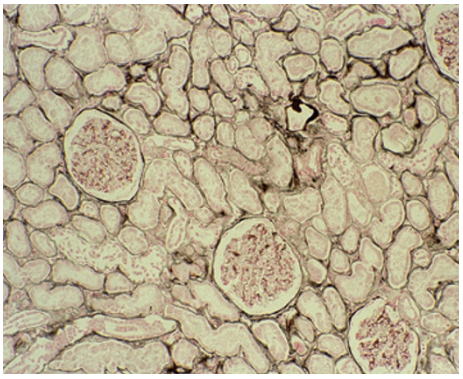
IN BRIEF

KIDNEY DISEASES

Modification of kidney barrier function by the urokinase receptor.

Wei, C. *et al. Nature Med.* **14**, 55–63 (2008)

Therapies aimed at the cellular level of progressive kidney disease — which is often initiated by podocyte dysfunction — are currently not available. Wei and colleagues show that induction of urokinase receptor signalling in podocytes leads to foot process effacement and urinary protein loss via a mechanism that includes lipid-dependent activation of αvβ3 integrin. Blockade of αvβ3 integrin reduced podocyte motility *in vitro* and lowered proteinuria in mice, and so could represent a novel therapy for kidney disease.



KINASE INHIBITORS

Identification of genotype-correlated sensitivity to selective kinase inhibitors by using high-throughput tumor cell line profiling.

McDermott, U. *et al. Proc. Natl Acad. Sci. USA* **104**,19936–19941 (2007)

A systematic interaction map of validated kinase inhibitors with Ser/Thr kinases.

Fedorov, O. *et al. Proc. Natl Acad. Sci. USA* **104**, 20523–20528 (2007)

There are few studies describing the selectivity of kinase inhibitors across panels of diverse kinases and/or cancer cell lines. McDermott and colleagues established a high-throughput screening platform to profile 500 cell lines derived from diverse epithelial cancers for sensitivity to 14 kinase inhibitors. Although most cell lines recapitulated known tumour-associated genotypes, the screen revealed low-frequency drug-sensitizing genotypes in tumour types not previously associated with drug susceptibility. Furthermore, comparison of drugs that were thought to target the same kinase revealed unsuspected functional relationships. Fedorov and colleagues evaluated the specificity of 156 kinase inhibitors against 60 human serine/threonine kinases using a thermal stability shift assay. The analysis revealed many unexpected cross-reactivities for inhibitors that were thought to be specific for certain targets. For example, a PKCβ inhibitor also inhibited PIM1 kinase, a suggested target for leukaemia treatment; indeed, this inhibitor suppressed growth of leukaemic cells. These studies reveal additional tumour types that could respond to established cancer therapies.

LUNG DISEASE

Cleavage of CXCR1 on neutrophils disables bacterial killing in cystic fibrosis lung disease.

Hartl, D. *et al. Nature Med.* **13**, 1423–1430 (2007)

The airways of individuals with cystic fibrosis are frequently colonized by bacterial pathogens, despite the presence of large numbers of neutrophils and interleukin 8 (IL8). Hartl and colleagues show that IL8 promotes neutrophilic bacterial killing through CXCR1; however, in the airways of individuals with cystic fibrosis, unopposed proteolytic activity in cleaved CXCR1 disables the bacterial-killing capacity of neutrophils. Protease inhibition restored CXCR1 expression and improved bacterial killing in these individuals, and so could represent a new pathophysiological mechanism in cystic fibrosis and other chronic lung diseases.