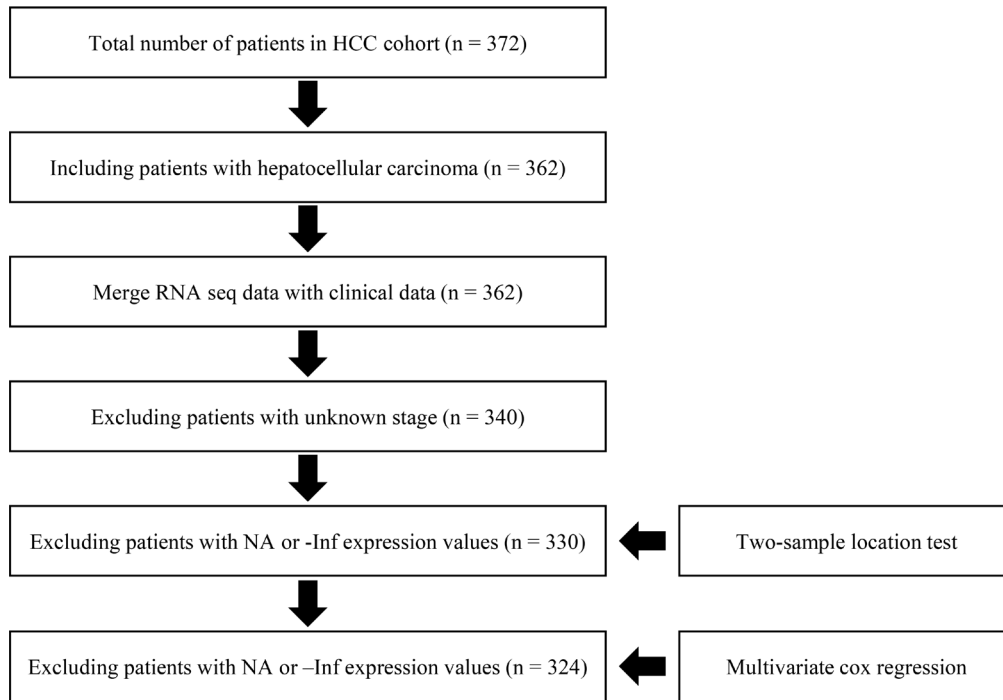
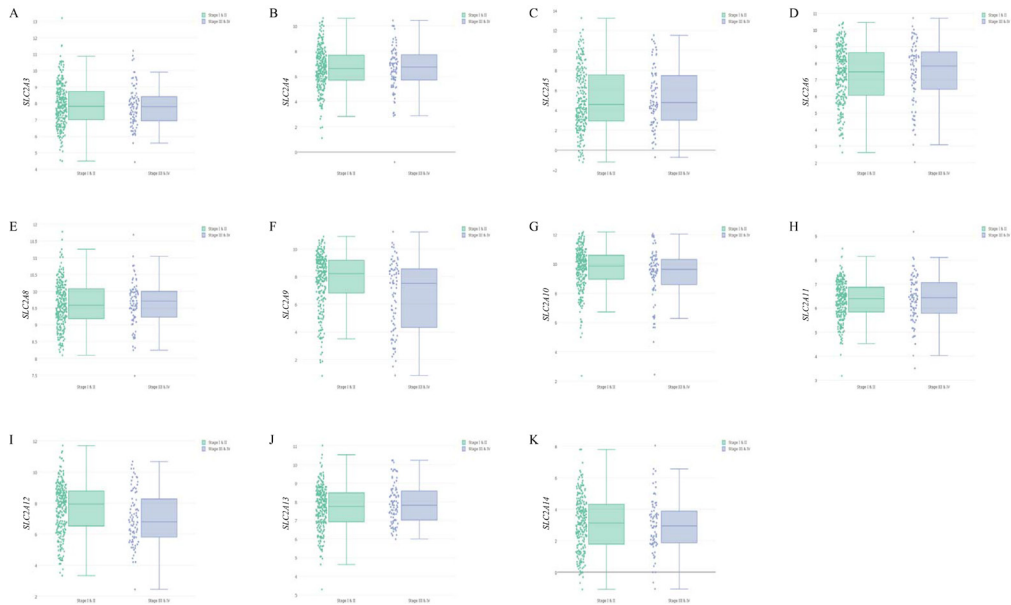


