

Original Article

Fascin-1 expression in advanced colorectal cancer is associated with the treatment efficacy of cetuximab

Hua-Jun Lu¹, Guo-Xiao Lv¹, Guo-Chao Ren¹, Jun-Kang Shao², Chao-Qun Wang²

¹Department of Oncological Radiotherapy, Affiliated Dongyang Hospital of Wenzhou Medical University, Dongyang, Zhejiang, China; ²Department of Pathology, Affiliated Dongyang Hospital of Wenzhou Medical University, Dongyang, Zhejiang, China

Received June 2, 2026; Accepted September 4, 2026; Epub September 15, 2026; Published September 30, 2026

Abstract: Objectives: Although several studies have reported that Fascin-1 is upregulated in colorectal cancer and promotes tumor progression, its relationship with therapeutic efficacy in patients with colorectal cancer remains unclear. This study aimed to investigate the effect of Fascin-1 protein expression on the efficacy of cetuximab treatment in patients with advanced colorectal cancer (CRC). Methods: Immunohistochemical (IHC) staining was used to evaluate the protein expression of Fascin-1 in tissues from 40 patients with advanced CRC. The RECIST criteria were applied to evaluate the efficacy of cetuximab-targeted therapy in CRC patients. Results: Among the 40 advanced CRC patients treated with cetuximab, 12 (30%, 12/40) achieved an objective response, and 28 (70%, 28/40) achieved disease control. IHC results revealed that 18 out of 40 CRC tissues (45%, 18/40) were positive for the Fascin-1 protein. Analysis of the relationship between Fascin-1 expression and treatment efficacy revealed that the objective response rate (ORR) in Fascin-1-positive CRC patients was 11.1% (2/18), which was significantly lower than that in Fascin-1-negative patients (45.5%, 10/22) ($P=0.018$). Similarly, the disease control rate (DCR) in Fascin-1-positive patients was 50.0% (9/18), which was also significantly lower than that of Fascin-1-negative patients (86.4%, 19/22) ($P=0.013$). Multiple logistic regression analysis revealed that Fascin-1 positivity was an independent factor associated with failure to achieve an objective response (odds ratio (OR)=6.667; 95% confidence interval (CI): 1.227-36.226; $P=0.028$) and failure to achieve disease control (OR=7.342; 95% CI: 1.068-50.456; $P=0.043$). ROC curve analysis revealed that Fascin-1 positivity predicted failure to achieve an objective response, with an area under the curve (AUC) value of 0.702 (95% CI: 0.531-0.874; $P=0.045$), and failure to achieve disease control, with an AUC value of 0.714 (95% CI: 0.538-0.890; $P=0.034$). Survival analysis revealed that Fascin-1 positivity was significantly associated with reduced 1-year progression-free survival (PFS) in these patients ($P=0.003$). Conclusions: Fascin-1 expression status is significantly correlated with the efficacy of cetuximab treatment. Combined intervention against Fascin-1 may be an effective strategy for improving the outcome of patients with RAS wild-type advanced CRC.

Keywords: Fascin-1, colorectal cancer, cetuximab, prognosis, immunohistochemistry

Introduction

Colorectal cancer (CRC) is a malignant tumor characterized by high global incidence and mortality rate, and approximately one-quarter of CRC patients present with distant metastasis at the time of initial diagnosis [1-3]. How to optimize its treatment regimen is an ongoing focus of research. Among the various therapeutic options, targeted treatment strategies have attracted increasing attention. In particular, epidermal growth factor receptor (EGFR)-targeted therapy has emerged as a pivotal advancement in the management of advanced

CRC. EGFR is a transmembrane glycoprotein receptor that activates downstream signaling pathways that regulate cell proliferation, differentiation, and survival. Aberrant activation or overexpression of EGFR is observed in a substantial proportion of CRC cases and is associated with disease progression and poor prognosis [4, 5].

Therapeutic monoclonal antibodies such as cetuximab and panitumumab bind specifically to the extracellular domain of EGFR, thereby inhibiting ligand-induced receptor activation, blocking downstream signaling cascades, and

suppressing tumor cell growth and survival. Clinical trials have demonstrated that when combined with standard chemotherapy, anti-EGFR agents significantly improve response rate, progression-free survival, and overall survival in patients with RAS wild-type advanced CRC [6]. The EGFR-targeted drug cetuximab has been extensively used to treat patients with RAS wild-type advanced CRC. However, its monotherapy efficacy is relatively low, with only approximately 10-20% of patients receiving a survival benefit [7, 8]. Therefore, the identification of additional predictive biomarkers and a better understanding of the mechanisms underlying therapeutic resistance are essential to optimize patient selection and maximize treatment benefit.

