

Article

Metastasis of Uveal Melanoma with Monosomy-3 is Associated with a Less Glycogenetic Gene Expression Profile and the Dysregulation of Glycogen Storage

Siranush Vardanyan, Anton Brosig, Hartmut Merz, Mahdy Ranjbar, Vinodh Kakkassery, Salvatore Grisanti, and Aysegül Tura

Supplementary Materials:

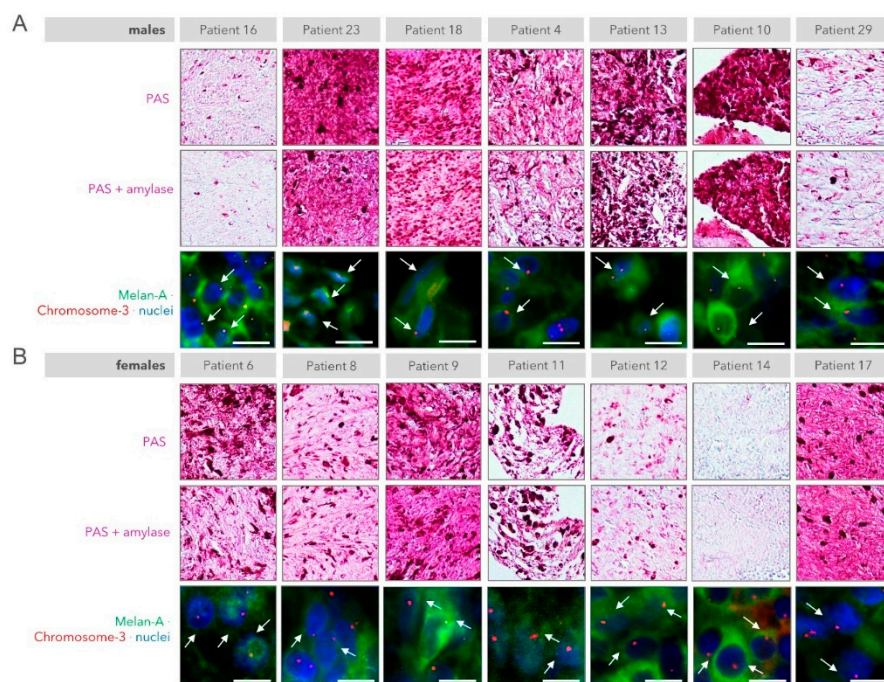


Figure S1. Estimated levels of the amylase-sensitive glycogen in the monosomy-3 tumors of the male versus female patients (n=7 each). **(A)** The amylase pretreatment has led to a slight to moderate weakening in the intensity of the PAS staining in all the male patients except for Patient #29, who did not demonstrate any difference (rightmost panel). **(B)** The tumors of the female patients did not exhibit a noticeable decline in the intensity of the PAS staining except for Patient #6 (leftmost panel), suggesting that the amylase-sensitive glycogen was less abundant in the monosomy-3 tumors of females. All the images of the PAS-stainings were acquired under an original magnification of 100X. The copy number of chromosome-3 (red) together with the melanoma marker protein Melan-A (green) was analyzed by Immuno-FISH. Nuclei were counterstained in blue with DAPI. Arrows indicate several examples of cells with monosomy-3. Scale bars

Table S1. Human genes involved in glycogen synthesis and breakdown (n = 67).

| Supplementary Table S1 | | | | | | | | | | | | | | | | | |
|--|-----------------|--|----------|--|---------------------|----------------------|------------------|----------------|--|-----------|---------------------|------------|---------------------|-----------|------------------|----------------|------------------------------------|
| not corrected for gene copy number: Tumors with complete information on the copy numbers of chromosome 3p and 3q | | | | | | | | | | | | | | | | | |
| corrected for gene copy number: Exclusion of the tumors with aberrations on the other chromosomes that harbor the analyzed genes | | | | | | | | | | | | | | | | | |
| 1. Preparatory steps / Dual regulators of glycogen synthesis* (n=6 genes) | | | | | | | | | | | | | | | | | |
| Symbol | NCBI Gene ID | Name | Locus | Expression (not corrected for gene copy number) | | | | | Expression (corrected for gene copy number) | | | | | | | | References for gene function |
| | | | | All (n=77) | Disomy-3 (n=38) | Monosomy-3 (n=39) | p - value | | All | Disomy -3 | | Monosomy-3 | | p - value | | | |
| | | | | Mean ± SD | Median (range) | Median (range) | un- corrected | corrected † | Mean ± SD | n | Median (range) | n | Median (range) | n | un- corrected | corrected † | |
| GCK | 2645 | glucokinase | 7p13 | 9.0 ± 3.3 | 9.0 (0.0-14.7) | 9.7 (0.0-14.2) | 0.21 | 1.00 | 8.9 ± 3.4 | 71 | 9.0 (0.0-14.7) | 36 | 9.7 (0.0-14.2) | 35 | 0.19 | 1.00 | [30] |
| PGM1* | 5236 | phosphoglucomutase 1 | 1p31.3 | 17.0 ± 1.4 | 15.8 (13.3-18.8) | 17.6 (15.9-18.9) | 0.00 | 0.11 | 17.1 ± 1.4 | 56 | 16.9 (13.3-18.8) | 32 | 17.7 (16.8-18.9) | 24 | 0.02 | 1.00 | [16,37,38] |
| PGM2* | 55276 | phosphoglucomutase 2 | 4p14 | 17.3 ± 0.8 | 17.0 (15.0-18.3) | 17.7 (16.0-19.5) | 0.00 | 0.00 | 17.2 ± 0.7 | 68 | 17.0 (15.0-18.3) | 36 | 17.6 (16.0-18.7) | 32 | 0.00 | 0.02 | [16,38] |
| PGM3* | 5238 | phosphoglucomutase 3 | 6q14.1 | 15.5 ± 0.8 | 15.6 (13.6-16.6) | 15.6 (13.8-16.8) | 0.58 | 1.00 | 15.7 ± 0.7 | 50 | 15.7 (14.0-16.6) | 24 | 16.0 (14.0-16.8) | 26 | 0.28 | 1.00 | [16,38] |
| PGM5* | 5239 | phosphoglucomutase 5 | 9q21.11 | 12.4 ± 1.2 | 11.8 (8.3-14.2) | 12.8 (10.5-15.5) | 0.00 | 0.02 | 12.4 ± 1.2 | 72 | 11.7 (8.3-14.2) | 36 | 12.8 (10.5-15.5) | 36 | 0.00 | 0.00 | [16,38] |
| UGP2 | 7360 | UDP-glucose pyrophosphorylase 2 | 2p15 | 17.6 ± 0.4 | 17.6 (16.4-18.7) | 17.9 (16.6-18.5) | 0.40 | 1.00 | 17.6 ± 0.4 | 67 | 17.6 (16.4-18.4) | 33 | 17.9 (16.6-18.2) | 34 | 0.30 | 1.00 | [16] |
| 2. De novo glycogen synthesis (n=5 genes) | | | | | | | | | | | | | | | | | |
| Symbol | NCBI Gene ID | Name | Locus | Expression (not corrected for gene copy number) | | | | | Expression (corrected for gene copy number) | | | | | | | | References for gene function |
| | | | | All (n=77) | Disomy-3 (n=38) | Monosomy-3 (n=39) | p - value | | All | Disomy -3 | | Monosomy-3 | | p - value | | | |
| | | | | Mean ± SD | Median (range) | Median (range) | un- corrected | corrected † | Mean ± SD | n | Median (range) | n | Median (range) | n | un- corrected | corrected † | |
| GBE1 | 2632 | 1,4-alpha-glucan branching enzyme 1 | 3p12.2 | 16.8 ± 0.7 | 17.3 (15.6-19.2) | 16.5 (15.4-17.1) | 0.00 | 0.00 | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | [15,16] |
| GYG1 | 2992 | glycogenin 1 | 3q24 | 18.3 ± 0.3 | 18.4 (17.7-19.2) | 18.2 (17.5-18.7) | 0.00 | 0.01 | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | [15,16] |
| GYG2 | 8908 | glycogenin 2 | Xp22.33 | 20.8 ± 1.0 | 21.3 (19.4-23.1) | 20.1 (18.9-22.2) | 0.00 | 0.00 | 20.6 ± 0.9 | 55 | 21.2 (19.4-22.7) | 29 | 19.9 (18.9-22.2) | 26 | 0.00 | 0.00 | [15,16] |
| GYS1 | 2997 | glycogen synthase 1 | 19q13.33 | 20.9 ± 0.8 | 20.7 | 20.7 | 0.43 | 1.00 | 20.9 ± 0.8 | 75 | 20.6 | 36 | 20.7 | 39 | 0.38 | 1.00 | [15,16,23] |

| | | | | | | | | | | | | | | | | | |
|------|------|---------------------|---------|-----------|-------------------|-------------------|-------------|------|-----------|----|------------------|-------------|-------------------|----|-------------|------|------------|
| | | | | | (18.7-22.7) | (19.7-22.2) | | | | | (18.7-22.7) | (19.7-22.2) | | | | | |
| GYS2 | 2998 | glycogen synthase 2 | 12p12.1 | 5.5 ± 4.3 | 0.0 (0.0-9.67) | 8.4 (0.0-10.7) | 0.00 | 0.19 | 5.5 ± 4.3 | 72 | 0.0 (0.0-9.7) | 37 | 8.3 (0.0-10.7) | 35 | 0.01 | 0.38 | [15,16,23] |

