**Metabolic reprogramming and dependencies associated with epithelial cancer stem cells uncoupled from epithelial-mesenchymal transition**

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**Supplemental Table 1**. Isotopologue distribution data of metabolites analyzed in PC-3M and PC-3S cells, after incubation with 50% [1,2-13C2]-glucose.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Metabolite** | **Cells** | **Tracer** | **Time (h)** | **m0 (%)** | | **m1 (%)** | | **m2 (%)** | | **m3 (%)** | | **m4 (%)** | | **m5 (%)** | | **m6 (%)** | | **Ʃm (%)** | | |
| **mean** | **SD** | **mean** | **SD** | **mean** | **SD** | **mean** | **SD** | **mean** | **SD** | **mean** | **SD** | **mean** | **SD** | **mean** | **SD** | |
| **Glucoseextra.** | PC-3M | 50% [1,2-13C2]-glucose | 0 | 53.37 | 0.28 | 0.23 | 0.06 | 45.99 | 0.12 | 0.35 | 0.09 | 0.06 | 0.09 | 0.00 | 0.14 | 0.00 | 0.05 | 46.63 | | 0.28 |
| PC-3S | 0 | 53.03 | 0.73 | 0.28 | 0.20 | 46.17 | 1.12 | 0.38 | 0.20 | 0.10 | 0.05 | 0.04 | 0.03 | 0.00 | 0.01 | 46.97 | | 0.73 |
| **Lactateextra.** | PC-3M | 50% [1,2-13C2]-glucose | 48 | 78.94 | 0.20 | 1.46 | 0.05 | 19.36 | 0.10 | 0.24 | 0.06 |  |  |  |  |  |  | 21.06 | | 1.83 |
| PC-3S | 48 | 79.92 | 0.85 | 0.69 | 0.34 | 19.30 | 0.43 | 0.08 | 0.08 |  |  |  |  |  |  | 20.08 | | 1.97 |
| **Palmitateintra.** | PC-3M | 50% [1,2-13C2]-glucose | 48 | 94.49 | 1.12 | 0.06 | 0.10 | 3.43 | 0.64 | 0.19 | 0.02 | 1.23 | 0.24 | 0.11 | 0.02 | 0.50 | 0.13 | 5.65 | | 0.99 |
| PC-3S | 48 | 92.18 | 0.22 | 0.00 | 0.00 | 5.02 | 0.08 | 0.18 | 0.05 | 1.96 | 0.05 | 0.08 | 0.02 | 0.59 | 0.06 | 7.91 | | 0.13 |
| **Stearateintra.** | PC-3M | 50% [1,2-13C2]-glucose | 24 | 98.11 | 0.47 | 0.00 | 0.00 | 1.86 | 0.30 | 0.05 | 0.05 | 0.52 | 0.13 | 0.39 | 0.07 | 0.28 | 0.08 | 3.25 | | 0.54 |
| PC-3S | 24 | 96.92 | 0.38 | 0.00 | 0.00 | 2.97 | 0.21 | 0.03 | 0.03 | 0.88 | 0.10 | 0.25 | 0.04 | 0.33 | 0.03 | 4.51 | | 0.32 |

Values are expressed as percentage of each isotopologue and denote mean and SD of n=3. Abbreviations: extra., extracellular; intra., intracellular.

**Supplemental Table 2**. Isotopologue distribution data of metabolites analyzed in PC-3M and PC-3S cells, after incubation with 100% [1,2-13C2]-glucose.

