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Identification and analysis of microplastics in peritumoral and tumor tissues of colorectal cancer

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The widespread occurrence of microplastics (MPs) in the environment has raised significant concerns regarding their potential health impacts, particularly in relation to carcinogenesis. This study aimed to identify and analyze microplastics present in peritumoral and tumor tissues of patients diagnosed with colorectal cancer (CRC). Utilizing advanced scanning electron microscopy (SEM) and laser direct infrared (LDIR) imaging systems, we systematically examined tissue samples to detect and characterize the microplastics. Our findings revealed a diverse array of microplastic types, notably polyvinyl chloride (PVC) and polyethylene (PE), within both peritumoral and tumor regions. Compared to adjacent non-cancerous tissues, tumor tissues exhibited a greater variety and distribution of microplastics. Furthermore, Clathrin—a key protein involved in endocytosis—was found to be highly expressed in colorectal cancer specimens, facilitating the substantial uptake of microplastics. These results suggest a potential association between exposure to microplastics and the pathogenesis of colorectal cancer. This study highlights the urgent need for increased awareness and regulatory measures aimed at mitigating microplastic pollution along with its associated health risks.

Microplastics (MPs) are pervasive environmental contaminants increasingly detected in marine, freshwater, and terrestrial ecosystems[1]. Defined as plastic particles smaller than 5 mm in diameter, microplastics arise from the degradation of larger plastic debris, manufacturing processes, and personal care products[2]. The widespread distribution of MPs in the environment raises significant concerns due to their potential infiltration into the food chain and human living spaces, leading to direct and indirect exposure through ingestion, inhalation, and dermal contact[3].

The implications of microplastic exposure on human health remain largely unclear; however, evidence indicates that microplastics can elicit adverse biological responses such as inflammation, cytotoxicity, and oxidative stress—potentially culminating in chronic health conditions[4]. Among various health risks associated with microplastics, the possible connection between their exposure and cancer is particularly concerning. Microplastics may serve as vectors for hazardous chemicals and pathogens that could amplify their toxicological effects[5].

Colorectal cancer (CRC) ranks among the most prevalent cancers globally, contributing significantly to morbidity and mortality rates[6]. Despite advancements in screening methodologies and treatment options, the pathogenesis of CRC remains complex—resulting from a multifactorial interplay involving genetic predispositions alongside environmental influences and lifestyle choices[7]. The potential role of environmental pollutants like microplastics in CRC development represents an emerging area of research that necessitates thorough investigation.

Recent studies have examined the presence of MPs within human tissues while underscoring their potential involvement in gastrointestinal diseases[8]. Nevertheless, comprehensive analyses focusing specifically on microplastics within colorectal cancer tissues are still limited. Advanced analytical techniques such as laser direct infrared imaging present a novel approach for accurately identifying and characterizing microplastics within biological samples with high precision[9]. This methodology facilitates a comprehensive spatial distribution

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and compositional analysis of microplastics within tissue matrices, thereby offering essential insights into their potential role in carcinogenesis.

This study aimed to address the existing gap in research by systematically identifying and analyzing microplastics (MPs) in both peritumoral and tumor tissues of colorectal cancer patients. By employing advanced imaging and spectroscopic techniques, we sought to quantify the concentration, types, and distribution patterns of microplastics within these tissues. Understanding the interactions between microplastics and colorectal tissues may elucidate their role in the pathogenesis of colorectal cancer and potentially inform future regulatory and public health strategies aimed at mitigating microplastic pollution and its associated risks.

Materials and methods

Human samples
Patients with CRC have been recruited from the Tianjin Union Medical Center. The inclusion criteria include ten patients diagnosed with stage I-IV colorectal cancer who are planning to undergo tumor surgical resection. Patients with a history of other malignancies or chronic inflammatory diseases were excluded. Informed consent was obtained from all participants, and the study was approved by the hospital's ethics review board (approval number: GZR2024035).

Tissue samples
During surgical resection, both tumor and adjacent peritumoral tissues (at least 5 cm away from the tumor margin) were collected. The samples were immediately placed in sterile containers and stored at -80 °C until further analysis. There are a total of 20 samples.

Microplastic extraction
Regarding the extraction of microplastics, there are previous studies as references[10,11]. Each sample was minced into small pieces using a sterile scalpel. All solvents must be filtered through a 0.45 μm polytetrafluoroethylene (PTFE) membrane (diameter 50 mm, pore size 0.45 μm, Shanghai Youmi, China) before use. All experimental consumables are glassware, which need to be rinsed with ethanol three times and then dried before use.

Tumor and adjacent normal tissues are weighed and recorded. Three times the volume of the sample in concentrated nitric acid (68%) is added to the sample. After digestion at room temperature for 42 h, the mixture is placed on a graphite heating plate (Shanghai Lichen Bangxi, China) for 3 h to digest the proteins.

Perform vacuum filtration using a steel membrane with a pore size of 13 μm. After multiple washes with ultrapure water and ethanol, immerse the resulting filter membrane in ethanol for ultrasonic treatment to disperse the particles on the filter membrane into the ethanol solution. Perform vacuum filtration again on the ethanol solution using a steel membrane with a pore size of 13 μm. After multiple ethanol washes, remove the filter membrane from the ethanol solution.Wash the filter membrane with ethanol multiple times, then place the ethanol solution in an infrared drying oven (WA70-1, Hangzhou Qiwei, China) to concentrate it to 150 μl. Subsequently, drop the concentrated solution onto a high-reflection glass (MY2108LD34, Agilent, USA). Once the ethanol has completely evaporated, perform LDIR testing.

Laser direct infrared imaging (LDIR)
The filtered microplastic particles were analyzed using a laser direct infrared imaging system (Agilent 8700, USA). Select the particle analysis mode, choose the method for establishing a microplastic spectral library, set up an automatic testing method (matching degree > 0.65, particle size range 20–500 μm), and conduct the test. This technique provides high-resolution images and spectral data, allowing for the identification of different types of plastics based on their infrared absorption spectra.

Scanning electron microscopy (SEM)
To study the morphology and surface characteristics of the microplastics, the samples were examined using a scanning electron microscope (Zeiss, Oberkirchen, Germany). The samples were coated with a thin layer of gold to enhance the conductivity and imaged at various magnifications.