Fascin-1, a key actin-bundling protein, is expressed at low levels or not at all in normal epithelial tissues but is upregulated in various tumors, including CRC. It significantly enhances the invasive and migratory capacities of tumor cells, and knockdown of Fascin-1 expression can inhibit the migratory ability of CRC cells [9-13]. As reported in our preliminary study published in the *Chinese Journal of Anatomy and Clinics* (Wang et al., 2020) [14], a positive correlation between EGFR and Fascin-1 expression was observed in CRC tissues. Patients with high coexpression of both markers exhibited poor prognosis, suggesting that Fascin-1 expression is associated with the efficacy of EGFR-targeted therapy.

On the basis of these findings, this study aimed to investigate the relationship between Fascin-1 protein expression and the efficacy of cetuximab treatment in patients with advanced CRC and to evaluate its clinical value as a biomarker for predicting therapeutic response. This information is intended to help optimize precise targeted therapeutic strategies for CRC, thereby improving outcomes.

Materials and methods

Patients and tissue samples

A total of 40 patients with advanced CRC who were hospitalized at the Affiliated Dongyang Hospital of Wenzhou Medical University (Dongyang, Zhejiang, China) between November 2016 and January 2023 were enrolled in this study. The cohort consisted of 26 males and 14

females, with a median age of 63 years (range, 39-82 years). All patients were diagnosed with RAS wild-type stage IV CRC and had received cetuximab-targeted therapy. Among them, 10 presented with left-sided colon cancer, 26 with rectal cancer, and 4 with right-sided colon cancer. CRC patients were staged according to the eighth edition of the American Joint Committee on Cancer (AJCC) Cancer Staging Manual [15]. The inclusion criteria were as follows: (1) patients with confirmed advanced CRC based on clinicopathologic or imaging evidence; (2) patients with RAS wild-type status, meeting the guideline indications for cetuximab therapy; (3) patients who underwent histopathologic examination at our institution; (4) patients who received at least two cycles of cetuximab-based treatment; and (5) patients with complete imaging data for pre- and posttreatment efficacy evaluation. Patients were excluded if they received fewer than two cycles of cetuximab therapy or lacked complete imaging data for efficacy assessment. All the enrolled patients received a combination regimen of cetuximab and chemotherapy in accordance with the Chinese Society of Clinical Oncology (CSCO) guidelines. Paraffin-embedded specimens from the 40 enrolled CRC patients were obtained from the Department of Pathology at our hospital. The study method followed the relevant guidelines and regulations of the Affiliated Dongyang Hospital of Wenzhou Medical University.

IHC analysis

Immunohistochemical (IHC) staining of the paraffin-embedded tissue sections was conducted using an Envision System (Dako, Glostrup, Denmark) in accordance with a previously described method [16-19]. A primary anti-Fascin-1 mouse monoclonal antibody (clone 55k-2; Santa Cruz Biotechnology, Santa Cruz, CA, USA) was applied at a dilution of 1:100, followed by detection with a universal horseradish peroxidase (HRP)-conjugated rabbit/mouse secondary antibody (Dako, Glostrup, Denmark). For negative controls, the primary antibody was omitted, and tissue sections were incubated with antibody diluent prior to secondary antibody application. A positive internal control for Fascin-1 immunoreactivity was established by staining interstitial fibers and vascular endothelial cells within the CRC tissue.

Assessment of staining

Fascin-1 expression in CRC cells was evaluated for both staining intensity and the proportion of positive cells, following the same scoring criteria reported previously [16]. Briefly, immunoreactivity was assessed semiquantitatively, with staining intensity graded as 0 (negative), 1 (weak), 2 (moderate), or 3 (strong), and the percentage of immunopositive tumor cells was scored as 0 (0%), 1 (1-25%), 2 (26-50%), 3 (51-75%), or 4 (76-100%). Samples were classified as Fascin-1 positive when the combined score (intensity + extent) was ≥ 3 and when distinct cytoplasmic staining was evident in at least 5% of the tumor cells. In the negative control, sections were incubated with the vehicle and secondary antibody, omitting the primary antibody to prevent nonspecific staining. As positive controls, the internal positive control cells within the CRC tissue specimens, specifically, interstitial fibroblasts and vascular endothelial cells, were evaluated, as these cell types are known to consistently exhibit positive Fascin-1 immunoreactivity. The presence of distinct Fascin-1 staining in these internal control cells was used to confirm the validity and sensitivity of the IHC assay. All tissue sections were independently evaluated and scored by two pathologists.

Treatment response evaluation

Treatment response was evaluated by two experienced oncologists according to the Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST 1.1) [20]. A response assessment was performed at the first scheduled radiological evaluation following the initiation of cetuximab therapy. A complete response (CR) was defined as the disappearance of all target lesions, which was sustained for a minimum of four weeks; a partial response (PR) was defined as a $\geq 30\%$ decrease in the sum of the diameters of the target lesions compared to the baseline, which was maintained for at least four weeks. Stable disease (SD) was defined as neither sufficient shrinkage to qualify for a PR nor a sufficient increase to qualify for PD. Progressive disease (PD) was defined as a $\geq 20\%$ increase in the sum of the diameters of the target lesions, taking as reference the smallest sum on study (including the baseline sum if it was the smallest), with the sum also demonstrating an absolute increase of at least 5 mm. The objective response rate (ORR) was

calculated as the percentage of patients who achieved either a CR or PR: $(\text{number of CR} + \text{PR cases} / \text{total number of cases}) \times 100.00\%$. The disease control rate (DCR) was calculated as the percentage of patients who achieved a CR, a PR, or SD: $(\text{number of CR} + \text{PR} + \text{SD cases} / \text{total number of cases}) \times 100.00\%$.

