New EPHAR 2027 – Symposium Proposals

- **Novel insights into function of ABC transporters**
  Prof. Dr. Ingolf Cascorbi and Prof. Dr. Oliver Langer

- **Animal Research in Pharmacology: Indispensable Necessity, Ethical Obligation, and the Road to Replacement**
- *Prof. Dr Kristina Lorenz and Prof. Dr. Maria Grundoch*

- **Emerging strategies in targeting nuclear receptor signaling**
  (Organizer: Bastian Schirmer)

Novel insights into function of ABC Transporters

Chairs

Prof. Dr. Ingolf Cascorbi — *Institute of Experimental and Clinical Pharmacology, University Hospital Schleswig-Holstein Kiel, Germany*

Prof. Dr. Oliver Langer — *Department of Clinical Pharmacology, Medical University of Vienna, Austria*

Symposium Description

ABC transporters play a crucial role as a defence and extraction mechanism at compartment barriers in the human body. Consequently, they have a significant impact on pharmacokinetic properties and thus on the intracellular concentration of drugs and various other endogenous and exogenous compounds. The characteristics of ABC transporters has been intensively investigated, but still major question on their mode of action. regulation and specificity remain open. For example, the intramolecular mechanism by which transported substrates stimulate the ATPase activity has not been identified or how conformational changes induced by nucleotide binding and hydrolysis result in the decrease of drug binding affinity and lead to the release of the transported substrate. New technology like CRIPSR/Cas 9 have led to the creation of knockout models allowing the determination of specific transmembrane transport rates and better understand of substrate specificities of the transporter itself or compound characteristics. Moreover, advanced PET imaging techniques allow the determination of the ABC transporter function and consequences for drug distribution in vivo.
Novel aspects regarding these topics will be presented by renowned international experts in the field covering structural function, drug specificity in (multi)-knock-out models and functional characterization in vivo through clinical studies applying advanced techniques.

Proposed Speakers

The table below lists primary speakers.

Speaker	Affiliation	Understanding the molecular function of ABCG2
Dr. Lazlo Homolya	*Institute of Enzymology, Research Centre for Natural Sciences, Budapest, Hungary. (homolya.laszlo@ttk.hu)*	Understanding the molecular function of ABCG2 [1, 2]
Dr. Meike Kähler	*Institute of Experimental and Clinical Pharmacology, University Hospital Schleswig-Holstein, Kiel, Germany (kaehler@pharmakologie.uni-kiel.de)*	Determination of ABC transporter specificity applying knock-out models [3,4]
Prof. Oliver Langer	*Department of Clinical Pharmacology, Medical University of Vienna, Austria (oliver.langer@meduniwien.ac.at)*	Imaging of P-gp activity in humans [5,6]

Selected Key References

1. Bartos and Homolya. Identification of Specific Trafficking Defects of Naturally Occurring Variants of the Human ABCG2 Transporter. Front Cell Dev Biol. 2021 Feb 9;9:61572

2. Mózner ...Homoloya *et al.* Revisiting the Role of the Leucine Plug/Valve in the Human ABCG2 Multidrug Transporter. Int J Mol Sci. 2025 Apr 24;26(9):4010.

3. Radtke … Kaehler. CRISPR/Cas9-induced knockout reveals the role of ABCB1 in the response to temozolomide, carmustine and lomustine in glioblastoma multiforme. Pharmacol Res. 2022 Nov;185:106510

4. Kasten … Kaehler Determination of ABC transporter specificity applying a human CRISPR/Cas9-derived knockout model. Submitted.