**A.** Isotopologue distribution data integrated in Isodyn.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Metabolite** | **Cells** | **Tracer** | **Time (h)** | **m0 (%)** | | **m1 (%)** | | **m2 (%)** | | **m3 (%)** | | **m4 (%)** | | **m5 (%)** | | **m6 (%)** | | **Ʃm (%)** | |
| **mean** | **SD** | **mean** | **SD** | **mean** | **SD** | **mean** | **SD** | **mean** | **SD** | **mean** | **SD** | **mean** | **SD** | **mean** | **SD** |
| **Glucoseextra.** | PC-3M / S | 100% [1,2-13C2]-glucose | 0 | 5.49 | 0.01 | 1.06 | 0.02 | 91.46 | 0.01 | 0.40 | 0.00 | 1.50 | 0.00 | 0.05 | 0.00 | 0.04 | 0.00 | 94.51 | 0.01 |
| **Lactateextra.** | PC-3M | 100% [1,2-13C2]-glucose | 24 | 66.66 | 0.18 | 1.61 | 0.01 | 31.18 | 0.17 | 0.54 | 0.00 |  |  |  |  |  |  | 33.34 | 0.18 |
| PC-3S | 24 | 67.62 | 0.18 | 1.51 | 0.01 | 30.52 | 0.16 | 0.35 | 0.00 |  |  |  |  |  |  | 32.38 | 0.18 |
| **Lactateextra.** | PC-3M | 100% [1,2-13C2]-glucose | 48 | 60.75 | 0.05 | 2.32 | 0.02 | 36.02 | 0.06 | 0.91 | 0.02 |  |  |  |  |  |  | 39.25 | 0.05 |
| PC-3S | 48 | 61.94 | 0.08 | 1.86 | 0.01 | 35.74 | 0.08 | 0.46 | 0.00 |  |  |  |  |  |  | 38.06 | 0.08 |
| **(Glu + Gln)extra.** | PC-3M | 100% [1,2-13C2]-glucose | 24 | 98.62 | 0.41 | 1.14 | 0.29 | 0.18 | 0.07 | 0.06 | 0.05 |  |  |  |  |  |  | 1.38 | 0.41 |
| **(C2-C4 fragment)** | PC-3S | 24 | 97.33 | 0.16 | 2.05 | 0.12 | 0.48 | 0.02 | 0.14 | 0.02 |  |  |  |  |  |  | 2.67 | 0.16 |
| **(Glu + Gln)extra.** | PC-3M | 100% [1,2-13C2]-glucose | 48 | 93.20 | 0.16 | 5.51 | 0.12 | 1.03 | 0.04 | 0.26 | 0.00 |  |  |  |  |  |  | 6.80 | 0.16 |
| **(C2-C4 fragment)** | PC-3S | 48 | 91.55 | 0.38 | 6.30 | 0.28 | 1.72 | 0.05 | 0.44 | 0.06 |  |  |  |  |  |  | 8.45 | 0.38 |
| **(Glu + Gln)extra.** | PC-3M | 100% [1,2-13C2]-glucose | 24 | 98.83 | 0.03 | 0.23 | 0.02 | 0.84 | 0.03 | 0.08 | 0.00 | 0.02 | 0.02 |  |  |  |  | 1.17 | 0.03 |
| **(C2-C5 fragment)** | PC-3S | 24 | 97.69 | 0.09 | 0.62 | 0.03 | 1.47 | 0.06 | 0.20 | 0.01 | 0.02 | 0.00 |  |  |  |  | 2.31 | 0.09 |
| **(Glu + Gln)extra.** | PC-3M | 100% [1,2-13C2]-glucose | 48 | 93.39 | 0.23 | 1.56 | 0.08 | 4.30 | 0.12 | 0.65 | 0.03 | 0.09 | 0.01 |  |  |  |  | 6.61 | 0.23 |
| **(C2-C5 fragment)** | PC-3S | 48 | 92.03 | 0.25 | 2.23 | 0.07 | 4.66 | 0.14 | 0.88 | 0.03 | 0.20 | 0.01 |  |  |  |  | 7.97 | 0.25 |
| **Alanineextra.** | PC-3M | 100% [1,2-13C2]-glucose | 24 | 79.85 | 0.31 | 0.26 | 0.20 | 19.89 | 0.32 | 0.00 | 0.00 |  |  |  |  |  |  | 20.15 | 0.31 |
| PC-3S | 24 | 82.54 | 0.67 | 0.12 | 0.11 | 17.34 | 0.59 | 0.00 | 0.00 |  |  |  |  |  |  | 17.46 | 0.67 |
| **Alanineextra.** | PC-3M | 100% [1,2-13C2]-glucose | 48 | 65.00 | 0.38 | 1.41 | 0.10 | 33.59 | 0.33 | 0.00 | 0.00 |  |  |  |  |  |  | 35.00 | 0.38 |
| PC-3S | 48 | 70.27 | 0.51 | 0.83 | 0.19 | 28.90 | 0.34 | 0.00 | 0.00 |  |  |  |  |  |  | 29.73 | 0.51 |
| **Glycineextra.** | PC-3M | 100% [1,2-13C2]-glucose | 24 | 99.27 | 0.07 | 0.73 | 0.06 | 0.00 | 0.01 |  |  |  |  |  |  |  |  | 0.73 | 0.07 |
| PC-3S | 24 | 99.06 | 0.15 | 0.94 | 0.15 | 0.00 | 0.00 |  |  |  |  |  |  |  |  | 0.94 | 0.15 |
| **Glycineextra.** | PC-3M | 100% [1,2-13C2]-glucose | 48 | 97.70 | 0.02 | 2.30 | 0.02 | 0.00 | 0.00 |  |  |  |  |  |  |  |  | 2.30 | 0.02 |
| PC-3S | 48 | 97.97 | 0.09 | 2.03 | 0.09 | 0.00 | 0.00 |  |  |  |  |  |  |  |  | 2.03 | 0.09 |
| **Serineextra.** | PC-3M | 100% [1,2-13C2]-glucose | 24 | 95.59 | 0.23 | 1.44 | 0.02 | 2.95 | 0.16 | 0.03 | 0.04 |  |  |  |  |  |  | 4.41 | 0.23 |
| PC-3S | 24 | 95.98 | 0.16 | 2.05 | 0.13 | 1.96 | 0.05 | 0.00 | 0.00 |  |  |  |  |  |  | 4.02 | 0.16 |
| **Serineextra.** | PC-3M | 100% [1,2-13C2]-glucose | 48 | 90.54 | 0.23 | 5.79 | 0.18 | 3.62 | 0.08 | 0.05 | 0.01 |  |  |  |  |  |  | 9.46 | 0.23 |
| PC-3S | 48 | 92.98 | 0.42 | 5.14 | 0.35 | 1.86 | 0.07 | 0.03 | 0.00 |  |  |  |  |  |  | 7.02 | 0.42 |
| **Prolineextra.** | PC-3M | 100% [1,2-13C2]-glucose | 24 | 99.59 | 0.53 | 0.09 | 0.12 | 0.22 | 0.32 | 0.05 | 0.07 | 0.00 | 0.00 | 0.00 | 0.00 |  |  | 0.41 | 0.53 |
| PC-3S | 24 | 99.97 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |  |  | 0.03 | 0.00 |
| **Prolineextra.** | PC-3M | 100% [1,2-13C2]-glucose | 48 | 98.63 | 0.10 | 0.00 | 0.00 | 1.34 | 0.10 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |  |  | 1.37 | 0.10 |
| PC-3S | 48 | 99.77 | 0.34 | 0.10 | 0.18 | 0.10 | 0.17 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |  |  | 0.23 | 0.34 |
