Cancer Screening and Prevention 2026 vol. **000(000)** | 000–000 Epub
DOI: 10.14218/CSP.2026.00029

Editorial

Olink Proteomic Research in Colorectal Cancer: Redefining Minimally Invasive Surgery through Biomarker-driven Insights

Zhenting Zhao[1,2#], Nan Wang[3#] and Pengyue Zhao[1*]

[1]*Department of General Surgery, First Medical Center of the Chinese PLA General Hospital, Beijing, China;* [2]*College of Life Science, Xinyang Normal University, Xinyang, China;* [3]*Department of Medical Administration, Traditional Chinese Medicine Hospital of Shijingshan District, Beijing, China*

Received: February 26, 2026 | **Revised:** April 01, 2026 | **Accepted:** April 15, 2026 | **Published online:** May 12, 2026

The study by Yan and colleagues in the *Journal of Proteome Research* (2025) represents a valuable contribution to the emerging integration of molecular profiling in surgical oncology.[1] By employing high-fidelity Olink proteomic profiling, the research provides the first plasma proteomic comparison between Endoscopic Super-Minimally Invasive Surgery (ESMIS) and laparoscopic surgery (LS) for colorectal cancer (CRC), moving beyond traditional clinical metrics to propose a data-driven framework for understanding surgical trauma and tumor biology. The identification of candidate diagnostic biomarkers (AMN, LRP1, FOXO1, PTPRJ) and surgery-specific injury markers (CALCA, PDGFC) offers tangible targets for translational development.

However, the true measure of an innovative study lies not only in its findings but in the scholarly discourse it generates regarding its context, limitations, and the pathway it opens. This editorial aims to fulfill that role. We will critically evaluate the work by Yan et al., recognizing its groundbreaking approach while constructively examining its scope. A key consideration is its exploratory nature, characterized by a single-center design and a limited sample size (n = 76), which, while appropriate for an initial proof-of-concept, necessarily restricts the generalizability of its conclusions. The translational value of proteomic biomarkers hinges on robust validation. Therefore, a crucial step in this appraisal is to contextualize this study within the wider landscape of CRC proteomics, which includes large-scale discovery cohorts involving thousands of patients. This contrast helps frame the findings of Yan et al. not as definitive clinical conclusions but rather as highly focused, biologically plausible hypotheses derived from a specific clinical scenario. These hypotheses now require, and deserve, rigorous testing in larger, multicenter prospective studies to assess their true potential for reshaping screening, surgical decision-making, and postoperative monitoring in CRC.

The study's design, featuring longitudinal plasma sampling and orthogonal validation, facilitates several important discoveries. The significant downregulation of proteins like AMN ($P < 0.001$) and LRP1 ($P < 0.001$) in CRC patients compared to healthy controls, consistent across both surgical cohorts, points to their potential fundamental role in tumor biology. The orthogonal validation via immunohistochemistry and Western blotting significantly strengthens the biological credibility of these plasma proteomic findings, for instance, showing a marked reduction (e.g., ~70% decrease in positive cells for FOXO1, $P < 0.001$) in tumor tissues.

The amplitude of postoperative increase for trauma-associated proteins like CALCA and PDGFC was notably lower in the ESMIS group compared to the LS group (inferred from fold-change differences in Fig. 4 of the original article), offering a quantitative molecular measure that aligns with the "super-minimally invasive" clinical premise of ESMIS. Furthermore, the identification of "inflection point" proteins (e.g., FOXO1, PTPRJ) that normalize after tumor resection presents a fascinating signature of the reversible "cancer state."

The value of this research lies in its potential to advance a translational pathway. The biomarkers identified form a toolkit that could, upon extensive future validation, address clinical needs across the perioperative continuum.

