Celebrity Endorsements of Cancer Screening

Celebrities often promote cancer screening by relating personal anecdotes about their own diagnosis or that of a loved one. Larson et al. (p. 693) examined the extent to which 360 women and 140 men without a history of cancer had seen or heard or been influenced by celebrity endorsements of screening mammography, prostate-specific antigen (PSA) testing, or sigmoidoscopy or colonoscopy. Most respondents reported they “had seen or heard a celebrity talk about” mammography (73% of women aged 40 years or older), PSA testing (63% of men aged 50 years or older), or sigmoidoscopy or colonoscopy (52% of adults aged 50 years or older). Among respondents who had seen or heard a celebrity endorsement, 25% said the endorsement made them more likely to undergo mammography, 31% said they were more likely to undergo PSA testing, and 37% were more likely to undergo sigmoidoscopy or colonoscopy.

Metastasis Suppression by Medroxyprogesterone Acetate

Medroxyprogesterone acetate, MPA—a progestin that is used in the contraceptive Depo-Provera and has been tested as a treatment for advanced breast cancer—increases the expression of the metastasis suppressor gene Nm23-H1 in hormone receptor-negative breast cancer cells in vitro via the glucocorticoid receptor. In this issue, Palmieri et al. (p. 632) tested whether the MPA-stimulated increase in Nm23-H1 expression would translate to a reduction in metastatic colonization in hormone receptor-negative breast cancer cells. The authors found that MPA treatment reduced the in vitro colony-forming ability of MDA-MB-231T human breast carcinoma cells but not MDA-MB-231T cells that had been transfected with an antisense Nm23-H1 construct. For in vivo experiments, mice harboring MDA-MD-231T micrometastases were randomly assigned to injection with MPA or vehicle. Mice injected with MPA developed fewer and smaller lung metastases than mice injected with vehicle.

In an editorial, Jordan (p. 619) notes that Palmieri’s results raise the possibility that the glucocorticoid receptor may be a target that can be exploited in the future treatment of estrogen receptor-negative breast cancer. He also notes the clinical challenge of preventing metastasis in a disease that is typically diagnosed after metastatic spread has already occurred.

EGFR Gene Copy Number and Gefitinib Sensitivity

Gefitinib specifically inhibits the epidermal growth factor receptor (EGFR), a tyrosine kinase that is overexpressed in non–small-cell lung cancer (NSCLC). Cappuzzo et al. (p. 643) measured EGFR gene copy number, EGFR gene mutations, EGFR protein expression, Akt phosphorylation status, time to progression, and overall survival in 102 patients with advanced NSCLC who were treated daily with gefitinib. After multivariable analysis, the authors found that only increased EGFR gene copy number detected by fluorescence in situ hybridization (FISH) was associated with overall survival and that patients with high EGFR gene copy number or high protein expression and phosphorylated Akt had the best outcome. They conclude that high EGFR copy number detected by FISH may be an effective molecular predictor of gefitinib efficacy in advanced NSCLC.

In a related editorial (p. 621), Kaye compares the results of Cappuzzo et al. with other recent findings. He hypothesizes that allele dilution resulting from gene amplification may be involved in gefitinib-responsive tumorigenesis.

Characterizing K-Cyclin in KSHV-Infected Cells

Kaposi sarcoma–associated human herpesvirus (KSHV) encodes K-cyclin, a D-type cyclin homolog. D-type cyclins bind to cyclin-dependent kinases (cdks) and phosphorylate various substrates; K-cyclin phosphorylates these substrates as well as substrates phosphorylated by cyclins A and E. Van Dross et al. (p. 656) further characterize K-cyclin in cells naturally infected with KSHV. They found that K-cyclin interacts with cdk2, cdk4, and cdk6 and with cyclin/cdk inhibitory proteins p21Cip1 and p27Kip1 in KSHV-infected cell lysates. Unlike D-type cyclins, whose expression is cell cycle-dependent, the level of K-cyclin was stable through-out the cell cycle, and the K-cyclin/cdk6 complex kinase was constitutively active. The half-life of K-cyclin was much longer than that of cyclin D2, probably because K-cyclin lacks a specific degradation sequence present in D-type cyclins. The authors conclude that the constitutive activation of K-cyclin/cdk complexes in KSHV-infected cells appears to result from the extended half-life of K-cyclin and may explain its role in Kaposi sarcoma.

Dose-Dense Chemotherapy in Small-Cell Lung Cancer

Because dose-intensity studies in small-cell lung cancer (SCLC) have conflicting results, Lorigan et al. (p. 666) carried out a phase III randomized trial in patients with better-prognosis SCLC to investigate whether doubling the dose density of ifosfamide, carboplatin, and etoposide (ICE) chemotherapy with blood-progenitor-cell support improved survival compared with standard ICE chemotherapy. They found that overall survival and 2-year survival were not different between the two arms. The treatment duration was shorter in the dose-dense arm than in the standard arm, albeit not statistically significantly so, and the number of treatment cycles complicated by neutropenic sepsis was higher in the standard arm than in the dose-dense arm. The authors concluded that dose-dense ICE chemotherapy was associated with shorter periods of treatment and less neutropenic sepsis than standard ICE but was not associated with improved overall survival.

Health Care Access and Cervical Cancer Screening

Invasive cervical cancer is highly preventable and treatable. Leyden et al. (p. 675) reviewed the medical records of 833 women who were diagnosed with invasive cervical cancer despite having access to cancer screening and treatment services. They found that 56% of cases were in women who had no Pap tests during the period 4–36 months prior to diagnosis, whereas 32% and 13% of cases were attributed to Pap test detection failure and to failure to follow up an abnormal test result, respectively. Most (81%) of the women with no Pap screening had had at least one outpatient visit 4–36 months prior to their cancer diagnosis. The authors conclude that an increase in Pap screening adherence would reduce the incidence of invasive cervical cancer among women with access to screening and treatment.