| **Citrateintra.** | PC-3M | 100% [1,2-13C2]-glucose | 24 | 65.84 | 0.63 | 2.33 | 0.16 | 19.74 | 0.07 | 5.24 | 0.25 | 4.90 | 0.30 | 1.36 | 0.24 | 0.58 | 0.21 | 34.16 | 0.63 |
| PC-3S | 24 | 59.83 | 0.51 | 3.73 | 0.06 | 20.81 | 0.12 | 6.94 | 0.11 | 6.12 | 0.17 | 1.78 | 0.04 | 0.79 | 0.02 | 40.17 | 0.51 |
| **Citrateintra.** | PC-3M | 100% [1,2-13C2]-glucose | 48 | 51.98 | 0.09 | 4.04 | 0.10 | 24.42 | 0.03 | 8.26 | 0.00 | 7.83 | 0.15 | 2.39 | 0.05 | 1.07 | 0.02 | 48.02 | 0.09 |
| PC-3S | 48 | 51.26 | 0.74 | 4.62 | 0.04 | 23.49 | 0.34 | 8.75 | 0.12 | 8.04 | 0.19 | 2.65 | 0.08 | 1.19 | 0.03 | 48.74 | 0.74 |
| **(Glu + Gln)intra.** | PC-3M | 100% [1,2-13C2]-glucose | 24 | 91.35 | 0.35 | 0.92 | 0.04 | 5.38 | 0.19 | 1.25 | 0.07 | 0.93 | 0.04 | 0.17 | 0.01 |  |  | 8.65 | 0.35 |
| PC-3S | 24 | 81.36 | 0.34 | 3.00 | 0.05 | 9.88 | 0.15 | 3.08 | 0.07 | 2.18 | 0.06 | 0.50 | 0.01 |  |  | 18.64 | 0.34 |
| **(Glu + Gln)intra.** | PC-3M | 100% [1,2-13C2]-glucose | 48 | 80.49 | 0.83 | 2.86 | 0.17 | 10.41 | 0.36 | 3.30 | 0.17 | 2.38 | 0.11 | 0.55 | 0.03 |  |  | 19.51 | 0.83 |
| PC-3S | 48 | 76.38 | 0.51 | 3.78 | 0.11 | 11.88 | 0.23 | 4.18 | 0.09 | 3.02 | 0.07 | 0.77 | 0.02 |  |  | 23.62 | 0.51 |
| **Fumarateintra.** | PC-3M | 100% [1,2-13C2]-glucose | 24 | 92.54 | 1.54 | 1.44 | 0.64 | 4.54 | 0.54 | 0.74 | 0.26 | 0.74 | 0.32 |  |  |  |  | 7.46 | 1.54 |
| PC-3S | 24 | 84.51 | 2.19 | 3.62 | 0.59 | 8.73 | 0.92 | 2.15 | 0.80 | 0.98 | 0.16 |  |  |  |  | 15.49 | 2.19 |
| **Fumarateintra.** | PC-3M | 100% [1,2-13C2]-glucose | 48 | 87.96 | 3.20 | 0.20 | 0.28 | 10.00 | 1.55 | 1.08 | 1.16 | 0.75 | 0.21 |  |  |  |  | 12.04 | 3.20 |
| PC-3S | 48 | 85.50 | 2.35 | 0.94 | 0.30 | 9.93 | 1.66 | 2.36 | 0.42 | 1.28 | 0.17 |  |  |  |  | 14.50 | 2.35 |
| **Malateintra.** | PC-3M | 100% [1,2-13C2]-glucose | 24 | 90.79 | 0.24 | 1.47 | 0.08 | 5.61 | 0.09 | 1.38 | 0.04 | 0.74 | 0.04 |  |  |  |  | 9.21 | 0.24 |
| PC-3S | 24 | 81.90 | 0.29 | 3.98 | 0.04 | 9.55 | 0.18 | 3.05 | 0.05 | 1.52 | 0.04 |  |  |  |  | 18.10 | 0.29 |
| **Malateintra.** | PC-3M | 100% [1,2-13C2]-glucose | 48 | 79.02 | 0.86 | 4.03 | 0.28 | 11.58 | 0.40 | 3.59 | 0.14 | 1.78 | 0.04 |  |  |  |  | 20.98 | 0.86 |
| PC-3S | 48 | 77.20 | 0.39 | 4.80 | 0.10 | 11.91 | 0.17 | 4.03 | 0.07 | 2.06 | 0.09 |  |  |  |  | 22.80 | 0.39 |
| **Aspartateintra.** | PC-3M | 100% [1,2-13C2]-glucose | 24 | 89.22 | 2.61 | 2.41 | 1.48 | 5.78 | 0.50 | 1.74 | 0.53 | 0.85 | 0.12 |  |  |  |  | 10.78 | 2.61 |
| PC-3S | 24 | 81.57 | 0.25 | 4.14 | 0.00 | 9.59 | 0.17 | 3.17 | 0.05 | 1.53 | 0.03 |  |  |  |  | 18.43 | 0.25 |
| **Aspartateintra.** | PC-3M | 100% [1,2-13C2]-glucose | 48 | 77.96 | 3.14 | 4.80 | 0.99 | 10.64 | 0.96 | 4.40 | 0.65 | 2.20 | 0.54 |  |  |  |  | 22.04 | 3.14 |
| PC-3S | 48 | 77.56 | 0.04 | 4.79 | 0.15 | 11.45 | 0.07 | 4.16 | 0.02 | 2.05 | 0.12 |  |  |  |  | 22.44 | 0.04 |
| **Pyruvateintra.** | PC-3M | 100% [1,2-13C2]-glucose | 24 | 63.49 | 2.44 | 1.40 | 0.28 | 33.08 | 2.09 | 2.04 | 0.23 |  |  |  |  |  |  | 36.51 | 2.44 |
| PC-3S | 24 | 69.27 | 2.18 | 3.81 | 0.80 | 25.14 | 2.95 | 1.78 | 0.21 |  |  |  |  |  |  | 30.73 | 2.18 |
| **Pyruvateintra.** | PC-3M | 100% [1,2-13C2]-glucose | 48 | 63.67 | 0.89 | 3.16 | 0.19 | 30.76 | 0.48 | 2.41 | 0.21 |  |  |  |  |  |  | 36.33 | 0.89 |
| PC-3S | 48 | 65.97 | 3.19 | 4.12 | 1.82 | 27.79 | 5.13 | 2.12 | 0.20 |  |  |  |  |  |  | 34.03 | 3.19 |
| **Lactateintra.** | PC-3M | 100% [1,2-13C2]-glucose | 24 | 68.18 | 0.88 | 0.64 | 0.04 | 27.93 | 0.75 | 3.25 | 0.09 |  |  |  |  |  |  | 31.82 | 0.88 |
| PC-3S | 24 | 72.16 | 1.53 | 0.56 | 0.09 | 24.48 | 1.37 | 2.80 | 0.15 |  |  |  |  |  |  | 27.84 | 1.53 |
| **Lactateintra.** | PC-3M | 100% [1,2-13C2]-glucose | 48 | 63.86 | 0.17 | 1.24 | 0.09 | 30.96 | 0.03 | 3.94 | 0.05 |  |  |  |  |  |  | 36.14 | 0.17 |
| PC-3S | 48 | 66.24 | 1.14 | 0.80 | 0.09 | 29.56 | 0.95 | 3.41 | 0.11 |  |  |  |  |  |  | 33.76 | 1.14 |
| **Alanineintra.** | PC-3M | 100% [1,2-13C2]-glucose | 24 | 73.55 | 0.30 | 1.03 | 0.18 | 23.28 | 0.21 | 2.14 | 0.22 |  |  |  |  |  |  | 26.45 | 0.30 |
| PC-3S | 24 | 78.42 | 0.71 | 1.68 | 0.08 | 17.94 | 0.54 | 1.96 | 0.10 |  |  |  |  |  |  | 21.58 | 0.71 |
| **Alanineintra.** | PC-3M | 100% [1,2-13C2]-glucose | 48 | 64.04 | 0.05 | 2.38 | 0.02 | 29.96 | 0.02 | 3.62 | 0.05 |  |  |  |  |  |  | 35.96 | 0.05 |
| PC-3S | 48 | 69.33 | 0.17 | 1.96 | 0.11 | 25.86 | 0.17 | 2.85 | 0.07 |  |  |  |  |  |  | 30.67 | 0.17 |

