**The solute carrier family 7 genes are potential diagnostic and prognostic biomarkers in Lower grade glioma**

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Supplementary Table1. Detailed information of glioma patients in the TCGA cohort

|  |  |  |
| --- | --- | --- |
| Variables | Group | Number |
| Age |  | 42.99 |
| Tumour weight |  | 329.59 |
| Gender | Female | 224 |
| Male | 282 |
| History of cancer | No | 210 |
| Yes | 129 |
| Histological type | Astrocytoma | 192 |
|  | Oligoastrocytoma | 129 |
|  | Oligodendroglioma | 185 |
| 2007 WHO grade | Grade2 | 243 |
| Grade3 | 262 |
| *IDH1* mutation | Wild-type | 113 |
|  | Mutant | 393 |
| *TP53* mutation | Wild-type  Mutant | 258  248 |
| Radiation therapy | No  Yes | 118  140 |
| Targeted therapy | No  Yes | 189  247 |
| Overall survival | Dead | 90 |
|  | Alive | 416 |
| Relapse-free | Relapse | 129 |
| survival | Non-relapse | 273 |

Supplementary Table2. Detailed information of glioma patients in the CGGA cohort

|  |  |  |
| --- | --- | --- |
| Variables | Group | Number |
| Age |  | 40.17 |
| Gender | Female | 193 |
| Male | 251 |
| Grade | II | 188 |
|  | III | 255 |
| *IDH1* mutation | Wild-type | 96 |
|  | Mutant | 307 |
| 1p19q\_codeletion | Wild-type  Mutant | 273  132 |
| Radiation therapy | No | 102 |
|  | Yes | 315 |
| Chemotherapy | No | 132 |
|  | Yes | 285 |
| Overall survival | Dead | 199 |
|  | Alive | 226 |
| Relapse-free | Relapse | 162 |
| survival | Non-relapse | 282 |

Supplementary Table3. Association between the clinicopathologic characteristics and patients’ mortality in the CGGA dataset

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Variables | Group | Alive | Dead | P value | Non-relapse | Relapse | P value | Statistical method |
| Age |  | 39.68 | 40.93 | 0.21 | 39.98 | 40.51 | 0.59 | Student t test |
| Gender | Female | 103 | 83 | 0.43 | 124 | 69 | 0.84 | Fisher’s exact test |
| Male | 123 | 116 | 158 | 93 |  |  |
| Grade | II | 122 | 54 | <0.001 | 138 | 50 | <0.001 | Fisher’s exact test |
|  | III | 104 | 145 |  | 144 | 111 |  |  |
| *IDH1* mutation | Wild-type | 34 | 60 | <0.001 | 66 | 30 | 0.15 | Fisher’s exact test |
|  | Mutant | 165 | 128 |  | 184 | 123 |  |  |
| X1p19q\_codeletion | Wild-type  Mutant | 115  91 | 145  36 | <0.001 | 166  83 | 107  49 | 0.74 | Fisher’s exact test |
| Radiation therapy | No | 60 | 39 | 0.16 | 67 | 35 | 0.91 | Fisher’s exact test |
|  | Yes | 163 | 150 |  | 203 | 112 |  |  |
| Chemotherapy | No | 75 | 56 | 0.4 | 95 | 37 | 0.02 | Fisher’s exact test |
|  | Yes | 148 | 135 |  | 172 | 113 |  |  |

Supplementary Table4. Linear regression alysis between clinicopathologic factors and SLC2 family gene expression in the CGGA dataset

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | Grade | Gender | Age | Radiotherapy | Chemotherapy | IDH mutation | X1p19q\_code1etion |
| SLC7A1 |  |  |  |  |  | +++ | +++ |
| SLC7A2 | - | +++ |  |  | - | - | -- |
| SLC7A3 |  |  |  |  |  | - |  |
| SLC7A4 |  |  | + |  |  |  | - |
| SLC7A5 |  |  |  |  |  | + | +++ |
| SLC7A6 |  |  |  | + |  |  | -- |
| SLC7A7 |  |  | - |  |  | --- | --- |
| SLC7A8 |  |  |  |  |  | --- |  |
| SLC7A9 |  |  |  |  |  | - | -- |
| SLC7A10 |  |  |  |  |  | --- | --- |
| SLC7A11 | - | + |  |  | -- |  |  |
| SLC7A14 | -- |  | + |  |  | +++ | +++ |

+, ++, +++ represent positive correlation with P value < .05, P value < .01 and P value < .001 respectively.