5. Mairinger … Langer. Imaging pulmonary P-glycoprotein activity with aerosolized [99mTc]Tc-sestamibi in mice. Eur J Pharm Sci. 2026 Jun 1;221:107517

6. Biali … Langer, [11C]Metoclopramide PET can detect a seizure-induced up-regulation of cerebral P-glycoprotein in epilepsy patients. Fluids Barriers CNS 2024 Oct 28;21(1):87

Animal Research in Pharmacology: Indispensable Necessity, Ethical Obligation, and the Road to Replacement

Chairs

Kristina Lorenz	*University of Würzburg, Germany*
Maria Grandoch	*University of Düsseldorf, Germany*

Symposium Description

Animal experimentation remains a cornerstone of biomedical and pharmacological research. Without *in vivo* models, the discovery and development of landmark drug classes — from insulin and vaccines to modern biologics and GLP-1 receptor agonists — would not have been possible. At the same time, the scientific community faces growing ethical, regulatory, and societal pressure to critically evaluate the continued use of animals in research, accelerate the validation of alternative methods, and communicate its work with greater transparency and openness.

This symposium addresses one of the most contested yet fundamental questions in modern pharmacology: *When is animal research truly indispensable, and where can it — or must it — be replaced?* By examining a high-profile drug development success story (GLP-1 agonists), the regulatory and industrial perspective on replacement testing, and the latest advances in 3Rs methodology, this session offers a balanced, evidence-based perspective.

The four speakers represent academia, industry and a major European scientific advocacy organisation. Together, they illustrate that the path forward is neither the blanket defence of animal use nor its uncritical abolition, but a rigorously science-driven, step-by-step transition guided by the 3Rs principles of **Replacement, Reduction, and Refinement**.

Proposed Speakers

Speaker	Affiliation	Topic
Prof. Dr. Timo D. Müller	*Institute for Diabetes and Obesity (IDO), Helmholtz Munich & Walther-Straub Institute, LMU Munich, Germany*	The roadmap to innovative drugs — GLP-1 agonists as a use case
Kirk Leech	*European Animal Research Association (EARA), London, United Kingdom*	Replacement of animal research? Science, politics, and the limits of wishful thinking
Dr. Gabi Itter	*Sanofi-Aventis Deutschland GmbH, Frankfurt, Germany (Head I3RS / IVRC, TIM)*	Animal vs. replacement tests in industry — what are the restrictions?
Prof. Reinoud Gosens	*University of Groningen, Netherlands*	The use of pluripotent stem cells for the study of neuroimmune interactions in asthma

Speaker Profiles and Talk Descriptions

Prof. Dr. Timo D. Müller (Munich)

The roadmap to innovative drugs — GLP-1 agonists as a use case

Timo D. Müller is Director of the Institute for Diabetes and Obesity (IDO) at Helmholtz Munich and Full Professor for Energy and Glucose Metabolism at the Walther-Straub Institute for Pharmacology and Toxicology, Ludwig-Maximilians-University Munich (LMU). He is one of the scientists who pioneered the concept of GLP-1-based dual- and triple-agonists for the treatment of obesity and type 2 diabetes, with more than 200 publications in *Nature*, *Cell*, *Cell Metabolism*, *Nature Medicine*, and *Nature Metabolism*. His most recent work, published in *Nature* (2026), describes a unimolecular quintuple agonist (GLP-1R–GIPR–PPARα/γ/δ) that corrects obesity and diabetes using the incretin pathway as a targeted delivery vehicle. He is an ERC Consolidator grant awardee and recipient of the Minkowski Prize of the EASD and the Werner-Creutzfeldt-Preis (2023).

His talk will trace the full arc from initial animal model discoveries in rodents through the progressive development of GLP-1-based pharmacotherapies to today's approved drugs (semaglutide, tirzepatide), illustrating at each step *why* animal experiments were essential, *where* they were complemented by alternative approaches, and *what* remains unanswerable without *in vivo* models — including species-specific receptor differences (e.g., GIP receptor between mouse and human) that demand careful translational judgement. This talk provides the framing for the subsequent discussion of replacement strategies.

Kirk Leech (London)

Replacement of animal research? Science, politics, and the limits of wishful thinking

Kirk Leech is Executive Director of the European Animal Research Association (EARA), a communications and advocacy organisation dedicated to promoting transparency and public understanding of the role of animal studies in advancing biomedical science. EARA works across Europe to foster open dialogue between the research community, policymakers, and the public on the continued scientific need for — and the welfare limits of — animal experimentation, while simultaneously supporting the uptake of New Approach Methodologies (NAMs) where scientifically justified. Leech has been a prominent voice at openness events across Europe, warning against the "wishful thinking" that all animal research can immediately be replaced by alternative methods and addressing the scientific distortions promoted by anti-animal-research advocacy groups.