3. Positive regulators of glycogen synthesis (n=19 genes)

| Symbol | NCBI Gene ID | Name | Locus | Expression (not corrected for gene copy number) | | | | | Expression (corrected for gene copy number) | | | | | | | | References for gene function |
|----------|---------------------|---|----------|--|---|---|------------------|----------------|--|------|------------------------------------|------|-------------------------------------|------|------------------|----------------|------------------------------------|
| | | | | All (n=77) Mean ± SD | Disomy-3 (n=38) Median (range) | Monosomy-3 (n=39) Median (range) | p - value | | All Mean ± SD | n | Disomy -3 Median (range) | n | Monosomy-3 Median (range) | n | p - value | | |
| | | | | | | | un- corrected | corrected † | | | | | | | un- corrected | corrected † | |
| ATG7 | 10533 | autophagy related 7 | 3p25.3 | 16.2 ± 0.4 | 16.4 (15.8-17.2) | 16.0 (14.9-17.0) | 0.00 | 0.00 | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | [15] |
| BAP1 | 8314 | BRCA1 associated protein 1 | 3p21.1 | 19.0 ± 1.5 | 20.2 (19.0-21.7) | 17.7 (15.9-19.8) | 0.00 | 0.00 | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | [22] |
| EPM2A | 7957 | EPM2A glucan phosphatase, laforin | 6q24.3 | 16.2 ± 0.8 | 16.7 (15.3-17.7) | 16.0 (14.5-17.2) | 0.00 | 0.00 | 16.5 ± 0.6 | 50 | 16.9 (15.6-17.6) | 24 | 16.1 (15.5-16.9) | 26 | 0.00 | 0.00 | [16] |
| INS | 3630 | insulin | 11p15.5 | 1.6 ± 4.1 | 0.0 (0.0-18.4) | 0.0 (0.0-12.7) | 0.89 | 1.00 | 1.7 ± 4.2 | 68 | 0.0 (0.0-18.4) | 34 | 0.0 (0.0-12.7) | 34 | 0.90 | 1.00 | [23] |
| INSR | 3643 | insulin receptor | 19p13.2 | 16.9 ± 0.4 | 17.1 (16.3-17.9) | 16.7 (16.2-17.7) | 0.00 | 0.00 | 17.0 ± 0.4 | 73 | 17.1 (16.5-17.9) | 35 | 16.7 (16.2-17.7) | 38 | 0.00 | 0.00 | [31] |
| IRS1 | 3667 | insulin receptor substrate 1 | 2q36.3 | 17.0 ± 0.9 | 17.3 (15.2-18.9) | 16.9 (14.0-19.1) | 0.01 | 0.52 | 17.0 ± 0.8 | 69 | 17.3 (15.4-18.9) | 32 | 16.9 (14.0-19.1) | 37 | 0.01 | 0.43 | [39] |
| IRS2 | 8660 | insulin receptor substrate 2 | 13q34 | 19.0 ± 0.6 | 19.2 (18.5-20.2) | 18.7 (17.3-20.2) | 0.00 | 0.00 | 19.0 ± 0.5 | 68 | 19.2 (18.5-20.1) | 34 | 18.8 (17.6-19.7) | 34 | 0.00 | 0.00 | [32] |
| IRS4 | 8471 | insulin receptor substrate 4 | Xq22.3 | 10.7 ± 3.8 | 13.6 (0.0-15.7) | 10.3 (0.0-13.1) | 0.00 | 0.00 | 10.7 ± 4.0 | 55 | 13.6 (0.0-15.7) | 29 | 10.5 (0.0-13.1) | 26 | 0.00 | 0.02 | [33] |
| NNAT | 4826 | neuronatin | 20q11.23 | 12.7 ± 2.5 | 12.6 (0.0-19.5) | 12.7 (9.0-18.6) | 0.39 | 1.00 | 12.6 ± 2.5 | 68 | 12.6 (0.0-19.5) | 34 | 12.7 (9.0-18.6) | 34 | 0.31 | 1.00 | [40] |
| PPARGC1A | 10891 | PPARG coactivator 1 alpha | 4p15.2 | 10.1 ± 3.0 | 11.2 (0.0-15.7) | 9.4 (0.0-14.1) | 0.01 | 0.46 | 10.3 ± 3.1 | 68 | 11.2 (0.0-15.7) | 36 | 9.6 (0.0-14.1) | 32 | 0.03 | 1.00 | [41] |
| PPP1CA | 5499 | protein phosphatase 1 catalytic subunit alpha | 11q13.2 | 21.0 ± 0.6 | 21.0 (19.8-22.4) | 21.0 (20.2-22.3) | 0.32 | 1.00 | 20.9 ± 0.6 | 66 | 20.9 (19.8-22.1) | 31 | 21.0 (20.2-22.0) | 35 | 0.22 | 1.00 | [15] |
| PPP1CB | 5500 | protein phosphatase 1 catalytic subunit beta | 2p23.2 | 19.2 ± 0.6 | 19.1 (18.1-20.1) | 19.4 (17.2-20.5) | 0.81 | 1.00 | 19.2 ± 0.6 | 67 | 19.1 (18.1-20.1) | 33 | 19.3 (17.2-20.0) | 34 | 0.63 | 1.00 | [15] |
| PPP1CC | 5501 | protein phosphatase 1 catalytic subunit gamma | 12q24.11 | 18.9 ± 0.4 | 19.1 (18.1-20.1) | 18.7 (18.0-19.7) | 0.01 | 0.46 | 18.9 ± 0.4 | 72 | 19.1 (18.1-20.1) | 37 | 18.7 (18.0-19.6) | 35 | 0.00 | 0.10 | [15,16] |
| PPP1R3A | 5506 | protein phosphatase 1 regulatory subunit 3A | 7q31.1 | 0.5 ± 1.8 | 0.0 (0.0-0.0) | 0.0 (0.0-8.61) | 0.02 | 1.00 | 0.5 ± 1.9 | 72 | 0.0 (0.0-0.0) | 37 | 0.0 (0.0-8.6) | 35 | 0.02 | 1.00 | [15,16] |

| | | | | | | | | | | | | | | | | | |
|---------|-------|--|----------|------------|---------------------|---------------------|-----------------|-------------|------------|----|---------------------|----|---------------------|----|-------------|-------------|---------|
| PPP1R3B | 79660 | protein phosphatase 1 regulatory subunit 3B | 8p23.1 | 17.2 ± 1.1 | 18.0 (16.1-20.4) | 16.5 (15.1-17.7) | 0.00 | 0.00 | 17.4 ± 0.8 | 44 | 17.9 (16.1-18.7) | 29 | 16.7 (15.8-17.7) | 15 | 0.00 | 0.00 | [15,16] |
| PPP1R3C | 5507 | protein phosphatase 1 regulatory subunit 3C | 10q23.32 | 18.6 ± 1.5 | 19.6 (15.9-21.4) | 17.7 (15.0-19.5) | 0.00 | 0.00 | 18.6 ± 1.5 | 76 | 19.6 (15.9-21.4) | 38 | 17.7 (15.0-19.5) | 38 | 0.00 | 0.00 | [15,16] |
| PPP1R3D | 5509 | protein phosphatase 1 regulatory subunit 3D | 20q13.33 | 16.6 ± 0.3 | 16.6 (16.0-18.2) | 16.6 (16.1-17.4) | 0.92 | 1.00 | 16.6 ± 0.3 | 68 | 16.6 (16.0-17.1) | 34 | 16.6 (16.1-17.1) | 34 | 0.79 | 1.00 | [15,16] |
| PRKAG2 | 51422 | protein kinase AMP-activated non-catalytic subunit gamma 2 | 7q36.1 | 16.1 ± 0.5 | 16.2 (14.9-17.0) | 16.0 (15.1-17.2) | <0.05 | 1.00 | 16.1 ± 0.4 | 71 | 16.2 (14.9-17.0) | 36 | 16.0 (15.1-16.6) | 35 | 0.02 | 1.00 | [15] |
| TRIM7 | 81786 | tripartite motif containing 7 | 5q35.3 | 11.6 ± 1.2 | 11.8 (9.4-15.6) | 11.3 (9.2-13.1) | 0.02 | 1.00 | 11.6 ± 1.1 | 70 | 11.8 (9.4-15.6) | 34 | 11.3 (9.2-13.1) | 36 | 0.10 | 1.00 | [16] |

4. Negative regulators of glycogen synthesis (n=37 genes)

| Symbol | NCBI Gene ID | Name | Locus | Expression (not corrected for gene copy number) | | | | | Expression (corrected for gene copy number) | | | | | | | References for gene function | |
|--------|---------------------|--|----------|--|---------------------|----------------------|------------------|----------------|--|----|---------------------|----|---------------------|----|------------------|------------------------------------|----------------|
| | | | | All (n=77) | Disomy-3 (n=38) | Monosomy-3 (n=39) | p - value | | All | | Disomy -3 | | Monosomy-3 | | p - value | | |
| | | | | Mean ± SD | Median (range) | Median (range) | un- corrected | corrected † | Mean ± SD | n | Median (range) | n | Median (range) | n | un- corrected | | corrected † |
| AGL | 178 | amylo-alpha-1, 6-glucosidase, 4-alpha-glucanotransferase | 1p21.2 | 15.0 ± 0.9 | 14.9 (12.9-16.5) | 14.9 (12.9-16.6) | 0.97 | 1.00 | 15.2 ± 0.8 | 56 | 15.0 (13.7-16.5) | 32 | 15.5 (13.8-16.6) | 24 | 0.23 | 1.00 | [15] |
| AMY1A | 276 | amylase alpha 1A | 1p21.1 | 1.3 ± 3.0 | 0.0 (0.0-8.8) | 0.0 (0.0-9.4) | 0.28 | 1.00 | 1.2 ± 2.9 | 56 | 0.0 (0.0-8.8) | 32 | 0.0 (0.0-8.3) | 24 | 0.75 | 1.00 | [15,44] |
| AMY1B | 277 | amylase alpha 1B | 1p21.1 | 1.0 ± 2.7 | 0.0 (0.0-9.0) | 0.0 (0.0-10.2) | 0.67 | 1.00 | 1.0 ± 2.8 | 56 | 0.0 (0.0-8.6) | 32 | 0.0 (0.0-10.2) | 24 | 0.44 | 1.00 | [15,44] |
| AMY2A | 279 | amylase alpha 2A | 1p21.1 | 2.6 ± 4.1 | 0.0 (0.0-10.2) | 0.0 (0.0-11.8) | 0.41 | 1.00 | 2.4 ± 4.1 | 56 | 0.0 (0.0-10.2) | 32 | 0.0 (0.0-11.8) | 24 | 0.17 | 1.00 | [15,44] |
| AMY2B | 280 | amylase alpha 2B | 1p21.1 | 12.6 ± 1.6 | 12.4 (10.1-16.2) | 13.0 (6.9-15.5) | 0.23 | 1.00 | 12.7 ± 1.4 | 56 | 12.4 (10.1-16.2) | 32 | 13.2 (10.7-14.8) | 24 | 0.05 | 1.00 | [15,44] |
| CALM1 | 801 | calmodulin 1 | 14q32.11 | 19.9 ± 0.4 | 19.7 (18.9-20.6) | 20.2 (19.7-20.9) | 0.00 | 0.00 | 19.9 ± 0.4 | 72 | 19.7 (18.9-20.6) | 36 | 20.2 (19.7-20.9) | 36 | 0.00 | 0.00 | [16] |
| CALM2 | 805 | calmodulin 2 | 2p21 | 19.8 ± 0.5 | 19.5 (18.2-20.1) | 20.1 (18.5-21.1) | 0.00 | 0.00 | 19.8 ± 0.5 | 67 | 19.5 (18.2-20.1) | 33 | 20.1 (18.5-20.6) | 34 | 0.00 | 0.00 | [16] |
| CALM3 | 808 | calmodulin 3 | 19q13.32 | 21.7 ± 0.6 | 21.8 (20.8-22.9) | 21.6 (20.5-22.7) | 0.12 | 1.00 | 21.7 ± 0.5 | 75 | 21.8 (20.8-22.9) | 36 | 21.6 (20.5-22.7) | 39 | 0.20 | 1.00 | [16] |
| G6PC | 2538 | glucose-6-phosphatase catalytic subunit | 17q21.31 | 0.9 ± 2.5 | 0.0 (0.0-7.3) | 0.0 (0.0-9.2) | 0.02 | 1.00 | 1.0 ± 2.5 | 62 | 0.0 (0.0-7.3) | 28 | 0.0 (0.0-9.2) | 34 | 0.05 | 1.00 | [16] |