Blank and quality control procedures
To ensure the accuracy and reliability of the experiment, several steps should be taken. Firstly, set up a reagent blank, solvent blank, and laboratory blank to monitor potential sources of contamination. Regularly calibrate using standard samples to improve accuracy and sensitivity. Additionally, calibrate instruments regularly and implement data quality control measures. Use specialized anti-static clothing, gloves, and dust-free workbenches to prevent secondary pollution. Finally, participate in an external quality control plan to verify the reliability of the testing methods. The test results of the blank control have been shown in Fig. S2.

Microplastic quantification
The number and size of the microplastic particles were quantified using an image analysis software (ImageJ 1.53t, NIH, Bethesda, MD, USA, https://imagej.net). The concentration of microplastics was calculated as particles per gram of tissue.

Statistical analysis
Data were analyzed using GraphPad Prism software (Graphpad Prism 9.5.1, https://shop.kkjs.net/gp/#/). Image editing and typesetting are done using Adobe Illustrator software (Adobe Illustrator 25.0.1, https://adobe.hmzs ya.com/ai/). Descriptive statistics were used to summarize the data. Differences in microplastic concentrations

between tumor and peritumoral tissues were evaluated using paired t-tests and Two-way ANOVA. Statistical significance was set at $P < 0.05$.

Cell experiments

Resistant strains and human colorectal cancer cell lines HCT-116 and LOVO were acquired from the Chinese Academy of Sciences Cell Bank (Shanghai, China). The cells were cultured in a specific cell culture medium (Gibco, Grand Island, NY, USA) supplemented with 10% fetal bovine serum (FBS, BI) and 1% penicillin/streptomycin (both from Gibco).All cultures were maintained in an incubator at 37℃ with 5% CO2.

The cells were treated with polystyrene fluorescent microspheres with a diameter of 80 nm, which were purchased from the Beisi Le Technology Development Center (Tianjin, China). The cells were then treated with microplastics at a concentration of 25 µg/mL, and relevant experimental procedures were performed after 48 h of treatment.

Si-Clathrin Heavy Chain 1 (CLTC) (human) and the negative control (NC) were procured from Jiangsu Saisofei Biotechnology Co. (Jiangsu, China), and cells were transfected with Lipofectamine 2000 (Invitrogen, Carlsbad, CA, USA) following the manufacturer's protocol.

The cells were cultured in 24-well chamber slides, harvested, fixed with 4% paraformaldehyde, and permeabilized with 0.01% Triton X-100 for 10 min. Subsequently, the cells were exposed to microplastics and CLTC. The nuclei were stained with 4′,6-diamidino-2-phenylindole (DAPI, 488 nm). Confocal microscopy was performed using a Nikon C2 Plus confocal microscope.

Contamination prevention

All the equipment and workspaces were thoroughly cleaned and checked for contamination prior to use. Procedural blanks were included in each batch of samples to monitor potential contamination during the extraction process.

Reproducibility

All experiments were conducted in triplicate to ensure the reproducibility of the results. Inter- and intra-assay variability was calculated to assess the consistency of the methods.

Results

Demographics and clinical characteristics of patients

The analysis of patient demographics and clinical characteristics is presented in Table 1 and S1. The average age of the patients was 69.9 years, with a standard deviation of 9.07 years. The mean BMI is 23.97 kg/cm^2 (BMI, Body Mass Index). Some studies have found a correlation between body mass index BMI and disease prevalence[12,13]. The patient's average carcinoembryonic antigen (CEA) level is 41.04 µg/L, and the average carbohydrate antigen 19-9 (CA19-9) level were 64.67 U/mL. These two indicators are closely related to colorectal cancer[14]. Half of the patients experienced rectal bleeding, the majority of patients (70%) had a pathological stage of pT3 or higher, and 40% of the patients had tumor metastasis. The analysis revealed that most patients frequently consumed bottled water (90%, 9 10) and had a habit of eating takeout food (80%, 8 10).

Characteristics of MPs in para-tumor and tumor tissues of human colorectal cancer were detected using LDIR and SEM

The results revealed distinct differences in the morphology and distribution of MPs between the two tissue types. These findings provide valuable insights into the role of MPs in the progression of colorectal cancer and may have implications for future diagnostic and therapeutic strategies.

We collected postoperative specimens encompassing both adjacent and tumor tissues from 10 colorectal cancer patients at Tianjin Medical University Cancer Hospital. Twenty samples were analyzed using SEM and the LDIR imaging system. The experimental steps are shown in Fig. 1a. The examination of patient V's samples, selected randomly, showed the size, composition, and quantity of various microplastics (MPs) in both adjacent and tumor tissues (Fig. 1b and c). The data indicated a notable presence of MPs in both types of tissues, with significant variations in their levels. We referred to previous research and classified the size of microplastics[15]. Further analysis of patients III and X showed that within the 0–30 µm size range, the percentage of MPs was notably higher in tumor tissues than in adjacent tissues (Fig. 1d and e). Figure 1f presents a comparison of particle diameters from five randomly selected patients, indicating that the MP diameters in both tissue types were predominantly below 100 µm. Additionally, there was a marked difference in the plastic content between the tumor and adjacent tissues.A comparison of MP content per gram of tissue for these five patients revealed distinct differences among tissue types (Fig. 1g). Additionally, we have selected the detection conditions for the tissues of patient III, as shown in Fig. S1.

Furthermore, an examination was conducted on the common microplastics found in the specimens from patients I and X, with the results being illustrated in Fig. 1h and i. The findings revealed that the MPs in these specimens were primarily concentrated below 100 µm, as shown in Table 2.The analysis of the remaining patients is shown in Table S2-S10. In summary, these results confirmed the presence of MPs in both tumors and adjacent tissues in patients with CRC.

Subsequently, electron microscopy imaging was performed on the MPs detected in 20 samples, with five randomly selected pairs of tumor and adjacent tissue images. These electron microscopy images matched the LDIR scanning images, and the results are shown in Fig. 2. Our analysis identified PP, PE, PVC, and PET in both the tumor and adjacent tissues (Fig. 2a–e), showing various morphologies, including particles, fibers, irregular shapes, and varying degrees of folding and fracturing (Fig. 2a and e).

