**Electronic Supplementary Material**

Sensitive Potential Prognostic Markers for Colorectal Cancer Surgery Screened by UPLC-Q-TOF-MS Combined with Metabolomics Technology: UDP-D-galactose

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Figure S1. Representative TIC chromatograms of (a) ESI+, control group (b) ESI+, CRC group (c) ESI-, control group (d) ESI-, CRC group of plasma samples.



Figure S2. Results of the metabolites of the plasma samples from 0 to 13 min, (a) ESI+, PCA score plot; (b) ESI+, PCA variable loading plot; (c) ESI+, OPLS-DA score plot; (d) ESI+, OPLS-DA variable importance in the projection plot.(e) ESI-, PCA score plot; (f) ESI-, PCA variable loading plot; (g) ESI-, OPLS-DA score plot; (h) ESI-, OPLS-DA variable importance in the projection plot.



Figure S3. Representative TIC chromatograms of (a) ESI+, control group (b) ESI+, CRC group (c) ESI-, control group (d) ESI-, CRC group of tissue samples.



Figure S4. Results of the metabolites of the tissue samples from 0 to 13 min, (a) ESI+, PCA score plot; (b) ESI+, PCA variable loading plot; (c) ESI+, OPLS-DA score plot; (d) ESI+, OPLS-DA variable importance in the projection plot.(e) ESI-, PCA score plot; (f) ESI-, PCA variable loading plot; (g) ESI-, OPLS-DA score plot; (h) ESI-, OPLS-DA variable importance in the projection plot.

Table S1. Relative concentrations of the metabolites in control, preoperative and CRC patients group measured by MassLynx

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| No. | Identified metabolites | Control group | Preoperative group | Postoperative group | *p* valuea | |
| Positive ion mode | | | | | | |
| 1 | Cysteine-S-sulfate | 25.8787 | 0.0020 | 0.0027 | 0.554 | |
| 2 | Prolyl-Arginine | 10.7284 | 0.0007 | 0.0004 | 0.408 | |
| 3 | TG(22:2(13Z,16Z)/18:2(9Z,12Z)/22:2(13Z,16Z)) | 204.1430 | 0.0087 | 0 | 0.328 | |
| 4 | (3-Nitroamino)alanine | 0.0081 | 25.3943 | 24.7309 | 0.910 | |
| 5 | Dihydrobiopterin | 11.3718 | 0.0494 | 0.0117 | 0.170 | |
| 6 | Aspartyl-Tryptophan | 1.3927 | 0.0316 | 0.0656 | 0.927 | |
| Negative ion mode | | | | | | |
| 7 | 7-Methylguanosine 5'-phosphate | 25.2951 | 0.2439 | 0.3578 | 0.852 |
| 8 | CDP-glycerol | 0 | 20.6762 | 21.2758 | 0.617 |
| 9 | DTDP-alpha-D-glucose(2-) | 46.9926 | 341.3774 | 367.4627 | 0.059 |
| 10 | CDP-glucose | 6.0673 | 94.3779 | 96.9996 | 0.188 |
| 11 | Caffeoyl aspartic acid | 0.5945 | 47.4157 | 56.6720 | 0.427 |
| 12 | 6-Mercaptopurine ribonucleoside triphosphate | 41.4453 | 0.3047 | 0.2043 | 0.760 |
| 13 | dTDP-D-glucose | 247.8531 | 7.8541 | 7.4517 | 0.480 |
| 14 | UDP-D-galactose | 213.5291 | 4.0342 | 9.2921 | 0.010\* |
| 15 | N-Gluconyl ethanolamine phosphate | 0.0544 | 42.4951 | 37.5443 | 0.555 |
| 16 | 6-Hydroxy-5-methoxyindole glucuronide | 61.7164 | 0 | 0 | - |
| 17 | Thioguanosine 5'-diphosphate | 164.5772 | 0.0145 | 0.0112 | 0.358 |

a *p* value was obtained from wilcoxon test between preoperative and postoperative group

Table S2. Markers selected indicated a difference between ESI+ and ESI- ion mode of plasm samples