| | | | | | | | | | | | | | | | | | |
|--------|--------|---|----------|------------|---------------------|---------------------|------|------|------------|------|---------------------|------|---------------------|------|------|------|---------|
| G6PC2 | 57818 | glucose-6-phosphatase catalytic subunit 2 | 2q31.1 | 6.2 ± 4.9 | 7.3 (0.0-12.3) | 9.2 (0.0-15.3) | 0.02 | 1.00 | 6.3 ± 4.9 | 70 | 7.2 (0.0-12.3) | 33 | 9.3 (0.0-15.3) | 37 | 0.03 | 1.00 | [16] |
| G6PC3 | 92579 | glucose-6-phosphatase catalytic subunit 3 | 17q21.31 | 20.3 ± 0.9 | 20.0 (18.5-21.7) | 20.7 (19.2-22.3) | 0.00 | 0.00 | 20.3 ± 0.9 | 62 | 19.8 (18.5-21.7) | 28 | 20.6 (19.2-22.0) | 34 | 0.00 | 0.02 | [16] |
| GAA | 2548 | glucosidase alpha, acid | 17q25.3 | 20.3 ± 0.7 | 20.1 (18.7-21.7) | 20.3 (19.4-22.0) | 0.02 | 1.00 | 20.1 ± 0.7 | 62 | 19.7 (18.7-21.7) | 28 | 20.3 (19.4-21.3) | 34 | 0.00 | 1.00 | [15,16] |
| GANC | 2595 | glucosidase alpha, neutral C | 15q15.1 | 16.7 ± 0.5 | 16.6 (14.9-17.3) | 16.8 (15.3-17.8) | 0.16 | 1.00 | 16.7 ± 0.5 | 72 | 16.6 (15.4-17.3) | 37 | 16.8 (15.9-17.8) | 35 | 0.20 | 1.00 | [45] |
| GCG | 2641 | glucagon | 2q24.2 | 0.4 ± 2.2 | 0.0 (0.0-16.3) | 0.0 (0.0-7.3) | 0.52 | 1.00 | 0.5 ± 2.3 | 70 | 0.0 (0.0-16.3) | 33 | 0.0 (0.0-7.3) | 37 | 0.47 | 1.00 | [46] |
| GCGR | 2642 | glucagon receptor | 17q25.3 | 6.6 ± 4.9 | 7.3 (0.0-14.5) | 9.5 (0.0-14.9) | 0.02 | 1.00 | 6.3 ± 5.0 | 62 | 7.2 (0.0-12.8) | 28 | 9.1 (0.0-14.9) | 34 | 0.01 | 0.99 | [46] |
| GCKR | 2646 | glucokinase regulator | 2p23.3 | 1.3 ± 3.0 | 0.0 (0.0-10.1) | 0.0 (0.0-9.7) | 0.29 | 1.00 | 1.1 ± 2.8 | 67 | 0.0 (0.0-8.8) | 33 | 0.0 (0.0-9.7) | 34 | 0.02 | 1.00 | [16] |
| GFPT1 | 2673 | glutamine--fructose-6-phosphate transaminase 1 | 2p13.3 | 17.0 ± 0.7 | 16.6 (15.5-17.4) | 17.4 (15.8-18.4) | 0.00 | 0.00 | 17.0 ± 0.7 | 67 | 16.6 (15.5-17.4) | 33 | 17.4 (15.8-18.4) | 34 | 0.00 | 0.00 | [34] |
| GSK3A | 2931 | glycogen synthase kinase 3 alpha | 19q13.2 | 19.3 ± 0.7 | 19.2 (18.2-21.3) | 19.2 (18.4-20.5) | 0.89 | 1.00 | 19.3 ± 0.7 | 75 | 19.2 (18.2-21.3) | 36 | 19.2 (18.4-20.5) | 39 | 0.77 | 1.00 | [23] |
| GSK3B | 2932 | glycogen synthase kinase 3 beta | 3q13.33 | 17.4 ± 0.3 | 17.6 (16.8-18.1) | 17.3 (16.2-17.8) | 0.00 | 0.00 | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | [15,23] |
| INPP5K | 51763 | inositol polyphosphate-5-phosphatase K | 17p13.3 | 19.2 ± 0.7 | 19.2 (18.0-21.0) | 19.1 (17.5-20.5) | 0.82 | 1.00 | 19.1 ± 0.7 | 68 | 19.2 (18.0-21.0) | 35 | 19.0 (18.0-20.3) | 33 | 0.62 | 1.00 | [47] |
| NHLRC1 | 378884 | NHL containing ubiquitin ligase 1 repeat E3 protein | 6p22.3 | 17.1 ± 1.0 | 17.1 (10.0-19.0) | 17.4 (16.6-18.2) | 0.01 | 0.97 | 17.2 ± 0.5 | 36 | 16.7 (15.7-17.3) | 6 | 17.4 (16.6-17.8) | 30 | 0.01 | 0.82 | [40] |
| NUDT14 | 256281 | nudix hydrolase 14 | 14q32.33 | 19.8 ± 1.0 | 19.4 (17.8-21.4) | 19.8 (18.8-21.9) | 0.01 | 0.94 | 19.8 ± 0.9 | 71 | 19.3 (17.9-21.4) | 35 | 19.8 (18.8-21.7) | 36 | 0.02 | 1.00 | [48] |
| PCK1 | 5105 | phosphoenolpyruvate carboxykinase 1 | 20q13.31 | 7.0 ± 3.8 | 6.9 (0.0-9.8) | 9.4 (6.1-12.8) | 0.00 | 0.00 | 6.8 ± 3.9 | 68 | 6.5 (0.0-9.8) | 34 | 9.3 (6.1-12.8) | 34 | 0.00 | 0.00 | [35] |
| PFKM | 5213 | phosphofructokinase, muscle | 12q13.11 | 19.4 ± 0.5 | 19.4 (17.9-20.2) | 19.5 (18.5-20.7) | 0.36 | 1.00 | 19.4 ± 0.4 | 72 | 19.4 (18.1-20.2) | 37 | 19.5 (18.5-20.2) | 35 | 0.57 | 1.00 | [49] |
| PHKA1 | 5255 | phosphorylase kinase regulatory subunit alpha 1 | Xq13.1 | 14.9 ± 1.9 | 15.5 (10.9-17.8) | 14.6 (9.7-17.4) | 0.05 | 1.00 | 14.9 ± 1.8 | 56 | 15.5 (10.9-17.8) | 29 | 14.6 (10.0-17.0) | 27 | 0.11 | 1.00 | [16] |

| | | | | | | | | | | | | | | | | | |
|----------|-------|--|----------|------------|---------------------|---------------------|------|------|------------|----|---------------------|----|---------------------|----|------|------|---------|
| PHKA2 | 5256 | phosphorylase kinase regulatory subunit alpha 2 | Xp22.13 | 16.8 ± 0.6 | 17.1 (15.8-18.3) | 16.5 (15.3-17.9) | 0.00 | 0.00 | 16.8 ± 0.6 | 56 | 17.1 (15.8-18.3) | 29 | 16.5 (15.3-17.9) | 27 | 0.00 | 0.03 | [16] |
| PHKB | 5257 | phosphorylase kinase regulatory subunit beta | 16q12.1 | 16.3 ± 0.8 | 16.0 (14.4-17.4) | 16.7 (15.3-18.1) | 0.00 | 0.03 | 16.4 ± 0.7 | 63 | 16.1 (14.7-17.4) | 33 | 16.9 (15.3-17.7) | 30 | 0.00 | 0.06 | [16] |
| PHKG1 | 5260 | phosphorylase kinase catalytic subunit gamma 1 | 7p11.2 | 13.9 ± 0.8 | 13.8 (11.9-16.3) | 14.1 (12.8-15.5) | 0.06 | 1.00 | 13.9 ± 0.8 | 71 | 13.7 (11.9-16.3) | 36 | 14.1 (12.8-15.5) | 35 | 0.02 | 1.00 | [16] |
| PHKG2 | 5261 | phosphorylase kinase catalytic subunit gamma 2 | 16p11.2 | 17.0 ± 0.6 | 16.9 (15.8-18.2) | 16.9 (16.2-17.9) | 0.84 | 1.00 | 17.0 ± 0.5 | 74 | 16.9 (15.8-18.2) | 37 | 16.9 (16.2-17.9) | 37 | 0.96 | 1.00 | [16] |
| PPP1R14C | 81706 | protein phosphatase 1 regulatory inhibitor subunit 14C | 6q25.1 | 8.9 ± 5.2 | 7.9 (0.0-12.2) | 12.6 (9.7-16.4) | 0.00 | 0.00 | 9.1 ± 5.2 | 50 | 7.9 (0.0-12.2) | 24 | 12.7 (9.7-16.4) | 26 | 0.00 | 0.00 | [36] |
| PRDM8 | 56978 | PR/SET domain 8 | 4q21.21 | 9.7 ± 3.4 | 9.1 (0.0-14.0) | 10.9 (0.0-17.9) | 0.00 | 0.06 | 9.8 ± 3.4 | 70 | 9.1 (0.0-14.0) | 35 | 11.1 (0.0-17.9) | 35 | 0.00 | 0.16 | [16,50] |
| PYGB | 5834 | glycogen phosphorylase B | 20p11.21 | 21.7 ± 1.0 | 22.1 (20.1-24.6) | 21.3 (19.7-23.2) | 0.00 | 0.29 | 21.7 ± 1.0 | 67 | 22.1 (20.1-24.6) | 33 | 21.3 (20.2-23.0) | 34 | 0.00 | 0.19 | [15,16] |
| PYGL | 5836 | glycogen phosphorylase L | 14q22.1 | 21.2 ± 1.3 | 21.6 (18.8-22.9) | 21.3 (16.8-23.7) | 0.48 | 1.00 | 21.2 ± 1.3 | 72 | 21.7 (18.8-22.9) | 36 | 21.4 (16.8-23.5) | 36 | 0.36 | 1.00 | [15,16] |
| PYGM | 5837 | glycogen phosphorylase, muscle associated | 11q13.1 | 13.2 ± 1.4 | 12.3 (10.2-15.1) | 13.9 (11.5-16.2) | 0.00 | 0.00 | 13.2 ± 1.3 | 66 | 12.2 (10.6-14.3) | 31 | 13.9 (11.5-16.0) | 35 | 0.00 | 0.00 | [15,16] |
| RBCK1 | 10616 | RANBP2-type and C3HC4-type zinc finger containing 1 | 20p13 | 20.0 ± 0.7 | 19.9 (18.9-21.8) | 19.7 (18.9-21.5) | 0.24 | 1.00 | 19.8 ± 0.6 | 67 | 19.8 (18.9-21.7) | 33 | 19.7 (18.9-20.7) | 34 | 0.29 | 1.00 | [51] |
| TFEB | 7942 | transcription factor EB | 6p21.1 | 15.3 ± 0.9 | 15.5 (13.2-17.3) | 15.2 (13.2-17.2) | 0.11 | 1.00 | 15.2 ± 0.7 | 36 | 15.7 (15.0-16.3) | 6 | 15.1 (13.9-17.2) | 30 | 0.04 | 1.00 | [52] |
| UGDH | 7358 | UDP-glucose 6-dehydrogenase | 6-4p14 | 16.8 ± 0.7 | 16.5 (15.1-18.2) | 16.8 (16.0-18.5) | 0.03 | 1.00 | 16.7 ± 0.6 | 68 | 16.5 (15.1-18.2) | 36 | 16.7 (16.0-17.9) | 32 | 0.21 | 1.00 | [53] |

n= number; n.a.: not analyzed; NCBI: National Center for Biotechnology Information; TCGA: The Cancer Genome Atlas; SD: standard deviation; UM: Uveal melanoma. *Genes that are involved in both the synthesis and degradation of glycogen.

P - values were determined by the Mann-Whitney U test. † Bonferroni correction.

Genes with a differential expression in monosomy-3-tumors that remained significant after Bonferroni correction were highlighted in colored background. References for gene function are presented in the main text.

Table S2. Genes with a lower expression level in the monosomy-3 tumors regardless of the gene copy number (n = 13),

Supplementary Table S2

Genes with a lower expression level in the monosomy-3 tumors regardless of the gene copy number (n=13) · Median expression (range) in log₂(FPKM-ug) units

