Ran As a Cancer Therapeutic Target

Yuen et al. Page 380

A shuttling molecule inside a cell, Ran is shown to be overproduced in breast and lung cancers. The overproduction of Ran is associated with early death and is exacerbated by mutations that lead to stimulation of the major growth-controlling pathways. Outside the body, cells can be killed by artificially switching off this overproduction of Ran, and mutations that lead to the activation of the same major growth-controlling pathways increase this killing effect dramatically. These findings from Yuen and colleagues suggest that Ran may be an important therapeutic target for human cancers that harbor these common growth-stimulating mutations and are resistant to standard therapy.

Immunotherapy against Pancreatic Cancer Stem Cells

Cioffi et al. Page 465

Pancreatic ductal adenocarcinoma is a highly aggressive and deadly disease that harbors a distinct population of cancer stem cells (CSC) and is not affected by conventional therapies, causing disease relapse and fast progression. Here, Cioffi and colleagues provide evidence for a new therapeutic approach using the EpCAM/CD3-bispecific antibody MT110, which is capable of activating and redirecting cytotoxic T cells to eliminate primary human pancreatic cancer cells. This antibody not only efficiently eradicates more differentiated pancreatic cancer cells but also targets the highly tumorigenic CSC in vivo. These results suggest MT110 as a promising new treatment modality for pancreatic ductal adenocarcinoma.

Prognostic Impact of HER2 in Esophageal Adenocarcinomas

Yoon et al. Page 546

The HER2/ErbB2 receptor regulates cell growth, survival, and differentiation. As with breast cancer, data show that HER2 targeted therapy improves survival in patients with advanced gastric cancer. Yoon and colleagues examined HER2 expression and gene amplification in untreated esophageal adenocarcinomas. HER2 positivity was present in 17% of cases, with a higher frequency in cancers with adjacent Barrett epithelium. HER2 positivity was unexpectedly associated with decreased tumor aggressiveness, particularly among Barrett-associated tumors. These data demonstrate that a subset of esophageal adenocarcinomas overexpress HER2, lending further support to the establishment of Barrett-associated tumors as biologically distinct entities.

HDAC Inhibition in Uveal Melanoma

Landreville et al. Page 408

There is a critical need to identify targeted molecular therapy for metastatic uveal melanoma, which is highly recalcitrant to all current therapies. Landreville and colleagues capitalized on the recent discovery of BAP1 mutations in metastasizing uveal melanoma, along with transcriptomic bioinformatic approaches, to identify histone deacetylase (HDAC) inhibitors as compounds capable of inducing cell-cycle arrest, apoptosis, and differentiation in cultured uveal melanoma cells and inducing growth arrest of uveal melanoma xenograft tumors in mice. These findings suggest that HDAC inhibitors may be effective in uveal melanoma, particularly in the early metastatic or adjuvant setting.
Clinical Cancer Research

Highlights of This Issue


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