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| No. | m/za | | Rt (min) | | VIP[1]b | | | *p* valuec | | | Formula | | Identified metabolites | | |
| Positive ion mode | | | |  | | |  | | |  | |  | |  |
| 1 | 201.2210 | | 3.13 | | 13.3191 | | | <0.0001 | | | C3H7NO5S2 | | Cysteine-S-sulfate | | |
| 2 | 271.3161 | | 4.31 | | 8.5782 | | | <0.0001 | | | C11H21N5O3 | | Prolyl-Arginine | | |
| 3 | 991.6210 | | 6.00 | | 36.1026 | | | <0.0001 | | | C65H114O6 | | TG(22:2(13Z,16Z)/18:2(9Z,12Z)/22:2(13Z,16Z)) | | |
| 4 | 149.1054 | | 6.03 | | 13.1070 | | | <0.0001 | | | C3H7N3O4 | | (3-Nitroamino)alanine | | |
| 5 | 239.2312 | | 8.30 | | 8.6113 | | | <0.0001 | | | C9H13N5O3 | | Dihydrobiopterin | | |
| 6 | 319.3126 | | 9.21 | | 12.2054 | | | <0.0001 | | | C15H17N3O5 | | Aspartyl-Tryptophan | | |
| Negative ion mode | |  | | | |  | | |  | | |  | |  |
| 7 | 378.2551 | | 4.73 | | 1.8775 | | | <0.0001 | | | C11H17N5O8P | | 7-Methylguanosine 5'-phosphate | | |
| 8 | 477.2550 | | 5.25 | | 1.7326 | | | <0.0001 | | | C12H21N3O13P2 | | CDP-glycerol | | |
| 9 | 564.3300 | | 5.30 | | 6.6807 | | | <0.0001 | | | C16H26N2O16P2 | | DTDP-alpha-D-glucose(2-) | | |
| 10 | 565.3170 | | 5.30 | | 3.6760 | | | <0.0001 | | | C15H25N3O16P2 | | CDP-glucose | | |
| 11 | 295.2448 | | 5.39 | | 2.3792 | | | <0.0001 | | | C13H13NO7 | | Caffeoyl aspartic acid | | |
| 12 | 524.2310 | | 5.40 | | 2.4810 | | | <0.0001 | | | C10H15N4O13P3S | | 6-Mercaptopurine ribonucleoside triphosphate | | |
| 13 | 564.3290 | | 5.52 | | 6.0846 | | | <0.0001 | | | C16H26N2O16P2 | | dTDP-D-glucose | | |
| 14 | 566.3018 | | 5.85 | | 2.5063 | | | <0.0001 | | | C15H24N2O17P2 | | UDP-D-galactose | | |
| 15 | 319.2030 | | 5.99 | | 2.2060 | | | <0.0001 | | | C8H18NO10P | | N-Gluconyl ethanolamine phosphate | | |
| 16 | 339.2974 | | 7.95 | | 3.00571 | | | <0.0001 | | | C15H17NO8 | | 6-Hydroxy-5-methoxyindole glucuronide | | |
| 17 | 459.2660 | | 8.8 | | 5.03227 | | | <0.0001 | | | C10H15N5O10P2S | | Thioguanosine 5'-diphosphate | | |

a m/z is available in the HMDB database

b variable importance in the projection (VIP) values were derived from OPLS-DA mode and its thresholds in positive mode and negative mode were 1.5 and 8.0, respectively.

c *p* value was obtained from wilcoxon test

Table S3. Markers selected indicated a difference between ESI+ and ESI- ion mode of tissue samples