Patient follow-up

Follow-up assessments were conducted by telephone interviews and outpatient visits every three months following treatment initiation and continued until patient death. CRC progression was confirmed through clinical imaging or pathologic examination. Progression-free survival (PFS) was defined as the time from the initiation of cetuximab therapy to disease progression, metastasis, or death from any cause, whichever occurred first.

Statistical analysis

Statistical analyses were performed using SPSS version 19.0 (SPSS Inc., Chicago, IL, USA). Categorical variables, including response rates and Fascin-1 expression status, are expressed as counts and percentages. The association between Fascin-1 expression and treatment response was evaluated using Pearson's chi-square test. Multivariate logistic regression analysis (forward stepwise likelihood ratio method) was conducted to identify independent factors associated with treatment response, and the results were presented as odds ratios (ORs) with 95% confidence intervals (CIs). Receiver operating characteristic (ROC) curve analysis was employed to assess the ability of Fascin-1 expression to predict treatment response. PFS rates were estimated using the Kaplan-Meier method, with the results expressed as median survival times and estimated 1-year PFS rates, and intergroup differences were compared using the log-rank test. A two-tailed P -value < 0.05 was considered significant.

Results

Fascin-1 expression in CRC tissues

Fascin-1 expression was predominantly localized in the cytoplasm of tumor cells. Among the 40 advanced CRC tissues included in this study, 18 were positive for Fascin-1, correspond-

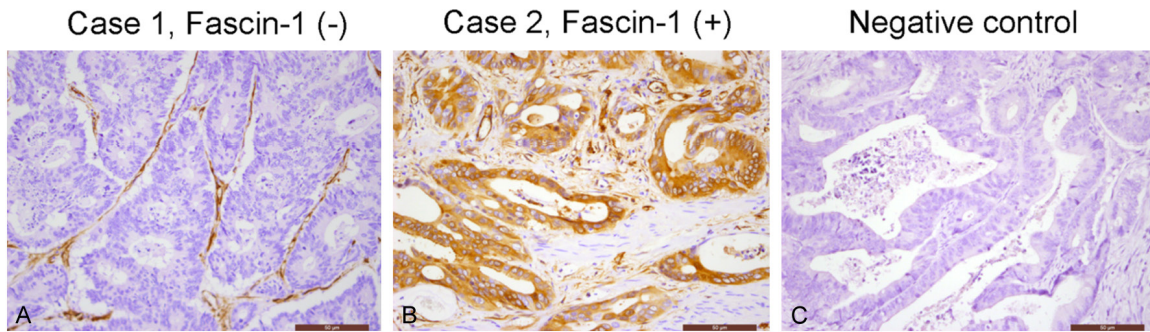


Figure 1. Immunohistochemical analysis of Fascin-1 expression in CRC tissues. A. In case 1, negative Fascin-1 expression was observed in cancer cells, and the patient's response to treatment was evaluated as a partial response (PR). B. In case 2, positive Fascin-1 expression was observed in cancer cells, and the patient's response to treatment was evaluated as progressive disease (PD). C. In the negative control group, all cells in the CRC tissue samples, including cancer cells and stromal cells, were negative for Fascin-1 expression.

Table 1. Association of Fascin-1 expression with ORR to cetuximab in advanced colorectal cancer patients

	No.	ORR		χ^2	P-value
		Responders, n (%)	Non-responders, n (%)		
Fascin-1 (-)	22	10 (45.5%)	12 (54.5%)	5.560	0.018
Fascin-1 (+)	18	2 (11.1%)	16 (88.9%)		

Abbreviation: ORR, objective response rate.

Table 2. Association of Fascin-1 expression with the DCR to cetuximab in advanced colorectal cancer patients

	No.	DCR		χ^2	P-value
		Controlled, n (%)	Uncontrolled, n (%)		
Fascin-1 (-)	22	19 (86.4%)	3 (13.6%)	6.234	0.013
Fascin-1 (+)	18	9 (50.0%)	9 (50.0%)		

Abbreviation: DCR, disease control rate.

ing to a positivity rate of 45% (18/40) (**Figure 1**).

Treatment response to cetuximab in patients with CRC

Among the 40 patients with advanced CRC, the response to cetuximab therapy was evaluated as follows: no patient achieved a CR, 12 achieved a PR, 16 had SD, and 12 had PD. Accordingly, the ORR was 30% (12/40), and the DCR was 70% (28/40).

