STOPPING THE SPREAD

Amifostine, a thiol-bearing compound, has already been approved by the FDA for use in protecting cells from the toxic effects of chemotherapy. Now, data from a new study by Grdina et al. (pages 135–141), indicate that amifostine may inhibit the formation of spontaneous metastases as well. The researchers administered amifostine to mice implanted with Sa-NH sarcoma cells, which have the propensity to form spontaneous pulmonary metastases. Although amifostine delayed the growth of the primary sarcomas only slightly, it reduced the incidence of pulmonary metastases significantly. Consistent with this anti-metastatic effect, amifostine also enhanced serum angiostatin four-fold over control levels. In vitro, Grdina et al. found that the active form of amifostine, WR-1065, inhibited matrix metalloproteinase (MMP) activity, an important component of tumor cell invasion. Similarly, WR-1065 inhibited the ability of Sa-NH sarcoma cells to migrate through Matrigel membranes. According to the investigators, amifostine shares antimetastatic properties with other thiols, including N-acetyl cysteine and captopril and thus offers significant potential in the development of therapies that prevent metastatic disease.

ANGLING IN ON ANGIOGENESIS

In order to grow, solid tumors must trigger the growth of new microvasculature, but the mechanisms involved in this intricate process are unclear. Using tumors grown in nude mice from v-Ha-Ras-transformed mouse mammary epithelial cells, Breier et al. (pages 142–148) offer insight into some of these mechanisms. They conclude that Ras is central to triggering angiogenesis and that transforming growth factor-beta1 (TGF-beta1) and hypoxia cooperate to induce vascular endothelial growth factor (VEGF) expression to promote angiogenesis. This cooperation may be important because it enhances the production of VEGF throughout the tumor, i.e. in both normoxic and hypoxic tumor tissue. Breier et al. also found that induction of VEGF receptors 1 and 2 (Flt-1 and Flk-1) accompanied the growth of the tumors and that this appeared to be a Ras-dependent process. They conclude that the central role of Ras may have important implications for antiangiogenic tumor therapy, such indications as the use of farnesyl transferase inhibitors, which inhibit Ras.

MICROSATELLITE INSTABILITY

DOESN'T MATCH WITH HODGKIN’S

In their study, Re et al. (pages 205–210) focus on the role of microsatellite instability (MSI) in the pathogenesis of classical Hodgkin’s disease (cHD). MSI is thought to result from a defect of DNA mismatch repair (MMR) genes, which have been implicated in several tumor types, but its role in cHD pathology is unclear. Re et al. evaluated Hodgkin and Reed-Sternberg (H/RS) derived cell lines for the presence of MSI. H/RS cells are clonal germinal center-derived B cells and account for less than 1% of the cells found in tissue affected by cHD. They also analyzed the expression of hMSH2 and hMLH1 proteins, which serve as markers of MMR activity in cells. Re et al. found that staining patterns of hMSH2 and hMLH1 proteins in H/RS cells were similar to those of nonmalignant lymph nodes; they conclude that MMR deficiency and MSI do not seem to be involved in cHD pathology, despite gross chromosomal abnormalities of H/RS cells.

Prostate Cancer Trials Progressing

Although screening for prostate cancer can lead to its early detection, the benefits of such screening have not been determined. Many believe, however, that treating the cancer by local eradication before it has metastasized may prevent progression and reduce mortality. According to de Koning et al. (pages 238–245), 2 large randomized screening trials currently in progress will have sufficient statistical power to detect a 20% difference in prostate cancer mortality among people who have and have not been screened for prostate cancer. The European trial is called the European Randomized Screening for Prostate Cancer (ERSPC) trial and the Prostate, Lung, Colorectal and Ovary (PLCO) cancer trial is taking place in the USA. So far, researchers have recruited over 215,000 subjects—about 80% of the hoped-for sample size. There are important differences between the 2 studies, but the design and other key features will allow joint evaluation. Considerable progress has been made in both trials, according to the researchers and they will show definitive results in 2005–2008.

Combined Fluorescence Lights Up Oral Cancer

Reporting on pages 246–253, Betz et al. seek to compare the effectiveness of normal white light inspection, combined fluorescence diagnosis (CFD) and each of the components of CFD alone in diagnosing oral cancer; CFD proved the most effective method, they found. Patients with oral cancer were first inspected with white light. They were then viewed with autofluorescence imaging, 1 of the 2 components of CFD. Under autofluorescence imaging, normal areas appeared green and malignant lesions appeared darker green. Then, after topical application of 5-aminolevulinic acid (5-ALA) and incubation, CFD was performed. After the application, tumors visible under white light were demarcated by bright red fluorescence (the second component of CFD), which contrasted with the green fluorescing normal tissue. By computer removal of the green signals of CFD, the researchers found that imaging detected a red fluorescence that was stronger in neoplastic tissue than in normal tissue. But the tumor borders were less well defined with the red fluorescence than with CFD. The authors conclude that CFD was clearly better for the identification of both tumor and borders than either the red or green fluorescing components of CFD or white light.

In this issue

Spotlight

Combined fluorescence diagnosis image of oral cancer.