specifically to the trapped biomarkers. The next step is to treat the sensor with an aqueous suspension of magnetic nanoparticles — tiny spheres containing iron oxide — to which the protein avidin has been attached. Avidin binds with high affinity to biotin, and so the magnetic nanoparticles become strongly linked to the biomarker–antibody complexes on the surface of the sensor. Finally, the authors activate the sensor by exposing it to a magnetic field. The resulting electronic readout is proportional to the extent of nanoparticle binding, and thus provides a quantitative measure of the amount of biomarker bound to the sensor's surface.

Bioassays that use GMR sensors to detect molecules sandwiched between a pair of antibodies (one immobilized and the other introduced in solution) have been reported previously[3,4]. But there are two factors that distinguish Gaster and colleagues' results[1] from the others. First, they have meticulously characterized their approach for several candidate analytes to prove its generality and its superiority to ELISA. And second, they demonstrate that their nanosensor can be used for multiplexing, so that as many as 64 assays can be performed on the same device. This capability is possible because of the specificity and sensitivity of their design, and because of the lack of biological-matrix interference.

The authors showed that their nanosensor assay system works in all biological fluids studied, including blood, urine, saliva and cell lysates — although the signal strength in saliva is less than that in other media, perhaps because the viscosity of saliva affects the binding kinetics of the assay. The authors also demonstrated that real-time readouts of binding are possible with their system, and that it can be used *in vivo* to follow the earliest stages of tumour progression by monitoring appropriate biomarkers. Turbidity and sample pH do not significantly affect the assay, but Gaster *et al*. found that the output signal is affected by temperature, so that hot or cold samples create undesirable spikes in the baseline of the electronic readout before they equilibrate to room temperature. The authors were able to correct for this, however, by processing the data using a mathematical algorithm. No other assay system, including ELISA, has such a combination of broad applicability, high sensitivity and low background 'noise' caused by biological-matrix interference.

It should be noted that Gaster and colleagues' approach does not actually prevent the biological matrix from physically interfering with antigen–antibody interactions. Nevertheless, such interference can be minimized by carefully screening antibodies to find those that don't interact with components of the biological matrix[2]. The assay could also be adversely affected by inadvertent exposure to strong magnetic fields, such as those present in nuclear magnetic resonance imaging scanners, but this can be prevented by appropriate shielding.

Gaster *et al*. speculate that their assay will be useful for several applications, such as studying protein–protein interactions and screening compounds for biological activity in drug-discovery programmes. Furthermore, the sensitivity and rapid responsiveness of the system permit biomarker monitoring with both high spatial and temporal resolution. This might open up exciting medical applications — for example, by tracking appropriate biomarkers, tumour responses to therapy could be anticipated before any effect becomes apparent. That could reduce the risk of untoward drug effects, and allow adjustments to be made to medication in a more timely way than is currently possible. ■

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STEM CELLS

A fateful age gap

Tim Stearns

When a stem cell divides, one sister cell differentiates and the other retains its stem-cell identity. Differences in the age of an organelle — the centriole — inherited at cell division may determine these differing fates.

One of the enduring mysteries of biology is how two genetically identical sister cells become different from each other after cell division. Stem cells are particularly interesting in this respect because they can divide so that one of the two resulting cells remains an undifferentiated stem cell while the other becomes a differentiated cell type. It has long been thought that such asymmetric cell division may reflect an underlying asymmetry in the segregation of a cellular component at division; the asymmetrically inherited component would have properties that allow it to control the fate of its recipient cell. In this issue (page 947), Wang *et al.*[1] present evidence that the centrosome, a multifunctional organelle that is common to all animal cells, might be such a determinant.

The centrosome is an ancient organelle[2] and is one of the cell structures that distinguishes eukaryotic cells (animal and plant cells) from prokaryotes (bacteria and archaea). It helps to form the microtubule cytoskeleton, a network of protein filaments that serve as tracks for moving cellular cargo. It also organizes the primary cilium, a whip-like structure that extends from the surface of cells. In most cells the primary cilium is non-motile, in contrast to the beating cilium of sperm cells, but it is responsive to chemical and mechanical signals outside the cell. For more than a century, the main function of the centrosome was thought to be organization of the mitotic spindle — the filamentous network that carries out the segregation of chromosomes at cell division. But it is now clear that the spindle can form without the centrosome, and that formation of a cilium is actually the centrosome's essential function[3]. This revelation is particularly exciting because it has coincided with the recognition that the primary cilium is a key signalling centre in vertebrate organisms, thereby placing it, and the centrosome, in the thick of important regulatory processes[4].

Each centrosome consists of a pair of cylindrical centrioles and associated microtubule-organizing material. The two centrioles in a pair usually lie in close association at right angles to each other. One centriole, the mother, has structural appendages that confer the ability to anchor microtubules and to organize a cilium; the other centriole, the daughter, lacks these appendages.

The centrosome duplicates once during the cell cycle, and it derives an intrinsic asymmetry from its mechanism of duplication. Centriole duplication is initiated by disengagement of the centriole pair at the end of mitosis, followed in S phase (the phase of DNA synthesis) by assembly of two new daughter centrioles, each adjacent to one of the existing centrioles. This pattern of duplication and segregation results in an age difference in the two centrosomes that are segregated to sister cells at division. One sister cell receives a centrosome containing a newly minted mother centriole (one that was a daughter centriole before duplication and cell division), and the other sister cell receives a centrosome containing the older mother centriole.

