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EDITORIAL

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Translational pharmacology: Closing the mechanistic gap

We have had the privilege of serving as guest editors for this special issue of Basic and Clinical Pharmacology and Toxicology, presenting a series of papers that highlight different aspects of translational pharmacology. Translation in research is most often described as the focused process of moving forward, that is, translating, basic discoveries into clinical practice. Within health research, and pharmacology in particular, there is often a considerable gap between our mechanistic understanding and the interventions that are applied in the treatment of patients. Closing this gap by translational approaches holds great promise, not only by moving laboratory discoveries into clinical practice but also by improving our understanding of already established treatment regimens (sometimes referred to as 'reverse translation'). Importantly, such translational work, be it in either direction, should not be viewed as a sequential process from basic to clinical pharmacology but would ideally involve an overlapping effort with direct collaboration between researchers from different disciplines within pharmacology.

This special issue contains two original articles and seven MiniReviews. In the first of the original contributions, Loucks et al.[1] demonstrate how improved understanding of genetic factors that affect risk of adverse events with anthracycline treatment can be used to guide treatment. In the second original article, Nabil et al.[2] provide a full (reverse) translational tale of the discovery that pregnane X receptor (PXR) activation with rifampicin led to an increase in plasma alkaline phosphatase in a clinical trial, a finding that was later investigated in both osteoblasts and two rodent models to understand the underlying molecular mechanism. The seven MiniReviews span widely. Uddin et al.[3] describe how expression of membrane transporters in cardiac tissue influences the risk of chemotherapy-induced cardiotoxicity and how our increased understanding of this can lead to safer treatments in the future. Chua et al.[4] similarly consider a common side-effect to chemotherapy, namely peripheral neuropathy, focusing on microtubule-targeting agents and how translational genetic studies covering both genome-wide association studies and functional genomic studies using pluripotent stem cells will bring us forward in our understanding of chemotherapy-induced neuropathy. Lim et al.[5] review pharmacological agents of current or potential future use as medical expulsive therapy in urolithiasis, leveraging both in vitro and in vivo studies to provide recommendations for candidate drug classes for further clinical investigation. Eisenmann et al.[6] review how pharmacokinetic knowledge can be used to improve the oral bioavailability of anticancer drugs by deploying intentional drug–drug interactions. Tornio et al.[7] also concerns drug–drug interactions and provides an overview of the available translational methods that can be used in assessing drug–drug interactions, including clinical pharmacokinetic studies, in vitro studies, and epidemiological studies, using a drug–drug interaction with clopidogrel as their case. Ingelman-Sundberg and Lauschke[8] provide a new framework for translational pharmacology in the form of 3D human liver spheroids, a method that more closely resembles human liver compared with historically used models, and review its use in studies of drug hepatotoxicity, metabolite formation and drug development for drugs in metabolic or infectious liver disease. Finally, Winterstein and Antonelli[9] illustrate method triangulation using the case of tympanic membrane perforations with otic quinolone therapy, reviewing a combination of mechanistic and real-world evidence studies and discussing the challenges in disseminating such translational studies.

As illustrated, the nine papers in this issue provide an array of considerations and applied examples of how translational thinking can move forward pharmacological research. In addition to the inherent value in the research endeavours described, it is our hope that they will inspire other researchers within pharmacology to consider translational approaches in their own research and to seek out collaborations outside their own subfield, to the benefit not only of the field of pharmacology but ultimately to patients at large. We recognise that this requires distancing from one's usual comfort zone; however, while challenging, the rewards far outweigh initial challenges. We can, from personal experience, testify to the fact that such collaborations rank among the most gratifying projects in our own career, both personally and scientifically.

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