His talk could provide an evidence-based overview of the current European political landscape — including the 2021–2023 European Citizens' Initiative calling for a phase-out of all animal research, which was rejected by the European Commission — and could distinguish between the aspirational narrative of immediate replacement and the scientific reality. He could outline where NAMs have genuinely advanced to offer valid replacements, where serious gaps remain, and what transparent communication by the research community can do to rebuild and maintain public trust.

Dr. Gabi Itter (Frankfurt)

Animal vs. replacement tests in industry — what are the restrictions?

Dr. Gabi Itter is Head of I3RS (Initiative for Innovation, Integration & Implementation of the 3Rs in Safety Sciences) and Head of IVRC (In Vitro Reference Centre) within the Translational and Investigative Medicine (TIM) unit of Sanofi-Aventis Deutschland GmbH, Frankfurt. With a career in pharmaceutical industry toxicology spanning regulatory safety testing, in vitro methodology development, and 3Rs implementation, she brings a unique perspective on the structural, regulatory, and scientific constraints that govern the use — and limit the replacement — of animal studies in drug development. Industry toxicology is subject to ICH, OECD, and EMA/FDA guidelines that prescribe specific animal studies as regulatory requirements for drug approval, meaning that the decision to use or replace animals is rarely made by scientists alone.

Her talk could explore the gap between what is scientifically feasible in the laboratory and what is regulatorily mandated, examining specific test areas (e.g., repeat-dose toxicity, reproductive toxicology, genotoxicity, immunogenicity) where replacement tests are emerging, partly validated, or still absent. She could address what industry can already replace today, what requires further validation before regulators will accept it, and what the pharmaceutical industry is doing — in collaboration with OECD, ICH, and NC3Rs — to accelerate this transition.

Prof Reinoud Gosens

The use of pluripotent stem cells for the study of neuroimmune interactions in asthma

Reinoud Gosens is Professor of Molecular Pharmacology at the University of Groningen and a member of GRIAC (Groningen Research Institute for Asthma and COPD). His group pioneered the differentiation of human pluripotent stem cells (hPSCs) into airway cholinergic and sensory neurons to model neuroplasticity and neuroimmune interactions in asthma in vitro. Using co-culture systems of hPSC-derived sensory neurons and mast cells, his team has demonstrated that physical neuron–mast cell contact drives differential gene expression in mast cells — linking airway innervation to the severity of asthmatic inflammation. This approach represents a paradigmatic example of 3Rs Replacement: a fully human, mechanistically informative in vitro model that replaces the rodent allergen-challenge model for the study of neuroimmune disease mechanisms.

Relevance to EPHAR 2027

This symposium addresses a theme of fundamental and urgent relevance to European pharmacology in 2027: the tension between the scientific necessity of animal models and the ethical, political, and societal imperative to reduce and replace them. This topic cuts across all areas of pharmacological research — from basic science to regulatory toxicology and clinical translation. By combining perspectives from academia, industry, and advocacy, the session offers a uniquely multi-stakeholder dialogue expected to attract pharmacologists, toxicologists, regulatory scientists, and industry representatives alike. The inclusion of a Dutch speaker acknowledges the Netherlands' internationally recognised leadership role in driving the transition to animal-free biomedical innovation.

Emerging strategies in targeting nuclear receptor signaling

Chairs

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Symposium Description

Nuclear receptors (NRs) remain central to modern pharmacology. Their ability to translate chemical signals into gene regulatory responses places them at the core of numerous physiological processes, including metabolism and immune regulation.

This symposium will provide insights into recent advances in understanding and pharmacologically manipulating NR signaling. It will highlight emerging concepts that move beyond classical agonist–antagonist paradigms, emphasizing novel strategies to achieve improved selectivity, efficacy, and safety in drug design. These include selective receptor modulators, allosteric ligands, tissue-specific

targeting approaches, and the modulation of co-regulator interactions and chromatin environments that influence receptor function.

