WEB WATCH

One-stop trial shop

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Researchers, physicians and patients have long demanded free access to clinical trial data while studies are in progress, rather than having to wait until the results are published. Current Controlled Trials Ltd, part of the Current Science Group of companies, has addressed this need by creating a free, international, searchable database of ongoing clinical trials. The *meta*Register of controlled trials (*m*RCT) is a valuable search engine for clinical studies that are underway in all areas of health care. Visitors can search by disease or sponsor for information on over 10,000 trials. The *m*RCT is not a complete record of all randomized trials worldwide, but does allow visitors to search databases of a number of organizations simultaneously. For example, with one click, a user can search for prostate cancer clinical trials that are sponsored by Oxford University, GlaxoSmithKline, the Leukaemia Research Fund, the Hong Kong Health Services Research Fund, the UK's Medical Research Council, the US Department of Veterans Affairs Cooperative Studies Program, and the National Institutes of Health. The site provides information on patient recruitment status, organizer contact details, reasons for trial termination, trial design and patient eligibility. Trial sponsors trying to recruit new patients can also enter information about their study. Information posted is not reviewed by Current Controlled Trials before being included in the database, and data accuracy is the responsibility of the contributor. The site does, however, have an advisory board made up of editors from a number of medical journals and executives from medical research organizations. Registrants can also receive regular updates by e-mail.

Kristine Novak

VACCINES

Trapping technology

In police circles, entrapment is frowned upon as a means of securing an arrest. But, as reported by Akira Takashima and colleagues in the January issue of *Nature Biotechnology*, it could be a legitimate way of creating cancer vaccines without having to resort to costly *ex vivo* approaches.

A promising way of generating cancer vaccines uses dendritic cells — specialized antigen-presenting cells. But to generate an effective vaccine, they must be collected from the patient and then subjected to time-consuming and costly 'customizing' procedures — in which they are expanded and loaded with tumour antigens and/or cytokine-encoding genes — before they can be re-administered to the patient. Could this lengthy *ex vivo* process be replaced by a simpler procedure?

Langerhans cells (LCs) — dendritic cells that reside in skin — generally stay put unless they are induced to mature. Maturation involves acquiring receptors for chemokines such as macrophage inflammatory protein 3β (MIP-3β), allowing them to move along a chemokine gradient from the epidermis to draining lymph nodes. This response can be triggered by haptens — small molecules that are not antigenic unless they are associated with a larger molecule such as a protein. But what if a 'decoy' lymph node could be produced that diverts LCs away from their real destination to a site where they can easily be pulsed with antigen? To this aim, the authors produced ethylene–vinyl–acetate (EVA) rods that released MIP-3β, and implanted them just under the abdominal skin of mice. Application of fluorescein isothiocyanate (FITC) — a hapten that also doubles up as a fluorescent signal for tracking LC migration — revealed that MIP-3β-expressing rods 'trapped' LCs by attracting them to the rods. By contrast, after 24 hours, a significant number of LCs had migrated from the epidermis to the draining lymph nodes in mice with either no implanted rods or rods expressing a control protein.

So, LCs can be trapped in one location, but can they also be loaded with tumour antigens? To investigate this, rods expressing ovalbumin were implanted with those expressing MIP-3β, and were, again, treated with a hapten. T cells harvested from the

GENOMIC INSTABILITY

A perfect mismatch

Inactivation of the DNA mismatch-repair machinery can drive tumorigenesis, as mutations in genes involved in cell growth and survival are not repaired. But does this mutator phenotype also mutate other repair genes to accelerate genomic instability and tumorigenesis? Sergei Malkhosyan and co-workers, reporting in the 18 December issue of *Proceedings of the National Academy of Sciences*, show that mutation of two mismatch-repair genes, rather than one, not only increases the mutation rate, but also changes the predominant type of mutation.

The SW48 human colon adenocarcinoma cell line lacks expression of the mismatch-repair gene *MLH1*, owing to promoter methylation, and contains a heterozygous frameshift mutation in another, *MSH6*. The authors analysed clones of this unstable cell line to isolate cells in which the wild-type allele of *MSH6* was also mutated — to generate $MLH1^{-/-}$ $MSH6^{-/-}$ cells — and cells in which the mutated *MSH6* allele had reverted to wild type — $MLH1^{-/-}$ $MSH6^{+/+}$ cells. The mutation rate and type were then determined in the two cell types, using the endogenous *HPRT* gene as a reporter.

The mutation rate was significantly higher in the double mutant cells: 2.3×10^{-5} per allele per replication, compared with 0.9×10^{-5}. Interestingly, the mutation spectrum was also different, depending on whether MSH6 was present. The mutations were all single point mutations, consistent with the mismatch-repair deficiency, but $MSH6^{+/+}$ cells predominantly had single base-pair insertions or deletions, whereas $MSH6^{-/-}$ cells predominantly had base substitutions and transitions, which resulted in missense or nonsense mutations.

So, mismatch repair — and the mutator phenotype that ensues when the process is deficient — is not quite as simple as we thought. The hypothesis that inactivation of *MLH1* would prevent all mismatch repair must be re-evaluated in light of these findings, and the idea that the mutator phenotype accelerates through a mutator 'cascade' gains further ground. The consequences of mutation in more than one mismatch-repair gene are now known, but the