-, --, --- represent negative correlation with P value < .05; P value < .01 and P value < .001 respectively.

Supplementary Table5. The GO terms and KEGG pathways that are significantly enriched for SLC7 family genes

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Source | Term name | Term id | Adjusted p value | Negative log10 of adjusted p value |
| GO:BP | amino acid transmembrane transport | GO:0003333 | 2.73E-25 | 24.56 |
| GO:BP | carboxylic acid transmembrane transport | GO:1905039 | 1.16E-22 | 21.94 |
| GO:BP | organic acid transmembrane transport | GO:1903825 | 1.26E-22 | 21.90 |
| GO:BP | amino acid transport | GO:0006865 | 2.37E-22 | 21.62 |
| GO:BP | L-alpha-amino acid transmembrane transport | GO:1902475 | 8.30E-21 | 20.08 |
| GO:BP | L-amino acid transport | GO:0015807 | 4.93E-20 | 19.31 |
| GO:BP | anion transmembrane transport | GO:0098656 | 9.94E-19 | 18.00 |
| GO:BP | carboxylic acid transport | GO:0046942 | 5.02E-18 | 17.30 |
| GO:BP | organic acid transport | GO:0015849 | 5.55E-18 | 17.26 |
| GO:BP | organic anion transport | GO:0015711 | 5.40E-16 | 15.27 |
| GO:BP | anion transport | GO:0006820 | 1.00E-14 | 14.00 |
| GO:BP | basic amino acid transmembrane transport | GO:1990822 | 4.63E-14 | 13.33 |
| GO:BP | basic amino acid transport | GO:0015802 | 5.00E-13 | 12.30 |
| GO:BP | ion transmembrane transport | GO:0034220 | 8.13E-12 | 11.09 |
| GO:BP | amino acid import across plasma membrane | GO:0089718 | 1.40E-10 | 9.85 |
| GO:BP | amino acid import | GO:0043090 | 3.73E-10 | 9.43 |
| GO:BP | transmembrane transport | GO:0055085 | 4.08E-10 | 9.39 |
| GO:BP | ion transport | GO:0006811 | 8.24E-10 | 9.08 |
| GO:BP | ornithine transport | GO:0015822 | 5.48E-09 | 8.26 |
| GO:BP | nitrogen compound transport | GO:0071705 | 5.16E-08 | 7.29 |
| GO:BP | organic substance transport | GO:0071702 | 3.64E-07 | 6.44 |
| GO:BP | import across plasma membrane | GO:0098739 | 4.70E-07 | 6.33 |
| GO:BP | transport across blood-brain barrier | GO:0150104 | 2.5E-06 | 5.60 |
| GO:BP | vascular transport | GO:0010232 | 2.65E-06 | 5.58 |
| GO:BP | import into cell | GO:0098657 | 4.39E-06 | 5.36 |
| GO:BP | L-ornithine transmembrane transport | GO:1903352 | 6.26E-06 | 5.20 |
| GO:BP | L-lysine transport | GO:1902022 | 6.26E-06 | 5.20 |
| GO:BP | L-lysine transmembrane transport | GO:1903401 | 6.26E-06 | 5.20 |
| GO:BP | L-arginine import across plasma membrane | GO:0097638 | 6.26E-06 | 5.20 |
| GO:BP | leukocyte migration | GO:0050900 | 1.49E-05 | 4.83 |
| GO:BP | L-arginine transmembrane transport | GO:1903400 | 1.75E-05 | 4.76 |
| GO:BP | neutral amino acid transport | GO:0015804 | 2.3E-05 | 4.64 |
| GO:BP | arginine transmembrane transport | GO:1903826 | 2.63E-05 | 4.58 |
| GO:BP | L-arginine transport | GO:1902023 | 3.75E-05 | 4.43 |
| GO:BP | arginine transport | GO:0015809 | 6.87E-05 | 4.16 |
| GO:BP | aromatic amino acid transport | GO:0015801 | 8.93E-05 | 4.05 |
| GO:BP | transport | GO:0006810 | 0.000577 | 3.24 |
| GO:BP | vascular process in circulatory system | GO:0003018 | 0.000722 | 3.14 |
| GO:BP | establishment of localization | GO:0051234 | 0.000768 | 3.11 |
| GO:BP | cation transport | GO:0006812 | 0.004593 | 2.34 |
| GO:BP | leucine import across plasma membrane | GO:0098713 | 0.005642 | 2.25 |
| GO:BP | tryptophan transport | GO:0015827 | 0.005642 | 2.25 |
| GO:BP | L-leucine import across plasma membrane | GO:1903801 | 0.005642 | 2.25 |
| GO:BP | localization | GO:0051179 | 0.01423 | 1.85 |
| GO:BP | leucine transport | GO:0015820 | 0.01578 | 1.80 |
| GO:BP | regulation of glutamine family amino acid metabolic process | GO:0000820 | 0.01578 | 1.80 |
| GO:BP | thyroid hormone transport | GO:0070327 | 0.025341 | 1.60 |
| GO:BP | branched-chain amino acid transport | GO:0015803 | 0.03714 | 1.43 |
| GO:BP | cell migration | GO:0016477 | 0.038956 | 1.41 |
| GO:BP | immune system process | GO:0002376 | 0.039686 | 1.40 |
| KEGG | Protein digestion and absorption | KEGG:04974 | 0.001875 | 2.73 |

