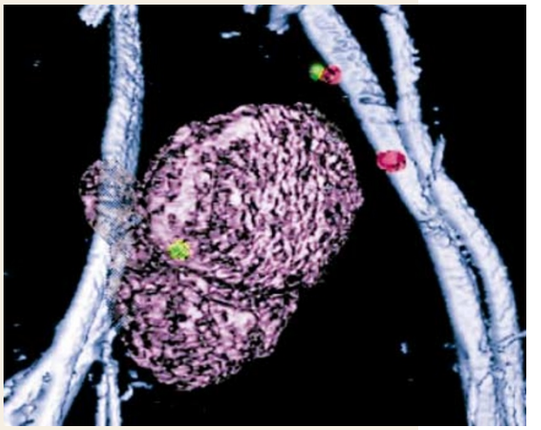
EARLY DETECTION

A perfect picture



Magnetic resonance imaging (MRI) is a useful non-invasive means of identifying lymph nodes that contain large metastatic tumours, but it cannot detect metastases at very early stages. Ralph Weissleder and colleagues have addressed this issue by using magnetic nanoparticles in conjuction with high-resolution MRI to find small, otherwise undetectable lymph-node metastases in patients with prostate cancer.

Lymphotropic superparamagnetic nanoparticles have a superparamagnetic iron oxide core that can be detected by MRI, surrounded by a dense packing of dextrans that allow maintenance of the nanoparticles in the circulation. Weissleder and colleagues used MRI to show that, after injection, the particles circulate and accumulate in the lymph nodes. In normal lymph nodes, this signal eventually decreases as the particles are taken up by macrophages. In lymph nodes that contain metastases, however, there is either a limited decrease in signal intensity, or discrete focal defects within the node, due to replacement of nodal architecture by the tumour. The image shows a three-dimensional reconstitution of the prostate (purple), metastatic (red) and non-metastatic (green) lymph nodes.

But how sensitive and accurate is this method of tumour detection? The authors analysed 334 lymph nodes taken from 80 patients with prostate cancer. As confirmed by surgical or biopsy analysis, standard MRI was only able to detect metastases in 45% of patients. MRI analysis of nanoparticle distribution, however, correctly identified all (100%) patients with nodal metastases. The technique also correctly identified 96% of patients that were metastasis-free.

Many of the metastases detected were less than 2 mm in diameter. This non-invasive technique is therefore a useful screening approach to identify patients that would not otherwise have been candidates for lymph-node surgery.

Kristine Novak

References and links

ORIGINAL RESEARCH PAPER Harisinghani, M. G. *et al.* Noninvasive detection of clinically occult lymph-node metastases in prostate cancer. *N. Engl. J. Med.* **348**, 2491–2499 (2003)

FURTHER READING Weissleder, R. Scaling down imaging: molecular mapping of cancer in mice. *Nature Rev. Cancer* **2**, 11–18 (2002)

WEB SITE

Centre for Molecular Imaging Research, Massachusetts General Hospital: http://www.mgh-cmir.org/

METASTASIS

Time to disperse

Imagine a dandelion flower that's 'gone to seed' — the smallest gust of wind disperses the seeds in every direction and you never know where this weed will grow next. Metastasis of tumour cells is similar — cells in the primary tumour undergo a sequence of genetic changes that cause the altered cells to migrate and form secondary tumours. But why do some patients with cancer develop metastases years after the primary tumour has been resected? As Schmidt-Kittler and colleagues report in *Proceedings of the National Academy of Sciences*, the answer challenges current views that metastasis is a late event in tumour formation.

The biological age of a tumour can be estimated from the number of chromosomal aberrations it contains, so a similar pattern of aberrations would be expected in metastases if cells migrate late in tumorigenesis. As bone is the preferred site of metastasis in patients with breast cancer, the authors began by isolating single disseminated cancer cells from the bone marrow of patients presenting with breast cancer with (M1) or without (M0) metastases. The cells were analysed by comparative genomic hybridization (CGH) — an *in situ* technique that is used to identify regions of amplification and deletion in the genome — and their chromosomal profile was compared with that of their matched primary tumour. The number of chromosomal aberrations was increased in M1 cells. But, to the authors' surprise, M0 cells had fewer chromosomal aberrations than either M1 cells or the primary tumours, indicating that the cancer cells migrate early in tumour development. So, how early does this migration occur?

The authors looked for chromosomal rearrangements that occurred during crisis — due to telomere shortening — and found that, unlike M1 cells, M0 cells had not undergone this process. As the passage through crisis is often completed early in tumour development, the M0 cells must migrate far earlier than previously thought. But are M0 cells really related to the primary tumour? The authors used a microsatellite polymerase chain reaction technique to identify loss of heterozygosity and showed that at least some M0 cells share sub-chromosomal deletions with the primary tumour. Cancer cells must therefore leave the breast tissue before the tumour is removed and accumulate the changes that generate the secondary tumour over time, which explains the long latency periods. So, targets for adjuvant therapies should be defined directly on disseminated cancer cells.

Emma Croager

References and links

ORIGINAL RESEARCH PAPER Schmidt-Kittler, O. *et al.* From latent disseminated cells to overt metastasis: genetic analysis of systemic breast cancer progression. *Proc. Natl Acad. Sci. USA* 13 Jun 2003 (doi:10.1073/pnas.1331931100)

WEB SITE

Christoph Klein's lab: www.ag-klein.de