Association between Fascin-1 expression and cetuximab treatment response

An evaluation of the relationship between Fascin-1 expression and treatment response revealed that patients with Fascin-1 positive CRC

exhibited a significantly lower ORR (11.1%, 2/18) compared to Fascin-1 negative CRC patients (45.5%, 10/22) ($P=0.018$) (**Table 1**). Similarly, the DCR was significantly lower in the Fascin-1-positive group (50.0%, 9/18) than in the Fascin-1-negative group (86.4%, 19/22) ($P=0.013$) (**Table 2**).

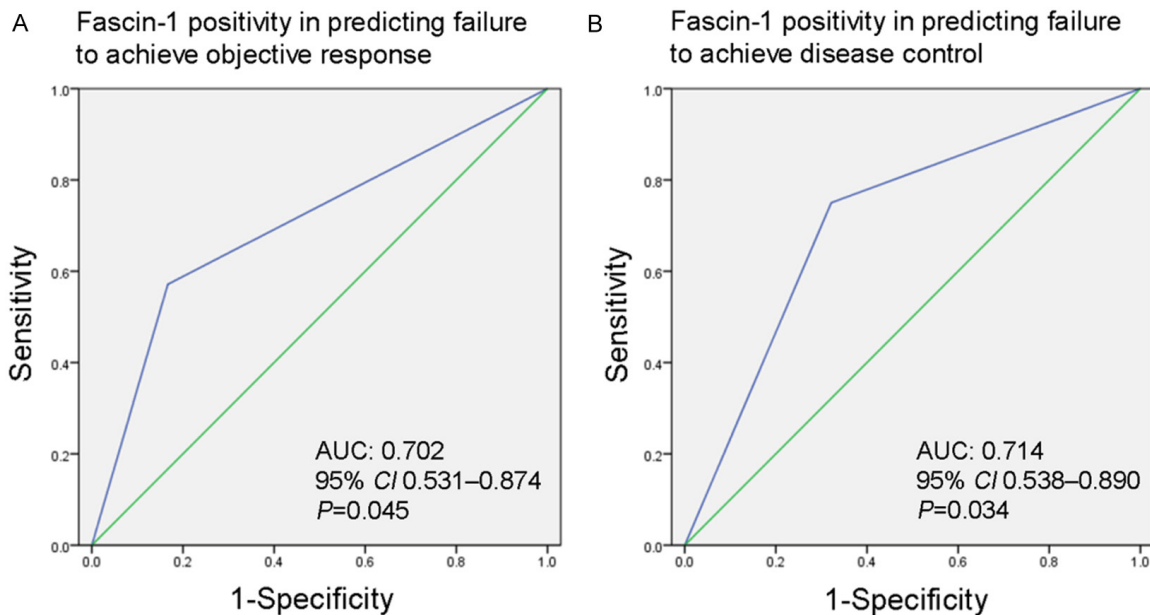
The relevant patient variables included sex, age, tumor location, Fascin-1 expression status, clinical stage, and RAS status. However, as all patients were at clinical stage IV and all had wild-type RAS status, these variables could not be stratified and thus were

not included in the model. Therefore, multivariate logistic regression analysis was performed, including sex, age, tumor location, and Fascin-1 expression status, to identify factors independently associated with treatment response. Variable selection was based on clinical relevance and the availability of sufficient variability within the dataset to allow meaningful stratification. The results demonstrated that Fascin-1 positivity was an independent factor associated with failure to achieve an objective response ($OR=6.667$; 95% CI : 1.227-36.226; $P=0.028$) and failure to achieve disease control ($OR=7.342$; 95% CI : 1.068-50.456; $P=0.043$) (**Table 3**). These findings suggest that the Fascin-1 expression status was a significant independent predictor of poor treatment response in this cohort.

Table 3. Multivariate logistic regression analysis (forward stepwise likelihood ratio method) of factors independently associated with treatment response

Variable	Failure to achieve ORR			Failure to achieve DCR		
	OR	95% CI	P-value*	OR	95% CI	P-value*
Gender (female vs. male)			0.122			0.417
Age (≥ 60 vs. <60)			0.588			0.533
Tumor site (left colon vs. right colon)			0.341			0.999
Tumor site (rectum vs. right colon)			0.785			0.999
Fascin-1 (positive vs. negative)	6.667	1.227-36.226	0.028	7.342	1.068-50.456	0.043

*A bold value of $P < 0.05$ indicates statistical significance. Abbreviations: ORR, objective response rate; DCR, disease control rate; OR, odds ratios; 95% CI, 95% confidence interval.

**Figure 2.** Receiver operating characteristic (ROC) curves demonstrating the predictive value of Fascin-1 positivity. A. ROC curve for the ability of Fascin-1 expression to predict failure to achieve an objective response. B. ROC curve for the ability of Fascin-1 expression to predict failure to achieve disease control.