Traditional clinical evaluation indicators, such as operative duration, intraoperative blood loss, and hospital stay, are unable to capture the subtle molecular changes induced by different surgical methods, which are key to understanding surgical trauma and tumor biology.[2] The downregulation of AMN, LRP1, and others offers a promising avenue for liquid biopsy development. However, the promising sensitivity and specificity of these markers, as suggested by the significant intergroup differences, now warrant validation in larger cohorts to determine their clinical performance metrics, such as the AUC of a combined panel. Current non-invasive screening methods have limitations in sensitivity and patient compliance. A multi-protein panel incorporating these markers could potentially improve early detection strategies, a pressing need given the rise of early-onset CRC.[3]

The proteomic data provide a molecular rationale for comparing surgical techniques. The attenuated response of trauma markers like CALCA/PDGFC after ESMIS offers an objective, quantitative measure to complement clinical assessments of invasiveness.

[*]**Correspondence to**: Pengyue Zhao, Department of General Surgery, First Medical Center of the Chinese PLA General Hospital, 28 Fuxing Road, Haidian District, Beijing 100853, China. ORCID: https://orcid.org/0000-0002-7813-1604. Tel: +86-15010112665, E-mail: zhaopengyue@301hospital.com.cn.
[#]These authors contributed equally to this manuscript.

How to cite this article: Zhao Z, Wang N, Zhao P. Olink Proteomic Research in Colorectal Cancer: Redefining Minimally Invasive Surgery through Biomarker-driven Insights. *Cancer Screen Prev* 2026;000(000):000–000. doi: 10.14218/CSP.2026.00029.

Table 1. Olink proteomic research in colorectal cancer

Year	First author	Country	Number of CRC patients	Purpose	Olink panel
2021	Monjazeb AM	USA	13	Interrogate changes in cytokines and chemokines among metastatic microsatellite stable colorectal cancer patients[6]	Immuno-Oncology
2022	Sun X	USA & China	160	Evaluate the role of circulating proteins in colorectal cancer development[7]	12 Olink Proseek panels (CAM, CRE, CVDII, CVDIII, DEV, INF, IRE, MET, NEU, NEX, ODA, ONCII)
2024	Xu X	China	33	Screen circulating immune protein expressions in the spectrum of responders and nonresponders[8]	Immuno-Oncology
2024	Wan Y	China	51	Investigate the changes in the content of tumor immune-related circulating proteins[9]	Immuno-Oncology
2025	Xiao C	China	52	Profile the proteome of intestinal tissue and offer valuable insights into potential biomarkers and therapeutic targets[10]	Oncology II
2025	Su H	China	49	Analyze saliva samples from CRC patients to identify candidate biomarkers[11]	Immuno-Oncology
2025	Pan ZK	China	619 samples	Systematically identify potential plasma protein targets for CRC[12]	None
2025	Jin H	China	149	Develop high-performance early diagnostic strategies for effective early detection and prevention[13]	Cardiometabolic
2025	Bai M	China	76	Analyze the peripheral immune proteome[14]	Immuno-Oncology
2025	Yan Y	China	76	Delineate ESMIS-versus laparoscopic surgery (LS)-associated molecular variations in CRC cohorts[1]	Organ damage
2026	Dhami J	UK	9,890	Clarify shared molecular mechanisms between CRC and inflammatory bowel disease[5]	None

In the future, validated proteomic signatures could contribute to more personalized surgical planning, helping to match surgical strategy to patient and tumor biology.[4]

The "inflection point" proteins create a conceptual roadmap for molecular recovery. Serial measurement of such signatures could objectively track a patient's return to a baseline state and potentially serve as an early indicator of complications or, in the long term, recurrence.

While the study by Yan et al. is groundbreaking as a proof-of-concept, a clear-eyed discussion of the subsequent steps and challenges is essential to map the route to clinical impact.