SLC2A2 (GLUT2) as a novel prognostic factor for hepatocellular carcinoma

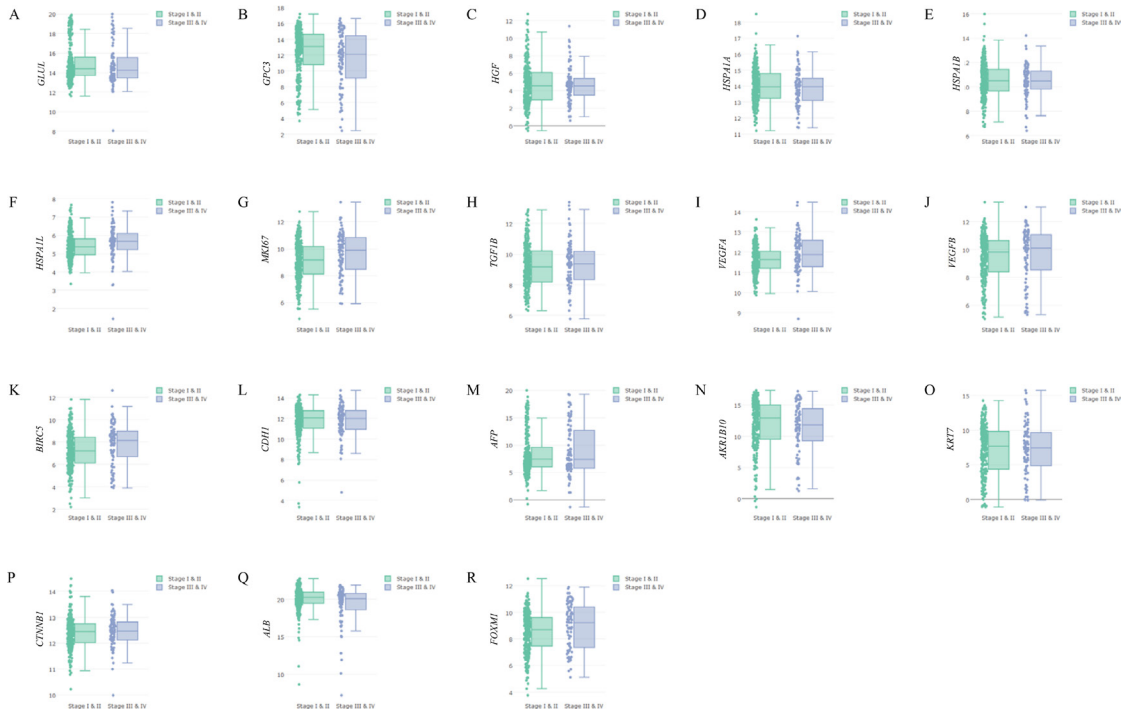
SUPPLEMENTARY MATERIALS



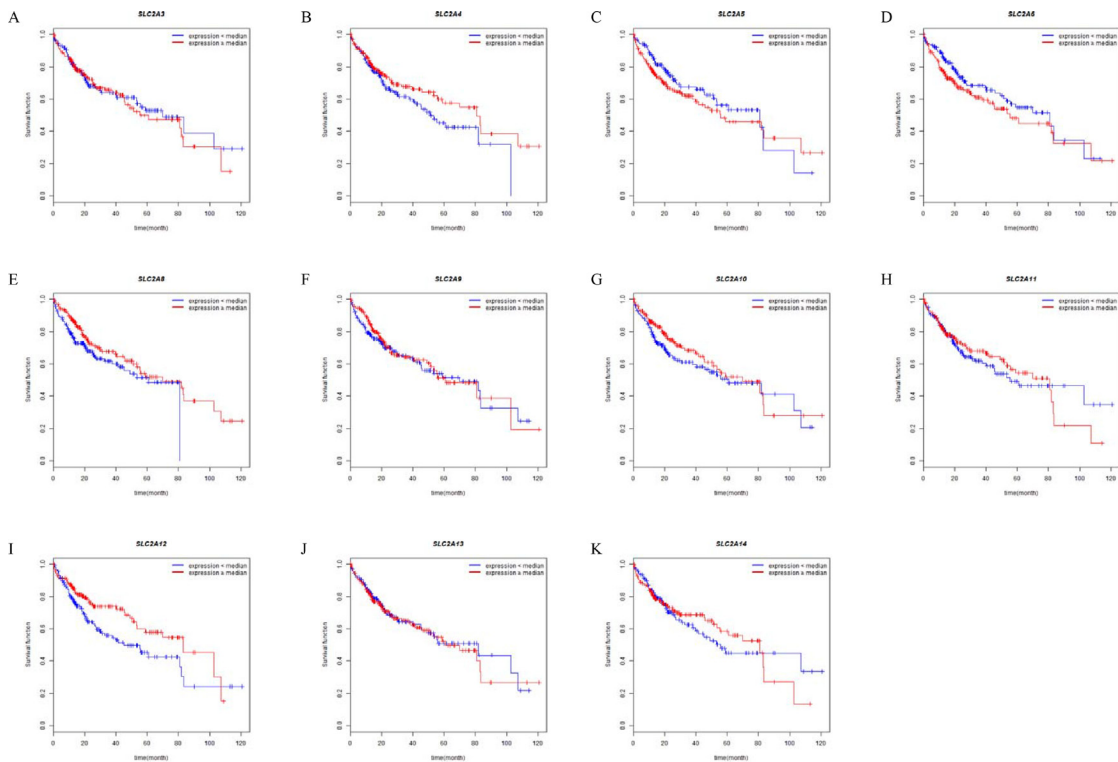
Supplementary Figure 1: Flow diagram of patient inclusion/exclusion criteria.



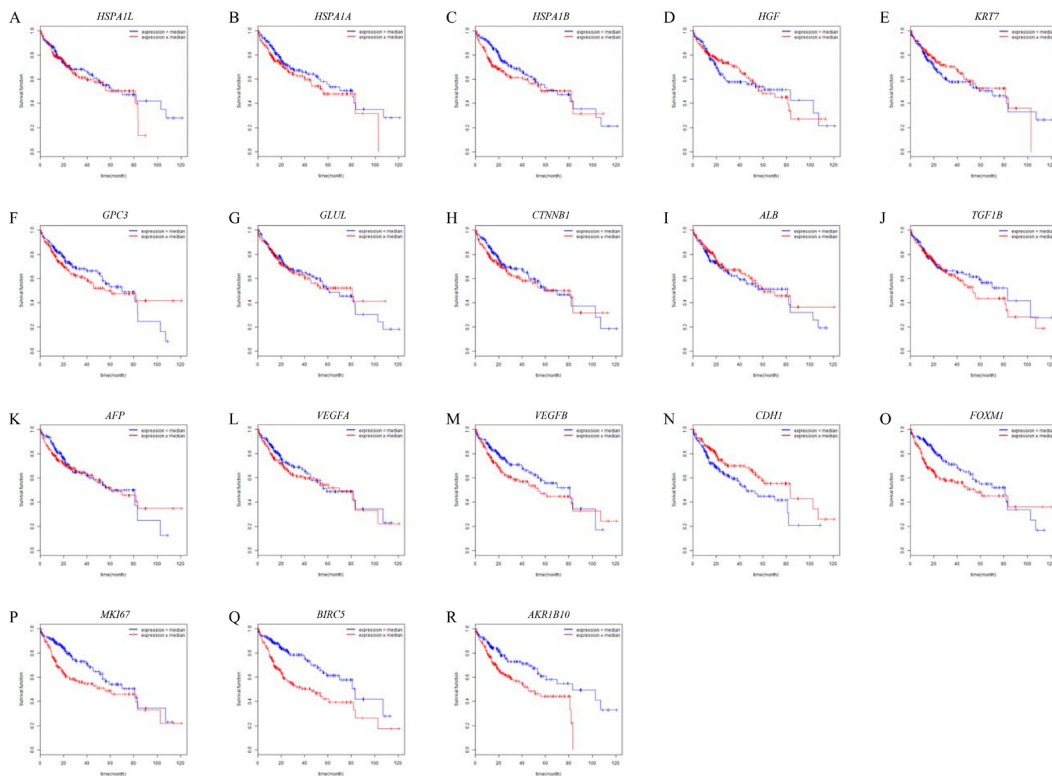
Supplementary Figure 2: Association of gene expression (SLC2A family) with clinical stages. Relations between clinical stages and the expression levels of genes were examined using boxplots and scatterplots. Central lines in boxes represent medians, boxes show interquartile ranges (IQR), and error bars show the full range of values, excluding outliers defined as being more than ± 1.5 IQR outside boxes. Scatter plots represent raw data.



