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Reducing safety-related attrition in drug development is a primary aim of the pharmaceutical industry, and gaining a better understanding of the safety profile of drug candidates as early as possible is crucial in achieving this goal. In a Perspective article, four major pharmaceutical companies — AstraZeneca, GlaxoSmithKline, Novartis and Pfizer — share their knowledge and experiences of the use of *in vitro* pharmacological profiling to detect undesirable off-target interactions of compounds. Using case studies, they demonstrate the impact of generating such data on the drug discovery process and recommend a minimal panel of targets for screening. The protein kinase C (PKC) family is an attractive target for drug discovery, but despite significant efforts the first drug specifically targeting a PKC isozyme is yet to receive approval. In their Review, Mochly-Rosen and colleagues consider the challenges in developing PKC modulators, assess their therapeutic potential in disorders including heart diseases, diabetic complications and cancer, and discuss recent clinical trials. Cancer is among the many indications for which inhibitors of the poly(ADP-ribose) polymerase (PARP) protein superfamily are being investigated. Although efforts have largely focused on PARP1, tankyrase 1 (TANK1) is beginning to emerge as a promising therapeutic target. Ashworth and colleagues review the diverse biological roles of TANK1 and discuss the clinical potential of TANK1-specific inhibitors in various cancers as well as non-oncological diseases such as pulmonary fibrosis. The complex and heterogeneous airway disease, asthma, remains inadequately controlled in some patients. In our final Review, Pelaia and colleagues discuss recent advances in the understanding of asthma pathobiology and the potential of biological therapies targeting specific cytokines to improve patient care.

EDITORIAL OFFICE

LONDON NatureReviews@nature.com
The Macmillan Building, 4 Crinan Street,
London N1 9XW, UK
Tel: +44 (0)20 7843 3620;
Fax: +44 (0)20 7843 3629

To subscribe and for more detailed information visit
www.nature.com/reviews/drugdisc

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NEW YORK nature@natureny.com
Nature Publishing Group, 75 Varick Street, 9th floor,
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Fax: +1 212 696 9006

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EDITORS


PETER KIRKPATRICK


ALEXANDRA FLEMMING


CHARLOTTE HARRISON


SARAH CRUNKHORN


ASHER MULLARD


MAN TSUEY TSE