



Overexpression of DNAJC12 predicts poor response to neoadjuvant concurrent chemoradiotherapy in patients with rectal cancer



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ABSTRACT

Genes associated with protein folding have been found to have certain prognostic significance in a subset of cancers. The aim of this study is to evaluate the clinical impact of DNAJC12 expression in patients with rectal cancers receiving neoadjuvant concurrent chemoradiotherapy (CCRT) followed by surgery. Through data mining from a public transcriptomic dataset of rectal cancer focusing on genes associated with protein folding, we found that DNAJC12, a member of the HSP40/DNAJ family, was the most significant such gene correlated with the CCRT response. We further evaluated the expression of DNAJC12 by immunohistochemistry in the pre-treatment tumor specimens from 172 patients with rectal cancers. From this set, we statistically analyzed the association of DNAJC12 expression with various clinicopathological factors, tumor regression grade, overall survival (OS), disease-free survival (DFS) and local recurrence-free survival (LRFS). High expression of DNAJC12 was significantly associated with advanced pre- and post-treatment tumor status ($P < 0.001$), advanced pre- and post-treatment nodal status ($P < 0.001$), increased vascular invasion ($P = 0.015$), increased perineural invasion ($P = 0.023$) and lower tumor regression grade ($P = 0.009$). More importantly, high expression of DNAJC12 was found to be correlated with poor prognosis for OS ($P = 0.0012$), DFS ($P < 0.0001$) and LRFS ($P = 0.0001$). In multivariate analysis, DNAJC12 overexpression still emerged as an independent prognosticator for shorter OS ($P = 0.040$), DFS ($P < 0.001$) and LRFS ($P = 0.016$). The data indicate that DNAJC12 overexpression acts as a negative predictive factor for the response to neoadjuvant CCRT and was significantly associated with shorter survival in patients with rectal cancers receiving neoadjuvant CCRT followed by surgery.

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1. Introduction

Colorectal cancer, a major cause of morbidity and mortality around the world, has an increasing incidence in Taiwan. Rectal cancer is characterized by the development of tumors in the portion of the

large bowel that lies in the pelvis, distal to the rectosigmoid junction and terminating at the anus. Although surgical resection usually is the cornerstone of curative treatment for rectal cancer that has no distant metastasis, neoadjuvant concurrent chemoradiotherapy (CCRT) plays an increasingly important role in treating not only patients with T3 or T4 rectal cancers, but also for those with clinically lymph node-positive disease (Bosset et al., 2006; Gerard et al., 2006; Sauer et al., 2004). Moreover, patients with distal rectal cancer and having a previous complete or partial response to neoadjuvant CCRT can receive sphincter-conserving low anterior resection, rather than the more

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