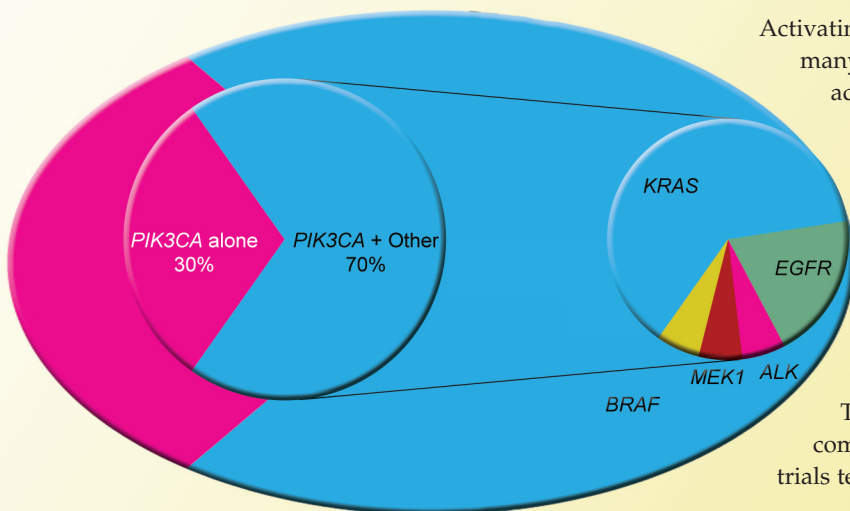


**PIK3CA-Mutant Lung Adenocarcinoma**Chaft *et al.* \_\_\_\_\_ Page 485

Activating mutations in *PIK3CA* have been identified in many solid tumors. To investigate *PIK3CA*-mutant lung adenocarcinomas, Chaft and colleagues examined the clinical and molecular characteristics of 1,125 patients, testing for driver mutations in *PIK3CA* and 8 other oncogenes. *PIK3CA* mutations were identified in 2% of lung adenocarcinoma specimens, potentially more than 3000 cases in the U.S. annually. Unlike the typical paradigm of driver-oncogene mutual exclusivity in lung adenocarcinomas, 70% tumors with a *PIK3CA* mutation harbored an additional driver mutation. These results support the necessity to comprehensively genotype patients enrolling in clinical trials testing agents that target the PIK pathway.

**c-Met and FAK in Medulloblastoma**Guessous *et al.* \_\_\_\_\_ Page 288

Medulloblastoma is the most common malignant pediatric brain tumor. It is an invasive neoplasm with poorly understood etiology. Guessous and colleagues uncover previously unknown molecular and functional interactions between the tyrosine kinases c-Met and FAK/Pyk2 in medulloblastoma. They show that c-Met activates FAK and Pyk2 and that FAK and Pyk2 mediate the invasive and malignant effects of c-Met in medulloblastoma. They show for the first time that combined inhibition of c-Met and FAK/Pyk2 has experimental therapeutic advantage. Their study therefore establishes proof-of-principle for the usefulness of combining existing clinically applicable small molecule inhibitors of c-Met and FAK/Pyk2 in medulloblastoma therapy.

**Efficacy of PF00299804 in Gastric Cancer**Nam *et al.* \_\_\_\_\_ Page 439

Recently, trastuzumab has shown clinical benefit in HER2 amplified gastric cancer. To explore its therapeutic potential, Nam and colleagues evaluated the activity and mechanisms of PF00299804, an irreversible pan-HER inhibitor, in gastric cancer cells. PF00299804 showed significant antitumor effects in HER2 amplified gastric cancer cells through inhibition of HER family heterodimer formation. The combination of PF00299804 with cytotoxic chemotherapeutic agents or molecularly targeted agents, including trastuzumab, CP751871 (IGF1R inhibitor), PD0325901 (ERK1/2 inhibitor), and PF04691502 (PI3K/mTOR inhibitor), produced synergistic effects. These findings strongly suggest that PF00299804, alone or in combination with other agents, can be used as a targeted therapy for the treatment of HER2 amplified gastric cancer.