Characteristics	Categories	Values
Gender	Male	8(80)
	Female	2(20)
Age(years)	NA	69.9 ± 9.07
BMI(kg/cm²)	NA	23.97 ± 2.47
CEA(μg/L)	NA	41.04 ± 105.33
CA19-9(U/mL)	NA	64.67 ± 141.64
Hematochezia, n(%)	Yes	5(50)
	No	5(50)
PDS, n(%)	pT1	2(20)
	pT2	1(10)
	pT3	4(40)
	pT4	3(30)
Metastasis, n(%)	Yes	4(40)
	No	6(60)
Differentiation status, n(%)	Well	1(10)
	Moderately	6(60)
	Poorly	3(30)
Smoking status, n(%)	Yes	3(30)
	No	7(70)
Drinking status, n(%)	Yes	5(50)
	No	5(50)
FDBW, n(%)	Never	1(10)
	1–3days/week	3(30)
	≥ 4days/week	6(60)
FTOC, n(%)	Never	2(20)
	1–3days/week	5(50)
	≥ 4days/week	3(30)

Table 1. Demographic and clinical characteristics of 10 patients. BMI: body mass index; CEA: carcinoembryonic antigen; CA19-9: carbohydrate antigen199; PDS: pathological diagnosis staging; FDBW: frequency of drinking bottled water; FTOC: frequency of take-out food consumption.

Distribution of common food-grade MPs in para-tumor and tumor tissues of human colorectal cancer

An increasing body of research has revealed that plastic particles can enter the human body through food, drinking water, and air, potentially accumulating in the digestive tract, lungs, and even bloodstream[16–19]. Building on this knowledge, we conducted an in-depth analysis to examine the presence of food-grade microplastics, specifically polyethylene (PE), polyethylene terephthalate (PET), polypropylene (PP), polystyrene (PS), and polyvinyl chloride (PVC), in both tumors and adjacent tissues from 10 colorectal cancer patients. Our findings revealed that food-grade MPs were detectable in all patient samples, with both the tumor and adjacent tissues showing the presence of these plastic particles (Fig. 3a). A detailed statistical analysis of all detected microplastics showed that PVC was the most prevalent, which may be attributed to the regular intake of bottled water, a known source of plastic contamination. Notably, a significant difference was observed in the concentration of plastic particles between tumor tissues and adjacent non-tumor tissues (Fig. 3b), suggesting a potential relationship between microplastic accumulation and the tumor microenvironment. Figure 3c illustrates the percentage distribution of different types of food-grade microplastics across all samples, highlighting a particularly high concentration of PVC compared with other types of plastics.

In addition to these findings, a more granular mass analysis of individual plastic types (PP, PE, PVC, PS, and PET) demonstrated consistent results across all samples, with noticeable mass differences between tumor and adjacent tissues (Fig. 3d and h). Collectively, these data confirmed the presence of PE, PET, PP, PS, and PVC in both adjacent and tumor samples of human colorectal tissues, with an increased concentration of PVC in tumor tissues.

The correlation between MPs, demographic characteristics, and clinical characteristics of CRC patients

To gain a more comprehensive understanding of the interplay between microplastics (MPs) and patient characteristics, we stratified patients into distinct subgroups based on lifestyle habits, clinical parameters, and demographic information. Intriguingly, our analysis revealed that patients with CEA levels exceeding 5 μg/L had significantly higher levels of PP in their tumor-adjacent tissues than other subgroups ($p = 0.019$, paired t-test, Table 3). This finding suggests that specific tumor markers, such as elevated CEA, may be linked to increased MP accumulation in certain tissues. Similarly, patients with CA19-9 levels > 27 U/mL showed notable increases
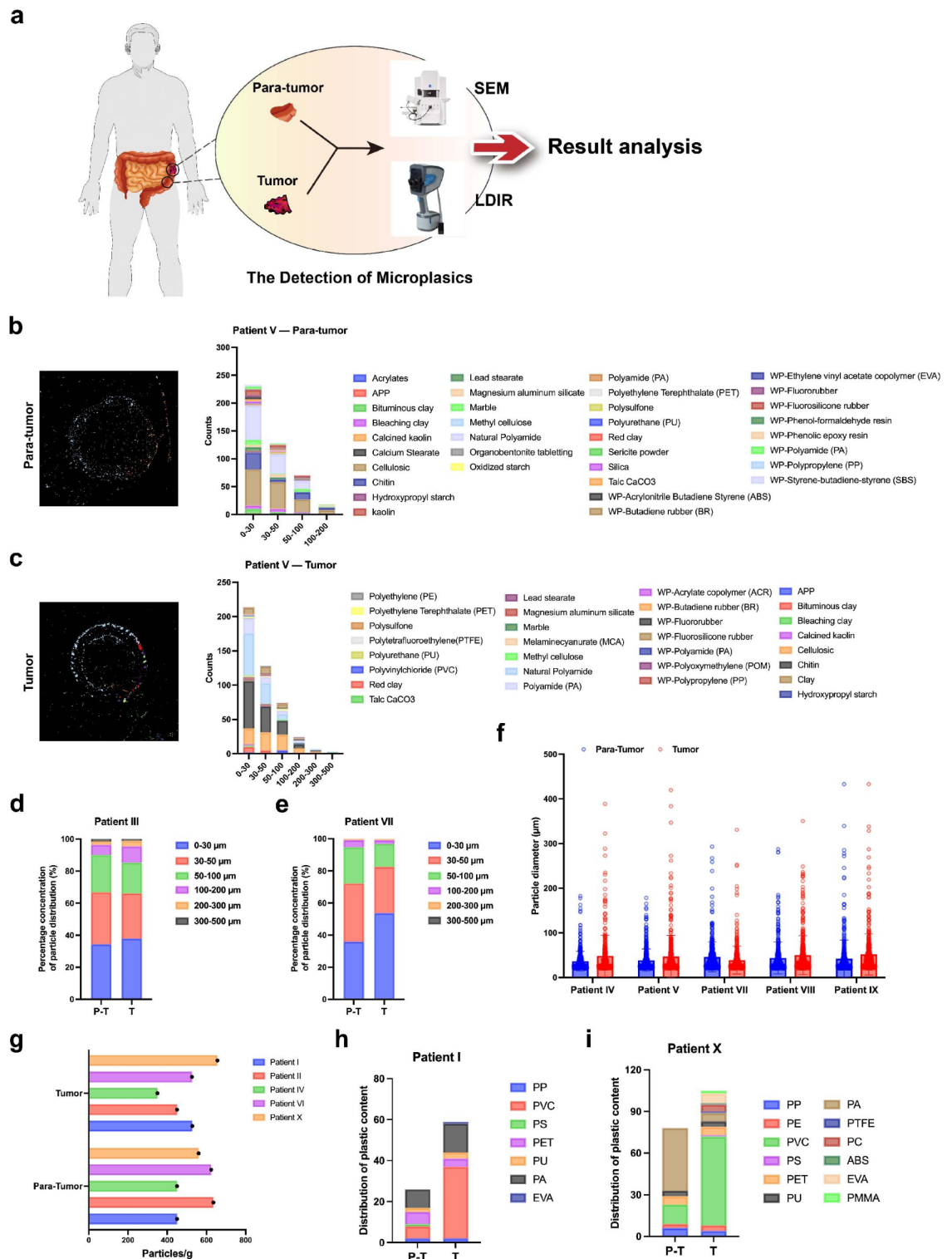
Fig. 1. The size and type of microplastics detected in the tumor and adjacent tissues of colorectal cancer patients using LDIR. (**A**) Schematic diagram of organization extraction and microplastic testing steps. (**B**,**C**). Distribution of microplastic sizes and contents across different types in tumor-adjacent (B) and tumor tissues (C) from patient samples. (**D**,**E**). Percentage distribution of microplastics by size in tumor-adjacent and tumor tissues in patients III (D) and VII (E). F. Statistical analysis of microplastic size across 20 samples. (**G**) Total amounts of microplastics in tumor and tumor-adjacent tissues from five randomly selected patients. (**H**,**I**). Distribution of common microplastics in tumor and tumor-adjacent tissues from patients I (H) and X (I). PT: para-tumor and T: tumor.