The most immediate step is validation in large, multicenter prospective cohorts. The study's sample size (n = 76) and single-center design are appropriate for its exploratory purpose but are insufficient to establish generalizable biomarkers or define clinical cut-offs. This scale of validation is the benchmark in the field. For instance, contemporary proteomic studies in CRC, such as the work by Dhami et al. (2026), have leveraged large population-based resources like the UK Biobank, including cohorts approaching 10,000 CRC cases.[5] The promising but focused findings of Yan et al. must be tested in similarly diverse and extensive populations to confirm their reliability and clinical utility across different demographics and disease stages (Table 1).[1,5–14]

It is important to acknowledge other limitations. The analysis was confined to the acute postoperative phase (72 h). Consequently, the long-term dynamics of these protein signatures and their correlation with hard clinical endpoints like overall survival or recurrence remain undefined and present a crucial avenue for future longitudinal research. Future studies should also address technology transfer to cost-effective assays and the integration of proteomic data with other omics layers for a more comprehensive molecular atlas.

The integration of proteomics with genomics, microbiomics, and metabolomics holds great promise for a systems-level understanding of CRC.[15,16] The immediate and essential next step is the rigorous validation of the protein panels identified in studies like Yan et al. in larger cohorts. The development of simple, interpretable protein-based scores represents a more immediately attainable clinical goal than complex, black-box AI models. Multi-omics and AI represent a strategic horizon, building upon validated biomarkers to enable future, more nuanced precision medicine.[17]

The work by Yan et al. serves as a crucial catalyst, adeptly bridging advanced proteomics with the nuanced field of minimally invasive surgery. It provides a compelling molecular proof-of-concept for the differential impact of ESMIS versus LS and delivers a focused set of biomarker candidates. By constructively acknowledging the limitations inherent in its pilot scale, most notably the need for validation in larger cohorts akin to contemporary large-scale studies, we can properly position its contribution. This study does not offer final answers but provides an excellently defined starting point. It outlines a clear translational pathway, from initial discovery through rigorous multicenter validation to potential integration into clinical decision-support frameworks. Embracing this pathway promises to advance CRC management towards a future of truly precision-guided surgical care, ultimately aiming for earlier detection, less invasive treatments, and improved patient outcomes.

Acknowledgments

None.

Funding

There was no funding support.

Conflict of interest

PYZ has served as an Editorial Board Member of *Cancer Screening and Prevention* since 2025. The other authors, ZTZ and NW, have no other potential conflicts of interest to declare.

Author contributions

Manuscript drafting and writing (ZTZ), table conception and drawing (NW), conception and design of the work (PYZ). All authors have approved the final version of the manuscript.

References

[1] Yan Y, Ma Y, Xiao P, Wang J, Xiao S, Linghu E, *et al*. Plasma Proteomic Profiling of Colorectal Cancer: Insights from Minimally Invasive Surgical Cohorts. J Proteome Res 2025;24(12):6252–6271. doi:10.1021/acs.jproteome.5c00785.

[2] Larmann J, Luedi MM. Biomarkers and Cellular Biology in Perioperative Medicine. Cells 2022;11(7):1147. doi:10.3390/cells11071147, PMID:35406711.

[3] Jayakrishnan T, Ng K. Early-Onset Gastrointestinal Cancers: A Review. JAMA 2025;334(15):1373–1385. doi:10.1001/jama.2025.10218, PMID:40674064.

[4] de Back TR, van Hooff SR, Sommeijer DW, Vermeulen L. Transcriptomic subtyping of gastrointestinal malignancies. Trends Cancer 2024;10(9):842–856. doi:10.1016/j.trecan.2024.06.007.

[5] Dhami J, Radhakrishnan SK, Russ D, Mondal S, Alzarooni A, Merodio LB, *et al*. A Network-Based Association of IBD and Colorectal Cancer Using Proteomics Data. Proteomics Clin Appl 2026;20(2):e70041. doi:10.1002/prca.70041.