Supplementary Table6. survival alyses between patients’ overall survival and *SLC7* family gene expression levels in the TCGA dataset

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Kaplan-Meier survival alysis | | | Univariate survival alysis | | | | Multivariate survival alysis | | | |
|  | Cutoff | Chisq | P value | OR | 2.5%CI | 97.5%CI | P value | OR | 2.5%CI | 97.5%CI | P value |
| SLC7A1 | 2344.65 | 18.08 | <0.001 | 0.44 | 0.28 | 0.71 | <0.001 | 0.59 | 0.35 | 1.03 | 0.06 |
| SLC7A2 | 953.82 | 3.28 | 0.07 | 1.70 | 0.98 | 2.88 | 0.05 | 1.67 | 0.87 | 3.12 | 0.11 |
| SLC7A3 | 23.98 | 4.22 | 0.04 | 1.49 | 0.93 | 2.37 | 0.10 | 1.18 | 0.68 | 2.01 | 0.56 |
| SLC7A4 | 42.37 | 5.49 | 0.02 | 0.37 | 0.17 | 0.73 | 0.01 | 0.38 | 0.16 | 0.81 | 0.02 |
| SLC7A5 | 2992.97 | 2.22 | 0.14 | 2.09 | 0.94 | 5.57 | 0.10 | 1.84 | 0.77 | 5.14 | 0.20 |
| SLC7A6 | 1035.24 | 4.82 | 0.03 | 1.83 | 0.99 | 3.27 | 0.05 | 1.86 | 0.94 | 3.58 | 0.07 |
| SLC7A7 | 267.91 | 16.64 | <0.001 | 2.73 | 1.72 | 4.38 | <0.001 | 2.66 | 1.56 | 4.60 | <0.001 |
| SLC7A8 | 317.67 | 13.04 | <0.001 | 0.43 | 0.26 | 0.70 | <0.001 | 0.44 | 0.26 | 0.77 | <0.001 |
| SLC7A9 | 4.30 | 3.72 | 0.05 | 1.24 | 0.78 | 1.96 | 0.35 | 1.09 | 0.65 | 1.84 | 0.74 |
| SLC7A10 | 210.45 | 11.40 | <0.001 | 2.03 | 0.99 | 3.96 | 0.04 | 1.57 | 0.67 | 3.56 | 0.28 |
| SLC7A11 | 809.53 | 4.07 | 0.04 | 0.47 | 0.29 | 0.77 | <0.001 | 0.54 | 0.31 | 0.95 | 0.03 |
| SLC7A14 | 652.60 | 15.82 | <0.001 | 0.39 | 0.24 | 0.62 | <0.001 | 0.38 | 0.21 | 0.67 | <0.001 |

