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PI3'-Kinase Inhibition Forestalls the Onset of MEK1/2 Inhibitor Resistance in BRAF-Mutated Melanoma ............... 143  
M.M. Deuker, V. Marsh Durban, W.A. Phillips, and M. McMahon  
Précis: Treatment with PI3K inhibitors enhances the depth of response to MEK1/2 inhibition and delays the development of drug-resistant tumors in BRAF-mutated melanoma mouse models.

### RESEARCH ARTICLES

Linking Tumor Mutations to Drug Responses via a Quantitative Chemical-Genetic Interaction Map ............... 154  
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Aberrant Glycosylation Promotes Lung Cancer Metastasis through Adhesion to Galectins in the Metastatic Niche .......................... 168
N.E. Reticker-Flynn and S.N. Bhatia
Précis: Changes in glycosyltransferase activity in lung cancer cells enhance surface presentation of the carbohydrate ligand T-antigen and potentiate metastasis via increased binding to tumor-mobilized galectin-3+ leukocytes.
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NOTCH Decoys That Selectively Block DLL/NOTCH or JAG/NOTCH Disrupt Angiogenesis by Unique Mechanisms to Inhibit Tumor Growth .......................... 182
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M. Sonoshita, Y. Itatani, F. Kakizaki, K. Sakimura, T. Terashima, Y. Katsuyama, Y. Sakai, and M.M. Taketo
Précis: NOTCH–DAB1 signaling promotes colon cancer cell invasion and progression by stimulating ABL-mediated phosphorylation of the ROHGEF TRIO at tyrosine residue 2681.
See commentary, p. 115

Reticker-Flynn and Bhatia found that tumor-derived IL6 induced CD11b+ galectin-3+ leukocyte mobilization from the bone marrow in a mouse model of lung adenocarcinoma. Metastatic cell lines and human non-small cell lung cancer samples exhibited increased surface presentation of the galectin-3 ligand, Thomsen-Friedenreich Antigen (T-Antigen). Elevated T-Antigen surface presentation was mediated by altered expression of the glycosyltransferases C2GnT2 and St6GalNAc4, which prevented T-Antigen glycan elongation. Restoration of T-Antigen glycan chain elongation decreased T-Antigen presentation, reduced tumor-cell galectin-3 binding, and inhibited experimental metastases in vivo. These results indicate that aberrant glycosyltransferase activities play a critical role in the early metastatic niche to promote metastatic progression of lung tumors. For details, please see the article by Reticker-Flynn and Bhatia on page 168.