Clinical Cancer Research

Contents

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Vol 13, No 1

Imaging, Diagnosis, Prognosis

Cancer Therapy: Clinical

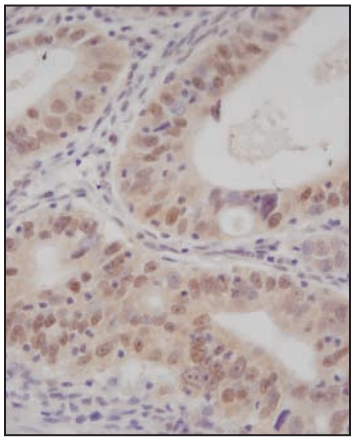
Cancer Therapy: Preclinical

Cancer Susceptibillity and Prevention

Acknowledgment to Reviewers

About the Cover

SMAD4 is a tumor suppressor gene whose inactivation by the various mechanisms frequently occurs in association with malignant progression. Cytoplasmic and nuclear expression levels of SMAD4 are increased in both low-grade and high-grade dysplasia but are gradually reduced as dysplasia progresses to gastric adenocarcinoma. This figure shows strong cytoplasmic and nuclear staining of SMAD4 in stage I of gastric carcinoma, but SMAD4 is gradually reduced as the carcinoma develops to subsequent stages, possibly owing to a modified two-hit model of tumor suppressor genes as proposed in the article. For more details, please see Wang *et al*. on page 102 of this issue.



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Clinical Cancer Research

13 (1)

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