human epidermal growth factor receptor 2 (HER2)/neu status in 252 primary breast cancer specimens obtained from Kyushu University Hospital, Japan.

The activation of Akt was assessed by immunohistochemical staining of phosphorylated Akt (pAkt). Positive staining for pAkt was shown in 84 cases (33%) and was significantly associated with HER2/neu overexpression ($P < 0.0001$). There was an inverse correlation between pAkt and expression of progesterone receptors ($P = 0.032$); no significant correlation between pAkt and estrogen receptor expression was found. The presence of pAkt was related to the incidence of lymph node metastases, suggesting that pAkt is associated with a more-malignant phenotype ($P = 0.008$). Analysis of the 107 patients undergoing postoperative hormone therapy demonstrated that there was a positive correlation between pAkt positivity and risk of disease recurrence ($P = 0.0161$).

The results indicate that inhibition of the Akt signaling pathways might increase the efficacy of hormone therapy and could improve the prognosis of patients undergoing postoperative adjuvant therapy. Analysis of pAkt activation and HER2/neu overexpression might be useful in predicting the effectiveness of postoperative hormone therapy in breast cancer patients.

Kate Matthews

Original article Tokunaga E *et al.* (2006) Akt is frequently activated in HER2/neu-positive breast cancers and associated with poor prognosis among hormone-treated patients. *Int J Cancer* 118:284–289

Improving antitumor dendritic-cell vaccination through depletion of regulatory T cells

Vaccination with tumor-RNA-transfected dendritic cells (DCs) induces specific T-cell responses in metastatic carcinoma patients; however, the activation and function of these tumor-specific cells might be suppressed by naturally occurring regulatory T cells (T_{REG}). Dannull and co-workers tested whether depletion of T_{REG} before DC vaccination could enhance $CD4^+$ and $CD8^+$ T-cell responses in 10 patients with metastatic renal-cell carcinoma and 1 with disseminated ovarian cancer.

T_{REG} were depleted from the peripheral blood of seven patients using a single intravenous

dose of a recombinant interleukin-2 diphtheria toxin conjugate, DAB₃₈₉IL-2, which binds to and selectively eliminates CD25-expressing T_{REG} , without affecting the viability of naive or memory T-cell populations. Four days later, patients received intradermal vaccination with 3 doses of 1×10^7 tumor-RNA-transfected DCs, given every other week. The tumor-specific T-cell responses were compared with those of the remaining four patients, who received DC vaccine only. Patients depleted of T_{REG} before vaccination had greater frequencies of tumor-specific $CD8^+$ T cells, and a trend toward increased frequencies of specific $CD4^+$ T cells, than patients who had not undergone T_{REG} depletion ($P = 0.011$ vs $P = 0.055$). The increase in $CD8^+$ T-cell numbers was still evident 13 weeks after the final vaccination.

The findings suggest that depletion of T_{REG} using DAB₃₈₉IL-2 can augment T-cell responses to weak tumor-associated antigens, a strategy that could be used to enhance a range of immunotherapeutic regimes. Further clinical investigations are required to optimize and define this approach, and to test whether it can reduce tumor burden.

Kate Matthews

Original article Dannull J *et al.* (2005) Enhancement of vaccine-mediated antitumor immunity in cancer patients after depletion of regulatory T cells. *J Clin Invest* 115:3623–3633

Hypofractionated intensity-modulated radiotherapy effective in localized prostate cancer

Researchers at the Cleveland Clinic, Ohio, have recently published an update of their experience with high-dose hypofractionated intensity-modulated radiotherapy in a cohort of patients with localized prostate cancer. To the authors' knowledge, this study has the longest follow-up period (median 66 months) of any investigation of hypofractionated radiotherapy. This paper reports excellent relapse-free survival rates and limited late toxicity in these patients.

The study enrolled a series of 100 consecutive patients, each of whom received a radiation dose of 70 Gy at 2.5 Gy per fraction, in 28 fractions over 5.5 weeks. The prostate and seminal vesicles were targeted in 62 patients with stage T3 disease. The remaining 38