Order	Types of MPs	Equivalent diameter (μm)	No.		Total no.
1	Acrylonitrile Butadiene Styrene (ABS)	0–100	0		0
		100–500	0		
2	Acrylate copolymer (ACR)	0–100	0		0
		100–500	0		
3	Ethylene vinyl acetate copolymer (EVA)	0–100	1		1
		100–500	0		
4	Polyamide (PA)	0–100	14		14
		100–500	0		
5	Polycarbonate (PC)	0–100	0		0
		100–500	0		
6	Polyethylene (PE)	0–100	0		0
		100–500	0		
7	Polyethylene Terephthalate (PET)	0–100	4		4
		100–500	0		
8	Polypropylene (PP)	0–100	0		0
		100–500	0		
9	Polyurethane (PU)	0–100	3		3
		100–500	0		
10	Polyvinylchloride (PVC)	0–100	32		35
		100–500	3		
11	Polystyrene (PS)	0–100	0		0
		100–500	0		
12	Polytetrafluoroethylene (PTFE)	0–100	0		0
		100–500	0		
13	Polyoxymethylene (POM)	0–100	0		0
		100–500	0		
14	Polymethylmethacrylate (PMMA)	0–100	0		0
		100–500	0		
Summary	Total number of MPs types	7	Total number of microplastic particles		57

Table 2. Detecting the content of various MPs in tumor specimens of patient I using the LDIR method.

in PVC concentrations in both tumor and tumor-adjacent tissues ($p = 0.031$; $p = 0.002$, paired t-test, Table 3), indicating a potential association between this biomarker and PVC exposure.

Moreover, lifestyle factors appeared to influence MP content. Patients who reported consuming food takeout more than three times per week exhibited significantly higher PVC levels in their tumor tissues ($p = 0.0007$, paired t-test, Table 4). Conversely, no significant differences in MP content were observed between the tumor and adjacent tissues among the other subgroups, suggesting that certain clinical or lifestyle characteristics may uniquely contribute to variations in MP distribution (Tables 3 and 4).

To strengthen the clinical relevance of these findings, we further explored the correlation between different MPs and various demographic and clinical characteristics of the patients. As anticipated, there was a strong positive correlation between PVC levels and the frequency of takeout food consumption ($r = 0.73$, $p < 0.05$, Pearson's correlation analysis, Fig. 4a), emphasizing the role of dietary choices in MP exposure. Additionally, the consumption frequency of PVC and takeaway food was positively correlated ($r = 0.73$, $p < 0.05$, Pearson's correlation analysis, Fig. 4b). PVC levels were positively correlated with CEA, CA19-9, and PDS levels ($r = 0.66$, $p < 0.05$; $r = 0.76$, $p < 0.05$; $r = 0.85$, $p < 0.01$, Pearson's correlation analysis, Fig. 4c–e).

Collectively, these findings reveal a complex relationship between the presence of MPs in human colorectal cancer-adjacent and tumor tissues and specific patient characteristics, including biomarkers, lifestyle factors, and dietary habits.

Inhibition of the endocytosis-related protein Clathrin prevents colorectal cancer cells from taking up microplastics

Several studies have demonstrated that Clathrin Heavy Chain 1 (CLTC) in tumor cells plays a key role in regulating the endocytosis-related protein clathrin, significantly influencing the endocytic capacity[20,21]. As illustrated in Fig. 5a, the expression levels of CLTC varied across different tumor types, suggesting its involvement in diverse cancer pathways. Additionally, as shown in Fig. 5b, CLTC expression was closely associated with patient survival and prognosis, highlighting its potential as a prognostic marker in oncology.

