**Supplementary Information**

**Untargeted metabolomics reveals molecular effects of ketogenic diet on healthy and tumor xenograft mouse models**

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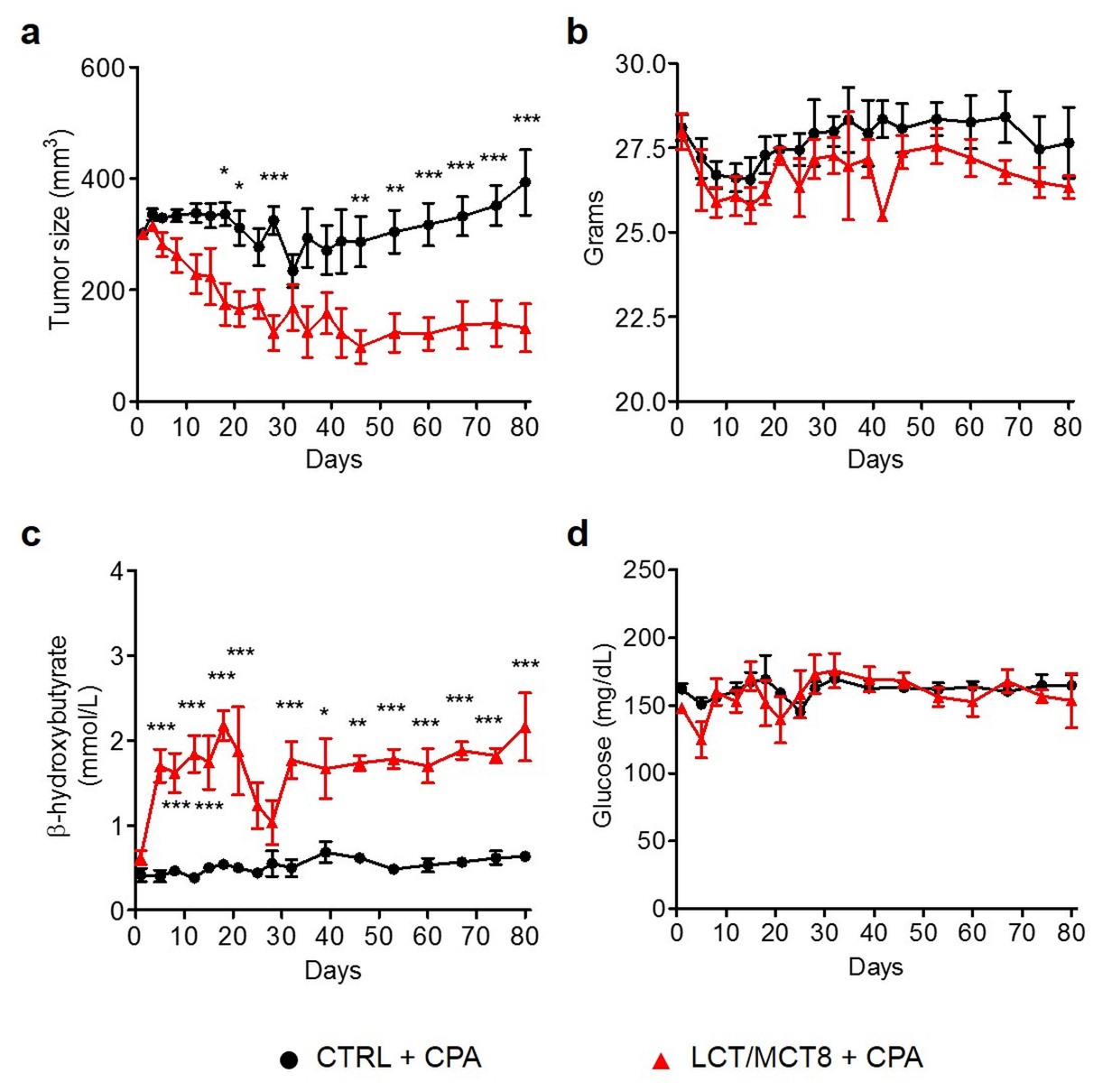
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**Supplementary figure S1.** Mean of the tumor size in MDA-MB-468 bearing mice under CTRL diet or LCT/MCT8 ketogenic diet (**a**). Average body weight variations in mice during dietary intervention (**b**). Average ketone bodies (mmol/L) (**c**) and blood glucose (mg/dL) levels (**d**) measured in blood of mice fed with the different diets.

Data are given as mean ± SEM. Statistical analysis was performed by using two-way ANOVA (Dunnett's multiple comparison test), \* *p* < 0.05, \*\* *p* < 0.01, \*\*\* *p* < 0.001; n = 5-6 mice.

