



Paper of the Quarter

Outstanding 3R-Research from North Rhine-Westphalia
- 1st Quarter of 2026 -

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 2026.

Congratulations to

René Geci

RWTH Aachen University & Kinpreda GmbH



for his publication

“Integration of in vitro and in silico approaches enables prediction of drug-induced liver injury”

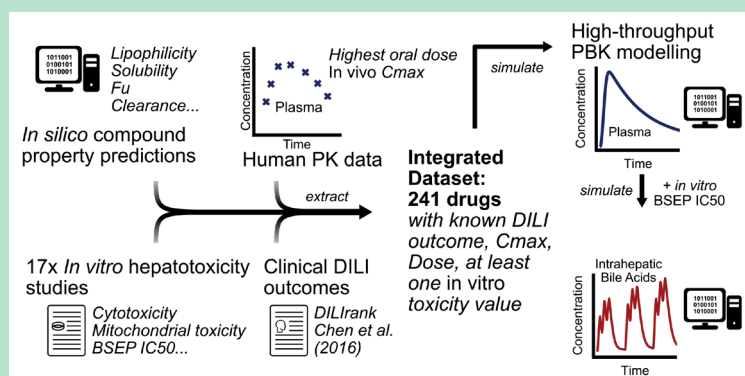
The “Paper of the Quarter” award was given to their publication because they strive in a special way to further develop the 3R principle—“Replace, Reduce, Refine”—which has been applied in laboratory animal science for more than 60 years.

The paper “Integration of in vitro and in silico approaches enables prediction of drug-induced liver injury” describes the development of a transparent and mechanistically grounded approach to predicting **drug-induced liver injury (DILI)** by linking in vitro toxicity data with in silico-based pharmacokinetic models.

The predictive performance of the approach is particularly noteworthy: across an integrated dataset of 241 drug substances, it achieves a ROC-AUC of up to 96%, and even up to 91% when using fully prospective, in silico-predicted pharmacokinetics. Because the approach preserves the interpretability that purely data-driven methods lack, **the model’s mechanistic traceability and compatibility with regulatory requirements are equally compelling**. By enabling the early identification of potentially hepatotoxic compounds, this approach can **make development processes more efficient and replace animal experiments in early safety assessment**.

His work therefore makes an important contribution, particularly to the **Replacement** principle of the 3Rs, and impres-

sively demonstrates the potential of **modern in vitro and in silico methods as forward-looking alternatives in the safety assessment of medicinal products**.



Data collection, analysis workflow and drug properties. Various literature datasets were integrated to obtain a dataset of 241 drugs with complete information on in vitro hepatotoxicity, clinical DILI outcome and pharmacokinetics. DILI prediction strategies of varying complexity were evaluated using the integrated dataset © Geci, René et al. “Integration of in vitro and in silico approaches enables prediction of drug-induced liver injury”

► You can read the original article here

[Geci, René et al. “Integration of in vitro and in silico approaches enables prediction of drug-induced liver injury.” Archives of toxicology vol. 100,5 \(2026\): 2029-2046.](#)

Q&A with the Winners

- 1st Quarter of 2026 -

How did this research come about?

Our research began with one relatively simple question: could high-throughput PBK simulations, a computational method we had been developing, add real value to the safety assessment of chemicals? PBK models can predict a substance's internal concentration, but they say nothing about its effect. So, we wanted to know how well chemical effects on humans could be predicted if this exposure information were combined with existing methods for predicting biological activity. Answering this, however, required a good case study: a setting where substance effects are reliably known, but where enough in vitro data are also available across enough compounds for a robust evaluation. Drug-induced liver injury was ideal, because clinical DILI outcomes of drugs are relatively well documented, and numerous public in vitro assays capture different mechanisms of liver toxicity. As we explored the literature, the project gradually grew. We integrated one dataset after another into a collection of hundreds of compounds, a scale that proved essential for distinguishing genuine predictive performance from noise. What began as a rather specific question eventually developed into a broader analysis of how well current DILI prediction methods work.

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

Our research contributes primarily to the Replacement principle of the 3Rs by showing that drug-induced liver injury can be predicted using human-relevant, animal-free methods. The approach combines toxicity measurements from human in vitro systems with in silico predictions of human pharmacokinetics, evaluated here across an integrated dataset of hundreds of drugs. This combination matters because an in vitro effect is only meaningful relative to expected patient concentrations, so relating the two is what makes reliable prediction possible. It also stays mechanistically transparent and interpretable, unlike many data-driven models, which is important for the 3Rs: regulators will only phase out animal testing once they can trust the alternatives, and interpretable, mechanism-based methods are far easier to scrutinise and justify. In practice, this can flag potentially hepatotoxic compounds earlier, support selection of safer candidates, and reduce ani-



The research group working on integration of in vitro and in silico methods for DILI prediction (From left to right: Ahenk Zeynep Sayin, Lars K pfer, Ren  Geci)

mal use in preclinical safety assessment, as a human-relevant alternative to animal studies whose concordance with human liver toxicity is itself limited.

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

Our main focus right now is to really establish how reliable high-throughput PBK predictions of human in vivo concentrations are, since we believe this is what is needed to bring them into routine use. We have already tested these predictions against large datasets of human concentration-time profiles and, for example in this work on DILI, have shown that they are useful not just for concentrations but for predicting real outcomes. What is still missing, however, is a clear definition of their applicability domains and a way to integrate prediction uncertainty into the simulations. We believe this is ultimately what is required to give both industry and regulators the confidence to rely on these methods. Our goal is therefore not only to develop the method further, but to build the scientific and technical framework needed for its practical use as an alternative to animal testing. To support this transition, we are currently founding a company called Kinpreda, dedicated to these problems and to bringing the methods into real safety assessment workflows.

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 November 30th, 2026**, please visit

► [PAPER OF THE QUARTER](#)

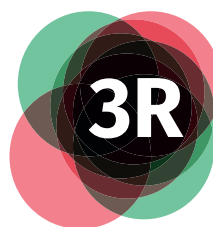
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Medical progress in line with best possible animal welfare

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