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DNA Methylation Levels at Chromosome 8q24 in Peripheral Blood Are Associated with 8q24 Cancer Susceptibility Loci
Kathryn Hughes Barry, Lee E. Moore, Joshua Sampson, Lijing Yan, Ann Meyer, Andrew J. Oler, Charles C. Chung, Zhaoqing Wang, Meredith Yeager, Laufey Amundadottir, and Sonja I. Berndt

Acknowledgment to Reviewers
ABOUT THE COVER

Ornithine decarboxylase (ODC) is the key rate-limiting enzyme in the synthesis of polyamines, and it is overexpressed in a variety of cancers, including pancreatic cancer. Activation of ODC signaling occurs at early stages of pancreatic precursor lesions and increases as the tumor progresses. Longitudinal profiling of tumor progression revealed that ODC and polyamine synthesis levels were increased in KrasG12D-activated genetically engineered mice and correlated with aggressiveness of tumor growth. The ODC inhibitor, efomithine (DFMO), caused modulation of ODC pathway signaling with significant inhibition of pancreatic ductal adenocarcinoma (PDAC) incidence, tumor cell proliferation, and increased expression of p21/p27 in KrasG12D mice. These preclinical data indicate that DFMO applied at clinically relevant dose levels has potential for chemoprevention of pancreatic cancer. The figure depicts immunofluorescence staining of pancreatic intraepithelial neoplasia (PanIN) lesions and PDAC showing membranous and cytoplasmic localization of ODC (green). Counter nuclei staining was performed with DAPI (blue). See the article by Mohammed and colleagues (beginning on page 1198) for more information.