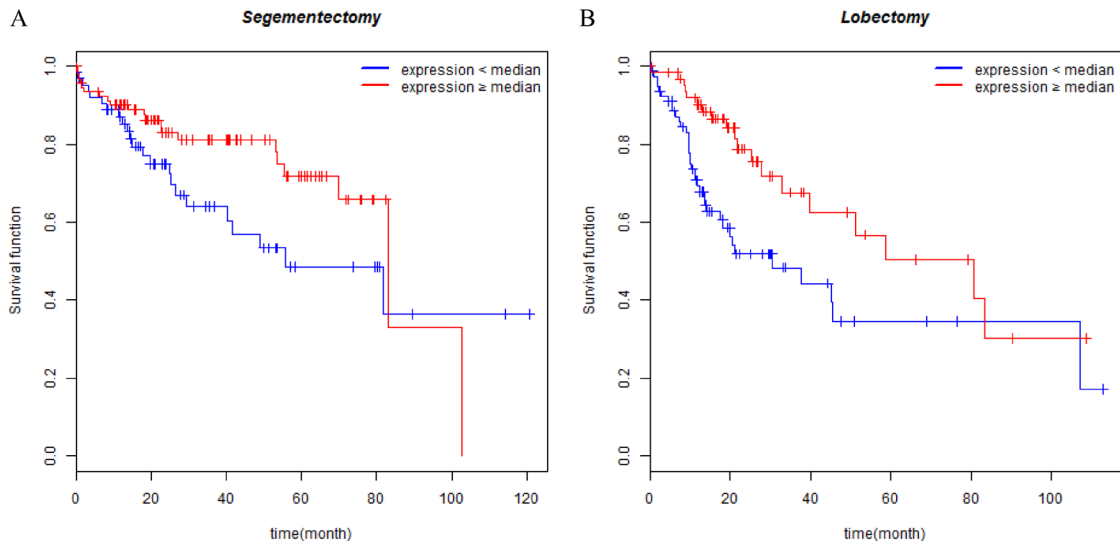
Supplementary Figure 3: Association of gene expression (previously known prognostic genes) with clinical stages. Relations between clinical stage and the expression levels of genes were examined using boxplots and scatterplots. Central lines in boxes represent medians, boxes show interquartile ranges (IQR), and error bars show the full range of values, excluding outliers defined as being more than ± 1.5 IQR outside boxes. Scatter plots represent raw data.



