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| **Supplementary Table 1.** Baseline characteristics  |  |
| **Variables** | **Control group (n=158)** | **Colorectal cancer group (n=70)** | **\**p* value** |
| Age (years) | 52.5 ± 8.5 | 63.1 ± 9.1 | <0.001 |
| Male  | 28 (17.7%) | 46 (65.7%) | <0.001 |
| Smoking history | 5 (3.2%) | 34 (50.0%) | <0.001 |
| Alcohol history | 52 (32.9%) | 33 (49.3%) | 0.031 |
| Body mass index (kg/m2) | 25.9 ± 3.5 | 24.0 ± 3.8 | 0.001 |
| Variables are expressed as mean ± SD or n (%). |  |  |
| \**p* value for comparing control group with colorectal cancer group. |  |

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| **Supplementary table 2**. Taxa showing a significant different abundance between late CRC with early CRC in the gut microbiota. |
| Taxon | t-statistic | Unadjusted *p* value | Adjusted *p* value |
| Phylum Bacteriodetes | 　 | 　 |  |
|  Family *Marinifilaceae* | 2.42  | 0.039  | 0.562  |
|  Genus *Odoribacter* | 2.42  | 0.039  | 0.779  |
|  Family *Rikenellaceae* | 2.81  | 0.037  | 0.550  |
|  Genus *Alistipes* | 2.81  | 0.037  | 0.779  |
|  Family *Prevotellaceae* | -2.68  | 0.039  | 0.562  |
|  Genus *Prevotella 9* | -2.68  | 0.039  | 0.562  |
| Phylum Firmicutes |  |  |  |
|  Family *Ruminococcaceae* |  |  |  |
|  Genus *Butyricicoccus* | -2.33  | 0.039  | 0.779  |
| The change of column (log2 fold) represents the multiplicative change in taxa abundance from late CRC to early CRC group.  |
| Negative numbers represent a trend of decreasing abundance in late CRC group compared with early CRC group. |

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| **Supplementary table 3.** Taxa showing a significant different abundance between late CRC with early CRC in the gut microbe-derived extracellular vesicles.  |
| Taxon | t-statistic | Unadjusted *p* value | Adjusted *p* value |
| Phylum Bacteriodetes | 　 | 　 |  |
|  Family *Rikenellaceae* | 3.15  | 0.024  | 0.322  |
|  Genus *Alistipes* | 3.15  | 0.024  | 0.529  |
| Phylum Firmicutes |  |  |  |
|  Family *Erysipelotrichaceae* | -2.98  | 0.010  | 0.165  |
|  Family *Lactobacillaceae* | -3.63  | 0.011  | 0.176  |
|  Genus *Lactobacillus* | -3.63  | 0.011  | 0.303  |
|  Family *Acidaminococcaceae* | 2.76  | 0.048  | 0.550  |
|  Genus *Phascolarctobacterium* | 2.76  | 0.048  | 0.762  |
| The change of column (log2 fold) represents the multiplicative change in taxa abundance from late CRC to early CRC group.  |
| Negative numbers represent a trend of decreasing abundance in late CRC group compared with early CRC group. |

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| **Supplementary table 4.** Taxa showing a significant different abundance between distal CRC with proximal CRC in the gut microbe-derived extracellular vesicles.  |
| Taxon | t-statistic | Unadjusted *p* value | Adjusted *p* value |
| Phylum Firmicutes | 　 | 　 | 　 |
|  Family *Ruminococcaceae* |  |  |  |
|  Genus *Ruminococcus 2* | -2.68  | 0.016  | 0.433  |
| The change of column (log2 fold) represents the multiplicative change in taxa abundance from distal CRC to proximal CRC group.  |
| Negative numbers represent a trend of decreasing abundance in distal CRC group compared with proximal CRC group. |