**Supplementary table 1.** Composition and energy supply of the different diets.

|  |  |  |
| --- | --- | --- |
|  | CTRL | LCT/MCT8 |
| Crude Protein % | 16.1 | 8.1 |
| LCT %a | 7.1 | 49.6 |
| MCT8 %b | 0 | 25 |
| MCT10 %b | 0 | 0 |
| Sugar % | 6 | 1 |
| Starch % | 51.2 | 0 |
| Crude fiber % | 10 | 9.9 |
| Crude ash % | 4.5 | 4.4 |
| Energy Kcal | 3609 | 7098 |
|  | per Kg | per Kg |
| Vitamin A (IU/IE) | 15 | 15 |
| Vitamin D3 (IU/IE) | 1.5 | 1.5 |
| Vitamin E (mg) | 150 | 150 |
| Vitamin K3 (mg) | 20 | 20 |
| Vitamin C (mg) | 30 | 30 |
| Copper (mg) | 11 | 11 |

CTRL, control; MCT8, 8-carbon medium-chain triglyceride;

a LCT composition: butter fat 11.7% and pork lard 88.3%

b MCT8 composition: pure oil

**Supplementary table 2.** Settings of PeakPickerHiRes

|  |  |
| --- | --- |
| Parameter | Value |
| **PeakPickerHiRes** |  |
| version | 2.3.0 |
| processOption | inmemory |
| debug | 0 |
| threads | 1 |
| no\_progress | false |
| force | false |
| test | false |
| **algorithm** |  |
| signal\_to\_noise | 0.1 |
| spacing\_difference\_gap | 4.0 |
| spacing\_differnece | 1.5 |
| missing | 1 |
| ms\_levels | 1 |
| report\_FWHM | false |
| report\_FWHM\_unit | relative(ppm) |
| **SignalToNoise** |  |
| max\_intensity | -1 |
| auto\_max\_stdev\_factor | 3.0 |
| auto\_max\_percentile | 95 |
| auto\_mode | 0 |
| win\_len | 200.0 |
| bin\_count | 30 |
| min\_required\_elements | 10 |
| noise\_for\_empty\_window | 1.0E20 |
| write\_log\_messages | true |

**Supplementary table 3.** Settings of FeatureFinderMetabo

|  |  |
| --- | --- |
| Parameter | Value |
| **FeatureFinderMetabo** |  |
| version | 2.3.0 |
| debug | 0 |
| threads | 1 |
| no\_progress | false |
| force | false |
| test | false |
| **common** |  |
| noise\_threshold\_int | 3000.0 |
| chrom\_peak\_snr | 3.0 |
| chorm\_fwhm | 5.0 |
| **mtd** |  |
| mass\_error\_ppm | 5.0 |
| reestimate\_mt\_sd | true |
| quant\_method | area |
| trace\_termination\_criterion | outlier |
| trace\_termination\_outliers | 5 |
| min\_sample\_rate | 0.5 |
| min\_trace\_length | 0.25 |
| max\_trace\_length | -1.0 |
| **epd** |  |
| enabled | true |
| width\_filtering | fixed |
| min\_fwhm | 0.25 |
| max\_fwhm | 60.0 |
| masstrace\_snr\_filtering | false |
| **ffm** |  |
| local\_ret\_range | 10.0 |
| local\_mz\_range | 6.5 |
| charge\_lower\_bound | 1 |
| charge\_upper\_bound | 3 |
| report\_summed\_ints | false |
| enable\_rt\_filtering | true |
| isotope\_filtering\_model | metabolites (5% RMS) |
| mz\_scoring\_13c | false |
| use\_smoothed\_intensities | true |
| report\_convex\_hulls | true |

**Supplementary table 4.** Settings of FeatureLinkerUnlabeled QT

|  |  |
| --- | --- |
| Parameter | Value |
| **FeatureLinkerUnlabeledQT** | **Value** |
| version | 2.3.0 |
| keep\_subelements | false |
| debug | 0 |
| threads | 1 |
| no\_progress | true |
| force | false |
| test | false |
| **algorithm** |  |
| use\_identifications | false |
| nr\_partitions | 100 |
| ignore\_charge | false |
| **distance\_rt** |  |
| max\_difference | 10.0 |
| exponent | 1.0 |
| weight | 1.0 |
| **distance\_mz** |  |
| max\_difference | 5.0 |
| unit | ppm |
| exponent | 2.0 |
| weight | 1.0 |
| **distance\_intensity** |  |
| exponent | 1.0 |
| weight | 0.0 |

**Supplementary table 5.** Settings of TextExporter

|  |  |
| --- | --- |
| Parameter | Value |
| **TextExporter** |  |
| version | 2.1.0 |
| replacement | \_ |
| quoting | None |
| no\_ids | False |
| debug | 0 |
| threads | 1 |
| no\_progress | false |
| force | false |
| test | false |
| **feature** |  |
| minimal | false |
| add\_metavalues | -1 |
| **id** |  |
| proteins\_only | false |
| peptides\_only | false |
| first\_dim\_rt | false |
| add\_metavalues | -1 |
| add\_hit\_metavalues | -1 |
| **consensus** |  |
| sorting\_method | None |
| sort\_by\_maps | false |
| sort\_by\_size | false |

**Supplementary table 6.** Settings of R Snippets in KNIME workflow

|  |  |
| --- | --- |
| Parameter | Value |
| **Blank Filter\_1** |  |
| blankFilterPassed | 14 |
| **ConsensusMapNormalization** |  |
| ignoreColsPattern | Blank |
| method | mean |
| outlier | 0.68, 1/0.68 |
| verbose | TRUE |
| **Pool Filter/RSD Filter** |  |
| poolFilterCount | 7 |
| maxRSD | 25 |
| **Biological Replicate Filter** |  |
| numInConditions | 3 |
| numInReplicates | 4 |