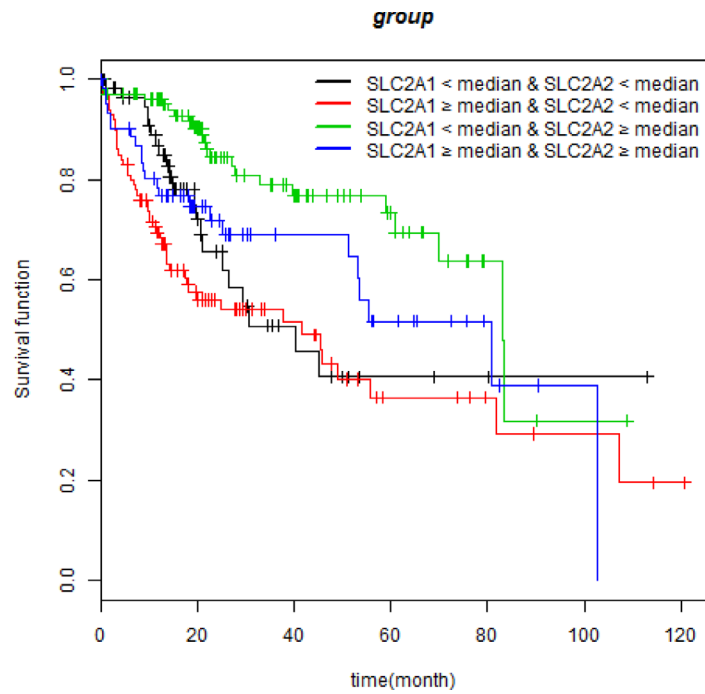
Supplementary Figure 4: Kaplan-Meier survival curves of HCC patients stratified by expression levels of SLC2A family genes. Overall survival analysis of HCC patients with respect to the expression levels of different genes was performed by Kaplan-Meier analysis. Expression levels are divided into low or high compared with the median (blue or red lines, respectively).



Supplementary Figure 5: Kaplan-Meier survival curves of HCC patients stratified by expression levels of previously known prognostic genes. Overall survival analysis of HCC patients with respect to the expression levels of different genes was performed by Kaplan-Meier analysis. Expression levels are divided into low or high compared with the median (blue or red lines, respectively).



Supplementary Figure 6: Kaplan-Meier survival curves of HCC patients stratified by expression levels of SLC2A2 in different surgery type (A) Segmentectomy (B) Lobectomy.



Supplementary Figure 7: Kaplan-Meier survival curves of HCC patients stratified by expression levels of SLC2A1 with SLC2A2.

Supplementary Table 1: Two-sample location test results comparing stage 1 & II and stage III & IV on SLC2A family gene expression

Gene name	Protein name	p-value	Test
<i>SLC2A3</i>	Glucose transporter 3	0.5598	Mann-Whitney U
<i>SLC2A4</i>	Glucose transporter 4	0.9914	Mann-Whitney U
<i>SLC2A5</i>	Glucose transporter 5	0.5582	Mann-Whitney U
<i>SLC2A6</i>	Glucose transporter 6	0.5048	Mann-Whitney U
<i>SLC2A8</i>	Glucose transporter 8	0.6690	Mann-Whitney U
<i>SLC2A9</i>	Glucose transporter 9	< 0.001***	Mann-Whitney U
<i>SLC2A10</i>	Glucose transporter 10	0.0666	Mann-Whitney U
<i>SLC2A11</i>	Glucose transporter 11	0.5943	Mann-Whitney U
<i>SLC2A12</i>	Glucose transporter 12	0.0037**	Mann-Whitney U
<i>SLC2A13</i>	Glucose transporter 13	0.3856	Mann-Whitney U
<i>SLC2A14</i>	Glucose transporter 14	0.5112	Mann-Whitney U

Supplementary Table 2: Two-sample location test results comparing stage 1 & II and stage III & IV on known prognostic gene expression