| Function* | #1-11. De novo glycogen synthesis & positive regulators of glycogen synthesis | | | | | | | | | | | #12,13. Negative regulators of glycogen synthesis | |
|-------------------------------|---|---------------------|---------------------|---------------------|---------------------|---------------------|---------------------|---------------------|--------------------|---------------------|---------------------|---|---------------------|
| Gene symbol | ATG7 | BAP1 | EPM2A | GBE1 | GYG1 | GYG2 | INSR | IRS2 | IRS4 | PPP1R3B | PPP1R3C | GSK3B | PHKA2 |
| Locus | 3p25.3 | 3p21.1 | 6q24.3 | 3p12.2 | 3q24 | Xp22.33 | 19p13.2 | 13q34 | Xq22.3 | 8p23.1 | 10q23.32 | 3q13.33 | Xp22.13 |
| Expression (n=80) | 16.2 (14.9-17.2) | 19.5 (15.9-21.7) | 16.2 (14.5-17.7) | 16.7 (15.4-19.2) | 18.2 (17.5-19.2) | 20.8 (18.9-23.1) | 17.0 (16.2-17.9) | 19.0 (17.3-20.2) | 10.9 (0.0-15.7) | 17.3 (15.1-20.4) | 18.5 (15.0-21.4) | 17.4 (16.2-18.1) | 16.7 (15.3-18.3) |
| Age (n=80) | ATG7 | BAP1 | EPM2A | GBE1 | GYG1 | GYG2 | INSR | IRS2 | IRS4 | PPP1R3B | PPP1R3C | GSK3B | PHKA2 |
| ≤Median (n=40) | 16.2 (15.3-17.2) | 19.6 (16.1-21.0) | 16.2 (14.5-17.5) | 16.8 (15.4-19.2) | 18.2 (17.7-19.1) | 20.8 (19.0-23.1) | 17.0 (16.2-17.9) | 18.9 (17.3-20.1) | 11.3 (0.0-15.7) | 17.3 (15.1-20.4) | 18.8 (15.6-21.4) | 17.4 (16.2-18.1) | 16.9 (15.5-18.3) |
| >Median (n=40) | 16.2 (14.9-17.1) | 19.4 (15.9-21.7) | 16.1 (14.6-17.7) | 16.6 (15.6-17.9) | 18.2 (17.5-19.2) | 20.9 (18.9-22.9) | 17.0 (16.2-17.7) | 19.0 (17.6-20.2) | 10.3 (0.0-15.3) | 17.2 (15.2-18.5) | 18.2 (15.0-21.3) | 17.4 (16.7-18.1) | 16.6 (15.3-17.9) |
| p - value [†] | 0.46 | 0.89 | 0.80 | 0.19 | 0.72 | 0.91 | 0.66 | 0.79 | 0.03 | 0.23 | 0.19 | 0.49 | 0.42 |
| Gender (n=80) | ATG7 | BAP1 | EPM2A | GBE1 | GYG1 | GYG2 | INSR | IRS2 | IRS4 | PPP1R3B | PPP1R3C | GSK3B | PHKA2 |
| Female (n=35) | 16.1 (14.9-17.1) | 19.6 (16.1-21.3) | 16.2 (15.0-17.7) | 16.7 (15.4-17.7) | 18.2 (17.5-19.2) | 21.3 (19.4-23.1) | 17.0 (16.2-17.9) | 19.1 (17.3-20.2) | 10.7 (0.0-15.0) | 17.5 (15.4-19.1) | 18.6 (15.6-21.4) | 17.4 (16.2-18.1) | 16.7 (16.1-18.0) |
| Male (n=45) | 16.3 (15.5-17.2) | 19.3 (15.9-21.7) | 16.1 (14.5-17.6) | 16.8 (15.6-19.2) | 18.3 (17.6-19.1) | 20.6 (18.9-22.0) | 16.9 (16.2-17.7) | 18.9 (17.6-20.2) | 10.9 (0.0-15.7) | 17.1 (15.1-20.4) | 18.4 (15.0-21.3) | 17.4 (16.7-18.0) | 16.7 (15.3-18.3) |
| p - value [†] | 0.18 | 0.83 | 0.31 | 0.87 | 0.26 | 0.00 | 0.92 | 0.39 | 0.77 | 0.21 | 0.40 | 0.87 | 0.66 |
| Eye color (n=30) | ATG7 | BAP1 | EPM2A | GBE1 | GYG1 | GYG2 | INSR | IRS2 | IRS4 | PPP1R3B | PPP1R3C | GSK3B | PHKA2 |
| Brown (n=15) | 16.3 (15.3-17.2) | 19.8 (16.6-21.7) | 16.3 (14.5-17.0) | 16.7 (15.7-17.6) | 18.2 (17.7-19.1) | 21.0 (19.4-23.1) | 17.0 (16.2-17.9) | 19.1 (17.3-20.2) | 11.3 (8.2-14.3) | 17.2 (15.4-19.1) | 18.5 (15.6-20.8) | 17.3 (16.8-18.1) | 17.0 (16.2-18.0) |
| Green (n=6) | 16.2 (15.6-16.5) | 19.1 (16.4-20.0) | 15.7 (14.9-17.2) | 16.6 (15.9-17.7) | 18.3 (17.9-18.9) | 20.6 (19.0-21.3) | 16.9 (16.3-17.2) | 19.2 (18.0-19.6) | 9.9 (0.0-14.6) | 16.3 (15.2-20.0) | 17.7 (16.9-19.7) | 17.5 (17.0-18.0) | 16.9 (15.8-17.5) |
| Blue (n=9) | 16.3 (15.6-17.1) | 19.8 (16.2-21.3) | 15.9 (15.0-17.4) | 16.9 (16.1-17.7) | 18.2 (18.0-18.5) | 21.3 (19.5-22.9) | 17.0 (16.4-17.4) | 19.0 (18.4-20.0) | 10.9 (9.2-14.9) | 17.5 (15.4-18.8) | 18.2 (17.5-20.9) | 17.3 (16.9-17.9) | 16.9 (16.1-17.6) |
| p - value ^{††} | 0.54 | 0.58 | 0.57 | 0.90 | 0.92 | 0.21 | 0.85 | 0.94 | 0.39 | 0.68 | 0.48 | 0.82 | 0.76 |
| Largest Basal Diameter (n=74) | ATG7 | BAP1 | EPM2A | GBE1 | GYG1 | GYG2 | INSR | IRS2 | IRS4 | PPP1R3B | PPP1R3C | GSK3B | PHKA2 |
| ≤13 mm (n=12) | 16.3 (15.6-17.2) | 20.0 (19.0-21.3) | 16.9 (14.9-17.7) | 16.9 (15.4-17.6) | 18.5 (17.9-19.0) | 21.7 (19.0-22.7) | 17.1 (16.3-17.5) | 19.1 (18.0-19.6) | 11.5 (8.2-15.0) | 17.5 (15.7-18.7) | 19.5 (16.9-20.9) | 17.5 (16.2-17.8) | 17.1 (15.8-17.5) |
| >13 mm (n=62) | 16.2 (14.9-17.1) | 19.0 (15.9-21.7) | 16.1 (14.5-17.6) | 16.7 (15.6-19.2) | 18.2 (17.5-19.2) | 20.7 (18.9-23.1) | 17.0 (16.2-17.9) | 18.9 (17.3-20.2) | 10.7 (0.0-15.7) | 17.1 (15.2-20.0) | 18.3 (15.0-21.4) | 17.3 (16.7-18.1) | 16.6 (15.3-18.3) |
| p - value [†] | 0.17 | 0.00 | 0.03 | 0.26 | <0.05 | 0.00 | 0.73 | 0.58 | 0.34 | 0.31 | 0.02 | 0.84 | 0.25 |
| Tumor thickness (n=76) | ATG7 | BAP1 | EPM2A | GBE1 | GYG1 | GYG2 | INSR | IRS2 | IRS4 | PPP1R3B | PPP1R3C | GSK3B | PHKA2 |
| < Median (n=37) | 16.1 (14.9-17.1) | 19.6 (16.3-21.3) | 16.3 (14.5-17.7) | 16.8 (15.4-17.9) | 18.3 (17.5-19.2) | 21.0 (19.0-22.7) | 17.1 (16.2-17.7) | 19.1 (17.3-20.1) | 10.7 (0.0-15.3) | 17.3 (15.3-18.8) | 18.7 (15.0-21.3) | 17.3 (16.2-18.1) | 16.7 (15.3-17.8) |
| ≥ Median (n=39) | 16.3 (15.3-17.2) | 19.3 (15.9-21.7) | 15.9 (14.6-17.5) | 16.7 (15.6-19.2) | 18.2 (17.6-19.1) | 20.7 (18.9-23.1) | 17.0 (16.3-17.9) | 19.0 (17.9-20.2) | 10.9 (0.0-15.7) | 17.2 (15.2-20.0) | 18.2 (15.6-21.4) | 17.4 (16.7-18.1) | 16.6 (15.8-18.3) |
| p - value [†] | 0.83 | 0.98 | 0.03 | 0.76 | 0.21 | 0.16 | 0.48 | 0.82 | 0.51 | 0.92 | 0.06 | 0.65 | 0.34 |

| AJCC Stage, clinical (n=80) | ATG7 | BAP1 | EPM2A | GBE1 | GYG1 | GYG2 | INSR | IRS2 | IRS4 | PPP1R3B | PPP1R3C | GSK3B | PHKA2 |
|---------------------------------------|---------------------|---------------------|---------------------|---------------------|---------------------|---------------------|---------------------|---------------------|--------------------|---------------------|---------------------|---------------------|---------------------|
| Stage IIA and -B (n=36) | 16.2 (14.9-17.0) | 19.7 (15.9-20.9) | 16.7 (14.8-17.7) | 16.9 (15.4-17.9) | 18.3 (17.5-19.2) | 21.1 (18.9-22.9) | 17.1 (16.3-17.7) | 19.1 (17.3-20.1) | 11.6 (0.0-15.3) | 17.6 (15.1-19.1) | 19.4 (15.0-21.4) | 17.5 (16.2-18.1) | 16.9 (15.3-17.8) |
| Stage IIIA-C (n=40) | 16.3 (15.3-17.2) | 19.0 (16.1-21.7) | 16.1 (14.5-17.5) | 16.7 (15.7-19.2) | 18.2 (17.6-19.1) | 20.6 (19.0-23.1) | 17.0 (16.2-17.9) | 19.0 (17.9-20.2) | 10.6 (0.0-15.7) | 16.9 (15.2-20.4) | 18.1 (15.6-21.1) | 17.3 (16.7-18.0) | 16.6 (15.8-18.3) |
| Stage IV (n=4) | 16.0 (15.6-16.6) | 18.8 (17.5-19.5) | 15.5 (15.0-16.2) | 16.6 (16.1-16.9) | 18.4 (18.0-19.0) | 20.3 (19.7-21.3) | 16.6 (16.4-16.8) | 18.6 (18.5-18.8) | 10.5 (0.0-11.1) | 15.8 (15.4-17.3) | 17.3 (16.7-18.2) | 17.4 (16.9-18.0) | 16.3 (16.2-16.5) |
| <i>p</i> - value ^{††} | 0.54 | 0.14 | 0.00 | 0.36 | 0.13 | 0.15 | 0.20 | 0.22 | 0.18 | 0.04 | 0.01 | 0.31 | 0.09 |
| Extrascleral Extension (n=80) | ATG7 | BAP1 | EPM2A | GBE1 | GYG1 | GYG2 | INSR | IRS2 | IRS4 | PPP1R3B | PPP1R3C | GSK3B | PHKA2 |
| No (n=71) | 16.2 (14.9-17.2) | 19.6 (16.1-21.7) | 16.2 (14.5-17.7) | 16.8 (15.4-19.2) | 18.2 (17.5-19.2) | 20.9 (18.9-23.1) | 17.0 (16.2-17.9) | 19.1 (17.3-20.2) | 10.9 (0.0-15.7) | 17.4 (15.1-20.4) | 18.6 (15.0-21.4) | 17.4 (16.2-18.1) | 16.8 (15.3-18.3) |
| Yes (n=9) | 16.1 (15.5-16.7) | 17.7 (15.9-20.3) | 15.3 (14.8-16.6) | 16.7 (16.1-17.5) | 18.2 (17.7-19.0) | 20.7 (19.0-21.3) | 16.6 (16.2-17.3) | 18.6 (18.0-19.5) | 10.2 (0.0-13.1) | 16.0 (15.4-17.9) | 17.3 (16.1-20.0) | 17.3 (16.9-18.0) | 16.5 (15.8-16.7) |
| <i>p</i> - value [†] | 0.44 | 0.10 | 0.02 | 0.65 | 0.90 | 0.16 | 0.04 | 0.11 | 0.04 | 0.01 | 0.02 | 0.99 | 0.01 |
| BAP1 expression (n=80) | ATG7 | BAP1 | EPM2A | GBE1 | GYG1 | GYG2 | INSR | IRS2 | IRS4 | PPP1R3B | PPP1R3C | GSK3B | PHKA2 |
| >Median (n=40) | 16.4 (15.8-17.2) | 20.1 (19.5-21.7) | 16.6 (15.1-17.7) | 17.2 (15.4-19.2) | 18.4 (17.7-19.2) | 21.3 (20.2-23.1) | 17.1 (16.3-17.9) | 19.2 (18.5-20.2) | 13.2 (0.0-15.3) | 18.0 (15.4-20.4) | 19.5 (16.7-21.4) | 17.6 (16.2-18.1) | 17.1 (16.1-18.3) |
| ≤Median (n=40) | 16.0 (14.9-17.0) | 17.8 (15.9-19.5) | 16.0 (14.5-17.5) | 16.5 (15.6-17.6) | 18.2 (17.5-18.7) | 20.1 (18.9-21.9) | 16.7 (16.2-17.7) | 18.7 (17.3-19.7) | 10.2 (0.0-15.7) | 16.4 (15.1-18.3) | 17.6 (15.0-21.1) | 17.3 (16.7-17.9) | 16.4 (15.3-17.5) |
| <i>p</i> - value [†] | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| Morphology (n=80) | ATG7 | BAP1 | EPM2A | GBE1 | GYG1 | GYG2 | INSR | IRS2 | IRS4 | PPP1R3B | PPP1R3C | GSK3B | PHKA2 |
| Spindle (n=43) | 16.3 (14.9-17.2) | 19.8 (16.1-21.7) | 16.5 (15.0-17.5) | 16.9 (15.4-19.2) | 18.3 (17.5-19.2) | 21.3 (19.4-23.1) | 17.1 (16.3-17.9) | 19.1 (17.9-20.2) | 11.2 (0.0-15.7) | 17.7 (15.4-20.4) | 19.4 (16.6-21.3) | 17.5 (16.2-18.1) | 17.1 (16.1-18.3) |
| Mixed / Spindle (n=14) | 16.3 (15.8-16.6) | 18.8 (15.9-21.0) | 15.8 (14.8-17.7) | 16.5 (15.9-17.7) | 18.2 (17.6-18.6) | 20.8 (19.0-21.8) | 17.0 (16.4-17.3) | 19.1 (18.3-20.2) | 10.6 (0.0-14.6) | 17.2 (15.7-20.0) | 18.0 (16.1-20.2) | 17.3 (16.7-18.0) | 16.6 (16.3-17.9) |
| Mixed / Epithelioid (n=7) | 16.0 (15.8-17.0) | 17.4 (16.3-19.9) | 15.7 (14.5-17.6) | 16.2 (15.7-17.9) | 18.2 (18.0-18.7) | 20.1 (19.5-21.0) | 16.6 (16.2-17.1) | 18.6 (18.1-19.2) | 10.5 (0.0-15.3) | 16.1 (15.2-18.5) | 17.9 (17.0-19.9) | 17.3 (17.2-17.8) | 16.4 (16.0-16.6) |
| Epithelioid (n=16) | 15.9 (15.5-16.7) | 17.9 (16.3-19.9) | 15.9 (14.7-17.2) | 16.7 (15.6-17.5) | 18.1 (17.6-18.7) | 19.8 (18.9-21.0) | 16.6 (16.2-17.3) | 18.5 (17.3-19.4) | 10.6 (0.0-14.4) | 16.2 (15.1-17.9) | 17.1 (15.0-21.4) | 17.4 (16.8-17.8) | 16.1 (15.3-16.8) |
| <i>p</i> - value ^{††} | 0.01 | 0.00 | 0.00 | 0.10 | 0.06 | 0.00 | 0.00 | 0.00 | 0.32 | 0.00 | 0.00 | 0.48 | 0.00 |
| Closed connective tissue loops (n=80) | ATG7 | BAP1 | EPM2A | GBE1 | GYG1 | GYG2 | INSR | IRS2 | IRS4 | PPP1R3B | PPP1R3C | GSK3B | PHKA2 |
| Absent (n=38) | 16.4 (15.3-17.2) | 19.8 (15.9-21.7) | 16.3 (14.8-17.6) | 16.9 (15.4-19.2) | 18.3 (17.7-19.2) | 21.0 (18.9-22.9) | 17.1 (16.3-17.7) | 19.1 (17.6-20.2) | 11.9 (0.0-15.3) | 17.8 (15.6-20.4) | 19.4 (15.0-21.3) | 17.5 (16.2-18.1) | 17.0 (15.3-18.3) |
| Present (n=42) | 16.1 (14.9-17.0) | 18.8 (16.1-20.8) | 16.1 (14.5-17.7) | 16.7 (15.6-17.9) | 18.2 (17.5-19.1) | 20.6 (19.0-23.1) | 16.8 (16.2-17.9) | 18.9 (17.3-20.2) | 10.4 (0.0-15.7) | 16.6 (15.1-18.9) | 18.1 (15.9-21.4) | 17.3 (16.7-18.0) | 16.6 (15.5-18.0) |
| <i>p</i> - value [†] | 0.01 | 0.00 | 0.34 | 0.23 | 0.04 | 0.06 | 0.03 | 0.22 | 0.00 | 0.00 | 0.02 | 0.17 | 0.07 |
| Mitotic count (n=80) | ATG7 | BAP1 | EPM2A | GBE1 | GYG1 | GYG2 | INSR | IRS2 | IRS4 | PPP1R3B | PPP1R3C | GSK3B | PHKA2 |
| 0-5 (n=63) | 16.3 (14.9-17.2) | 19.6 (15.9-21.7) | 16.3 (14.5-17.7) | 16.7 (15.4-19.2) | 18.3 (17.5-19.2) | 20.9 (18.9-23.1) | 17.0 (16.2-17.9) | 19.0 (17.3-20.2) | 10.9 (0.0-15.7) | 17.5 (15.1-20.4) | 18.8 (15.0-21.4) | 17.4 (16.2-18.1) | 16.8 (15.3-18.3) |