Fascin-1 positivity as a predictor of poor cetuximab treatment response in advanced CRC

The ROC curve analysis revealed that Fascin-1 positivity predicted failure to achieve an objective response with an area under the curve (AUC) value of 0.702 (95% CI: 0.531-0.874; $P=0.045$) (**Figure 2A**) and failure to achieve disease control with an AUC value of 0.714 (95% CI: 0.538-0.890; $P=0.034$) (**Figure 2B**).

Correlation of Fascin-1 expression with progression-free survival in advanced CRC patients

To evaluate the effect of Fascin-1 expression on survival outcome, we examined its associa-

tion with PFS in the 40 patients with advanced CRC included in this study. The 1-year PFS rate for the overall cohort was 17.5%.

As illustrated in **Figure 3**, patients with positive Fascin-1 expression ($n=18$) had a mean PFS of 4.9 months and an estimated 1-year PFS rate of 5.6%, which was significantly lower than that of patients with negative Fascin-1 expression ($n=22$), who had a mean PFS of 8.4 months and an estimated 1-year PFS rate of 27.3% ($P=0.003$).

Discussion

CRC is among the most prevalent and lethal malignancies worldwide, with metastasis being

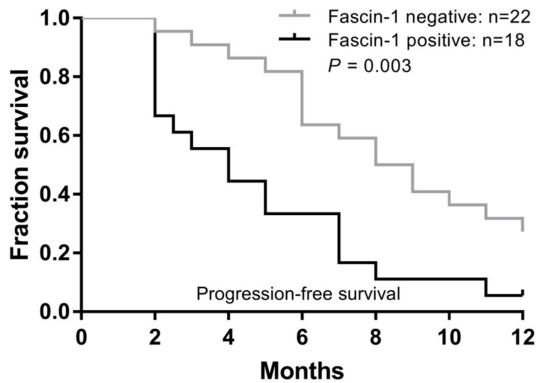


Figure 3. Association between Fascin-1 expression and progression-free survival (PFS) in advanced CRC patients. *P*-values were calculated using the Mantel-Cox log-rank test.

a key factor contributing to poor prognosis [1, 21]. Currently, targeted therapy has become a mainstay in the treatment of advanced CRC; however, its efficacy and the underlying mechanisms of drug resistance have garnered significant research attention. The detection of biomarkers associated with targeted therapy, such as KRAS, NRAS, and BRAF gene mutations, to guide anti-EGFR therapy, has become a routine practice in the management of CRC [22]. Studies have shown that patients with KRAS-mutant CRC do not benefit from treatment with cetuximab, whereas those with wild-type KRAS may benefit from clinical treatment [23]. Accordingly, all patients with advanced CRC included in the present study were confirmed to have wild-type RAS. Although cetuximab is widely used to treat RAS wild-type advanced CRC, its overall efficacy remains limited, with monotherapy conferring a survival benefit in only approximately 10-20% of patients, and acquired resistance frequently develops [7, 8]. Therefore, the identification of predictive biomarkers for the response to cetuximab is highly important for precision therapy and for improving treatment outcome in patients with advanced CRC.

Fascin-1, a key actin-bundling protein, promotes cell motility, migration, and tumor cell invasion and metastasis by facilitating the formation of filopodia, lamellipodia, and microspikes on the cell membrane [24, 25]. Previous studies have demonstrated that FSCN1 expression is upregulated in various malignancies, including lung cancer, esophageal squamous cell carcinoma, and CRC, and significantly enhances

the invasive and migratory capabilities of cancer cells [24, 26-28]. In our preliminary study published in a Chinese journal (Wang et al., 2020) [14], we observed a positive correlation between EGFR and Fascin-1 expression in CRC tissues, and patients with high coexpression of both markers exhibited poor prognosis. Furthermore, in triple-negative breast cancer, EGFR positively regulates Fascin-1 expression via the MAPK (ERK1/2) pathway, and cotargeting of EGFR and Fascin-1 resulted in significantly improved therapeutic efficacy compared to that of single-agent treatment [17]. These findings suggest that Fascin-1 expression may be associated with the efficacy of EGFR-targeted therapies.

In the present study, we demonstrated that the Fascin-1 expression status is significantly associated with the efficacy of cetuximab treatment in patients with RAS wild-type advanced CRC. Specifically, patients with Fascin-1-positive tumors had significantly lower ORR and DCR than those with Fascin-1-negative tumors did. Multivariate logistic regression analysis further revealed Fascin-1 positivity as an independent predictor of poor response to cetuximab. In conjunction with the results of the ROC curve analysis, these findings suggest that Fascin-1 expression may serve as a predictive biomarker for cetuximab resistance in advanced CRC and could have clinical implications for patient stratification and treatment optimization.

