Nature Reviews Drug Discovery | AOP, published online 15 March 2013; doi:10.1038/nrd3984–nrd3987

IN BRIEF

INFLAMMATORY DISORDERS

Of mice and humans

This study investigated changes in gene expression in individuals with trauma, burns and endotoxaemia, and compared them with gene expression changes in mouse models of these conditions. Although gene expression patterns were similar in humans with trauma, burns and endotoxaemia (supporting the view that these injuries invoke a common reaction), there was a low correlation between the changes in gene expression in humans and in mouse models of either of the three conditions. This suggests that the mouse models used in this study are poor indicators of human inflammatory conditions.

ORIGINAL RESEARCH PAPER Seok, J. *et al.* Genomic responses in mouse models poorly mimic human inflammatory diseases. *Proc. Natl. Acad. Sci. USA* **110**, 3507–3512 (2013)

LEAD IDENTIFICATION

New inhibitors of sonic hedgehog signalling

The sonic hedgehog protein is involved in cancer progression. To identify new sonic hedgehog inhibitors, Petrova *et al.* screened for a small-molecule inhibitor of Hedgehog acetyltransferase, an enzyme involved in sonic hedgehog palmitoylation and regulation of sonic hedgehog signalling. From a series of hits generated from initial screens, four lead compounds were selected based on their potency and drug-like scaffold, one of which was shown to inhibit autocrine and paracrine sonic hedgehog signalling in cells.

ORIGINAL RESEARCH PAPER Petrova, E. *et al.* Inhibitors of Hedgehog acetyltransferase block Sonic Hedgehog signaling. *Nature Chem. Biol.* 17 Feb 2013 (doi:10.1038/nchembio.1184)

PHARMACOKINETICS

Single-cell imaging adds insight into drug action

Poly(ADP ribose) polymerase 1 (PARP1) inhibitors have had little clinical success. Thurber *et al.* used real-time *in vivo* single-cell pharmacokinetic imaging of a PARP1 inhibitor to show that the lack of clinical effect is probably not due to tumour cells receiving insufficient concentrations of a PARP1 inhibitor. They then used imaging data to model and predict the distribution of the PARP1 inhibitor in situations in which it would be difficult to experimentally determine pharmacokinetics, such as subcellular distribution in humans. The authors note that single-cell pharmacokinetic imaging could aid the understanding of other drugs in other diseases.

ORIGINAL RESEARCH PAPER Thurber, G.M. *et al.* Single-cell and subcellular pharmacokinetic imaging allows insight into drug action *in vivo*. *Nature Commun.* **4**, 1504 (2013)

CARDIOVASCULAR DISEASE

Secrets of an ageing heart

Ageing is a risk factor for cardiovascular disease. This study showed that microRNA-34a (miR-34a) expression is induced in the ageing mouse heart and contributes to the decline in cardiac function. Genetic inhibition of miR-34a reduced age- and myocardial infarction-associated cardiomyocyte death and fibrosis. The authors showed that the target of miR-34a was protein phosphatase 1 regulatory subunit 10 (PPP1R10), which is involved in apoptosis and DNA repair. Overexpression of this target reduced telomere shortening, DNA damage responses and apoptosis in cardiomyocytes. In mice, genetic inhibition of miR-34a caused upregulation of PPP1R10 in the heart and reduced cardiac DNA damage after acute myocardial infarction.

ORIGINAL RESEARCH PAPER Boon, R. A. *et al.* MicroRNA-34a regulates cardiac ageing and function. *Nature* **495**, 107–110 (2013)