| | | | | | | | | | | | | | |
|---|---------------------|---------------------|---------------------|---------------------|---------------------|---------------------|---------------------|---------------------|--------------------|---------------------|---------------------|---------------------|---------------------|
| >5-10 (n=11) | 16.1 (15.6-16.4) | 19.3 (17.5-20.3) | 16.1 (15.0-17.2) | 16.8 (16.1-17.7) | 18.0 (17.6-18.5) | 21.0 (19.0-22.6) | 16.8 (16.4-17.3) | 19.1 (18.5-20.2) | 10.9 (8.1-14.3) | 16.7 (15.4-18.8) | 18.0 (16.9-20.3) | 17.6 (16.9-17.9) | 16.5 (16.1-17.9) |
| >11 (n=6) | 16.1 (15.6-16.5) | 18.9 (16.3-19.8) | 16.0 (14.6-16.5) | 16.6 (15.9-17.9) | 18.3 (17.9-18.7) | 20.0 (19.4-20.5) | 16.7 (16.3-17.3) | 18.5 (18.1-19.4) | 10.7 (0.0-13.0) | 16.1 (15.6-17.6) | 17.4 (15.6-18.9) | 17.3 (16.9-17.6) | 16.5 (16.0-17.2) |
| <i>p</i> - value ^{††} | 0.11 | 0.34 | 0.23 | 0.82 | 0.05 | 0.03 | 0.42 | 0.24 | 0.54 | 0.06 | 0.04 | 0.48 | 0.40 |
| Tumor infiltrating lymphocytes density (n=80) | ATG7 | BAP1 | EPM2A | GBE1 | GYG1 | GYG2 | INSR | IRS2 | IRS4 | PPP1R3B | PPP1R3C | GSK3B | PHKA2 |
| Mild (n=71) | 16.3 (14.9-17.2) | 19.6 (16.1-21.7) | 16.2 (14.5-17.7) | 16.8 (15.7-19.2) | 18.3 (17.5-19.2) | 20.9 (18.9-23.1) | 17.0 (16.2-17.9) | 19.1 (17.3-20.2) | 10.9 (0.0-15.7) | 17.4 (15.2-20.4) | 18.7 (15.6-21.4) | 17.5 (16.7-18.1) | 16.8 (15.8-18.3) |
| Moderate (n=7) | 16.0 (15.5-16.7) | 17.5 (16.3-19.9) | 15.9 (14.7-16.6) | 16.4 (15.4-17.5) | 18.1 (17.7-18.7) | 19.8 (19.0-22.2) | 16.6 (16.2-17.5) | 18.6 (17.6-19.1) | 9.2 (0.0-13.1) | 16.1 (15.1-17.9) | 17.3 (15.0-18.4) | 17.2 (16.2-17.8) | 16.1 (15.3-16.7) |
| Heavy (n=2) | 16.1 (15.8-16.4) | 17.5 (15.9-19.0) | 15.4 (14.8-15.9) | 15.9 (15.6-16.2) | 18.0 (17.9-18.2) | 19.9 (19.4-20.4) | 16.7 (16.5-16.8) | 18.7 (18.5-18.8) | 10.1 (9.4-10.9) | 16.0 (16.0-16.1) | 16.0 (15.9-16.1) | 16.9 (16.8-17.1) | 16.0 (15.8-16.3) |
| <i>p</i> - value ^{††} | 0.22 | 0.06 | 0.05 | 0.03 | 0.17 | 0.11 | 0.24 | 0.03 | 0.07 | 0.02 | 0.00 | 0.06 | 0.00 |
| Tumor infiltrating macrophages density (n=80) | ATG7 | BAP1 | EPM2A | GBE1 | GYG1 | GYG2 | INSR | IRS2 | IRS4 | PPP1R3B | PPP1R3C | GSK3B | PHKA2 |
| Mild (n=40) | 16.1 (15.3-17.1) | 19.6 (16.1-21.3) | 16.4 (15.0-17.7) | 16.9 (15.9-19.2) | 18.3 (17.6-19.2) | 21.0 (19.0-22.7) | 17.1 (16.4-17.7) | 19.1 (17.9-20.1) | 11.2 (0.0-15.7) | 17.6 (15.4-20.4) | 19.4 (16.6-21.4) | 17.6 (16.7-18.1) | 16.9 (16.1-18.3) |
| Moderate (n=29) | 16.2 (14.9-17.1) | 19.0 (15.9-21.7) | 16.0 (14.6-17.4) | 16.6 (15.9-17.7) | 18.2 (17.5-19.1) | 20.6 (18.9-23.1) | 16.8 (16.2-17.9) | 18.9 (17.6-20.2) | 10.6 (0.0-14.6) | 16.8 (15.1-18.9) | 18.0 (15.0-21.1) | 17.3 (16.8-17.9) | 16.6 (15.3-18.0) |
| Heavy (n=11) | 16.3 (15.8-17.2) | 19.0 (16.6-21.0) | 15.9 (14.5-17.0) | 16.6 (15.4-17.1) | 18.2 (17.9-18.4) | 20.7 (19.4-22.9) | 16.6 (16.2-17.5) | 18.8 (17.3-20.0) | 10.5 (8.2-14.6) | 16.8 (15.2-19.1) | 17.8 (15.9-19.6) | 17.3 (16.2-18.1) | 16.5 (15.8-17.5) |
| <i>p</i> - value ^{††} | 0.29 | 0.39 | 0.00 | 0.00 | 0.08 | 0.39 | 0.12 | 0.43 | <0.05 | 0.03 | 0.00 | 0.02 | 0.49 |
| Pigmentation (n=80) | ATG7 | BAP1 | EPM2A | GBE1 | GYG1 | GYG2 | INSR | IRS2 | IRS4 | PPP1R3B | PPP1R3C | GSK3B | PHKA2 |
| Mild (n=39) | 16.1 (14.9-17.1) | 19.6 (16.1-21.3) | 16.5 (15.3-17.7) | 17.0 (16.1-19.2) | 18.3 (17.5-19.2) | 20.9 (18.9-22.7) | 17.1 (16.3-17.7) | 19.1 (17.9-20.1) | 11.4 (0.0-15.7) | 17.6 (15.6-20.4) | 19.3 (15.9-21.4) | 17.6 (16.7-18.1) | 17.0 (16.1-18.3) |
| Moderate (n=27) | 16.2 (15.5-17.2) | 19.0 (16.2-21.7) | 15.9 (14.6-16.9) | 16.6 (15.6-17.6) | 18.2 (17.7-19.0) | 20.7 (19.0-23.1) | 16.8 (16.2-17.9) | 18.8 (17.3-20.2) | 10.3 (0.0-14.6) | 16.6 (15.1-18.9) | 17.8 (15.0-20.8) | 17.3 (16.8-18.0) | 16.6 (15.3-18.0) |
| Heavy (n=14) | 16.4 (15.7-17.0) | 19.2 (15.9-20.9) | 15.8 (14.5-17.2) | 16.5 (15.4-17.2) | 18.2 (17.9-18.9) | 20.6 (19.4-22.9) | 16.6 (16.2-17.7) | 19.1 (18.3-20.0) | 10.1 (0.0-13.5) | 16.9 (15.2-19.1) | 18.5 (15.6-20.1) | 17.3 (16.2-18.1) | 16.5 (15.8-17.2) |
| <i>p</i> - value ^{††} | 0.34 | 0.67 | 0.00 | 0.00 | 0.43 | 0.72 | 0.11 | 0.28 | 0.00 | 0.01 | 0.00 | 0.04 | 0.08 |
| Necrosis (n=80) | ATG7 | BAP1 | EPM2A | GBE1 | GYG1 | GYG2 | INSR | IRS2 | IRS4 | PPP1R3B | PPP1R3C | GSK3B | PHKA2 |
| Absent (n=63) | 16.2 (15.3-17.2) | 19.6 (16.1-21.7) | 16.2 (14.5-17.7) | 16.8 (15.4-17.9) | 18.3 (17.5-19.2) | 20.9 (19.0-23.1) | 17.0 (16.2-17.9) | 19.1 (17.6-20.2) | 10.9 (0.0-15.7) | 17.3 (15.1-20.4) | 18.8 (15.0-21.4) | 17.4 (16.2-18.1) | 16.8 (15.3-18.0) |
| Present (n=17) | 16.2 (14.9-16.8) | 19.3 (15.9-21.0) | 15.9 (14.6-17.2) | 16.7 (16.1-19.2) | 18.2 (17.6-19.0) | 20.7 (18.9-22.9) | 16.8 (16.2-17.6) | 18.7 (17.3-20.2) | 10.9 (0.0-14.6) | 16.8 (15.4-18.6) | 17.7 (15.9-20.6) | 17.4 (16.9-18.0) | 16.5 (16.0-18.3) |
| <i>p</i> - value [†] | 0.72 | 0.69 | 0.09 | 0.60 | 0.21 | 0.27 | 0.45 | 0.40 | 0.12 | 0.51 | 0.00 | 0.86 | 0.14 |
| Body-Mass-Index (n=53) | ATG7 | BAP1 | EPM2A | GBE1 | GYG1 | GYG2 | INSR | IRS2 | IRS4 | PPP1R3B | PPP1R3C | GSK3B | PHKA2 |
| <25.0 (n=17) | 16.2 (14.9-16.9) | 19.6 (16.2-20.9) | 16.4 (15.3-17.4) | 16.9 (15.6-17.7) | 18.2 (17.6-18.9) | 20.9 (19.4-23.1) | 17.2 (16.5-17.9) | 19.1 (17.3-20.2) | 11.4 (0.0-14.9) | 17.7 (15.2-19.1) | 19.0 (15.9-21.4) | 17.5 (16.8-18.1) | 16.9 (15.8-18.0) |