Notably, although previous studies have suggested that right-sided colon cancer may be associated with reduced efficacy of anti-EGFR therapies [29-31], the present multivariate analysis, which included tumor location along with other clinicopathologic factors, revealed that the Fascin-1 expression status was the sole independent factor associated with the response to cetuximab in our cohort. These results underscore the potential dominant role of Fascin-1 in modulating treatment outcome, even in the context of known confounding variables such as tumor location. However, given the small number of right-sided colon cancer cases (*n*=4) in this study, these findings should be interpreted with caution and warrant further validation in larger cohorts.

Consistent with its impact on treatment response, Fascin-1 positivity was also significantly associated with poor PFS in patients treated

with cetuximab. The 1-year PFS rate was markedly lower in Fascin-1-positive patients (5.6%) than in their Fascin-1-negative counterparts (27.3%). This survival disadvantage is likely attributable, at least in part, to the reduced efficacy of cetuximab in the presence of Fascin-1 expression, highlighting the use of Fascin-1 as both a predictive marker and a prognostic marker in this clinical setting.

The mechanistic link between Fascin-1 and resistance to EGFR-targeted therapy remains to be fully elucidated, but evidence provides a plausible basis for our observations. In our preliminary study, we observed a positive correlation between EGFR and Fascin-1 expression in CRC tissues, and patients whose expression of both markers was high had poor prognosis [14]. Moreover, studies in triple-negative breast cancer have demonstrated that EGFR positively regulates Fascin-1 expression through the MAPK (ERK1/2) signaling pathway and that cotargeting of EGFR and Fascin-1 resulted in significantly improved therapeutic efficacy compared to single-agent treatment [17]. These findings, together with our current results, suggest that Fascin-1 may function downstream of EGFR signaling and contribute to cetuximab resistance. It is therefore plausible that combined inhibition of EGFR and Fascin-1 could overcome resistance and increase therapeutic efficacy in RAS-wild-type advanced CRC. Further preclinical and clinical studies are warranted to explore this hypothesis.

Several limitations of this study should be acknowledged. First, the sample size was relatively small ($n=40$), which may have limited the statistical power and generalizability of our findings. Second, this was a single-center study, and selection bias cannot be entirely excluded. Third, although we observed a significant association between Fascin-1 expression and cetuximab efficacy, the underlying molecular mechanisms were not directly investigated in this cohort, and the proposed regulatory relationship between EGFR and Fascin-1 in CRC remains to be experimentally validated. Fourth, the lack of *in vitro* or *in vivo* validation of combined EGFR and Fascin-1 targeting precludes definitive conclusions regarding the therapeutic potential of such a strategy.

Future studies with larger, multicenter cohorts are needed to validate the predictive value of

Fascin-1 for the response to cetuximab in RAS-wild-type advanced CRC. Additionally, mechanistic investigations are warranted to clarify the precise molecular pathways through which Fascin-1 modulates resistance to anti-EGFR therapy. Preclinical models, including patient-derived xenografts and organoids, could be employed to evaluate the efficacy of combined EGFR and Fascin-1 inhibition. Ultimately, prospective clinical trials will be necessary to determine whether Fascin-1 status can guide treatment decisions and show whether cotargeting Fascin-1 represents a viable strategy to improve outcome in this patient population.

Based on the findings of the current study and the literature, we propose that the assessment of Fascin-1 expression should be considered an integral component of the clinical decision-making process for patients with RAS wild-type advanced CRC who are receiving cetuximab therapy. We believe that identifying patients with Fascin-1-positive tumors may help to stratify individuals who are less likely to benefit from anti-EGFR monotherapy could inform the selection of alternative or combination treatment strategies. In our view, integrating Fascin-1 status into routine pathologic evaluation, following validation in larger clinical trials, may facilitate personalized therapy and improve clinical outcomes.

Conclusion

Fascin-1 positivity was significantly associated with a reduced response to cetuximab and poor progression-free survival in patients with RAS wild-type advanced colorectal cancer. Multivariate analysis revealed that Fascin-1 was an independent predictive biomarker for cetuximab resistance, underscoring a possible role in patient stratification and therapeutic decision-making. Although these findings require validation in larger, multicenter cohorts and further mechanistic investigation, the assessment of Fascin-1 expression may inform personalized treatment strategy and improve outcome in this patient population.

Acknowledgements

During the preparation of this manuscript, the authors utilized DeepSeek (online version, available at deepseek.com) exclusively for language polishing and editing to enhance the

readability and clarity of the text. After using this tool, the authors meticulously reviewed, revised, and verified all the content to ensure the accuracy, scientific validity, and integrity of the presented data and conclusions. The authors assume full and sole responsibility for the final content of this work and confirm that no AI-generated substantive content has been incorporated into the manuscript. This study was supported by a grant from the Key Science and Technology Project of Jinhua City (no. 2023-3-017).

A waiver of informed consent was granted for patients who were deceased at the time of enrollment. For all the other participants, informed consent to participate in the study was obtained from the individuals themselves or from their legal guardians/next of kin, in accordance with national legislation and institutional requirements.