[6] Monjazeb AM, Giobbie-Hurder A, Lako A, Thrash EM, Brennick RC, Kao KZ, *et al*. A Randomized Trial of Combined PD-L1 and CTLA-4 Inhibition with Targeted Low-Dose or Hypofractionated Radiation for Patients with Metastatic Colorectal Cancer. Clin Cancer Res 2021;27(9):2470–2480. doi:10.1158/1078-0432.CCR-20-4632, PMID:33568343.

[7] Sun X, Shu XO, Lan Q, Laszkowska M, Cai Q, Rothman N, *et al*. Prospective Proteomic Study Identifies Potential Circulating Protein Biomarkers for Colorectal Cancer Risk. Cancers (Basel) 2022;14(13):3261. doi:10.3390/cancers14133261, PMID:35805033.

[8] Xu X, Ai L, Hu K, Liang L, Lv M, Wang Y, *et al*. Tislelizumab plus cetuximab and irinotecan in refractory microsatellite stable and RAS wild-type metastatic colorectal cancer: a single-arm phase 2 study. Nat Commun 2024;15(1):7255. doi:10.1038/s41467-024-51536-x, PMID:39179622.

[9] Wan Y, Luo W, Song X, Zhao Y, Han Z, Shen J, *et al*. A Targeted Proteomics Approach Reveals a Serum Protein Signature as a Diagnostic Biomarker for Colorectal Cancer. J Inflamm Res 2024;17:10755–10768. doi:10.2147/JIR.S492356, PMID:39677294.

[10] Xiao C, Wu H, Long J, You F, Li X. Olink Profiling of Intestinal Tissue Identifies Novel Biomarkers For Colorectal Cancer. J Proteome Res 2025;24(2):599–611.doi:10.1021/acs.jproteome.4c00728,PMID:39757570.

[11] Su H, Gu X, Zhang W, Lin F, Lu X, Zeng X, *et al*. Identification of Salivary Biomarkers in Colorectal Cancer by Integrating Olink Proteomics and Metabolomics. J Proteome Res 2025;24(5):2542–2552. doi:10.1021/acs.jproteome.5c00091, PMID:40183281.

[12] Pan ZK, Wu MH, Shi H, Ni YJ, Geng QL, Ye JS. Associations of plasma protein levels with risk of colorectal cancer: a proteome-wide Mendelian randomization study. Clin Proteomics 2025;22(1):24. doi:10.1186/s12014-025-09545-5, PMID:40462010.

[13] Jin H, Deng K, Qi S, Deng Z, Pu L, Xu D, *et al*. Plasma Proteomic High-Performance Biomarkers for Early Diagnosis of Colorectal Cancer. J Proteome Res 2025;24(10):5177–5189. doi:10.1021/acs.jproteome.5c00483, PMID:40927999.

[14] Bai M, Li N, Yin X, Huang C, Li W, Yang J, *et al*. An anti-PD-1 antibody (SCT-I10A) plus anti-EGFR antibody (SCT200) and chemotherapy for RAS/BRAF wild-type metastatic colorectal cancer: A phase Ib study. Cancer Lett 2025;634:218061. doi:10.1016/j.canlet.2025.218061, PMID:41005455.

[15] Zhou K, Yang C, Li Y. Multi-omics in colorectal cancer liver metastasis: applications and research advances. Cancer Biol Med 2025;22(6):618–38. doi:10.20892/j.issn.2095-3941.2025.0066, PMID:40574729.

[16] Sharma A, Kumar R, Yadav G, Garg P. Artificial intelligence in intestinal polyp and colorectal cancer prediction. Cancer Lett 2023;565:216238. doi:10.1016/j.canlet.2023.216238, PMID:37211068.

[17] Iacucci M, Santacroce G, Maeda Y, Majumder S, Hassan C, Shung DL, *et al*. Artificial intelligence in inflammatory bowel disease: bridging innovation, implementation and impact. Nat Rev Gastroenterol Hepatol 2026. doi:10.1038/s41575-026-01190-z, PMID:41857227.