| | | | | | | | | | | | | | |
|--|---------------------|---------------------|---------------------|---------------------|---------------------|---------------------|---------------------|---------------------|--------------------|---------------------|---------------------|---------------------|---------------------|
| ≥25.0 (n=36) | 16.2 (15.3-17.2) | 19.4 (16.1-21.7) | 16.0 (14.5-17.6) | 16.7 (15.4-17.9) | 18.3 (17.7-19.1) | 20.8 (18.9-22.7) | 16.9 (16.2-17.7) | 18.9 (17.9-20.2) | 10.8 (0.0-15.3) | 17.1 (15.3-20.4) | 18.3 (15.6-20.4) | 17.4 (16.2-18.0) | 16.5 (15.8-17.6) |
| <i>p</i> - value [†] | 0.82 | 0.47 | 0.08 | 0.32 | 0.20 | 0.27 | 0.12 | <0.05 | 0.47 | 0.65 | 0.80 | 0.67 | 0.14 |
| Progression (n=80) | ATG7 | BAP1 | EPM2A | GBE1 | GYG1 | GYG2 | INSR | IRS2 | IRS4 | PPP1R3B | PPP1R3C | GSK3B | PHKA2 |
| Censored (n=50) | 16.3 (15.5-17.2) | 19.8 (16.1-21.7) | 16.4 (14.6-17.7) | 16.9 (15.4-19.2) | 18.3 (17.5-19.2) | 21.1 (19.4-23.1) | 17.1 (16.3-17.9) | 19.1 (17.3-20.2) | 11.3 (0.0-15.7) | 17.6 (15.6-20.4) | 19.1 (15.0-21.4) | 17.5 (16.2-18.1) | 17.0 (15.3-18.3) |
| Progression (n=30) | 16.0 (14.9-17.0) | 18.0 (15.9-20.6) | 15.6 (14.5-17.4) | 16.6 (15.7-17.7) | 18.1 (17.7-19.0) | 20.2 (18.9-22.6) | 16.7 (16.2-17.4) | 18.7 (17.9-20.1) | 10.5 (0.0-15.0) | 16.4 (15.1-18.8) | 17.3 (15.6-20.4) | 17.4 (16.8-18.0) | 16.5 (15.5-17.8) |
| <i>p</i> - value [†] | 0.01 | 0.00 | 0.00 | 0.02 | 0.01 | 0.00 | 0.00 | 0.00 | 0.09 | 0.00 | 0.00 | 0.55 | 0.00 |
| Metastases (n=80) | ATG7 | BAP1 | EPM2A | GBE1 | GYG1 | GYG2 | INSR | IRS2 | IRS4 | PPP1R3B | PPP1R3C | GSK3B | PHKA2 |
| No (n=54) | 16.3 (15.5-17.2) | 19.8 (16.1-21.7) | 16.4 (14.6-17.7) | 16.9 (15.4-19.2) | 18.3 (17.5-19.2) | 21.1 (19.0-23.1) | 17.1 (16.2-17.9) | 19.1 (17.3-20.2) | 11.7 (0.0-15.7) | 17.6 (15.6-20.4) | 19.2 (15.0-21.4) | 17.5 (16.2-18.1) | 17.0 (15.3-18.3) |
| Yes (n=26) | 16.0 (14.9-17.0) | 17.9 (15.9-20.3) | 15.6 (14.5-16.9) | 16.5 (15.7-17.7) | 18.1 (17.7-19.0) | 19.9 (18.9-22.6) | 16.6 (16.2-17.7) | 18.7 (17.9-20.1) | 10.5 (0.0-14.3) | 16.3 (15.1-18.8) | 17.3 (15.6-20.3) | 17.3 (16.8-18.0) | 16.3 (15.5-17.6) |
| <i>p</i> - value [†] | 0.01 | 0.00 | 0.00 | 0.00 | 0.02 | 0.00 | 0.00 | 0.00 | 0.02 | 0.00 | 0.00 | 0.15 | 0.00 |
| Disease specific survival (n=78) | ATG7 | BAP1 | EPM2A | GBE1 | GYG1 | GYG2 | INSR | IRS2 | IRS4 | PPP1R3B | PPP1R3C | GSK3B | PHKA2 |
| Alive or dead due to other causes (n=58) | 16.3 (15.3-17.2) | 19.8 (16.1-21.7) | 16.4 (14.6-17.7) | 16.9 (15.4-19.2) | 18.3 (17.5-19.2) | 21.2 (19.0-23.1) | 17.1 (16.3-17.9) | 19.1 (17.3-20.2) | 11.7 (0.0-15.7) | 17.6 (15.1-20.4) | 19.2 (15.0-21.4) | 17.5 (16.2-18.1) | 17.0 (15.3-18.3) |
| Dead due to UM-metastases (n=20) | 15.9 (14.9-17.0) | 17.9 (15.9-20.2) | 15.6 (14.5-16.8) | 16.5 (15.7-16.9) | 18.2 (17.9-19.0) | 19.9 (18.9-21.5) | 16.6 (16.2-17.7) | 18.7 (18.0-19.4) | 10.5 (0.0-11.5) | 16.3 (15.2-17.3) | 17.2 (15.6-19.5) | 17.3 (16.9-18.0) | 16.3 (15.8-16.9) |
| <i>p</i> - value [†] | 0.03 | 0.00 | 0.00 | 0.00 | 0.08 | 0.00 | 0.00 | 0.00 | 0.03 | 0.00 | 0.00 | 0.04 | 0.00 |

*References for gene function are listed in Supplementary Table 1. Genes with a differential expression are highlighted in color. n: number. [†]Mann-Whitney U test · ^{††}Kruskal-Wallis test

Table S3. Genes with a higher expression level in the monosomy-3 tumors regardless of the gene copy number (n = 9).

| Supplementary Table S3 | | | | | | | | | |
|--|---|---------------------|---|---------------------|---------------------|---------------------|-------------------|--------------------|---------------------|
| Genes with a higher expression level in the monosomy-3 tumors regardless of the gene copy number (n=9) · Median expression (range) | | | | | | | | | |
| Function* | #1,2. Dual regulators of glycogen synthesis | | #3-9. Negative regulators of glycogen synthesis | | | | | | |
| Gene symbol | PGM2 | PGM5 | CALM1 | CALM2 | G6PC3 | GFPT1 | PCK1 | PPP1R14C | PYGM |
| Locus | 4p14 | 9q21.11 | 14q32.11 | 2p21 | 17q21.31 | 2p13.3 | 20q13.31 | 6q25.1 | 11q13.1 |
| Expression (n=80) | 17.4 (15.0-19.5) | 12.3 (8.3-15.5) | 20.0 (18.9-20.9) | 19.8 (18.2-21.1) | 20.4 (18.5-22.3) | 17.0 (15.5-18.4) | 8.4 (0.0-12.8) | 10.9 (0.0-16.4) | 13.2 (10.2-16.2) |
| Age (n=80) | PGM2 | PGM5 | CALM1 | CALM2 | G6PC3 | GFPT1 | PCK1 | PPP1R14C | PYGM |
| ≤Median (n=40) | 17.5 (16.0-19.5) | 12.5 (10.0-15.0) | 20.0 (19.1-20.6) | 19.7 (18.5-20.7) | 20.4 (18.5-22.3) | 17.0 (15.5-18.4) | 8.3 (0.0-12.8) | 10.4 (0.0-16.4) | 13.0 (10.3-16.2) |
| >Median (n=40) | 17.3 (15.0-18.9) | 12.2 (8.3-15.5) | 19.9 (18.9-20.9) | 20.0 (18.2-21.1) | 20.4 (18.8-22.0) | 17.0 (15.5-18.4) | 8.7 (0.0-12.2) | 11.0 (0.0-14.8) | 13.3 (10.2-16.0) |

| | | | | | | | | | |
|----------------------------------|---------------------|---------------------|---------------------|---------------------|---------------------|---------------------|-------------------|--------------------|---------------------|
| <i>p</i> - value [†] | 0.83 | 0.20 | 0.95 | 0.55 | 0.43 | 0.60 | 0.82 | 0.56 | 0.28 |
| Gender (n=80) | PGM2 | PGM5 | CALM1 | CALM2 | G6PC3 | GFPT1 | PCK1 | PPP1R14C | PYGM |
| Female (n=35) | 17.5 (15.0-19.5) | 12.2 (8.3-14.2) | 19.9 (18.9-20.6) | 19.8 (18.5-20.7) | 20.4 (18.7-21.7) | 16.9 (15.5-18.4) | 8.9 (0.0-12.8) | 11.1 (0.0-16.4) | 13.4 (11.0-16.2) |
| Male (n=45) | 17.4 (15.8-18.9) | 12.3 (10.0-15.5) | 20.0 (19.1-20.9) | 19.9 (18.2-21.1) | 20.5 (18.5-22.3) | 17.0 (15.8-18.4) | 8.3 (0.0-11.7) | 9.9 (0.0-14.4) | 13.0 (10.2-15.7) |
| <i>p</i> - value [†] | 0.62 | 0.72 | 0.46 | 0.74 | 0.74 | 0.93 | 0.48 | 0.57 | 0.17 |
| Eye color (n=30) | PGM2 | PGM5 | CALM1 | CALM2 | G6PC3 | GFPT1 | PCK1 | PPP1R14C | PYGM |
| Brown (n=15) | 17.1 (15.8-19.5) | 12.0 (10.0-15.0) | 20.0 (19.4-20.5) | 19.6 (18.2-20.7) | 20.7 (19.9-22.3) | 16.9 (15.5-18.0) | 7.3 (0.0-11.7) | 9.9 (0.0-14.4) | 12.5 (11.5-15.7) |
| Green (n=6) | 17.9 (17.5-18.9) | 12.0 (8.3-14.3) | 19.8 (19.4-20.0) | 19.8 (19.0-21.1) | 20.4 (18.8-21.4) | 16.9 (16.3-18.4) | 8.8 (7.6-10.1) | 12.0 (0.0-14.8) | 13.7 (12.2-14.5) |
| Blue (n=9) | 17.2 (15.0-18.4) | 12.4 (11.0-13.7) | 19.9 (18.9-20.6) | 19.7 (18.7-20.5) | 20.6 (18.9-21.7) | 16.6 (15.7-17.8) | 9.0 (0.0-12.2) | 9.9 (0.0-16.4) | 13.9 (11.0-16.0) |
| <i>p</i> - value ^{††} | 0.13 | 0.85 | 0.58 | 0.96 | 0.61 | 0.40 | 0.50 | 0.91 | 0.42 |
| Largest Basal Diameter (n=74) | PGM2 | PGM5 | CALM1 | CALM2 | G6PC3 | GFPT1 | PCK1 | PPP1R14C | PYGM |
| ≤13 mm (n=12) | 16.9 (16.0-18.9) | 11.9 (8.3-13.9) | 19.9 (18.9-20.4) | 19.5 (18.5-21.1) | 20.6 (18.7-21.7) | 16.6 (15.7-18.4) | 7.0 (0.0-10.1) | 9.0 (0.0-11.9) | 12.8 (10.6-15.4) |
| >13 mm (n=62) | 17.5 (15.0-19.5) | 12.3 (10.5-15.5) | 20.0 (18.9-20.9) | 20.0 (18.2-20.7) | 20.4 (18.5-22.3) | 17.0 (15.5-18.4) | 8.9 (0.0-12.8) | 11.3 (0.0-14.8) | 13.2 (10.2-16.2) |
| <i>p</i> - value [†] | 0.25 | 0.19 | 0.88 | 0.11 | 0.64 | 0.06 | 0.04 | 0.03 | 0.45 |
| Tumor thickness (n=76) | PGM2 | PGM5 | CALM1 | CALM2 | G6PC3 | GFPT1 | PCK1 | PPP1R14C | PYGM |
| < Median (n=37) | 17.4 (15.9-18.9) | 12.5 (10.3-15.5) | 19.9 (18.9-20.9) | 19.9 (18.5-20.6) | 20.4 (18.7-22.3) | 16.9 (15.5-18.3) | 8.8 (0.0-12.2) | 10.8 (0.0-14.7) | 13.1 (10.2-16.0) |
| ≥ Median (n=39) | 17.4 (15.0-19.5) | 12.0 (8.3-14.3) | 20.0 (18.9-20.8) | 19.6 (18.2-21.1) | 20.5 (18.5-22.0) | 17.0 (15.5-18.4) | 8.3 (0.0-12.8) | 11.3 (0.0-14.8) | 13.2 (10.3-16.2) |
| <i>p</i> - value [†] | 0.96 | 0.20 | 0.43 | 0.26 | 0.39 | 0.67 | 0.98 | 0.96 | 0.93 |
| AJCC Stage, clinical (n=80) | PGM2 | PGM5 | CALM1 | CALM2 | G6PC3 | GFPT1 | PCK1 | PPP1R14C | PYGM |
| Stage IIA and -B (n=36) | 17.2 (15.0-18.9) | 12.0 (10.3-13.9) | 19.9 (18.9-20.8) | 19.7 (18.5-20.6) | 20.2 (18.7-21.9) | 16.8 (15.5-18.0) | 7.6 (0.0-9.9) | 9.6 (0.0-13.7) | 13.0 (10.2-15.4) |
| Stage IIIA-C (n=40) | 17.5 (15.8-19.5) | 12.4 (8.3-15.5) | 20.0 (19.1-20.9) | 19.8 (18.2-21.1) | 20.5 (18.5-22.3) | 17.0 (15.5-18.4) | 9.0 (0.0-12.8) | 11.6 (0.0-14.8) | 13.4 (10.3-16.2) |
| Stage IV (n=4) | 18.0 (17.5-18.4) | 13.0 (12.4-13.4) | 20.2 (20.1-20.6) | 20.3 (20.1-20.5) | 20.7 (19.8-21.5) | 17.5 (16.6-17.8) | 9.9 (6.1-12.2) | 14.1 (9.6-16.4) | 13.7 (12.8-16.0) |

