of human tracheobronchial epithelial cells. To elucidate the pathway, they used both pharmacological agents and dominant negative mutant proteins that specifically inhibit various steps of the cellular signalling pathway. Dominant negative mutant protein, when overexpressed in the cell, specifically inhibits the activity of endogenous protein. For example, they found that the dominant negative protein kinase C δ (PKCδ) and rottlerin (a pharmacological inhibitor of PKCδ) abolished PMA-stimulated *SPRR1B* gene expression. Furthermore, mitogen-activated kinase kinase 1 (MKK1) inhibitors and its mutant protein suppressed PMA-enhanced SPRR1B promoter activity. However, mutants of extracellular signal-regulated kinases 1 and 2, downstream targets of MKK1, did not affect SPRR1B promoter regulation, indicating involvement of a yet unidentified extracellular-signal-related kinase (ERK)-like kinase in PMA-stimulated expression of SPRR1B.

The future

Currently, the team is repeating the process using human lung cancer cell lines to see if they show any defects in the pathways. 'If we can understand these early precancerous cellular changes, we might be able to reverse them before it is too late. Alternatively, if we can find a way to detect pre-cancerous cells within a few months of their onset, we might be able to prevent the development of full-blown cancer,' says Reddy. Further studies include the examination of lung biopsies to identify the stage at which *SPRR1B* gene expression is lost. Loss of gene expression could be developed as a diagnostic tool for lung cancer.

One treatment approach, says Reddy, would be to use cornification as a targeted cancer treatment. 'If you could induce cornification in cancer cells this would kill them and/or consequently slow the growth of the cancer.'

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People

Two transcription regulation experts join Science Board

CIStem Molecular Corporation (San Diego, CA, USA) has appointed two leading experts to their Scientific Board. The addition of the transcriptional regulation experts, Keith Tamamoto and James Kadonaga, to the Board is hoped to help in the company's aim to develop technologies for the characterization and commercialization of genetic regulatory circuits that control gene expression.

Yamamoto is currently Professor and Chairman of the Department of Cellular and Molecular Pharmacology at the University of California (San Diego, CA, USA) and has made significant contributions to the knowledge of signalling and gene regulation mechanisms through intracellular receptors that mediate the actions of several essential hormone classes. He is also the outgoing Chairman of the Advisory Committee to the NIH Center for Scientific Review, is a member of the National Academy of Sciences and a Fellow of the American Academy of Arts and Sciences.

Kadonaga is currently Professor of Molecular Biology at the University of California and has focussed on transcriptional regulation and chromatin structure. His research has included the development of sequence-specific DNA affinity chromatography, cloning of transcription factor Sp1, discovery of the downstream core promoter element (DPE), the use of chromatin templates to recreate ligand-regulated transcription by nuclear factors *in vitro*, and the cloning of factors that mediate chromatin assembly.

Change in investment adviser and manager for the IBT

The Board of International Biotechnology Trust plc (London, UK) has appointed Schroder Ventures Life Sciences Advisors to be their investment advisers and Schroder Investment Management Ltd to oversee the administration of the company. These appointments follow the termination of the previous contract with Rothschild Asset Management.

The Board has negotiated an annual investment management fee of 1.35% of gross assets. Incentive fee arrangements have also been put in place, which include benchmarks and hurdle rates in line with industry practices. The Board consulted several substantial shareholders before making this appointment and will be publishing a circular outlining certain proposals. These proposals are aimed to enable shareholders who wish to retain their investment in the international biotechnology sector to do so through a vehicle whose initial net value will comprise of not less than 50% of the company's assets.

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