Supplementary Table7. survival alyses between patients’ overall survival and *SLC7* family gene expression levels in the CGGA dataset

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Kaplan-Meier survival alysis | | | Univariate survival alysis | | | | Multivariate survival alysis | | | |
|  | Cutoff | Chisq | P value | OR | 2.5%CI | 97.5%CI | P value | OR | 2.5%CI | 97.5%CI | P value |
| SLC7A1 | 5.28 | 4.58 | 0.03 | 1.84 | 1.10 | 3.13 | 0.02 | 1.75 | 1.02 | 2.98 | 0.04 |
| SLC7A2 | 1.45 | 2.25 | 0.13 | 1.44 | 0.98 | 2.12 | 0.06 | 1.23 | 0.90 | 1.68 | 0.20 |
| SLC7A3 | 0.56 | 17.00 | 0.00 | 2.23 | 1.49 | 3.35 | 0.00 | 1.54 | 1.14 | 2.10 | 0.01 |
| SLC7A4 | 0.11 | 13.10 | 0.00 | 0.47 | 0.28 | 0.77 | 0.00 | 0.74 | 0.52 | 1.05 | 0.09 |
| SLC7A5 | 34.36 | 5.68 | 0.02 | 1.55 | 1.06 | 2.29 | 0.03 | 2.01 | 1.43 | 2.81 | 0.00 |
| SLC7A6 | 3.62 | 27.75 | 0.00 | 3.15 | 2.08 | 4.80 | 0.00 | 1.88 | 1.31 | 2.70 | 0.00 |
| SLC7A7 | 4.96 | 21.75 | 0.00 | 2.42 | 1.62 | 3.63 | 0.00 | 1.45 | 1.05 | 2.01 | 0.02 |
| SLC7A8 | 7.84 | 6.30 | 0.01 | 1.74 | 1.16 | 2.63 | 0.01 | 1.52 | 1.10 | 2.08 | 0.01 |
| SLC7A9 | 0.45 | 3.65 | 0.06 | 1.75 | 1.19 | 2.58 | 0.00 | 0.77 | 0.55 | 1.09 | 0.15 |
| SLC7A10 | 2.68 | 2.70 | 0.10 | 1.31 | 0.87 | 1.99 | 0.20 | 1.03 | 0.73 | 1.43 | 0.88 |
| SLC7A11 | 2.49 | 1.27 | 0.26 | 1.43 | 0.97 | 2.12 | 0.07 | 1.22 | 0.88 | 1.70 | 0.24 |
| SLC7A14 | 2.34 | 10.51 | 0.00 | 0.59 | 0.40 | 0.87 | 0.01 | 0.96 | 0.69 | 1.33 | 0.80 |

Supplementary Table8. survival alyses between RFS and *SLC7* family gene expression levels in the TCGA dataset

