Microfluid cell-capture chip isolates circulating tumor cells from patients with NSCLC

Despite the dramatic responses to EGFR therapy observed in patients with non-small-cell lung cancers (NSCLC) that harbor activating mutations in *EGFR*, the majority of patients relapse—often because their tumors acquire secondary *EGFR* mutations. Maheswaran and colleagues evaluated the ability of a microfluid cell-capture chip, which contains microposts coated with antibodies against epithelial-cell adhesion molecules, to isolate circulating tumor cells (CTCs) from patients with NSCLC.

The device successfully isolated CTCs (median 74 cells/ml) from each of 27 patients with advanced NSCLC. These isolated CTCs were then used in mutational analysis of *EGFR*. The presence of the *EGFR* T790M mutation, which confers drug resistance, in pretreatment tumor specimens was associated with greatly reduced progression-free survival compared with tumor specimens that lacked this mutation (7.7 months and 16.5 months, respectively; $P<0.001$). The *EGFR* activating mutation was identified in 11 of 12 patients for whom CTCs, plasma samples and primary tumor specimens were available. CTC genotyping, therefore, had 92% sensitivity to detect such mutations, whereas plasma genotyping (which identified mutations in 4 of 12 patients) had 33% sensitivity ($P=0.009$). Moreover, increased CTC numbers were associated with clinical progression and the emergence of additional *EGFR* mutations after therapy. Conversely, a decline in CTC numbers was associated with a radiographically evident response to therapy.

The authors suggest that the cell-capture chip can reliably isolate CTCs in an acceptable quantity and with satisfactory purity for use in molecular studies.

Original article Maheswaran S *et al.* (2008) Detection of mutations in *EGFR* in circulating lung-cancer cells. *N Engl J Med* **359:** 366–377

Novel bispecific antibody causes tumor regression in patients with non-Hodgkin lymphoma

Clinical data indicate a role for cytotoxic T lymphocytes in the control of tumor growth. However, immunotherapy strategies that induce antitumor T-cell responses have been characterized by low response rates. Bargou *et al.* assessed the efficacy of blinatumomab—an antibody with dual specificity for CD19 and CD3 antigens—in patients with non-Hodgkin lymphoma who relapsed after standard treatments.

This ongoing study has so far included 38 patients (with hematologic malignancies such as follicular lymphoma, mantle-cell lymphoma and chronic lymphocytic leukemia), who received blinatumomab for 4–8 weeks at doses of 0.0005–0.06 mg/m^2 daily. Target cells that expressed CD19 were depleted in the blood of patients who received ≥0.005 mg/m^2 of the drug; this decline was shown to be caused by apoptosis. Among 38 patients, 4 complete and 7 partial tumor regressions occurred in patients who received ≥0.015 mg/m^2 blinatumomab, which suggests that the response is dose-dependent. Tumor regression was observed in all 7 patients treated with 0.06 mg/m^2 blinatumomab. The majority of tumor shrinkage occurred within the first 4 weeks of therapy, and no relapse had been observed at the date of publication in patients treated with 0.03 mg/m^2 and 0.06 mg/m^2 blinatumomab. In patients who received blinatumomab doses ≥0.015 mg/m^2, tumor-cell depletion was observed in the blood, lymph nodes, spleen, bone marrow and liver.

These results suggest that blinatumomab is a promising new anticancer agent. Clinical trials that investigate the efficacy of bispecific antibodies, in hematologic and solid tumors, are warranted.

Original article Bargou R *et al.* (2008) Tumor regression in cancer patients by very low doses of a T cell-engaging antibody. *Science* **321:** 974–977

Predictors of response to erlotinib in patients with advanced NSCLC

Previous studies in patients with non-small-cell lung cancer have shown that mutations in the genes that encode tyrosine kinase domains of EGFR are strongly associated with response to EGFR tyrosine kinase inhibitors and could be used as molecular markers.

Zhu *et al*. assessed a subset of patients from the phase III, BR.21 trial of erlotinib in patients with advanced non-small-cell lung cancer, to investigate the effect of *KRAS* mutations, *EGFR* copy number and mutation status on response

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