Technology Watch

INTERFERING WITH MIGRATION

Joan Brugge and colleagues used a high-throughput small interfering (si)RNA-screening approach to identify genes that are involved in epithelial cell migration by focusing on the generation of a highly validated dataset. This contrasts with the prevalent strategy of selectively analysing a few strong hits with minimal validation of most primary hits.

The authors performed a high-throughput wound-healing screen with breast epithelial cells and used siRNAs that targeted 1,081 human genes that encode proteins that are predicted to influence cell migration and adhesion. The primary screen identified 34 genes that negatively regulate cell migration, 32 that have a positive role in cell migration and 29 that affect metabolism. Extensive validation of all the hits yielded 66 high-confidence genes that, when downregulated, either accelerated or impaired migration; 42 of these high-confidence genes had no prior association with motility or adhesion. Informatics analysis highlighted three main signalling nodes — β-catenin, β1 integrin and actin. This screen provides a resource of high-confidence data, annotated at the level of migration effects, cell morphology features, patterns of motility over time and pathway interactions. A fully interactive database is hosted by the Cell Migration Consortium (http://www.cellmigration.org/resource/discovery/brugge/simpson2008_rnai.cgi).

ORIGINAL RESEARCH PAPER Simpson, K. J. *et al.* Identification of genes that regulate epithelial cell migration using an siRNA screening approach. *Nature Cell Biol.* 10 Aug 2008 (doi:10.1038/ncb1762)

PROTEOMICS GOES LIVE

Quantitative proteomics has largely been limited to *in vitro* systems. Krüger *et al.* now show that SILAC (stable isotope-labelled amino acids), a versatile and successful method for quantitative proteomics in cell-culture-based systems or microorganisms, can be applied to mammalian model systems.

Krüger *et al.* report the development of a mouse SILAC diet that leads to complete labelling of the F2 progeny without affecting development, growth and behaviour. The authors propose that these mice can serve as internal standards to analyse the proteome of knockout mice. Mass spectrometry analysis of incorporation levels allowed for the determination of incorporation rates of proteins from blood cells and organs. SILAC analysis from various organs that lack expression of members of the integrin pathway — β1 integrin, β-parvin or the integrin tail-binding protein kindlin-3 — confirmed the absence of these proteins. This study also revealed a deficit of structural proteins in the plasma membrane of Kindlin-3-deficient erythrocytes, providing a molecular explanation for the severe anaemia seen in Kindlin-3-knockout mice. The authors elegantly show that this approach can be used to quantitatively compare proteomes from knockout mice and thereby determine protein functions under complex *in vivo* conditions.

ORIGINAL RESEARCH PAPER Krüger, M. *et al.* SILAC mouse for quantitative proteomics uncovers kindlin-3 as an essential factor for red blood cell function. *Cell* **134**, 353–364 (2008).

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