Disclosure of conflict of interest

None.

Abbreviations

FSCN1, Fascin-1; CRC, colorectal cancer; IHC, immunohistochemistry; ORR, objective response rate; DCR, disease control rate; CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease; PFS, progression-free survival.

Address correspondence to: Hua-Jun Lu, Department of Oncological Radiotherapy, Affiliated Dongyang Hospital of Wenzhou Medical University, 60 Wu Ning Xi Road, Dongyang, China. E-mail: luhua-jun1215@hotmail.com; Chao-Qun Wang, Department of Pathology, Affiliated Dongyang Hospital of Wenzhou Medical University, 60 Wu Ning Xi Road, Dongyang, China. E-mail: chaoqunw869@163.com

References

- [1] Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I and Jemal A. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 2024; 74: 229-263.
- [2] Guo L, Wang L, Cai L, Zhang Y, Feng X, Zhu C, Gao W, Cardoso R, Yang H, Dai M, Brenner H and Chen H. Global distribution of colorectal cancer staging at diagnosis: an evidence synthesis. *Clin Gastroenterol Hepatol* 2025; 23: 2088-2101.
- [3] Montes AF, Alonso V, Aguilar EA, Élez E, Alfonso PG, Castro CG, Maurel J, García RV, Tocino RV and Urtasun JA. 2025 Updated version v1.0 SEOM-GEMCAD-TTD clinical guidelines for the systemic treatment of metastatic colorectal cancer (2022). *Clin Transl Oncol* 2025; 27: 1845-1850.
- [4] Yun S, Kwak Y, Nam SK, Seo AN, Oh HK, Kim DW, Kang SB and Lee HS. Ligand-independent epidermal growth factor receptor overexpression correlates with poor prognosis in colorectal cancer. *Cancer Res Treat* 2018; 50: 1351-1361.
- [5] Krasinskas AM. EGFR signaling in colorectal carcinoma. *Patholog Res Int* 2011; 2011: 932932.
- [6] Zhang C, Liu L, Lv Y, Li J, Cao C, Lu J, Wang S, Du B and Yang X. Chemotherapy plus panitumumab/cetuximab versus chemotherapy plus bevacizumab in wild-type KRAS/RAS metastatic colorectal cancer: a meta-analysis. *Expert Rev Anticancer Ther* 2022; 22: 1333-1347.
- [7] Jonker DJ, O'Callaghan CJ, Karapetis CS, Zalcberg JR, Tu D, Au HJ, Berry SR, Krahn M, Price T, Simes RJ, Tebbutt NC, van Hazel G, Wierzbiicki R, Langer C and Moore MJ. Cetuximab for the treatment of colorectal cancer. *N Engl J Med* 2007; 357: 2040-2048.
- [8] Cunningham D, Humblet Y, Siena S, Khayat D, Bleiberg H, Santoro A, Bets D, Mueser M, Hestricks A, Verslype C, Chau I and Van Cutsem E. Cetuximab monotherapy and cetuximab plus irinotecan in irinotecan-refractory metastatic colorectal cancer. *N Engl J Med* 2004; 351: 337-345.
- [9] Chen Y, He M, Cui L, Zhang J, Huang H and Tao Z. MiR-145 encapsulated small extracellular vesicles inhibit colorectal cancer progression by downregulating fascin actin-bundling protein 1 expression. *Stem Cell Res Ther* 2025; 16: 343.
- [10] Wu Y, Zhou Y, Gao H, Wang Y, Cheng Q, Jian S, Ding Q, Gu W, Yao Y, Ma J, Wu W, Li Y, Tong X, Song X and Ma S. LYAR promotes colorectal cancer progression by upregulating FSCN1 expression and fatty acid metabolism. *Oxid Med Cell Longev* 2021; 2021: 9979707.
- [11] Izdebska M, Zielińska W, Krajewski A and Grzanka A. Fascin in migration and metastasis of breast cancer cells - a review. *Adv Med Sci* 2023; 68: 290-297.
- [12] Shi Y, Xu Y, Xu Z, Wang H, Zhang J, Wu Y, Tang B, Zheng S and Wang K. TKI resistant-based prognostic immune related gene signature in LUAD, in which FSCN1 contributes to tumor progression. *Cancer Lett* 2022; 532: 215583.