Previously, researchers have found that endocytic proteins can affect cell uptake of microplastics[22,23], but there has been no research on the effects of endocytic proteins on colorectal cancer cells. To investigate whether CLTC influences the uptake of MPs by colorectal cancer cells, we conducted a series of in vitro experiments.
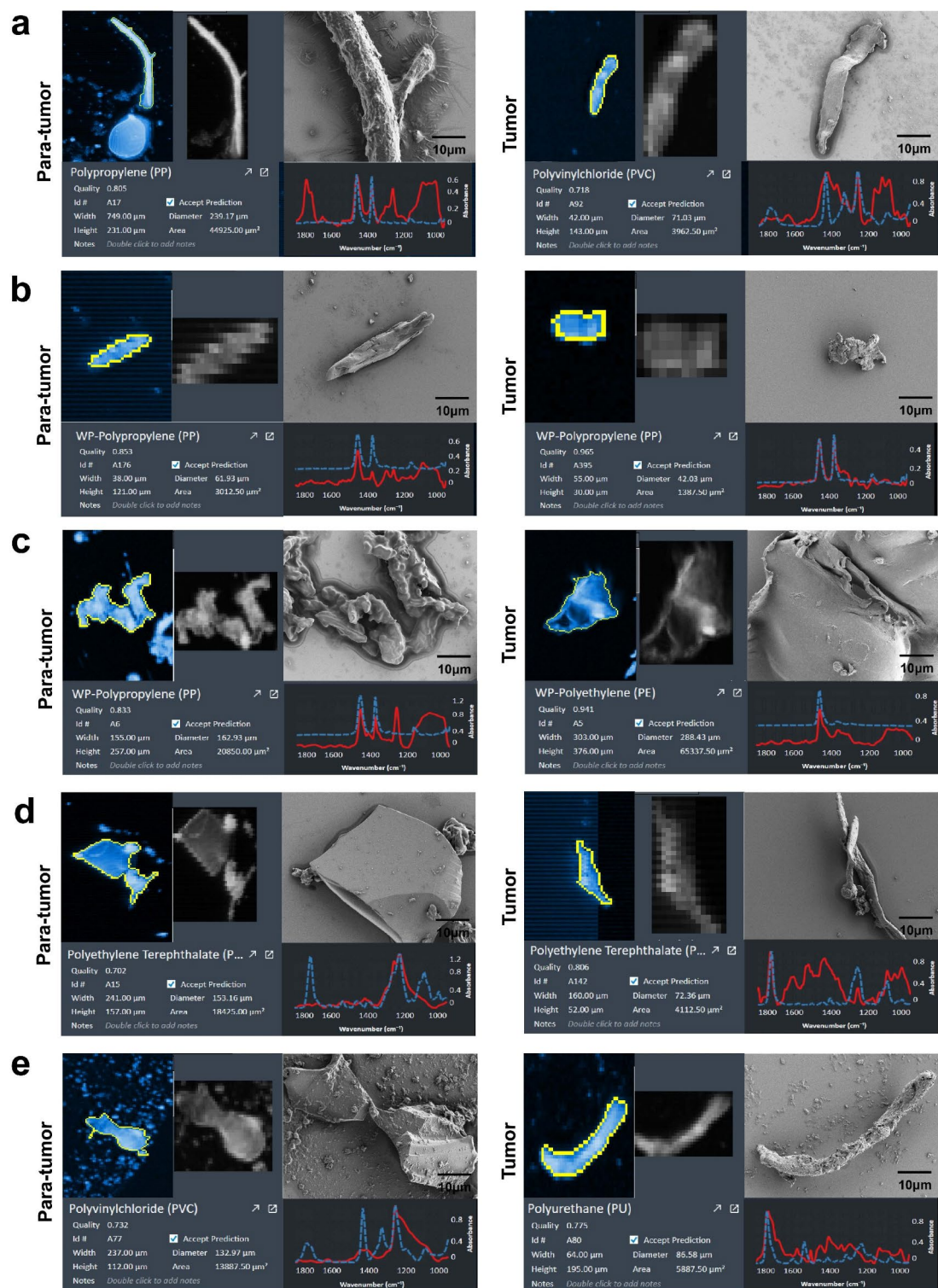
Fig. 2. Representative LDIR and SEM images of MP in adjacent and tumor tissues of human colorectal cancer. (**A–E**) PP (A–C), PVC (A, E), PE (C), PET (D), and PU (E) were detected in colon cancer tumors and adjacent tissues, showcasing various forms of microplastics, including particles, fibers, irregular shapes, and varying degrees of folding and breaking. PP, Polypropylene; PVC: Polyvinylchloride; PE: Polyethylene; PET: Polyethylene Terephthalate; PU: Polyurethane.
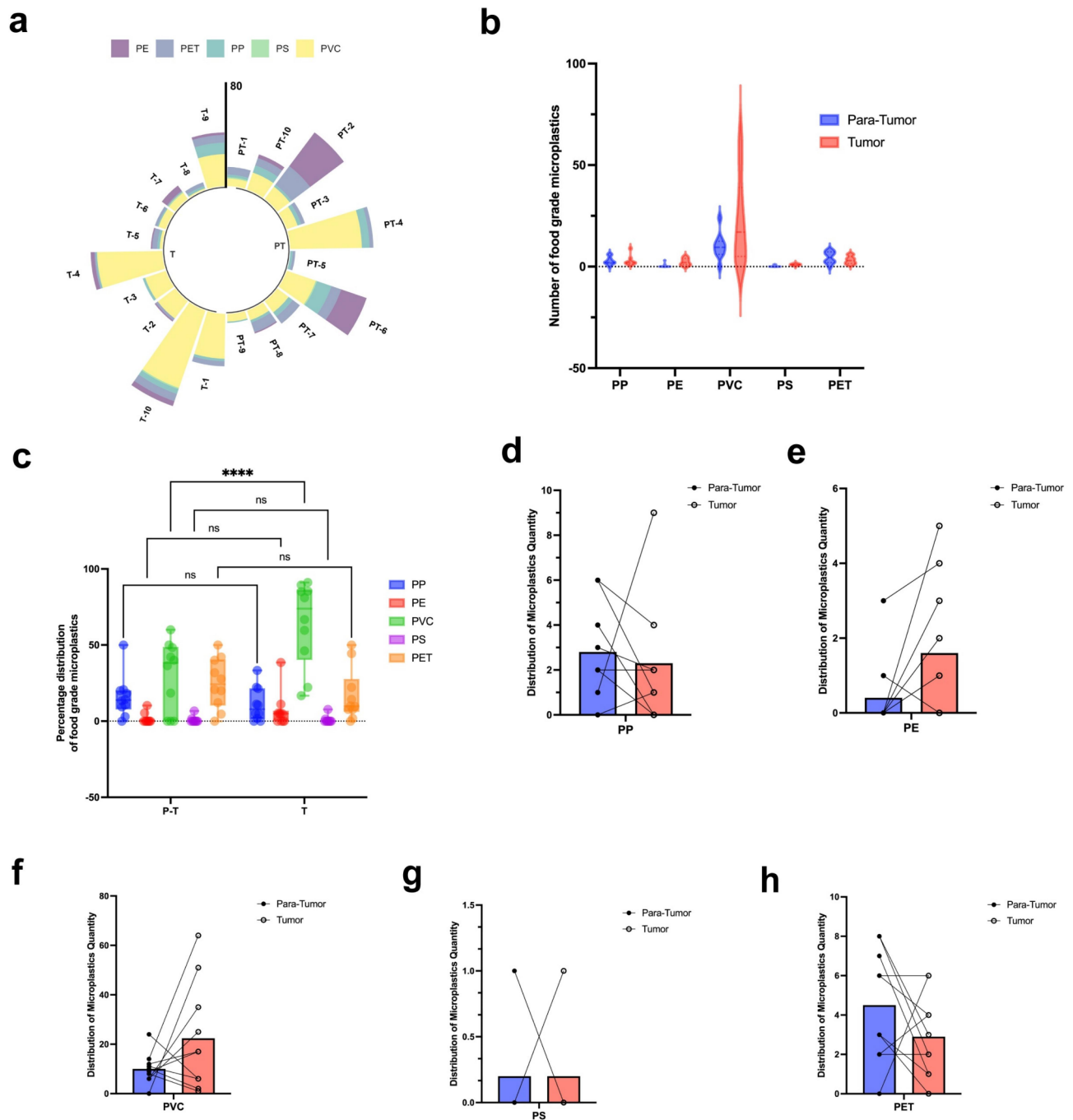
Fig. 3. The comparative analysis of MP content in adjacent and tumor tissues of human colorectal cancer. (**A**) Distribution of various food-grade microplastics in human colorectal tumor and adjacent tissues. (**B**) Comparison of the amounts of PP, PE, PVC, PS, and PET across 20 tumor-adjacent and tumor tissue samples. (**C**) Percentage comparison of different types of food-grade microplastics between tumor and tumor-adjacent tissues. (**D–H**) Detailed distribution of PP (D), PE (E), PVC (F), PS (G), and PET (H) in each pair of tumor-adjacent and tumor tissue samples. PT: para-tumor; T: tumor. $**p < 0.01$, $***p < 0.001$, $****p < 0.0001$ and data are analyzed by paired t test. PP, polypropylene; PE, polyethylene; PVC, polyvinyl chloride; PS, polystyrene; PET: Polyethylene Terephthalate.