Might there be a correlation between the asymmetric fates of dividing stem cells and differences in the age of the centrioles inherited at cell division? Wang *et al*.[1] addressed this question by studying the asymmetric divisions of radial glial cells, a type of neural stem cell that is important for the development of the mammalian cerebral cortex. These cells are highly polarized, stretching between the epithelial surface of the cerebral ventricles

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50 YEARS AGO

In his presidential address to the British Association at York on September 2, Sir James Gray pleaded strongly for a wider outlook in the teaching of science and stressed the need for a considered judgment as to the proportion of our total educational effort which should be devoted to the training of scientists and technicians — upon whom we depend for maintaining or extending our standard of living — and the proportion which should be expended on raising the intellectual standards whereby the bulk of the population forms its judgments on matters which are susceptible to personal prejudice or political propaganda. Sir James recognized the implications of Dr. Trenaman's inquiry into the impact of the mass media and maintained that the key to the problem lies in the schools. The responsibility resting on secondary school teachers is not easily exaggerated, and Sir James pointed out that really inspired teachers, working with adequate but simple equipment, would achieve far more for general education than specialists in highly equipped laboratories.
From *Nature* 17 October 1959.

100 YEARS AGO

The British School of Archaeology at Athens has made further important discoveries on the site of the city of Sparta. The great temple of Artemis Orthia has been now completely cleared. The site known as the Menelaion, at Therapne, about two miles south-east of Sparta, has been partially examined. The sanctuary of Menelaus and Helen, mentioned by Herodotus, Livy, Pausanias, and Polybius, was a favourite resort of the Spartan ladies, where the goddess was believed to confer the gift of beauty on her worshippers. The discovery of Mycenaean remains on this site suggests that this was the famous palace of Menelaus.
From *Nature* 14 October 1909.

50 & 100 YEARS AGO

and the adjoining layer of cells. The nucleus in these elongated radial glial cells moves up and down during the cell-division cycle, with mitosis occurring at the apical end, adjacent to the ventricle. After division, one cell remains a radial glial cell while the other differentiates into a neuron or a neuronal precursor that migrates away from the ventricular zone.

When Wang *et al.* labelled the centrioles in developing mouse brain with fluorescently tagged proteins, they found that the older mother centriole was preferentially inherited by the cell that retained the stem-cell fate. To test whether this pattern is important for stem-cell function, they used RNA interference to remove the protein ninein, a component of the centriolar appendages required for mother-centriole functions. Strikingly, when ninein was removed, centriole asymmetry was lost, and the pool of stem cells became depleted, suggesting that inheritance of the older mother centriole is crucial for maintaining stem-cell fate in radial glial cells.

How does the older mother centriole specify stem-cell fate after cell division? On the basis of the properties of centrioles, I consider three possibilities. First, the mother centriole initiates the formation of a primary cilium at the beginning of the cell cycle in most cells. A recent report[5] indicates that the cell that inherits the older mother centriole usually projects a cilium before its sister, and that the sister cell thus differs in its response to signals mediated by the cilium. Such a temporal difference in receptiveness to external differentiation signals might result in a cell-fate difference in recently divided cells.

A second possibility is that the older and newer mother centrioles differ in their complement of anchored microtubules during the cell cycle before division. As anchored microtubules can serve as tracks on which to move components towards the centrosome, the older mother centriole might accumulate proteins[6] or RNA[7] that influence cell fate after division.

Last, it has been proposed that stem cells are maintained by asymmetric segregation of a set of 'stem' chromosomes, all of a similar replicative age[8]. Such asymmetric chromosome segregation is at odds with the known mechanisms of mitosis, but has been observed in some types of mammalian stem-cell division[9]. Perhaps the older mother centriole maintains a connection to the chromosomes (the nuclear envelope notwithstanding) from one mitosis, through interphase to the next mitosis, allowing all similarly aged sister chromatids (the copies of a replicated chromosome) to segregate together.

Possibly the most exciting result from Wang and colleagues' work[1] is that their findings are remarkably similar to those of studies[10] of male germline stem cells in the fruitfly *Drosophila melanogaster*. In that system, the older centrosome also stays in the stem cell, and this asymmetric segregation is part of a stereotyped division choreographed by signals from the stem-cell niche. We can hope that a unifying mechanistic principle of differentiation will be revealed by future experiments investigating this remarkable organelle and its behaviour during division. ■

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MATERIALS SCIENCE

Quasicrystals from nanocrystals

Alfons van Blaaderen

Quasicrystals have a host of unusual physical properties. These intermediates between amorphous solids and regular crystalline materials can now be made to self-assemble from nanoparticles.

The discovery of quasicrystals about 25 years ago[1,2] brought about a paradigm shift in solid-state physics. The observation that the arrangement of atoms in these solids exhibited long-range order yet lacked the three-dimensional periodicity and translational symmetry that characterizes conventional crystals puzzled physicists[3–5] — not least because certain 'forbidden' rotational symmetries occur in these materials. Initially discovered in certain exotic metal alloys, quasicrystals were later found in more common mixtures of elements and even in soft matter[3]: liquid crystals, surfactants and polymers. Adding to this growing list, Talapin *et al.*[6] (page 964 of this issue) now report that binary colloidal nanoparticle

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