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Expression of Cell Cycle Regulators P21 and P27 as Predictors of Disease Outcome in Colorectal Carcinoma.

Al-Maghrabi J, Al-Ahwal M, Buhmeida A, Syrjänen K, Sibyani A, Emam E, Ghanim A, Al-Qahtani M.

Department of Pathology, King Abdul-Aziz University, P.O. Box 80205, Jeddah, 21589, Saudi Arabia, jalmaghrabi@hotmail.com.

Abstract

BACKGROUND:

Recent studies suggest that aberrations in cell cycle checkpoint controllers are a common feature in human malignancies and predict prognosis independent of stage.

OBJECTIVES:

This study correlated two cell cycle regulators (p27 and p21) with clinical and pathological variables in colorectal cancer (CRC) patients to assess their role as prognostic factors.

PATIENTS AND METHODS:

A series of 65 CRC patients were analyzed for p27 and p21 expression in their tumors using immunohistochemistry.

RESULTS:

Forty-six percent of tumors showed positive nuclear p27 expression, whereas 72% of cases were completely p21 negative. There were no significant correlations between p27 and p21 expression and gender, age, lymph node involvement, stage, and grade. However, p27 (but not p21) expression revealed highly significant correlation with tumor location ($p < 0.01$), depth of invasion ($p < 0.03$), and lympho-vascular invasion ($p < 0.02$). Tumors with high p27 expression showed a higher recurrence rate than tumors with no expression ($p < 0.03$). In Kaplan-Meier survival analysis, there was a significant ($p = 0.046$) difference in disease-free survival (DFS) between p27-positive and p27-negative tumors in favor of the latter. p21 did not show any predictive value of DFS ($p < 0.7$). Neither p27 nor p21 did predict disease-specific survival (DSS) in Kaplan-Meier analysis, but DSS time was much shorter for p27-positive tumors. In multivariate (Cox) model, p27 lost its value as independent predictor of DFS, and none of the covariates were independent predictors of DSS.

CONCLUSION:

p27 expression seems to be more powerful than p21 expression in providing useful prognostic information in CRC, particularly in predicting the patients at high risk for recurrent disease. Larger cohort and longer follow-up are needed to fully elucidate the value of p27 (and p21) as independent predictors of disease outcome.