Values are expressed as percentage of each isotopologue and denote mean and SD of n=3. Abbreviations: extra., extracellular; Gln, glutamine; Glu, glutamate; intra., intracellular.

**B.** Isotopologue distribution data not integrated in Isodyn

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Metabolite** | **Cells** | **Tracer** | **Time (h)** | **m0 (%)** | | **m1 (%)** | | **m2 (%)** | | **m3 (%)** | | **m4 (%)** | | **m5 (%)** | | **m6 (%)** | | **Ʃm (%)** | |
| **mean** | **SD** | **mean** | **SD** | **mean** | **SD** | **mean** | **SD** | **mean** | **SD** | **mean** | **SD** | **mean** | **SD** | **mean** | **SD** |
| **Riboseintra.** | PC-3M | 100% [1,2-13C2]-glucose | 24 | 52.61 | 1.24 | 20.73 | 0.41 | 10.08 | 0.16 | 8.32 | 0.36 | 7.80 | 0.13 | 0.45 | 0.24 |  |  | 47.39 | 1.24 |
| PC-3S | 24 | 74.67 | 0.20 | 11.94 | 0.06 | 4.80 | 0.02 | 4.65 | 0.17 | 3.74 | 0.06 | 0.20 | 0.05 |  |  | 25.33 | 0.20 |

Values are expressed as percentage of each isotopologue and denote mean and SD of n=3. Abbreviations: intra., intracellular.