We used viral vectors to knock down CLTC in the colorectal cancer cell lines HCT116 and LOVO, and cultured these cells in the presence of microplastics. We validated the efficiency of knocking out CLTC using Western blot (Fig. 5c). Previous studies have shown that intestinal cells have a certain uptake effect on microplastics[24,25]. Research has found that smaller sized microplastics are easily ingested, so we chose microplastics with a diameter of 80 nm to treat cells[24,26,27]. After a 48-hour incubation period, we assessed the capacity of the cells to internalize microplastics. Fluorescence microscopy analysis revealed that in both HCT116 (Fig. 5d) and LOVO (Fig. 5e)

MPs (/g)	CEA(µg/L)			CA19-9(U/mL)			PDS		
	≤5 (n=6)	>5 (n=4)	p	≤27(n=8)	>27(n=2)	p	≤ pT2c(n=3)	> pT2c (n=7)	p
PP-PT	13	27	0.019*	28	12	0.368	8	32	0.435
PE-PT	34	24	0.967	55	3	0.587	1	57	0.358
PVC-PT	43	103	0.063	76	70	0.031*	19	127	0.307
PS-PT	1	1	0.779	2	0	0.486	0	2	0.356
PET-PT	41	20	0.599	52	9	0.64	17	44	0.869
PP-T	15	8	0.787	18	5	0.912	4	19	0.479
PE-T	9	7	0.847	9	7	0.103	6	10	0.679
PVC-T	86	138	0.157	109	115	0.002**	9	215	0.055
PS-T	0	2	0.06	1	1	0.286	0	2	0.356
PET-T	20	9	0.452	22	7	0.675	8	21	0.832

Table 3. The comparison of MPs contents based on the frequency of CEA, CA19-9 and PDS among 10 patients. PT: para-tumor; T: tumor; PP: Polypropylene; PE: polythene; PVC: polyvinyl chloride; PS: polystyrene; PET: Polyethylene Terephthalate; CEA: carcinoembryonic antigen; CA19-9: Carbohydrate antigen199; PDS: Pathological diagnosis staging; Significant correlations are highlighted in asterisk. Data are analyzed by paired t test.

MPs (/g)	FDBW(days/week)			FTOC(days/week)		
	≤3 (n=4)	>3 (n=6)	p	≤3 (n=7)	>3 (n=3)	p
PP-PT	11	29	0.358	22	14	0.701
PE-PT	0	58	0.130	55	3	0.178
PVC-PT	26	120	0.355	70	76	0.243
PS-PT	1	1	>0.999	1	1	>0.999
PET-PT	18	43	0.220	46	15	0.466
PP-T	6	17	0.511	16	7	0.688
PE-T	6	10	0.765	9	7	0.438
PVC-T	60	164	0.407	64	150	0.0007***
PS-T	1	1	>0.999	1	1	>0.999
PET-T	9	20	0.825	18	11	0.655

Table 4. The comparison of MPs contents based on the frequency of CEA, CA19-9 and PDS among 10 patients. PT: para-tumor; T: tumor; PP: Polypropylene; PE: polythene; PVC: polyvinyl chloride; PS: polystyrene; PET: Polyethylene Terephthalate; FDBW: frequency of drinking bottled water; FTOC: frequency of take-out food consumption. Significant correlations are highlighted in asterisk. Data are analyzed by paired t test.

cells, the siCLTC-treated cells exhibited a significantly reduced ability to uptake microplastics compared to wild-type and siNC (negative control) cells. These findings suggest that CLTC plays a critical role in the internalization of microplastics by colorectal cancer cells, further supporting its role in endocytosis.