Gene name	Protein name	p-value	Test
<i>GLUL</i>	Glutamate synthetase	0.1538	Mann-Whitney U
<i>GPC3</i>	Glypican 3	0.0513	Mann-Whitney U
<i>HGF</i>	Hepatocyte growth factor	0.9271	Mann-Whitney U
<i>HSPA1A</i>	Heat shock protein 70	0.3292	T-test
<i>HSPA1B</i>	Heat shock protein 70	0.8217	Mann-Whitney U
<i>HSPA1L</i>	Heat shock protein 70	0.0066**	Mann-Whitney U
<i>MKI67</i>	Ki67	0.0093**	Mann-Whitney U
<i>TGF1B</i>	Transforming growth factor-β	0.5530	T-test
<i>VEGFA</i>	Vascular endothelial growth factor A	0.0054**	Welch's t-test
<i>VEGFB</i>	Vascular endothelial growth factor B	0.2145	Mann-Whitney U
<i>BIRC5</i>	Survivin	0.0072**	Mann-Whitney U
<i>CDH1</i>	E-cadherin	0.9687	Mann-Whitney U
<i>AFP</i>	Alpha-fetoprotein	0.7938	Mann-Whitney U
<i>AKR1B10</i>	Aldo-keto reductase family 1 B10	0.2571	Mann-Whitney U
<i>KRT7</i>	Cytokeratin-7	0.8784	Mann-Whitney U
<i>CTNNB1</i>	β-catenin	0.3805	Mann-Whitney U
<i>ALB</i>	Albumin	0.0528	Mann-Whitney U
<i>FOXM1</i>	Forkhead box protein M1	0.0299*	Mann-Whitney U

Supplementary Table 3: Comparison of SLC2A2 expression according to races

Race	Total	SLC2A2 expression (mean ± SD)
White	185	12.80 ± 1.93
Asian	158	12.48 ± 2.39
Black or American	17	12.85 ± 0.95
American Indian or Alaska native	2	10.22 ± 4.84
Unknown	10	12.76 ± 1.60

Supplementary Table 4: Test for equality of survival distributions for the different levels of SLC2A family gene expression

Gene name	Protein name	Significance	Median survival (months)	
			Low expression	High expression
<i>SLC2A3</i>	Glucose transporter 3	No significance	70.01	55.35
<i>SLC2A4</i>	Glucose transporter 4	No significance	51.25	80.68
<i>SLC2A5</i>	Glucose transporter 5	No significance	80.68	55.65
<i>SLC2A6</i>	Glucose transporter 6	No significance	80.68	55.35
<i>SLC2A8</i>	Glucose transporter 8	No significance	60.84	70.01
<i>SLC2A9</i>	Glucose transporter 9	No significance	70.01	60.84
<i>SLC2A10</i>	Glucose transporter 10	No significance	60.84	70.01
<i>SLC2A11</i>	Glucose transporter 11	No significance	60.84	70.01
<i>SLC2A12</i>	Glucose transporter 12	No significance	55.35	83.18
<i>SLC2A13</i>	Glucose transporter 13	No significance	81.67	60.84
<i>SLC2A14</i>	Glucose transporter 14	No significance	53.29	80.68

Supplementary Table 5: Test for equality of survival distributions for the different levels of previously known prognostic gene expression

Gene name	Protein name	Significance (<i>p</i> -value)	Median survival (months)	
			Low expression	High expression
<i>GLUL</i>	Glutamate synthetase	No significance	60.84	80.68
<i>GPC3</i>	Glypican 3	No significance	70.01	55.35
<i>HGF</i>	Hepatocyte growth factor	No significance	83.18	55.65
<i>HSPA1A</i>	Heat shock protein 70	No significance	70.01	55.35
<i>HSPA1B</i>	Heat shock protein 70	No significance	70.01	55.65
<i>HSPA1L</i>	Heat shock protein 70	No significance	60.84	80.68
<i>MKI67</i>	Ki67	Significance (0.0027**)	70.01	55.35
<i>TGF1B</i>	Transforming growth factor- β	No significance	83.18	53.35
<i>VEGFA</i>	Vascular endothelial growth factor A	No significance	58.84	70.01
<i>VEGFB</i>	Vascular endothelial growth factor B	No significance	80.68	53.29
<i>BIRC5</i>	Survivin	Significance (< 0.001***)	83.18	37.75
<i>CDH1</i>	E-cadherin	No significance	53.29	83.18
<i>AFP</i>	Alpha-fetoprotein	No significance	58.84	60.84
<i>AKR1B10</i>	Aldo-keto reductase family 1 B10	Significance (< 0.001***)	83.18	45.07
<i>KRT7</i>	Cytokeratin-7	No significance	58.84	80.68
<i>CTNNB1</i>	β -catenin	No significance	70.01	60.84
<i>ALB</i>	Albumin	No significance	80.68	60.84
<i>FOXMI</i>	Forkhead box protein M1	Significance (< 0.001***)	80.68	48.95