**Supplemental Table 3**. Isotopologue distribution data of metabolites analyzed in PC-3M and PC-3S cells, after incubation with 100% [U-13C5]-glutamine.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Metabolite** | **Cells** | **Tracer** | **Time (h)** | **m0 (%)** | | **m1 (%)** | | **m2 (%)** | | **m3 (%)** | | **m4 (%)** | | **m5 (%)** | | **m6 (%)** | | **Ʃm (%)** | |
| **mean** | **SD** | **mean** | **SD** | **mean** | **SD** | **mean** | **SD** | **mean** | **SD** | **mean** | **SD** | **mean** | **SD** | **mean** | **SD** |
| **Glucoseextra.** | PC-3M / S | 100% [U-13C5]-glutamine | 0 | 99.95 | 0.01 | 0.02 | 0.02 | 0.01 | 0.02 | 0.00 | 0.01 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.05 | 0.01 |
| **Lactateextra.** | PC-3M | 100% [U-13C5]-glutamine | 24 | 98.39 | 0.02 | 0.21 | 0.01 | 0.23 | 0.00 | 1.17 | 0.01 |  |  |  |  |  |  | 1.61 | 0.02 |
| PC-3S | 24 | 98.33 | 0.02 | 0.35 | 0.02 | 0.25 | 0.00 | 1.07 | 0.00 |  |  |  |  |  |  | 1.67 | 0.02 |
| **Lactateextra.** | PC-3M | 100% [U-13C5]-glutamine | 48 | 97.58 | 0.26 | 0.59 | 0.22 | 0.33 | 0.01 | 1.49 | 0.04 |  |  |  |  |  |  | 2.42 | 0.26 |
| PC-3S | 48 | 98.15 | 0.02 | 0.44 | 0.01 | 0.29 | 0.00 | 1.12 | 0.01 |  |  |  |  |  |  | 1.85 | 0.02 |
| **(Glu + Gln)extra.** | PC-3M | 100% [U-13C5]-glutamine | 24 | 24.43 | 0.75 | 0.87 | 0.20 | 2.91 | 0.31 | 71.79 | 1.06 |  |  |  |  |  |  | 75.57 | 0.75 |
| **(C2-C4 fragment)** | PC-3S | 24 | 26.97 | 1.21 | 1.88 | 0.39 | 4.01 | 0.21 | 67.14 | 1.78 |  |  |  |  |  |  | 73.03 | 1.21 |
| **(Glu + Gln)extra.** | PC-3M | 100% [U-13C5]-glutamine | 48 | 30.83 | 0.39 | 2.95 | 0.12 | 7.65 | 0.06 | 58.56 | 0.40 |  |  |  |  |  |  | 69.17 | 0.39 |
| **(C2-C4 fragment)** | PC-3S | 48 | 33.23 | 0.11 | 4.09 | 0.15 | 7.73 | 0.03 | 54.95 | 0.08 |  |  |  |  |  |  | 66.77 | 0.11 |
| **(Glu + Gln)extra.** | PC-3M | 100% [U-13C5]-glutamine | 24 | 23.30 | 0.68 | 0.68 | 0.01 | 2.63 | 0.06 | 1.78 | 0.13 | 71.61 | 0.61 |  |  |  |  | 76.70 | 0.68 |
| **(C2-C5 fragment)** | PC-3S | 24 | 25.79 | 1.09 | 1.42 | 0.07 | 3.56 | 0.20 | 1.54 | 0.20 | 67.70 | 1.14 |  |  |  |  | 74.21 | 1.09 |
| **(Glu + Gln)extra.** | PC-3M | 100% [U-13C5]-glutamine | 48 | 29.62 | 0.34 | 2.90 | 0.00 | 7.61 | 0.06 | 1.64 | 0.06 | 58.23 | 0.40 |  |  |  |  | 70.38 | 0.34 |
| **(C2-C5 fragment)** | PC-3S | 48 | 32.10 | 0.11 | 3.94 | 0.02 | 7.50 | 0.01 | 1.53 | 0.07 | 54.92 | 0.20 |  |  |  |  | 67.90 | 0.11 |
| **Alanineextra.** | PC-3M | 100% [U-13C5]-glutamine | 24 | 98.30 | 0.09 | 0.00 | 0.00 | 0.30 | 0.01 | 1.40 | 0.09 |  |  |  |  |  |  | 1.70 | 0.09 |
| PC-3S | 24 | 98.69 | 0.08 | 0.00 | 0.00 | 0.27 | 0.01 | 1.04 | 0.07 |  |  |  |  |  |  | 1.31 | 0.08 |
| **Alanineextra.** | PC-3M | 100% [U-13C5]-glutamine | 48 | 97.30 | 0.21 | 0.02 | 0.03 | 0.49 | 0.02 | 2.19 | 0.16 |  |  |  |  |  |  | 2.70 | 0.21 |
| PC-3S | 48 | 98.08 | 0.16 | 0.03 | 0.05 | 0.39 | 0.02 | 1.50 | 0.10 |  |  |  |  |  |  | 1.92 | 0.16 |
| **Glycineextra.** | PC-3M | 100% [U-13C5]-glutamine | 24 | 99.83 | 0.02 | 0.13 | 0.04 | 0.04 | 0.06 |  |  |  |  |  |  |  |  | 0.17 | 0.02 |
| PC-3S | 24 | 99.86 | 0.06 | 0.11 | 0.05 | 0.03 | 0.03 |  |  |  |  |  |  |  |  | 0.14 | 0.06 |
| **Glycineextra.** | PC-3M | 100% [U-13C5]-glutamine | 48 | 99.79 | 0.17 | 0.18 | 0.15 | 0.03 | 0.02 |  |  |  |  |  |  |  |  | 0.21 | 0.17 |
| PC-3S | 48 | 99.83 | 0.09 | 0.15 | 0.10 | 0.02 | 0.01 |  |  |  |  |  |  |  |  | 0.17 | 0.09 |
| **Serineextra.** | PC-3M | 100% [U-13C5]-glutamine | 24 | 99.87 | 0.07 | 0.11 | 0.09 | 0.02 | 0.03 | 0.00 | 0.00 |  |  |  |  |  |  | 0.13 | 0.07 |
| PC-3S | 24 | 99.93 | 0.06 | 0.04 | 0.06 | 0.02 | 0.01 | 0.00 | 0.00 |  |  |  |  |  |  | 0.07 | 0.06 |
| **Serineextra.** | PC-3M | 100% [U-13C5]-glutamine | 48 | 99.62 | 0.13 | 0.32 | 0.11 | 0.04 | 0.02 | 0.02 | 0.01 |  |  |  |  |  |  | 0.38 | 0.13 |
| PC-3S | 48 | 99.75 | 0.09 | 0.19 | 0.13 | 0.04 | 0.04 | 0.02 | 0.00 |  |  |  |  |  |  | 0.25 | 0.09 |
| **Prolineextra.** | PC-3M | 100% [U-13C5]-glutamine | 24 | 94.02 | 0.34 | 0.00 | 0.00 | 0.00 | 0.00 | 0.67 | 0.12 | 0.00 | 0.00 | 5.31 | 0.22 |  |  | 5.98 | 0.34 |
| PC-3S | 24 | 98.35 | 2.54 | 0.11 | 0.19 | 0.16 | 0.27 | 0.43 | 0.74 | 0.15 | 0.27 | 0.70 | 0.96 |  |  | 1.65 | 2.54 |
| **Prolineextra.** | PC-3M | 100% [U-13C5]-glutamine | 48 | 79.87 | 1.20 | 0.81 | 0.38 | 0.39 | 0.15 | 4.04 | 0.36 | 0.00 | 0.00 | 14.89 | 0.31 |  |  | 20.13 | 1.20 |
| PC-3S | 48 | 85.09 | 0.84 | 1.49 | 0.05 | 1.51 | 0.04 | 3.75 | 0.06 | 1.88 | 0.23 | 5.54 | 0.49 |  |  | 14.18 | 0.66 |
