BIOPHYSICS

Fashionable cells

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How can cells deform yet maintain optimal function? Probing the similarities in the properties of a cell's network of structural filaments, and those of soft glassy materials, may help in tackling this question.

Most of the cells that make up our body are supported by a cytoskeleton, an internal network of protein filaments. This network does not merely act as a scaffold that defines cell shape and organizes intracellular organelles, but also allows the cell to be malleable and motile, and adapt to strains imposed internally and externally. As they report in *Nature Materials*, Bursac *et al.*[1] have combined observations of the cytoskeleton in action with some principles derived from condensed-matter physics to offer a fresh perspective on cytoskeletal dynamics.

The need for a cell to deform while maintaining function is most obvious in the smooth muscle cell, which is embedded in the wall of hollow organs such as the urinary bladder, lungs (airways) and uterus. These organs undergo large changes in volume, implying substantial changes in cell length. Surprisingly, these drastic alterations in cell dimensions do not appear to affect cell function. The concept of plastic length adaptation was first developed for the smooth muscle of airways[2,3], to explain how muscle can generate maximal force over a large range of lengths. It then soon became evident that the network of contractile and cytoskeletal filaments in smooth muscle is in a constant state of rearrangement, driven by the strains applied to the network.

Like the cytoskeleton, soft glassy materials such as pastes, colloids and foams can accommodate drastic changes of shape. Such changes occur when a cold glass, a rigid solid, is heated to a temperature at which it starts to behave as a malleable fluid. As they go about their daily business of adhering and spreading, crawling and invading, or contracting and relaxing, the cells of our body seem to orchestrate their mechanical properties in much the same way as happens in soft glasses around the glass transition temperature (which marks the crossover point between solid and fluid characteristics). But instead of changing temperature, the cell modulates something else, although with much the same effect — an 'effective temperature'[4].

Bursac *et al.*[1] reveal further details of the behaviour of the cytoskeletal and contractile filament network of smooth muscle cells, and its striking resemblance to how soft glassy materials respond to stress and strain. Their experiments involved attaching a microbead to the cytoskeleton of cultured smooth muscle cells from human airways, then following its spontaneous movements. They find that the microbead's movement reflects motion associated with molecular-scale rearrangements of the filament network. Most of the time nothing of great interest happens; motions are sub-diffusive, suggesting that proteins are trapped in a cage formed by weakly interacting structural proteins in a 'crowded', out-of-equilibrium microenvironment. But these sub-diffusive motions are punctuated by intermittent events thought to reflect 'hops' of the structural proteins out of one cage and into another, driven by the tendency of the discrete constituents of the crowded environment to settle slowly into a slightly more stable configuration.

An analogous hopping phenomenon has been observed in colloidal glasses[5], and the slow settling process is known as ageing. Ageing can be reversed by a process called rejuvenation, when a soft glass is subjected to a large shear that breaks up constraints and restores the previous state of disequilibrium. Bursac

CANCER

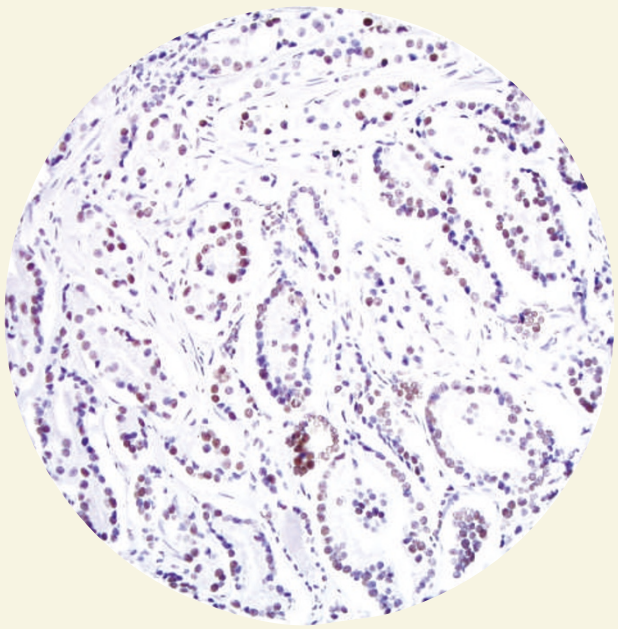
A changing global view

Global gene-expression profiles have emerged as a way to divide tumours that look similar into subgroups with distinct prognoses. But they can be technically demanding and difficult to implement as a routine clinical assay. Siavash Kurdistani and colleagues show elsewhere in this issue (*Nature* **435,** 1262–1266; 2005) that taking a different global view — of histone modification — can provide a similar indicator, for prostate cancer at least, that may translate easily to the clinic.

Histone proteins, around which DNA is wrapped to pack it into the nucleus, can be chemically modified in several places by the addition of acetyl or methyl groups. These modifications are reversible and can affect the expression of the associated genes. Cancer cells are known to have unusual patterns of histone modification, but so far work has focused on individual genes and their contribution to cancer development and progression.

In contrast, Kurdistani and colleagues looked at global levels of the acetylation or methylation of five different residues in histones H3 and H4 in prostate tumour samples. They used antibodies that were specific for each modification to highlight any differences; for example, the photo here shows a section of low-grade prostate cancer tissue (Gleason score 6) stained with an antibody against dimethylated arginine 3 of histone H4.

The authors found, from two independent sets of prostate cancer samples, that histone modification patterns can forecast the risk that a low-grade tumour will recur after surgical removal. How the observed global changes in histone modifications relate to the regulation of genes relevant to prostate cancer development is not known. However, using immunochemistry to detect bulk histone modifications in cancer samples is relatively easy, so these findings could be translated directly into prognostic markers for clinical use. **Barbara Marte**



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