| | | | | | | | | | |
|---|---------------------|---------------------|---------------------|---------------------|---------------------|---------------------|-------------------|--------------------|---------------------|
| <i>p</i> - value ^{††} | 0.06 | 0.12 | 0.06 | 0.06 | 0.24 | 0.26 | 0.01 | <0.01 | 0.08 |
| Extrascleral Extension (n=80) | PGM2 | PGM5 | CALM1 | CALM2 | G6PC3 | GFPT1 | PCK1 | PPP1R14C | PYGM |
| No (n=71) | 17.4 (15.0-19.5) | 12.3 (8.3-15.5) | 19.9 (18.9-20.9) | 19.8 (18.2-20.7) | 20.4 (18.5-22.3) | 16.9 (15.5-18.4) | 8.3 (0.0-12.8) | 9.9 (0.0-16.4) | 13.1 (10.2-16.2) |
| Yes (n=9) | 17.5 (16.4-18.9) | 12.4 (10.9-14.4) | 20.1 (19.6-20.4) | 20.2 (19.6-21.1) | 20.7 (19.1-21.9) | 17.6 (16.6-18.4) | 9.2 (0.0-12.2) | 11.9 (8.7-14.8) | 13.9 (11.5-16.0) |
| <i>p</i> - value [†] | 0.36 | 0.65 | 0.25 | 0.06 | 0.30 | 0.04 | 0.06 | <0.05 | 0.16 |
| BAP1 expression (n=80) | PGM2 | PGM5 | CALM1 | CALM2 | G6PC3 | GFPT1 | PCK1 | PPP1R14C | PYGM |
| >Median (n=40) | 17.1 (15.0-18.3) | 12.0 (8.3-14.2) | 19.7 (18.9-20.4) | 19.5 (18.2-20.3) | 20.1 (18.5-21.7) | 16.6 (15.5-17.5) | 7.1 (0.0-10.3) | 8.0 (0.0-14.4) | 12.5 (10.2-15.7) |
| ≤Median (n=40) | 17.9 (16.5-19.5) | 12.6 (10.5-15.5) | 20.2 (19.2-20.9) | 20.1 (19.1-21.1) | 20.6 (18.9-22.3) | 17.4 (16.5-18.4) | 9.3 (0.0-12.8) | 12.3 (0.0-16.4) | 13.8 (10.3-16.2) |
| <i>p</i> - value [†] | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 |
| Morphology (n=80) | PGM2 | PGM5 | CALM1 | CALM2 | G6PC3 | GFPT1 | PCK1 | PPP1R14C | PYGM |
| Spindle (n=43) | 17.3 (15.0-18.7) | 12.0 (8.3-14.3) | 19.8 (18.9-20.6) | 19.6 (18.2-20.5) | 20.1 (18.5-21.7) | 16.8 (15.5-17.9) | 7.5 (0.0-12.8) | 8.9 (0.0-16.4) | 12.7 (10.3-16.0) |
| Mixed / Spindle (n=14) | 17.2 (16.1-18.2) | 12.7 (10.7-15.5) | 20.0 (19.4-20.9) | 19.6 (18.7-20.2) | 20.6 (18.8-21.9) | 16.8 (15.8-17.7) | 8.9 (0.0-10.3) | 11.7 (0.0-14.4) | 13.5 (11.4-16.2) |
| Mixed / Epithelioid (n=7) | 17.6 (16.5-18.2) | 12.9 (11.9-14.4) | 20.1 (19.9-20.4) | 20.1 (19.7-20.2) | 20.4 (19.4-22.3) | 17.4 (16.9-18.3) | 9.5 (0.0-11.7) | 12.2 (9.2-13.2) | 14.0 (10.2-15.6) |
| Epithelioid (n=16) | 17.9 (16.5-19.5) | 12.5 (11.6-14.2) | 20.2 (19.4-20.8) | 20.1 (19.6-21.1) | 20.6 (19.1-21.6) | 17.9 (16.6-18.4) | 9.3 (0.0-11.4) | 12.1 (9.7-14.8) | 13.6 (11.2-15.5) |
| <i>p</i> - value ^{††} | 0.06 | 0.02 | <0.01 | <0.01 | 0.19 | <0.01 | 0.01 | <0.01 | 0.05 |
| Closed connective tissue loops (n=80) | PGM2 | PGM5 | CALM1 | CALM2 | G6PC3 | GFPT1 | PCK1 | PPP1R14C | PYGM |
| Absent (n=38) | 17.1 (15.0-19.5) | 12.0 (10.0-15.0) | 19.8 (18.9-20.8) | 19.6 (18.2-20.7) | 20.2 (18.5-21.9) | 16.8 (15.5-18.0) | 7.5 (0.0-9.9) | 8.9 (0.0-14.4) | 13.0 (10.2-15.4) |
| Present (n=42) | 17.7 (16.0-18.9) | 12.5 (8.3-15.5) | 20.0 (19.2-20.9) | 20.0 (19.0-21.1) | 20.5 (18.9-22.3) | 17.1 (15.5-18.4) | 9.1 (0.0-12.8) | 11.8 (0.0-16.4) | 13.5 (10.3-16.2) |
| <i>p</i> - value [†] | <0.01 | 0.23 | 0.01 | <0.01 | 0.35 | <0.01 | <0.01 | <0.01 | 0.02 |
| Mitotic count (n=80) | PGM2 | PGM5 | CALM1 | CALM2 | G6PC3 | GFPT1 | PCK1 | PPP1R14C | PYGM |
| 0-5 (n=63) | 17.3 (15.0-18.9) | 12.2 (8.3-15.0) | 19.9 (18.9-20.8) | 19.7 (18.2-21.1) | 20.4 (18.5-22.3) | 16.9 (15.5-18.4) | 8.1 (0.0-12.8) | 9.8 (0.0-14.8) | 13.0 (10.2-16.2) |
| >5-10 (n=11) | 17.6 (16.8-18.4) | 12.4 (11.1-15.5) | 20.1 (19.4-20.9) | 20.0 (19.2-20.5) | 20.0 (19.1-21.7) | 16.9 (15.8-18.4) | 9.3 (6.1-12.2) | 11.9 (0.0-16.4) | 13.9 (11.4-16.0) |

| | | | | | | | | | |
|---|---------------------|---------------------|---------------------|---------------------|---------------------|---------------------|-------------------|---------------------|---------------------|
| >11 (n=6) | 17.7 (16.9-19.5) | 12.6 (12.0-13.1) | 20.2 (19.7-20.4) | 20.1 (19.9-20.7) | 20.6 (19.2-22.0) | 17.5 (16.6-18.0) | 9.6 (7.2-9.9) | 11.9 (7.9-13.3) | 13.0 (11.5-13.7) |
| <i>p</i> - value ^{††} | 0.14 | 0.66 | 0.18 | 0.10 | 0.83 | 0.25 | 0.01 | 0.05 | 0.09 |
| Tumor infiltrating lymphocytes density (n=80) | PGM2 | PGM5 | CALM1 | CALM2 | G6PC3 | GFPT1 | PCK1 | PPP1R14C | PYGM |
| Mild (n=71) | 17.5 (15.0-19.5) | 12.2 (8.3-15.5) | 19.9 (18.9-20.9) | 19.8 (18.2-21.1) | 20.3 (18.5-22.3) | 16.9 (15.5-18.4) | 8.3 (0.0-12.8) | 9.9 (0.0-16.4) | 13.0 (10.2-16.2) |
| Moderate (n=7) | 17.4 (16.0-17.9) | 13.5 (12.5-14.2) | 20.3 (19.7-20.5) | 20.2 (18.5-20.6) | 20.7 (19.1-21.3) | 17.8 (16.6-18.0) | 9.1 (0.0-11.4) | 13.2 (9.8-14.2) | 13.9 (13.2-15.5) |
| Heavy (n=2) | 17.1 (16.9-17.3) | 12.2 (11.8-12.7) | 20.3 (20.1-20.6) | 19.7 (19.6-19.8) | 21.2 (20.6-21.9) | 17.6 (17.4-17.7) | 9.3 (8.6-9.9) | 11.9 (11.6-12.2) | 13.7 (13.5-13.9) |
| <i>p</i> - value ^{††} | 0.77 | 0.04 | 0.02 | 0.32 | 0.26 | 0.05 | 0.19 | 0.05 | 0.03 |
| Tumor infiltrating macrophages density (n=80) | PGM2 | PGM5 | CALM1 | CALM2 | G6PC3 | GFPT1 | PCK1 | PPP1R14C | PYGM |
| Mild (n=40) | 17.5 (16.1-18.7) | 12.3 (10.7-15.5) | 19.8 (18.9-20.9) | 19.8 (18.8-20.5) | 19.9 (18.5-21.7) | 17.0 (15.5-18.4) | 7.4 (0.0-12.8) | 9.6 (0.0-16.4) | 12.8 (10.2-16.2) |
| Moderate (n=29) | 17.3 (15.8-19.5) | 12.3 (8.3-14.2) | 20.0 (19.5-20.5) | 19.9 (18.2-21.1) | 20.7 (19.1-22.0) | 17.0 (15.5-18.4) | 9.0 (0.0-11.4) | 11.6 (0.0-14.8) | 13.4 (10.6-15.7) |
| Heavy (n=11) | 16.7 (15.0-18.9) | 11.9 (10.0-15.0) | 20.2 (18.9-20.8) | 19.7 (18.5-20.4) | 20.8 (19.9-22.3) | 17.2 (15.9-18.0) | 9.1 (0.0-11.7) | 9.8 (0.0-12.8) | 13.5 (11.4-15.6) |
| <i>p</i> - value ^{††} | 0.30 | 0.90 | 0.06 | 0.56 | <0.01 | 0.91 | 0.10 | 0.20 | 0.05 |
| Pigmentation (n=80) | PGM2 | PGM5 | CALM1 | CALM2 | G6PC3 | GFPT1 | PCK1 | PPP1R14C | PYGM |
| Mild (n=39) | 17.5 (16.1-18.7) | 12.3 (10.5-15.5) | 19.9 (18.9-20.9) | 19.9 (18.8-20.6) | 19.9 (18.5-21.7) | 17.0 (15.7-18.4) | 7.5 (0.0-12.8) | 9.9 (0.0-16.4) | 12.9 (10.2-16.2) |
| Moderate (n=27) | 17.2 (15.8-18.9) | 12.7 (10.0-14.4) | 20.1 (19.4-20.6) | 19.9 (18.2-21.1) | 20.7 (19.8-22.0) | 17.1 (15.5-18.4) | 8.9 (0.0-12.2) | 11.6 (0.0-14.7) | 13.4 (11.4-16.0) |
| Heavy (n=14) | 17.0 (15.0-19.5) | 12.0 (8.3-15.0) | 20.0 (18.9-20.8) | 19.6 (18.5-20.7) | 20.9 (19.9-22.3) | 17.1 (16.2-18.0) | 9.3 (0.0-11.7) | 11.4 (0.0-14.8) | 13.7 (10.6-15.6) |
| <i>p</i> - value ^{††} | 0.30 | 0.64 | 0.15 | 0.50 | <0.01 | 0.99 | 0.07 | 0.56 | 0.06 |
| Necrosis (n=80) | PGM2 | PGM5 | CALM1 | CALM2 | G6PC3 | GFPT1 | PCK1 | PPP1R14C | PYGM |
| Absent (n=63) | 17.5 (15.8-19.5) | 12.4 (10.0-15.5) | 20.0 (18.9-20.9) | 19.8 (18.2-21.1) | 20.3 (18.7-22.3) | 16.9 (15.5-18.4) | 8.3 (0.0-12.8) | 9.9 (0.0-16.4) | 13.0 (10.2-16.2) |
| Present (n=17) | 17.3 (15.0-18.9) | 12.2 (8.3-14.2) | 20.0 (18.9-20.7) | 20.0 (18.7-20.6) | 20.5 (18.5-22.0) | 17.1 (16.0-18.0) | 9.2 (0.0-11.4) | 11.6 (0.0-14.8) | 13.5 (11.4-15.5) |
| <i>p</i> - value [†] | 0.90 | 0.37 | 0.84 | 0.37 | 0.18 | 0.37 | 0.14 | 0.34 | 0.34 |
| Body-Mass-Index | PGM2 | PGM5 | CALM1 | CALM2 | G6PC3 | GFPT1 | PCK1 | PPP1R14C | PYGM |