- [13] Dif L, Manaud G and Moreau V. Fascin-1 in primary liver cancers, perspectives for targeted therapy. *Biochim Biophys Acta Rev Cancer* 2025; 1880: 189361.
- [14] Wang CQ WQ, Wang Y, Du Z, Shao JK and Huang BF. Correlation and clinical significance of epidermal growth factor receptor 1 and Fascin-1 expression in colorectal cancer. *Chin J Anat Clin* 2020; 25: 180-184.
- [15] Amin MB, Greene FL, Edge SB, Compton CC, Gershengwald JE, Brookland RK, Meyer L, Gress DM, Byrd DR and Winchester DP. The eighth edition AJCC cancer staging manual: continuing to build a bridge from a population-based to a more “personalized” approach to cancer staging. *CA Cancer J Clin* 2017; 67: 93-99.
- [16] Wang CQ, Tang CH, Chang HT, Li XN, Zhao YM, Su CM, Hu GN, Zhang T, Sun XX, Zeng Y, Du Z, Wang Y and Huang BF. Fascin-1 as a novel diagnostic marker of triple-negative breast cancer. *Cancer Med* 2016; 5: 1983-1988.
- [17] Wang CQ, Li Y, Huang BF, Zhao YM, Yuan H, Guo D, Su CM, Hu GN, Wang Q, Long T, Wang Y, Tang CH and Li X. EGFR conjunct FSCN1 as a novel therapeutic strategy in triple-negative breast cancer. *Sci Rep* 2017; 7: 15654.
- [18] Lu SP, Jiang LJ, Wang Y, Shao JK, Du ZQ, Huang BF and Wang CQ. Expression of Fascin-1 and its diagnostic value in liver cancer. *Sci Rep* 2024; 14: 10049.
- [19] Jin LL, Lu HJ, Shao JK, Wang Y, Lu SP, Huang BF, Hu GN, Jin HC and Wang CQ. Relevance and mechanism of STAT3/miR-221-3p/Fascin-1 axis in EGFR TKI resistance of triple-negative breast cancer. *Mol Cell Biochem* 2024; 479: 3037-3047.
- [20] Jang HJ, Kim BC, Kim HS, Kim JH, Song HH, Kim JB, Park JJ, Yoon SN, Woo JY and Zang DY. Comparison of RECIST 1.0 and RECIST 1.1 on computed tomography in patients with metastatic colorectal cancer. *Oncology* 2014; 86: 117-121.
- [21] Han B, Zheng R, Zeng H, Wang S, Sun K, Chen R, Li L, Wei W and He J. Cancer incidence and mortality in China, 2022. *J Natl Cancer Cent* 2024; 4: 47-53.
- [22] Baranov E and Nowak JA. Pathologic evaluation of therapeutic biomarkers in colorectal adenocarcinoma. *Surg Pathol Clin* 2023; 16: 635-650.
- [23] Kassouf E, Tabchi S and Tehfe M. Anti-EGFR therapy for metastatic colorectal cancer in the era of extended RAS gene mutational analysis. *BioDrugs* 2016; 30: 95-104.
- [24] Li Z, Shi J, Zhang N, Zheng X, Jin Y, Wen S, Hu W, Wu Y and Gao W. FSCN1 acts as a promising therapeutic target in the blockade of tumor cell motility: a review of its function, mechanism, and clinical significance. *J Cancer* 2022; 13: 2528-2539.
- [25] Sarantelli E, Mourkakis A, Zacharia LC, Stylianou A and Gkretsi V. Fascin-1 in cancer cell metastasis: old target-new insights. *Int J Mol Sci* 2023; 24: 11253.
- [26] Sun Q, Liu R, Zhang H, Zong L, Jing X, Ma L, Li J and Zhang L. Fascin actin-bundling protein 1 regulates non-small cell lung cancer progression by influencing the transcription and splicing of tumorigenesis-related genes. *PeerJ* 2023; 11: e16526.
- [27] Qin D, Wang R, Liu Q, Wang Z, He Y and Cai H. FSCN1 regulates TGF-beta signalling to promote esophageal squamous cell carcinoma metastasis via stabilizing THBS1 mRNA. *Commun Biol* 2025; 8: 1805.
- [28] Shi S, Zheng HC and Zhang ZG. Roles of Fascin mRNA expression in colorectal cancer: meta-analysis and bioinformatics analysis. *Mol Clin Oncol* 2020; 13: 119-128.
- [29] Wang F, Bai L, Liu TS, Yu YY, He MM, Liu KY, Luo HY, Zhang DS, Jin Y, Wang FH, Wang ZQ, Wang DS, Qiu MZ, Ren C, Li YH and Xu RH. Right-sided colon cancer and left-sided colorectal cancers respond differently to cetuximab. *Chin J Cancer* 2015; 34: 384-393.
- [30] Brulé SY, Jonker DJ, Karapetis CS, O’Callaghan CJ, Moore MJ, Wong R, Tebbutt NC, Underhill C, Yip D, Zalcberg JR, Tu D and Goodwin RA. Location of colon cancer (right-sided versus left-sided) as a prognostic factor and a predictor of benefit from cetuximab in NCIC CO.17. *Eur J Cancer* 2015; 51: 1405-1414.
- [31] Wang ZX, Wu HX, He MM, Wang YN, Luo HY, Ding PR, Xie D, Chen G, Li YH, Wang F and Xu RH. Chemotherapy with or without anti-EGFR agents in left- and right-sided metastatic colorectal cancer: an updated meta-analysis. *J Natl Compr Canc Netw* 2019; 17: 805-811.