| **Citrateintra.** | PC-3M | 100% [U-13C5]-glutamine | 24 | 32.36 | 0.31 | 3.84 | 0.21 | 10.03 | 0.08 | 7.72 | 0.35 | 30.15 | 0.71 | 9.92 | 0.10 | 5.98 | 0.17 | 67.64 | 0.31 |
| PC-3S | 24 | 40.94 | 0.28 | 6.83 | 0.00 | 11.60 | 0.07 | 5.95 | 0.17 | 23.52 | 0.51 | 6.79 | 0.05 | 4.37 | 0.05 | 59.06 | 0.28 |
| **Citrateintra.** | PC-3M | 100% [U-13C5]-glutamine | 48 | 40.94 | 1.33 | 6.83 | 0.12 | 12.16 | 0.29 | 5.85 | 0.14 | 23.72 | 0.77 | 6.17 | 0.09 | 4.33 | 0.14 | 59.06 | 1.33 |
| PC-3S | 48 | 45.50 | 0.24 | 7.81 | 0.06 | 11.77 | 0.09 | 5.63 | 0.05 | 20.12 | 0.07 | 5.55 | 0.02 | 3.62 | 0.04 | 54.50 | 0.24 |
| **(Glu + Gln)intra.** | PC-3M | 100% [U-13C5]-glutamine | 24 | 22.97 | 0.06 | 2.69 | 0.15 | 3.04 | 0.15 | 12.36 | 0.37 | 3.91 | 0.07 | 55.05 | 0.70 |  |  | 77.03 | 0.06 |
| PC-3S | 24 | 31.52 | 0.59 | 6.59 | 0.01 | 5.27 | 0.00 | 15.67 | 0.05 | 4.09 | 0.00 | 36.86 | 0.63 |  |  | 68.48 | 0.59 |
| **(Glu + Gln)intra.** | PC-3M | 100% [U-13C5]-glutamine | 48 | 27.29 | 0.78 | 5.71 | 0.15 | 4.81 | 0.10 | 14.68 | 0.07 | 4.10 | 0.02 | 43.40 | 1.03 |  |  | 72.71 | 0.78 |
| PC-3S | 48 | 35.73 | 0.27 | 7.07 | 0.02 | 5.27 | 0.01 | 14.13 | 0.07 | 3.74 | 0.01 | 34.06 | 0.36 |  |  | 64.27 | 0.27 |
| **Fumarateintra.** | PC-3M | 100% [U-13C5]-glutamine | 24 | 36.24 | 1.09 | 1.46 | 0.20 | 10.73 | 0.27 | 0.45 | 0.60 | 51.11 | 0.86 |  |  |  |  | 63.76 | 1.09 |
| PC-3S | 24 | 40.65 | 1.22 | 5.83 | 1.04 | 15.31 | 0.46 | 0.19 | 0.28 | 38.02 | 2.08 |  |  |  |  | 59.35 | 1.22 |
| **Fumarateintra.** | PC-3M | 100% [U-13C5]-glutamine | 48 | 45.77 | 0.06 | 4.58 | 0.90 | 13.67 | 0.40 | 0.31 | 0.44 | 35.67 | 1.00 |  |  |  |  | 54.23 | 6.62 |
| PC-3S | 48 | 48.55 | 1.20 | 4.44 | 1.74 | 13.59 | 0.50 | 0.00 | 0.00 | 33.42 | 1.05 |  |  |  |  | 51.45 | 1.20 |
| **Malateintra.** | PC-3M | 100% [U-13C5]-glutamine | 24 | 31.49 | 0.54 | 3.94 | 0.16 | 11.58 | 0.25 | 9.36 | 0.10 | 43.64 | 1.00 |  |  |  |  | 68.51 | 0.54 |
| PC-3S | 24 | 38.29 | 1.12 | 8.06 | 0.24 | 14.63 | 0.28 | 6.41 | 0.25 | 32.61 | 0.85 |  |  |  |  | 61.71 | 1.12 |
| **Malateintra.** | PC-3M | 100% [U-13C5]-glutamine | 48 | 43.16 | 0.56 | 6.94 | 0.17 | 13.09 | 0.20 | 5.62 | 0.12 | 31.19 | 0.47 |  |  |  |  | 56.84 | 0.56 |
| PC-3S | 48 | 45.07 | 0.55 | 8.24 | 0.01 | 13.21 | 0.02 | 5.95 | 0.12 | 27.53 | 0.42 |  |  |  |  | 54.93 | 0.55 |
| **Aspartateintra.** | PC-3M | 100% [U-13C5]-glutamine | 24 | 34.89 | 0.45 | 3.93 | 0.12 | 11.60 | 0.22 | 8.71 | 0.16 | 40.88 | 0.86 |  |  |  |  | 65.11 | 0.45 |
| PC-3S | 24 | 40.31 | 1.21 | 8.35 | 0.14 | 14.84 | 0.30 | 5.84 | 0.18 | 30.65 | 0.97 |  |  |  |  | 59.69 | 1.21 |
| **Aspartateintra.** | PC-3M | 100% [U-13C5]-glutamine | 48 | 47.73 | 1.89 | 6.65 | 0.05 | 12.36 | 0.23 | 4.88 | 0.18 | 28.38 | 1.43 |  |  |  |  | 52.27 | 1.89 |
| PC-3S | 48 | 48.42 | 0.65 | 8.25 | 0.11 | 13.06 | 0.20 | 5.17 | 0.02 | 25.11 | 0.34 |  |  |  |  | 51.58 | 0.65 |
| **Pyruvateintra.** | PC-3M | 100% [U-13C5]-glutamine | 24 | 88.86 | 4.26 | 1.37 | 0.67 | 1.53 | 0.60 | 8.24 | 3.00 |  |  |  |  |  |  | 13.46 | 2.05 |
| PC-3S | 24 | 91.27 | 3.21 | 1.96 | 0.90 | 1.44 | 0.38 | 5.33 | 1.92 |  |  |  |  |  |  | 8.73 | 3.21 |
| **Pyruvateintra.** | PC-3M | 100% [U-13C5]-glutamine | 48 | 87.10 | 2.14 | 2.68 | 0.45 | 2.10 | 0.35 | 8.12 | 1.36 |  |  |  |  |  |  | 12.90 | 2.14 |
| PC-3S | 48 | 86.32 | 7.40 | 3.39 | 1.75 | 2.39 | 1.30 | 7.90 | 4.34 |  |  |  |  |  |  | 17.91 | 1.40 |
| **Lactateintra.** | PC-3M | 100% [U-13C5]-glutamine | 24 | 98.70 | 0.40 | 0.00 | 0.00 | 0.05 | 0.08 | 1.25 | 0.32 |  |  |  |  |  |  | 1.30 | 0.40 |
| PC-3S | 24 | 97.71 | 0.79 | 0.00 | 0.00 | 0.44 | 0.37 | 1.85 | 0.42 |  |  |  |  |  |  | 2.29 | 0.79 |
| **Lactateintra.** | PC-3M | 100% [U-13C5]-glutamine | 48 | 96.92 | 1.08 | 1.16 | 0.69 | 0.53 | 0.31 | 1.39 | 0.08 |  |  |  |  |  |  | 3.08 | 1.08 |
| PC-3S | 48 | 98.86 | 0.18 | 0.00 | 0.00 | 0.00 | 0.01 | 1.13 | 0.17 |  |  |  |  |  |  | 1.14 | 0.18 |
| **Alanineintra.** | PC-3M | 100% [U-13C5]-glutamine | 24 | 97.74 | 0.26 | 0.58 | 0.16 | 0.40 | 0.07 | 1.28 | 0.03 |  |  |  |  |  |  | 2.26 | 0.26 |
| PC-3S | 24 | 96.93 | 0.19 | 1.40 | 0.06 | 0.52 | 0.15 | 1.15 | 0.01 |  |  |  |  |  |  | 3.07 | 0.19 |
| **Alanineintra.** | PC-3M | 100% [U-13C5]-glutamine | 48 | 96.82 | 0.12 | 1.01 | 0.11 | 0.48 | 0.04 | 1.69 | 0.01 |  |  |  |  |  |  | 3.18 | 0.12 |
| PC-3S | 48 | 96.90 | 0.21 | 1.23 | 0.20 | 0.50 | 0.02 | 1.36 | 0.01 |  |  |  |  |  |  | 3.10 | 0.21 |