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| No. | m/za | Rt (min) | VIP[1]b | *p* valuec | Formula | Identified metabolites | Average variationd |
| Positive ion mode | | | | | | | |
| 1 | 274.2737 | 3.45 | 6.7695 | 0.0444 | C10H18N4O5 | N2-Succinoylarginine | -0.3 |
| 2 | 454.2833 | 5.71 | 13.1266 | <0.0001 | C13H19N4O12P | SAICAR | 10.5 |
| 3 | 313.3032 | 5.72 | 8.9020 | <0.0001 | C14H19NO7 | Tyramine glucuronide | 9.9 |
| 4 | 498.3910 | 5.75 | 8.3513 | <0.0001 | C21H22O14 | Methyl 4,6-di-O-galloyl-beta-D-glucopyranoside | 7.2 |
| 5 | 993.6370 | 5.75 | 5.6034 | 0.0001 | C65H116O6 | TG(22:2(13Z,16Z)/22:0/18:3(9Z,12Z,15Z)) | 35.6 |
| 6 | 438.3285 | 6.04 | 24.9719 | <0.0001 | C17H19N4O8P | Riboflavin cyclic-4',5'-phosphate | 16.0 |
| 7 | 324.3072 | 6.64 | 6.7374 | <0.0001 | C13H25O7P | DHAP(10:0) | 885.1 |
| 8 | 341.3117 | 6.71 | 8.8588 | <0.0001 | C12H23NO10 | Lactosamine | 9.2 |
| 9 | 546.3137 | 7.01 | 11.0132 | <0.0001 | C16H24N2O15P2 | 4,6-Dideoxy-4-oxo-dTDP-D-glucose | 3.8 |
| 10 | 385.3041 | 7.10 | 6.7931 | <0.0001 | C13H24NO10P | Phosphatidylserine | -0.9 |
| 11 | 488.3240 | 7.32 | 9.2120 | <0.0001 | C14H26N4O11P2 | Citicoline | 6.3 |
| 12 | 329.2059 | 7.64 | 8.3142 | <0.0001 | C10H12N5O6P | Cyclic AMP | 9.4 |
| 13 | 425.3140 | 7.93 | 6.2400 | 0.0019 | C12H19N4O7P2S | Thiamine pyrophosphate | 0.6 |
| 14 | 263.2500 | 8.00 | 5.8273 | <0.0001 | C9H17N3O6 | Creatine riboside | 5.1 |
| 15 | 589.3815 | 8.29 | 7.8718 | <0.0001 | C18H29N3O15P2 | dTDP-4-acetamido-4,6-dideoxy-D-galactose | -1.0 |
| 16 | 545.4890 | 8.31 | 7.6496 | <0.0001 | C20H35NO16 | Lacto-N-triaose | -1.0 |
| 17 | 494.4007 | 8.52 | 10.1016 | <0.0001 | C19H26O15 | 2-O-Galloylsucrose | 13.9 |
| 18 | 809.5710 | 8.75 | 5.8453 | 0.0003 | C23H38N7O17P3S | Acetyl-CoA | 13.7 |
| 19 | 381.3325 | 9.13 | 5.5265 | <0.0001 | C14H23NO11 | N-Acetyl-9-O-lactoylneuraminic acid | 1.3 |
| Negative ion mode | | | | | | | |
| 20 | 329.2059 | 3.26 | 1.5473 | 0.0006 | C10H12N5O6P | Cyclic AMP | 92.3 |
| 21 | 331.2218 | 3.63 | 2.5418 | <0.0001 | C10H14N5O6P | Deoxyadenosine monophosphate | -0.7 |
| 22 | 295.2448 | 5.37 | 2.7523 | 0.0018 | C13H13NO7 | Caffeoyl aspartic acid | 2.4 |
| 23 | 452.3225 | 5.73 | 5.1433 | <0.0001 | C19H16O13 | 3,4-Hexahydroxydiphenoylarabinose | 1.3 |
| 24 | 947.6090 | 5.75 | 1.5327 | <0.0001 | C61H118O6 | TG(i-21:0/i-17:0/i-20:0) | 14.6 |
| 25 | 566.3018 | 6.04 | 1.6245 | 0.0002 | C15H24N2O17P2 | UDP-D-galactose | -0.5 |
| 26 | 488.3240 | 6.64 | 1.6333 | <0.0001 | C14H26N4O11P2 | Citicoline | 19.1 |
| 27 | 490.3618 | 7.51 | 1.6004 | <0.0001 | C16H23N6O10P | L-2-Aminoadipate adenylate | 14.0 |
| 28 | 283.2407 | 7.67 | 1.7570 | <0.0001 | C10H13N5O5 | Guanosine | 1.5 |
| 29 | 403.1764 | 7.87 | 1.9740 | 0.002 | C9H15N3O11P2 | CDP | 0.6 |
| 30 | 347.2212 | 8.03 | 1.5530 | <0.0001 | C10H14N5O7P | Adenosine monophosphate | -0.5 |
| 31 | 279.2454 | 8.04 | 2.2266 | <0.0001 | C13H13NO6 | N-[4'-hydroxy-(E)-cinnamoyl]-L-aspartic acid | 0.8 |
| 32 | 492.3864 | 8.55 | 2.5375 | <0.0001 | C22H20O13 | 6-Methoxyluteolin 7-glucuronide | 2.5 |
| 33 | 355.1709 | 8.67 | 3.1088 | 0.0006 | C14H14INO2 | 3-Iodothyronamine | -0.3 |
| 34 | 851.6070 | 8.80 | 2.0952 | <0.0001 | C10H19NO8 | N-(1-Deoxy-1-fructosyl)threonine | 1.3 |
| 35 | 851.5623 | 9.46 | 1.5512 | 0.0001 | C25H40N7O18P3S | Acetoacetyl-CoA | -0.9 |
| 36 | 852.6390 | 10.07 | 1.5049 | 0.0012 | C25H43N8O17P3S | L-3-Aminobutyryl-CoA | -0.9 |
| 37 | 588.9011 | 10.40 | 1.5456 | <0.0001 | C37H64O5 | DG | -0.7 |
| 38 | 118.0880 | 10.65 | 1.7724 | <0.0001 | C4H6O4 | Succinic acid | -0.8 |

a m/z is available in the HMDB database

b variable importance in the projection (VIP) values were derived from OPLS-DA mode and its thresholds in positive mode and negative mode were 1.5 and 5.5, respectively.

c *p* value was obtained from Wilcoxon test

d average variation was calculated as follows:  
Positive values indicated that the metabolite concentration in CRC group was relatively high to the control group. In a similar way that negative values indicated the metabolite concentration in CRC group was relatively low to the control group.