gy radiation) = 20 mice for one time point (survival period after thoracic irradiation: 30 minutes). Since the entire lung is processed in one go for histological examinations, an additional 20 animals per time point would be needed for corresponding expression analyses at the RNA and protein level. Complementary mouse tumor models would require exactly this number of animals. Either with regard to therapeutic modulation of radiation-induced normal tissue toxicity, many additional animals would be needed. Corresponding studies using a reliable “in vivo-like” model, particularly for dose determination and for narrowing down the correct time point, could significantly reduce the animal numbers. Furthermore, the proposed lung organoid model has the potential to better reflect corresponding findings than mouse models, which could then completely replace certain animal experiments.

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

We would like to produce these organoids in larger quantities using an automated process. Therefore, we are currently working on the feasibility of using bioreactors. We are also exploring other organ systems and organoids, such as the kidney.

## 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 February 28<sup>th</sup>, 2026**, please visit

► [PAPER OF THE QUARTER](#)

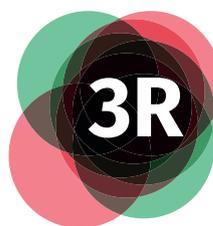
## 3R-Kompetenznetzwerk NRW

*Medical progress in line with best possible animal welfare*

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