Valuesare expressed as percentage of each isotopologue and denote mean and SD of n=3. Abbreviations: extra., extracellular; Gln, glutamine; Glu, glutamate; intra., intracellular.

**Supplemental Table 4**. Biochemical data used in Isodyn analysis

**A.** Extracellular concentrations of metabolites measured in the 13C-based experiments with 100% [1,2-13C2]-glucose (Supplemental Table 2) or 100% [U-13C5]-glutamine (Supplemental Table 3), performed in parallel.

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **PC-3M cells** | | | | | | **PC-3S cells** | | | | | |
|  | **CONCENTRATIONS (mM)** | | | | | | **CONCENTRATIONS (mM)** | | | | | |
|  | **0 h** | | **24 h** | | **48 h** | | **0 h** | | **24 h** | | **48 h** | |
| **Metabolite** | **Mean** | **SD** | **Mean** | **SD** | **Mean** | **SD** | **Mean** | **SD** | **Mean** | **SD** | **Mean** | **SD** |
| Glucose | 10.005 | 0.188 | 7.176 | 0.080 | 2.741 | 0.062 | 10.005 | 0.188 | 7.493 | 0.028 | 4.910 | 0.114 |
| Lactate | 1.402 | 0.037 | 7.498 | 0.535 | 17.536 | 0.526 | 1.402 | 0.037 | 6.980 | 0.128 | 13.608 | 0.125 |
| Glutamine | 1.824 | 0.043 | 1.289 | 0.045 | 0.431 | 0.029 | 1.824 | 0.043 | 1.190 | 0.259 | 0.730 | 0.049 |
| Glutamate | 0.336 | 0.010 | 0.478 | 0.009 | 0.616 | 0.015 | 0.336 | 0.010 | 0.586 | 0.007 | 0.822 | 0.011 |

**B.** Extracellular concentrations of amino acids measured in additional experiments.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **PC-3M cells** | | | | **PC-3S cells** | | | |
|  | **CONCENTRATIONS (mM)** | | | | **CONCENTRATIONS (mM)** | | | |
|  | **0 h** | | **48 h** | | **0 h** | | **48 h** | |
| **Metabolite** | **Mean** | **SD** | **Mean** | **SD** | **Mean** | **SD** | **Mean** | **SD** |
| **Glutamine** | **1.363** | **0.019** | **1.007** | **0.012** | **1.306** | **0.022** | **0.731** | **0.023** |
| **Glutamate** | **0.319** | **0.007** | **0.418** | **0.008** | **0.307** | **0.007** | **0.512** | **0.012** |
| **Alanine** | **0.226** | **0.006** | **0.479** | **0.007** | **0.224** | **0.006** | **0.481** | **0.007** |
| **Serine** | **0.391** | **0.009** | **0.355** | **0.008** | **0.377** | **0.005** | **0.251** | **0.007** |
| **Glycine** | **0.291** | **0.005** | **0.302** | **0.005** | **0.282** | **0.007** | **0.358** | **0.007** |
| **Proline** | **0.277** | **0.002** | **0.317** | **0.007** | **0.270** | **0.008** | **0.215** | **0.007** |
| **aa  Pyr** |  |  |  |  |  |  |  |  |
| Cysteine | 0.148 | 0.002 | 0.117 | 0.002 | 0.141 | 0.004 | 0.081 | 0.003 |
| Threonine | 0.186 | 0.008 | 0.178 | 0.003 | 0.179 | 0.004 | 0.158 | 0.008 |
| **aa  a-KG** |  |  |  |  |  |  |  |  |
| Histidine | 0.095 | 0.002 | 0.095 | 0.002 | 0.091 | 0.002 | 0.082 | 0.003 |
| Arginine | 0.890 | 0.017 | 0.847 | 0.012 | 0.861 | 0.021 | 0.813 | 0.010 |
| **aa  OAA** |  |  |  |  |  |  |  |  |
| Aspartate | 0.112 | 0.005 | 0.122 | 0.007 | 0.114 | 0.004 | 0.145 | 0.005 |
| Asparagine | 0.561 | 0.007 | 0.559 | 0.009 | 0.539 | 0.006 | 0.498 | 0.010 |
| **aa  Fum** |  |  |  |  |  |  |  |  |
| Valine | 0.205 | 0.007 | 0.187 | 0.002 | 0.199 | 0.007 | 0.167 | 0.004 |
| Methionine | 0.097 | 0.003 | 0.090 | 0.003 | 0.094 | 0.002 | 0.075 | 0.004 |
| Tyrosine | 0.125 | 0.002 | 0.123 | 0.005 | 0.121 | 0.002 | 0.119 | 0.008 |
| Phenylalanine | 0.122 | 0.002 | 0.118 | 0.003 | 0.118 | 0.003 | 0.098 | 0.004 |
| **aa  AcCoA** |  |  |  |  |  |  |  |  |
| Isoleucine | 0.356 | 0.008 | 0.304 | 0.004 | 0.351 | 0.006 | 0.307 | 0.008 |
| Leucine | 0.396 | 0.009 | 0.333 | 0.005 | 0.384 | 0.004 | 0.326 | 0.007 |
| Lysine | 0.254 | 0.011 | 0.242 | 0.005 | 0.244 | 0.005 | 0.211 | 0.005 |