Discussion

This study identified microplastics (MPs) in both peritumoral and tumor tissues of colorectal cancer patients, highlighting their accumulation in the human body, especially in cancerous environments. The notable presence of MPs in both tissues raises questions regarding the role of environmental pollutants in cancer development.

Our findings confirm a different concentration of MPs in tumor tissues compared to adjacent peritumoral tissues, consistent with previous research showing MP accumulation in human organs, such as the lungs and liver[28–30]. This suggests that MPs may contribute to or be retained in the tumor environment, potentially triggering inflammation, oxidative stress, and immune dysregulation, all of which are linked to cancer progression[31–34]. Further studies are needed to determine whether this accumulation causes or results from cancer. Characterization of MPs using LDIR and SEM showed that most MPs were smaller than 100 µm and consisted of PE, PVC, and PET. Their small size allows penetration into cells, potentially disrupting their function, signaling, or inducing genotoxic effects[28,35]. MPs with rough surfaces may increase cell interactions, triggering chronic inflammation linked to colorectal cancer, promoting mutations, and fostering tumor growth[36].

The correlation between MPs levels and lifestyle factors, such as takeout food and bottled water consumption, is consistent with research showing that single-use plastics are a major source of human MP exposure. MPs can leach from packaging into food and drinks, especially with heat or prolonged storage. The higher MP levels in patients with more frequent takeout and bottled water use suggest that dietary exposure may contribute to disease development over time.
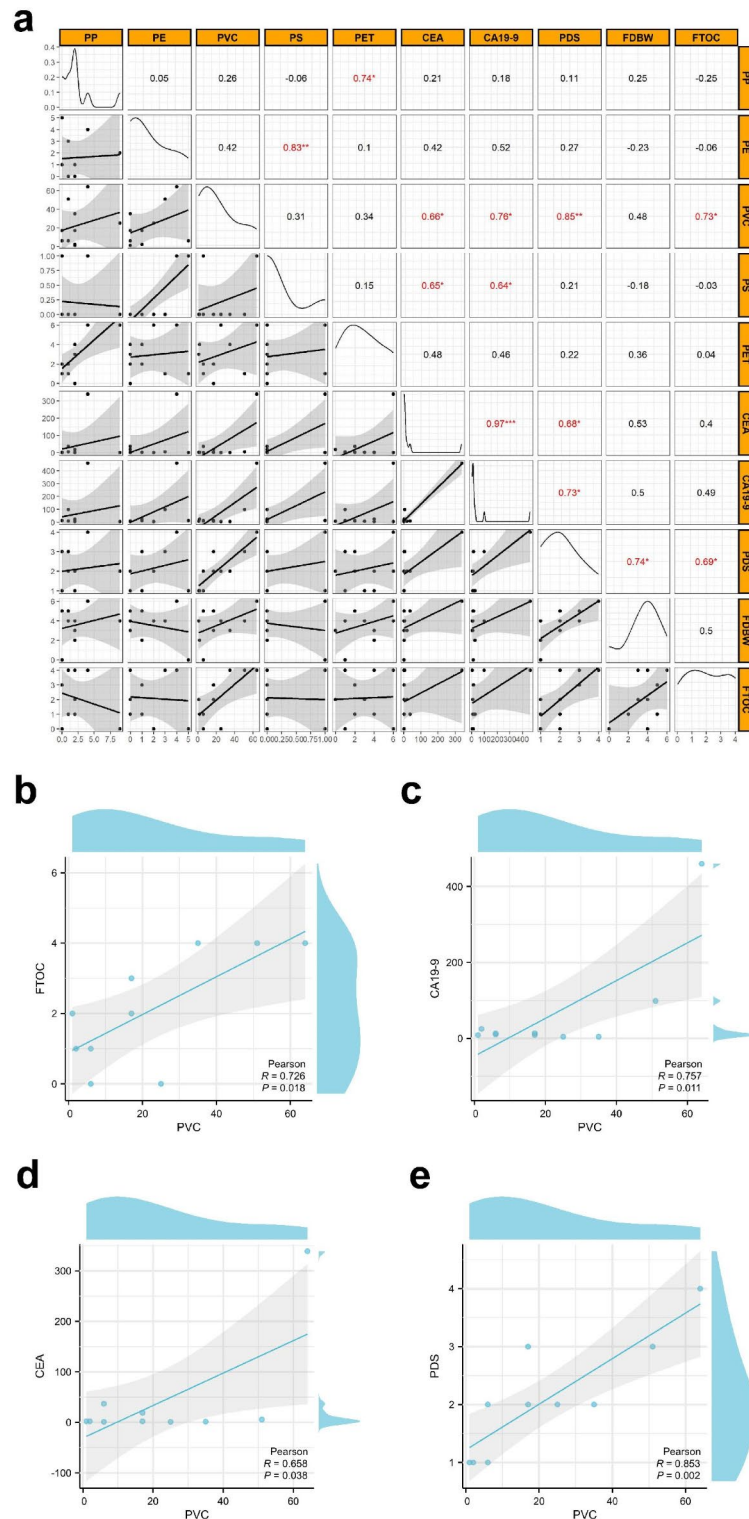
Fig. 4. Relationships between microplastic (MP) concentrations and patients' clinical characteristics. (**A**) Diagonal plots show the data distribution in logarithmic ratios; lower plots present scatter plots of the data, and upper plots display the correlation coefficients (r). The significant correlations are highlighted in red. (**B–E**). Correlation between PVC and clinical characteristics of CA19-9 (C), CEA (D), PDS (E), and lifestyle habits (B) in patients. $*p < 0.05$; $**p < 0.01$; $***p < 0.001$ and data are analyzed by Pearson's correlation analysis. PP, polypropylene; PE, polyethylene; PVC, polyvinyl chloride; PS, polystyrene; PET: Polyethylene Terephthalate. CEA, carcinoembryonic antigen; CA19-9: Carbohydrate antigen199; PDS: Pathological diagnosis staging; FDBW, frequency of drinking bottled water; FTOC, frequency of food intake.
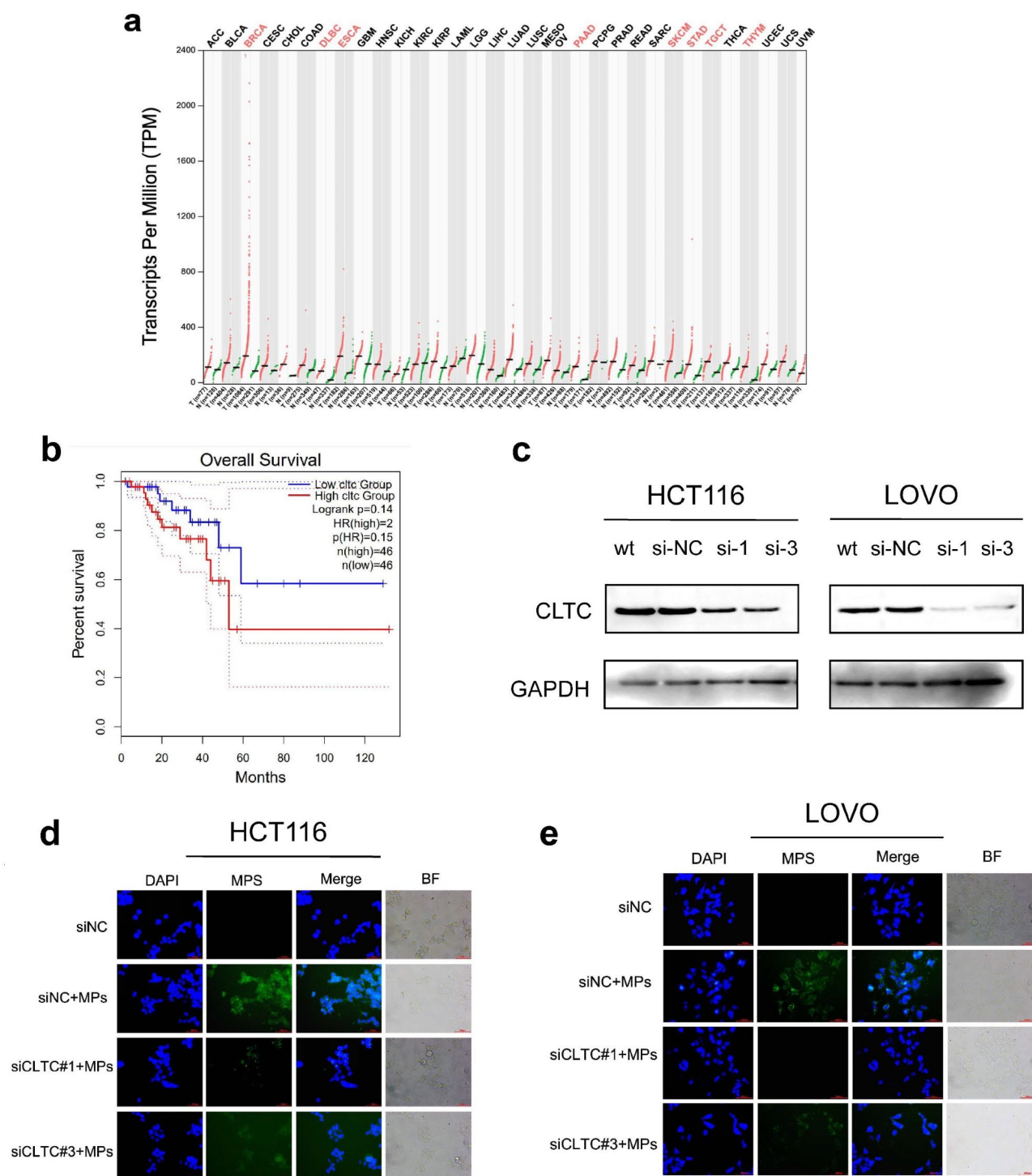
Fig. 5. Inhibition of Clatherin can prevent the uptake of microplastics by colorectal cancer cells. Expression of clatherin in different tumor types and adjacent tissues. B. Impact of clatherin on the survival rate of patients with colorectal cancer C-D. CLTC knockdown inhibits the uptake of microplastics by HCT116 (C) and LOVO (D) colon cancer cells.