Supplementary Table 6: C-index and Area Under the Curve (AUC) at 5 years of SLC2A family gene expression

Gene name	Protein name	C-index	AUC at 5 years
<i>SLC2A3</i>	Glucose transporter 3	0.503	0.499
<i>SLC2A4</i>	Glucose transporter 4	0.580	0.657
<i>SLC2A5</i>	Glucose transporter 5	0.608	0.567
<i>SLC2A6</i>	Glucose transporter 6	0.543	0.588
<i>SLC2A8</i>	Glucose transporter 8	0.562	0.515
<i>SLC2A9</i>	Glucose transporter 9	0.531	0.479
<i>SLC2A10</i>	Glucose transporter 10	0.553	0.522
<i>SLC2A11</i>	Glucose transporter 11	0.520	0.590
<i>SLC2A12</i>	Glucose transporter 12	0.519	0.548
<i>SLC2A13</i>	Glucose transporter 13	0.522	0.522
<i>SLC2A14</i>	Glucose transporter 14	0.508	0.562

Supplementary Table 7: C-index and Area Under the Curve (AUC) at 5 years of known prognostic gene expression

Gene name	Protein name	C-index	AUC at 5 years
<i>GLUL</i>	Glutamate synthetase	0.467	0.555
<i>GPC3</i>	Glypican 3	0.520	0.524
<i>HGF</i>	Hepatocyte growth factor	0.525	0.490
<i>HSPA1A</i>	Heat shock protein 70	0.536	0.542
<i>HSPA1B</i>	Heat shock protein 70	0.545	0.541
<i>HSPA1L</i>	Heat shock protein 70	0.521	0.504
<i>MKI67</i>	Ki67	0.619	0.582
<i>TGF1B</i>	Transforming growth factor- β	0.541	0.585
<i>VEGFA</i>	Vascular endothelial growth factor A	0.546	0.512
<i>VEGFB</i>	Vascular endothelial growth factor B	0.512	0.528
<i>BIRC5</i>	Survivin	0.629	0.623
<i>CDH1</i>	E-cadherin	0.584	0.558
<i>AFP</i>	Alpha-fetoprotein	0.555	0.511
<i>AKR1B10</i>	Aldo-keto reductase family 1 B10	0.584	0.599
<i>KRT7</i>	Cytokeratin-7	0.544	0.519
<i>CTNNB1</i>	β -catenin	0.554	0.417
<i>ALB</i>	Albumin	0.575	0.516
<i>FOXMI</i>	Forkhead box protein M1	0.622	0.600

Supplementary Table 8: Tissue distribution and substrates binding affinity of GLUT isoforms

Gene name	Protein name	Major site expression	High binding affinity
<i>SLC2A1</i>	GLUT 1	Ubiquitous	Glucose, FDG
<i>SLC2A2</i>	GLUT 2	Liver, islets, kidney, small intestine	Glucosamine
<i>SLC2A3</i>	GLUT 3	Brain, nerve cells	Glucose, FDG
<i>SLC2A4</i>	GLUT 4	Muscle, fat, heart	Glucose, glucosamine
<i>SLC2A5</i>	GLUT 5	Intestine, kidney, testis	Fructose
<i>SLC2A6</i>	GLUT 6	Spleen, leukocytes, brain	Cytochalasin B
<i>SLC2A7</i>	GLUT7	Small intestine, colon, testis	Fructose
<i>SLC2A8</i>	GLUT 8	Testis, brain, muscle, adipocyte, blastocyst	Glucose
<i>SLC2A9</i>	GLUT 9	Liver, kidney	-
<i>SLC2A10</i>	GLUT 10	Liver, pancreas	2-Deoxy glucose
<i>SLC2A11</i>	GLUT 11	Heart, muscle	-
<i>SLC2A12</i>	GLUT 12	Heart, prostate, mammary gland	-
<i>SLC2A13</i>	GLUT 13	Brain	<i>myo</i> -inositol