Abbreviations: -KG, -ketoglutarate; aa, amino acid; AcCoA, acetyl-CoA; Fum, fumarate; OAA, oxaloacetate; Pyr, pyruvate.**Supplemental Table 5**. Isotopologue distribution data of metabolites analyzed in PC-3M and PC-3S cells, after incubation with 100% [U-13C6]-glucose.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Metabolite** | **Cells** | **Tracer** | **Time (h)** | **m0 (%)** | | **m1 (%)** | | **m2 (%)** | | **m3 (%)** | | **m4 (%)** | | **m5 (%)** | | **m6 (%)** | | **Ʃm (%)** | |
| **mean** | **SD** | **mean** | **SD** | **mean** | **SD** | **mean** | **SD** | **mean** | **SD** | **mean** | **SD** | **mean** | **SD** | **mean** | **SD** |
| **Serineextra.** | PC-3M | 100% [U-13C6]-glucose | 48 | 90.78 | 0.15 | 1.37 | 0.09 | 0.72 | 0.01 | 7.13 | 0.07 |  |  |  |  |  |  | 9.22 | 0.15 |
| PC-3S | 48 | 86.91 | 0.46 | 5.78 | 0.34 | 3.17 | 0.13 | 4.13 | 0.05 |  |  |  |  |  |  | 13.09 | 0.46 |
| **Glycineextra.** | PC-3M | 100% [U-13C6]-glucose | 48 | 98.56 | 0.16 | 0.26 | 0.05 | 1.18 | 0.11 |  |  |  |  |  |  |  |  | 1.44 | 0.16 |
| PC-3S | 48 | 96.11 | 0.07 | 0.26 | 0.08 | 3.64 | 0.15 |  |  |  |  |  |  |  |  | 3.89 | 0.07 |

Values are expressed as percentage of each isotopologue and denote mean and SD of n=3. Abbreviations: extra., extracellular.

**Supplemental Table 6**. PC-3M-overexpressed metabolic gene set.

|  |  |  |  |
| --- | --- | --- | --- |
|  | **GENE SYMBOL** | **GENE DESCRIPTION** | **KEGG PATHWAY** |
| 1 | **BCAT1** | Branched chain aminoacid transaminase 1, cytosolic | Valine\_ leucine and isoleucine degradation |
| 2 | **HS3ST3A1** | Heparan sulfate (glucosamine) 3Osulfotransferase 3A1 | Glycosaminoglycan biosynthesis heparan sulfate |
| 3 | **CYP1B1** | Cytochrome P450, family 1, subfamily B, polypeptide 1 | Steroid hormone biosynthesis |
| 4 | **SLC22A3** | Solute carrier family 22 (organic cation transporter), member 3 | Transport |
| 5 | **ALDH1A2** | Aldehyde dehydrogenase 1 family, member A2 | Retinol metabolism |
| 6 | **PDE3B** | Phosphodiesterase 3B, cGMPinhibited | Purine metabolism |
| 7 | **CBS** | Cystathionine betasynthase | Cysteine and methionine metabolism  Glycine\_ serine and threonine metabolism |
| 8 | **ST6GAL1** | ST6 betagalactosamide alpha2,6sialyltranferase 1 | NGlycan biosynthesis |
| 9 | **GALNT14** | Polypeptide Nacetylgalactosaminyltransferase 14 | Mucin type OGlycan biosynthesis |
| 10 | **AGMAT** | Agmatine ureohydrolase (agmatinase) | Arginine and proline metabolism |
| 11 | **SLC27A2** | Solute carrier family 27 (fatty acid transporter), member 2 | PPAR signaling pathway |
| 12 | **ASS1** | Argininosuccinate synthase 1 | Arginine and proline metabolism  Alanine\_ aspartate and glutamate metabolism |
| 13 | **GUCY1A3** | Guanylate cyclase 1, soluble, alpha 3 | Purine metabolism |
| 14 | **ABCB11** | ATPbinding cassette, subfamily B (MDR/TAP), member 11 | Bile secretion |
| 15 | **SLC1A3** | Solute carrier family 1 (glial high affinity glutamate transporter), mem 3 | Glutamatergic synapse  ABC transporters |
| 16 | **GLDC** | Glycine dehydrogenase (decarboxylating) | Glycine\_ serine and threonine metabolism |
| 17 | **DGKG** | Diacylglycerol kinase, gamma 90kDa | Glycerolipid metabolism  Glycerophospholipid metabolism  Phosphatidylinositol signaling system |
| 18 | **SLCO3A1** | Solute carrier organic anion transporter family, member 3A1 | Transport |
| 19 | **ADCY7** | Adenylate cyclase 7 | GnRH signaling pathway  Calcium signaling pathway  Purine metabolism |
| 20 | **CA9** | Carbonic anhydrase IX | Nitrogen metabolism |
| 21 | **SLC7A8** | Large neutral amino acids transporter small subunit 2 | Protein digestion and absortion |

**Supplemental Table 7**. GSEA with enrichment scores for PC-3M metabolic gene set in human tumors. Expression datasets retrieved from TCGA (<https://tcga-data.nci.nih.gov/tcga/>). Here the samples have been grouped based on their tumor stage: T1, T2, T3, T4 or Metastasis. The contiguous pathological states have been analyzed as a single group or as separate groups in order to obtain the highest correlation with the gene signature. Shown are the 11 datasets for which significant enrichment is observed for the PC-3M metabolic geneset in association with tumor stage (FDR ≤ 0.250).

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **ES** | **NES** | **FDR** | **nº samples** |
| **1 OV Ovarian serous cystadenocarcinoma** | 0.61 | 1.86 | 0.004 | 563 |
| **2 DLBC Lymphoid neoplasm diffuse large B-cell lymphoma** | 0.51 | 1.5 | 0.029 | 35 |
| **3 STAD Stomach adenocarcinoma** | 0.46 | 1.46 | 0.07 | 330 |
| **4 ACC Adrenocortical carcinoma** | 0.43 | 1.36 | 0.086 | 75 |
| **5 BLCA Bladder urothelial carcinoma** | 0.46 | 1.37 | 0.118 | 128 |
| **6 MESO Mesothelioma** | 0.39 | 1.29 | 0.143 | 69 |
| **7 UCEC Uterine corpus edometrial carcinoma** | 0.42 | 1.31 | 0.159 | 155 |
| **8 READ Rectum adenocarcinoma** | 0.39 | 1.24 | 0.168 | 93 |
| **9 LAML Acute myeloid leukemia** | 0.4 | 1.26 | 0.170 | 155 |
| **10 HNSC Head and neck squamous cell carcinoma** | 0.38 | 1.21 | 0.203 | 442 |
| **11 UVM Uveal melanoma** | 0.43 | 1.24 | 0.245 | 27 |