The mechanisms by which MPs contribute to colorectal cancer remain unclear, but several hypotheses include acting as carriers for harmful substances such as heavy metals, inducing oxidative stress that leads to DNA damage, and causing immune dysregulation or chronic inflammation, all of which may promote tumor growth[37–40].

Future research should explore the molecular effects of MPs on gene expression, DNA damage, and cellular signaling in cancer cells. Additionally, investigating strategies to reduce MP exposure through lifestyle changes

or regulations could help mitigate the risks. In the future, we can also focus on the risks of microplastics to the human body and use some risk assessment models[41].

Conclusion

In conclusion, our study provides new evidence for the presence of MPs in both peritumoral and tumor tissues of colorectal cancer patients. The greater abundance of MPs in tumor tissues and their association with lifestyle factors, such as takeout food consumption and bottled water intake, underscore the need for heightened awareness of the potential impact of environmental pollutants on human health. Future research is crucial to elucidate the mechanisms by which MPs contribute to cancer development and to develop strategies for reducing human exposure to MPs.

Data availability

All data generated or analyzed during this study are included in this article or in the supplementary information files.

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Author contributions

Wen Pan, Jie Hao, Mingqing Zhang, and Hui Liu performed most of the experiments, analyzed the data, and wrote the manuscript. Fei Tian and Chong Chen performed some experiments, collected clinical samples, and recorded patient information. Haiyang Zhang, Ming Gao and Xipeng Zhang designed the experiments and edited the manuscript. All authors have reviewed the manuscript. Haiyang Zhang is the guarantor of this work, has full access to all data in the study, and takes responsibility for the integrity of the data and accuracy of the data analysis.

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Declarations

Competing interests

The authors declare no competing interests.

Ethical approval

All experiments were performed in accordance with relevant guidelines and regulations. All patients provided informed consent, and the Ethics Committee of the Tianjin Union Medical Center of Nankai University approved all aspects of this study (approval number: GZR2024035).

Additional information

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