| 1. De novo glycogen synthesis** | | | | | | | | | | | | | |
|--|----------|--------------|-----------------|--------------------------|--------------------------|-------|-----------------|-------------|--------------------------|--------------------------|-------|-------------|-------------|
| GBE1 | 3p12.2 | ILMN_1789702 | 65.5 ± 86.9 | 42.2 (4.7_585.5) | 29.0 (0.8_171.5) | -1.46 | 0.09 | 1.00 | 37.7 (0.8_210.2) | 43.2 (2.9_585.5) | 1.15 | 0.71 | 1.00 |
| GYG1 | 3q24 | ILMN_2230862 | 235.3 ± 225.3 | 132.0 (9.9_887.9) | 105.7 (31.8_755.8) | -1.25 | 0.85 | 1.00 | 110.8 (31.8_773.2) | 105.7 (9.9_887.9) | -1.05 | 0.47 | 1.00 |
| GYG2 | Xp22.33 | ILMN_2245686 | 1.2 ± 8.5 | -0.5 (-5.8_28.1) | -0.7 (-7.3_43.0) | n.a. | 0.38 | 1.00 | -0.9 (-7.3_28.1) | -0.3 (-5.8_43.0) | n.a. | 0.36 | 1.00 |
| | | ILMN_2319424 | 1065.9 ± 754.1 | 1091.4 (273.9_5024.6) | 660.4 (181.8_1602.9) | -1.65 | 0.00 | 0.04 | 1252.1 (655.4_5024.6) | 631.9 (181.8_2439.0) | -1.98 | 0.00 | 0.01 |
| | | ILMN_1684017 | 117.4 ± 99.7 | 129.5 (-4.5_625.5) | 67.1 (-3.0_200.8) | -1.93 | 0.02 | 0.52 | 139.7 (0.2_625.5) | 65.6 (-4.5_313.5) | -2.13 | 0.00 | 0.02 |
| 2. Positive regulators of glycogen synthesis** | | | | | | | | | | | | | |
| ATG7 | 3p25.3 | ILMN_1790978 | 164.0 ± 86.6 | 172.0 (4.2_392.6) | 114.2 (27.2_335.6) | -1.51 | 0.01 | 0.29 | 130.5 (11.0_334.3) | 168.6 (4.2_392.6) | 1.29 | 0.29 | 1.00 |
| BAP1 | 3p21.1 | ILMN_1768363 | 87.2 ± 65.6 | 96.4 (-0.4_251.8) | 56.2 (-1.0_184.2) | -1.72 | 0.01 | 0.13 | 65.9 (2.4_205.4) | 89.9 (-1.0_251.8) | 1.36 | 0.14 | 1.00 |
| EPM2A | 6q24.3 | ILMN_1719468 | 34.1 ± 22.9 | 33.4 (-4.5_95.6) | 24.7 (-7.6_63.7) | -1.35 | 0.09 | 1.00 | 37.1 (-4.5_95.6) | 25.1 (-7.6_93.5) | -1.48 | 0.10 | 1.00 |
| | | ILMN_1788156 | 0.8 ± 4.3 | 0.9 (-4.2_22.2) | -0.7 (-5.9_5.4) | n.a. | <0.05 | 1.00 | 0.6 (-5.9_22.2) | 0.1 (-4.2_7.4) | -6.00 | 0.35 | 1.00 |
| INSR | 19p13.2 | ILMN_1670918 | 8.3 ± 8.8 | 7.0 (-1.6_20.7) | 7.0 (-1.6_49.1) | 1.00 | 0.85 | 1.00 | 5.7 (-1.4_18.1) | 7.2 (-1.6_49.1) | 1.26 | 0.71 | 1.00 |
| IRS2 | 13q34 | ILMN_2083469 | 531.3 ± 463.8 | 381.3 (58.9_1794.7) | 309.6 (48.3_1461.4) | -1.23 | 0.82 | 1.00 | 366.2 (58.9_1696.2) | 392.0 (48.3_1794.7) | 1.07 | 0.71 | 1.00 |
| IRS4 | Xq22.3 | ILMN_1712774 | 25.5 ± 37.1 | 17.8 (6.5_215.7) | 14.4 (3.9_52.9) | -1.24 | 0.29 | 1.00 | 12.2 (6.5_215.7) | 17.8 (3.9_199.8) | 1.46 | 0.32 | 1.00 |
| PPP1R3B | 8p23.1 | ILMN_2131103 | -0.5 ± 3.5 | -0.7 (-7.4_10.0) | -1.8 (-7.3_5.8) | n.a. | 0.34 | 1.00 | -1.3 (-7.4_10.0) | -1.3 (-7.3_6.3) | n.a. | 0.87 | 1.00 |
| PPP1R3C | 10q23.32 | ILMN_1736670 | 418.5 ± 507.6 | 352.4 (-0.7_2020.3) | 85.9 (-1.6_2063.4) | -4.1 | 0.01 | 0.22 | 209.8 (21.7_1774.9) | 155.6 (-1.6_2063.4) | -1.35 | 0.37 | 1.00 |
| 3. Negative regulators of glycogen synthesis** | | | | | | | | | | | | | |
| CALM1 | 14q32.11 | ILMN_1778242 | 1194.4 ± 611.7 | 1013.2 (457.7_2604.7) | 987.3 (422.5_2908.2) | -1.03 | 1.00 | 1.00 | 1077.5 (457.7_2908.2) | 865.3 (422.5_2055.0) | -1.25 | 0.10 | 1.00 |
| CALM2 | 2p21 | ILMN_1687858 | 2341.5 ± 1318.3 | 2381.2 (677.6_4147.6) | 2303.9 (536.1_6124.7) | -1.03 | 0.71 | 1.00 | 2043.8 (708.3_4479.9) | 2468.1 (536.1_6124.7) | 1.21 | 0.33 | 1.00 |
| G6PC3 | 17q21.31 | ILMN_2127477 | 467.7 ± 265.9 | 395.5 (37.9_1361.0) | 425.2 (35.1_1120.1) | 1.08 | 0.75 | 1.00 | 412.1 (133.3_1361.0) | 412.9 (35.1_1120.1) | 1.00 | 0.87 | 1.00 |

| | | | | | | | | | | | | | |
|--|----------|------------------|---------------|-------------------------|-------------------------|-------|------|------|-------------------------|-------------------------|-------|------|------|
| GFPT1 | 2p13.3 | ILMN_ 2220187 | 241.9 ± 151.7 | 168.3 (63.5_770.3) | 229.3 (137.1_931.7) | 1.36 | 0.05 | 1.00 | 174.5 (110.8_393.6) | 206.3 (63.5_931.7) | 1.18 | 0.33 | 1.00 |
| GSK3B | 3q13.33 | ILMN_ 1779376 | 525.6 ± 418.5 | 408.4 (88.1_1572.4) | 528.1 (77.2_1942.5) | 1.29 | 0.85 | 1.00 | 404.0 (88.1_1572.4) | 563.3 (77.2_1942.5) | 1.39 | 0.08 | 1.00 |
| PCK1 | 20q13.31 | ILMN_ 2197381 | -2.7 ± 3.8 | -3.9 (-9.9_5.9) | -2.4 (-9.0_5.8) | n.a. | 0.45 | 1.00 | -3.9 (-9.9_5.9) | -2.4 (-9.0_4.6) | n.a. | 0.57 | 1.00 |
| PHKA2 | Xp22.13 | ILMN_ 1814074 | 846.8 ± 643.3 | 623.7 (109.6_2289.3) | 679.1 (167.3_2590.5) | 1.09 | 0.80 | 1.00 | 567.1 (136.7_1946.6) | 726.5 (109.6_2590.5) | 1.28 | 0.11 | 1.00 |
| PPP1R14C | 6q25.1 | ILMN_ 1664855 | -0.4 ± 5.6 | -2.4 (-7.8_14.7) | -0.5 (-8.3_24.7) | n.a. | 0.40 | 1.00 | -2.4 (-7.8_24.7) | -0.8 (-8.3_14.7) | n.a. | 0.39 | 1.00 |
| PYGM | 11q13.1 | ILMN_ 1720849 | 1.1 ± 4.6 | 0.4 (-5.0_13.0) | 0.6 (-7.7_19.2) | 1.50 | 0.97 | 1.00 | 0.2 (-7.7_7.3) | 0.6 (-5.0_19.2) | 3.00 | 0.45 | 1.00 |
| 4. Dual regulators of glycogen synthesis** | | | | | | | | | | | | | |
| PGM2 | 4p14 | ILMN_ 1673543 | 98.2 ± 64.4 | 84.4 (24.6_265.5) | 90.0 (1.1_318.3) | 1.07 | 0.19 | 1.00 | 86.0 (1.1_254.9) | 82.0 (24.3_318.3) | -1.05 | 0.94 | 1.00 |
| PGM5 | 9q21.11 | ILMN_ 2271149 | 2.5 ± 9.1 | 1.1 (-6.6_47.8) | -0.1 (-5.8_37.7) | n.a. | 0.09 | 1.00 | 0.9 (-5.1_37.7) | 0.3 (-6.6_47.8) | -3.00 | 0.09 | 1.00 |
| | | ILMN_ 1781388 | 9.3 ± 19.2 | 3.6 (-4.0_107.0) | 3.0 (-4.1_78.9) | -1.20 | 0.78 | 1.00 | 3.8 (-4.1_30.9) | 2.6 (-3.2_107.0) | -1.46 | 0.95 | 1.00 |
| | | ILMN_ 1709590 | 16.8 ± 21.7 | 10.0 (-3.6_115.2) | 8.8 (0.2_44.9) | -1.14 | 0.54 | 1.00 | 13.1 (-0.2_94.0) | 7.4 (-3.6_115.2) | -1.77 | 0.28 | 1.00 |

GEO: Gene Expression Omnibus; n.a.: not analyzed; TCGA: The Cancer Genome Atlas; UM: Uveal melanoma.

Multiple probes were available for GYG2, EPM2A, and PGM5. Genes with a differential expression are indicated in bold.

*Fold changes were calculated only for the probes with positive median values after background subtraction. Negative fold change values indicate the downregulation of genes.

**References for gene function provided in the main text. † Mann-Whitney U test. †† with Bonferroni correction.



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