Advances in genomics, structural biology, and systems pharmacology have revealed that NR activity is highly context dependent. These insights are transforming pharmacological thinking, enabling the development of drugs that will fine-tune receptor activity in a pathway- or tissue-specific manner, with the aim of minimizing adverse effects traditionally associated with systemic receptor activation or inhibition.

The symposium will also highlight the translational implications of targeting nuclear receptors in major disease areas. By bringing together cutting-edge perspectives from molecular, cellular, and translational research, this symposium aims at stimulating new ideas at the interface of nuclear receptor biology and drug discovery.

Proposed Speakers

The table below lists primary and alternative speakers..

#	Speaker	Affiliation	Topic
1	**Karolien De Bosscher**	*VIB-UGent Center for Medical Biotechnology, Belgium*	Selective modulation of glucocorticoid receptor signaling (1–5)
1	**Jan Tuckermann** *bzw. Sabine Vettorazzi*	*Institute of Comparative Molecular Endocrinology and Physiology, Universität Ulm, Germany*	Decoding and exploiting cell type–specific glucocorticoid receptor signaling (6–8)
1	**Eckardt Treuter**	*Karolinska Institutet, Stockholm, Sweden*	Beyond NR: The role of nuclear receptor coregulators and transcriptional complexes (9–11)
2	**Antonio Moschetta**	*Università “Aldo Moro”, Bari, Italy*	Linking nuclear receptor signaling to metabolic and liver diseases (12–16)
2	**Daniel Merk**	*LMU München, Germany*	New approaches to discover and refine selective nuclear receptor modulators (17–19)
2	**Bart Staels**	*Université de*	Nuclear receptors in metabolic

#	Speaker	Affiliation	Topic
		Lille / Institut Pasteur de Lille	and cardiovascular disease (20–23)
2	**Nina Henriette Uhlenhaut**	*TU München / Helmholtz Zentrum München, germany*	Metabolic Programming by GR (24–27)

Selected Key References

1. Bougarne N, Paumelle R, Caron S, Hennuyer N, Mansouri R, Gervois P, et al. PPARalpha blocks glucocorticoid receptor alpha-mediated transactivation but cooperates with the activated glucocorticoid receptor alpha for transrepression on NF-kappaB. Proc Natl Acad Sci U S A. 2009 May 5;106(18):7397–402. doi:10.1073/PNAS.0806742106 PubMed PMID: 19376972.

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3. *Antwi MB, Lefere S, Clarisse D, Koorneef L, Heldens A, Onghena L, et al. PPARα-ERRα crosstalk mitigates metabolic dysfunction-associated steatotic liver disease progression. Metabolism. 2025 Mar 1;164. doi:10.1016/J.METABOL.2024.156128 PubMed PMID: 39743041.*

4. *Clarisse D, Van Moortel L, Van Leene C, Gevaert K, De Bosscher K. Glucocorticoid receptor signaling: intricacies and therapeutic opportunities. Trends Biochem Sci. 2024 May 1;49(5):431–44. doi:10.1016/J.TIBS.2024.01.012 PubMed PMID: 38429217.*

5. *Antwi MB, Jennings A, Lefere S, Clarisse D, Geerts A, Devisscher L, et al. Unlocking therapeutic potential: exploring cross-talk among emerging nuclear receptors to combat metabolic dysfunction in steatotic liver disease. npj metabolic health and disease. 2024 Dec 1;2(1). doi:10.1038/S44324-024-00013-6 PubMed PMID: 40603501.*

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16. *Cariello M, Zerlotin R, Pasculli E, Piccinin E, Peres C, Porru E, et al. Intestinal FXR Activation via Transgenic Chimera or Chemical Agonism Prevents Colitis-Associated and Genetically-Induced Colon Cancer. Cancers (Basel). 2022 Jul 1;14(13). doi:10.3390/CANCERS14133081 PubMed PMID: 35804854.*

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