TP53 mutation is associated with poor survival in patients with head and neck cancer

Mutation of the *TP53* gene (which encodes the tumor suppressor protein p53) is a molecular alteration commonly observed in squamous-cell carcinoma of the head and neck. Poeta *et al.* conducted a prospective multicenter trial to examine the association between *TP53* status and survival in patients with this cancer type.

Tumor DNA samples from 420 patients were examined for mutations in *TP53*. All mutations were classified as being either disruptive or nondisruptive on the basis of the degree of predicted disruption to the protein structure. In total, *TP53* mutations were found in tumors from 53.3% of the study population.

After a median follow-up of 6.2 years, 232 patients had died, 121 from head and neck cancer. Patients with any *TP53* mutation had a significantly lower rate of overall survival than did patients with wild-type *TP53* (hazard ratio [HR] 1.4, 95% CI 1.1–1.8). Stratification of patients according to type of *TP53* mutation revealed an even greater risk of death in patients with disruptive *TP53* mutations (HR 1.7, 95% CI 1.3–2.4). The risk of death in patients with nondisruptive mutations, on the other hand, was not significantly different from that of patients with wild-type *TP53* (HR 1.2, 95% CI 0.9–1.7). In multivariate analysis adjusted for pathologic nodal stage, type of treatment, site of primary tumor, smoking history and average alcohol use, presence of any *TP53* mutation was associated with decreased survival (HR 1.32, 95% CI 1.01–1.73). The authors conclude that *TP53* mutation status is highly prognostic in patients with squamous-cell carcinoma of the head and neck.

Original article Poeta ML *et al.* (2007) *TP53* mutations and survival in squamous-cell carcinoma of the head and neck. *N Engl J Med* **357:** 2552–2561

Stroma-specific *TP53* alterations correlate with clinical outcome in breast cancer

Studies have suggested that cross-talk between neoplasms and the surrounding microenvironment can regulate tumor behavior. High-frequency mutations of *TP53* have been identified in neoplastic breast epithelium and the surrounding stroma. A study by Patocs *et al.* has evaluated the role of genomic alterations of *TP53* in epithelial and stromal cells in hereditary and sporadic breast cancers.

The authors assessed *TP53* mutation status, loss of heterozygosity (LOH) and allelic imbalance in 43 and 175 DNA samples from patients with hereditary and sporadic breast cancer, respectively. *TP53* mutations were identified in 74.4% of samples from the hereditary-cancer group and 42.3% of samples from the sporadic-cancer group ($P<0.001$). *TP53* mutations in epithelium or stroma were associated with increased frequency of allelic imbalance or LOH in both groups; however, the association was more prominent in the sporadic group. In the sporadic group, 66 microsatellite loci linked to LOH or allelic imbalance were associated with mutated *TP53*; by contrast, only one locus (2p25.1) in stromal cells from the hereditary group was associated with mutated *TP53*. In the sporadic group, stromal *TP53* mutation status was significantly associated with lymph-node metastases ($P=0.003$). Finally, five stromal loci in the sporadic tumors were associated with nodal metastases in the absence of *TP53* mutations.

The authors conclude that stroma-specific LOH or allelic imbalance is associated with *TP53* mutation status and nodal metastases in sporadic but not hereditary breast cancer.

Original article Patocs A *et al.* (2007) Breast-cancer stromal cells with *TP53* mutations and nodal metastases. *N Engl J Med* **357:** 2543–2551

Capecitabine and oxaliplatin are effective treatments in advanced esophagogastric cancer

For patients with advanced esophagogastric cancer, combined epirubicin, cisplatin and fluorouracil (ECF) is a widely used regimen in Europe; however, continuous fluorouracil administration requires central venous access, while cisplatin requires hydration and causes renal toxic effects, hearing loss, neuropathy, and emesis. A randomized noninferiority trial has examined whether fluorouracil and cisplatin can be replaced by capecitabine and oxaliplatin, respectively, in the ECF regimen.

This study included 1,002 patients who were randomized to receive epirubicin and cisplatin plus either fluorouracil (ECF, $n=263$) or capecitabine (ECX, $n=250$), or epirubicin and oxaliplatin plus either fluorouracil (EOF, $n=245$)