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Kaplan-Meier survival alysis | | | Univariate survival alysis | | | | Multivariate survival alysis | | | |
|  | Cutoff | Chisq | P value | OR | 2.5%CI | 97.5%CI | P value | OR | 2.5%CI | 97.5%CI | P value |
| SLC7A1 | 2875.59 | 11.23 | 0.00 | 0.57 | 0.37 | 0.87 | 0.01 | 0.62 | 0.43 | 0.89 | 0.01 |
| SLC7A2 | 694.93 | 2.49 | 0.11 | 0.62 | 0.38 | 1.00 | 0.05 | 0.68 | 0.45 | 1.03 | 0.07 |
| SLC7A3 | 62.72 | 9.89 | 0.00 | 2.75 | 1.43 | 5.33 | 0.00 | 1.35 | 0.83 | 2.21 | 0.23 |
| SLC7A4 | 7.51 | 3.63 | 0.06 | 0.68 | 0.45 | 1.05 | 0.08 | 0.71 | 0.50 | 1.01 | 0.06 |
| SLC7A5 | 4818.30 | 0.06 | 0.80 | 1.18 | 0.77 | 1.79 | 0.45 | 0.98 | 0.69 | 1.39 | 0.92 |
| SLC7A6 | 783.46 | 0.65 | 0.42 | 0.78 | 0.51 | 1.19 | 0.24 | 0.96 | 0.68 | 1.36 | 0.83 |
| SLC7A7 | 174.42 | 9.37 | 0.00 | 1.91 | 1.23 | 2.99 | 0.00 | 1.83 | 1.25 | 2.67 | 0.00 |
| SLC7A8 | 357.84 | 9.58 | 0.00 | 0.60 | 0.39 | 0.92 | 0.02 | 0.61 | 0.43 | 0.86 | 0.01 |
| SLC7A9 | 8.00 | 3.52 | 0.06 | 1.74 | 1.04 | 2.89 | 0.03 | 1.27 | 0.85 | 1.89 | 0.25 |
| SLC7A10 | 5.30 | 3.87 | 0.05 | 1.65 | 1.07 | 2.55 | 0.02 | 1.29 | 0.90 | 1.86 | 0.17 |
| SLC7A11 | 890.00 | 6.30 | 0.01 | 0.57 | 0.36 | 0.89 | 0.01 | 0.61 | 0.43 | 0.88 | 0.01 |
| SLC7A14 | 793.34 | 10.12 | 0.00 | 0.48 | 0.31 | 0.73 | 0.00 | 0.60 | 0.42 | 0.87 | 0.01 |

Supplementary Table9. survival alyses between RFS and *SLC7* family gene expression levels in the CGGA dataset

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Kaplan-Meier survival alysis | | | Univariate survival alysis | | | | Multivariate survival alysis | | | |
|  | Cutoff | Chisq | P value | OR | 2.5%CI | 97.5%CI | P value | OR | 2.5%CI | 97.5%CI | P value |
| SLC7A1 | 37.39 | 11.66 | 0.00 | 4.03 | 1.82 | 9.57 | 0.00 | 2.81 | 1.63 | 4.85 | 0.00 |
| SLC7A2 | 4.66 | 8.51 | 0.00 | 0.19 | 0.07 | 0.46 | 0.00 | 0.30 | 0.11 | 0.81 | 0.02 |
| SLC7A3 | 0.32 | 1.57 | 0.21 | 1.43 | 0.97 | 2.11 | 0.07 | 1.30 | 0.93 | 1.81 | 0.13 |
| SLC7A4 | 0.83 | 0.16 | 0.69 | 1.45 | 0.96 | 2.18 | 0.08 | 1.14 | 0.80 | 1.61 | 0.47 |
| SLC7A5 | 53.23 | 29.30 | 0.00 | 3.71 | 2.40 | 5.77 | 0.00 | 2.42 | 1.74 | 3.36 | 0.00 |
| SLC7A6 | 5.34 | 0.00 | 1.00 | 0.78 | 0.52 | 1.15 | 0.21 | 1.04 | 0.74 | 1.46 | 0.82 |
| SLC7A7 | 2.06 | 0.00 | 0.95 | 0.80 | 0.50 | 1.28 | 0.34 | 1.00 | 0.68 | 1.47 | 0.99 |
| SLC7A8 | 7.70 | 6.72 | 0.01 | 2.06 | 1.37 | 3.08 | 0.00 | 1.89 | 1.35 | 2.65 | 0.00 |
| SLC7A9 | 0.32 | 5.70 | 0.02 | 0.64 | 0.43 | 0.95 | 0.03 | 0.66 | 0.47 | 0.91 | 0.01 |
| SLC7A10 | 7.29 | 5.32 | 0.02 | 1.71 | 0.94 | 3.10 | 0.08 | 1.74 | 1.08 | 2.80 | 0.02 |
| SLC7A11 | 5.95 | 12.49 | 0.00 | 0.41 | 0.24 | 0.67 | 0.00 | 0.50 | 0.30 | 0.82 | 0.01 |
| SLC7A14 | 2.57 | 1.23 | 0.27 | 2.04 | 1.38 | 3.02 | 0.00 | 1.41 | 1.01 | 1.97 | 0.05 |