

Identification of NEK6 as a potential biomarker for prognosis in glioma, a Pan-Cancer Analysis

Supplementary Material

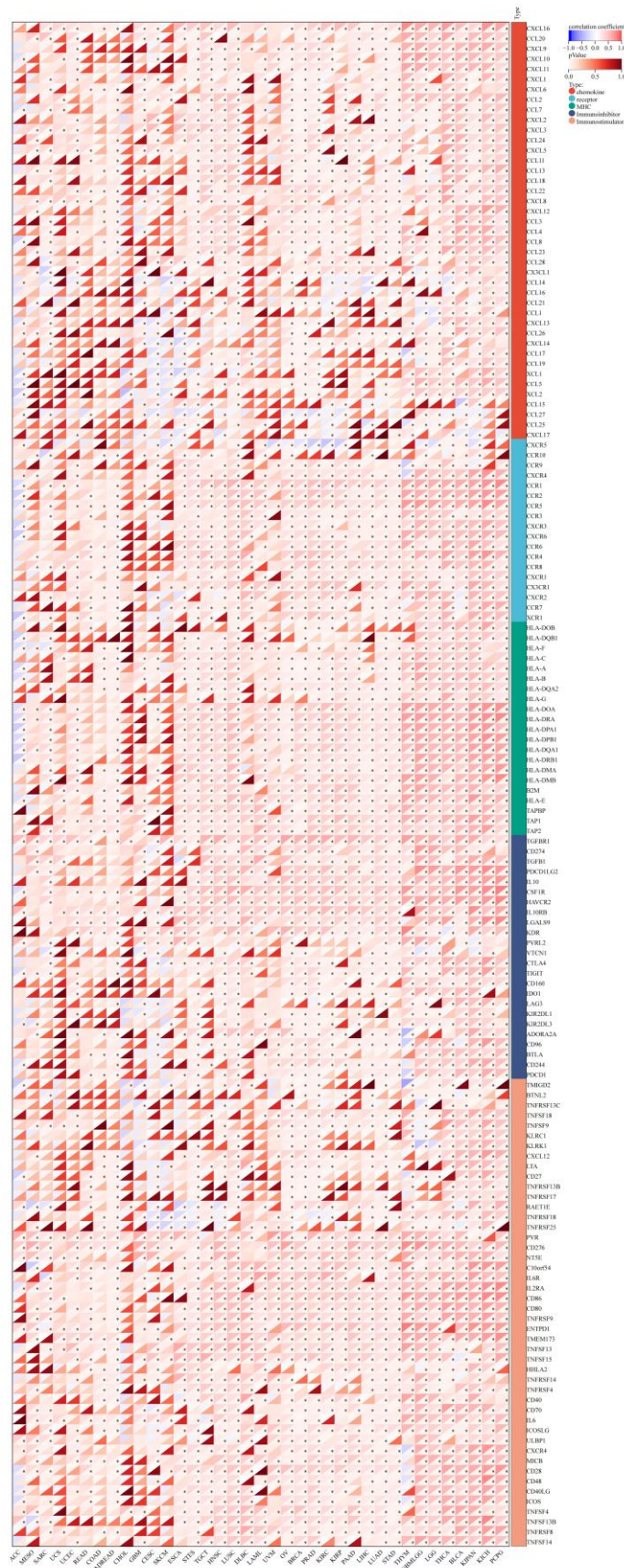
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Supplementary Figure 1 Spearman's correlation analyses showing the correlations between NEK6 expression and immune-related genes in five immune pathways in pan-cancer.



Supplementary Table 1 Clinicopathological information of the patients in CGGA_325.

Variables	NEK6 Expression		P value
	High (N=157)	Low (N=156)	
Age (Years)			
Mean (SD)	46.4 (11.8)	39.9 (11.2)	<0.001
Median [Min, Max]	45.0 [11.0, 79.0]	39.0 [8.00, 74.0]	
Gender			
Female	55 (35.0%)	61 (39.1%)	0.53
Male	102 (65.0%)	95 (60.9%)	
Radiation Therapy			
Treated	113 (72.0%)	128 (82.1%)	0.153
Untreated	36 (22.9%)	26 (16.7%)	
Missing	8 (5.1%)	2 (1.3%)	
Chemotherapy			
TMZ-treated	105 (66.9%)	85 (54.5%)	0.0228
Untreated	45 (28.7%)	65 (41.7%)	
Missing	7 (4.5%)	6 (3.8%)	
IDH Mutation Status			
Mutant	50 (31.8%)	117 (75.0%)	<0.001
Wildtype	106 (67.5%)	39 (25.0%)	
Missing	1 (0.6%)	0 (0%)	
X1p19q Codeletion Status			
Codel	4 (2.5%)	58 (37.2%)	<0.001
Non-codel	146 (93.0%)	97 (62.2%)	
Missing	7 (4.5%)	1 (0.6%)	
Grade			
2	19 (12.1%)	79 (50.6%)	<0.001
3	34 (21.7%)	40 (25.6%)	
4	101 (64.3%)	36 (23.1%)	
Missing	3 (1.9%)	1 (0.6%)	

Supplementary Table 2 Clinicopathological information of the patients in CGGA_693.

Variables	NEK6 Expression		P value
	High (N=329)	Low (N=328)	
Age (Years)			
Mean (SD)	44.8 (13.6)	42.1 (11.0)	0.00497
Median [Min, Max]	45.0 [11.0, 76.0]	42.0 [14.0, 73.0]	
Missing	0 (0%)	1 (0.3%)	
Gender			
Female	139 (42.2%)	144 (43.9%)	0.727
Male	190 (57.8%)	184 (56.1%)	
Radiation Therapy			
Treated	257 (78.1%)	244 (74.4%)	0.1
Untreated	56 (17.0%)	75 (22.9%)	
Missing	16 (4.9%)	9 (2.7%)	
Chemotherapy			
TMZ-treated	251 (76.3%)	229 (69.8%)	0.038
Untreated	66 (20.1%)	90 (27.4%)	
Missing	12 (3.6%)	9 (2.7%)	
IDH Mutation Status			
Mutant	129 (39.2%)	204 (62.2%)	<0.001
Wildtype	197 (59.9%)	79 (24.1%)	
Missing	3 (0.9%)	45 (13.7%)	
X1p19q Codeletion Status			
Codel	27 (8.2%)	110 (33.5%)	<0.001
Non-codel	280 (85.1%)	174 (53.0%)	
Missing	22 (6.7%)	44 (13.4%)	
Grade			
2	56 (17.0%)	116 (35.4%)	<0.001
3	104 (31.6%)	144 (43.9%)	
4	169 (51.4%)	68 (20.7%)	

Supplementary Table 3 Clinicopathological information of the patients in GSE16011.

Variables	NEK6 Expression		P value
	High (N=136)	Low (N=135)	
Age (Years)			
Mean (SD)	54.0 (14.3)	46.2 (14.1)	<0.001
Median [Min, Max]	56.0 [14.4, 80.7]	44.6 [11.7, 81.2]	
Missing	1 (0.7%)	0 (0%)	
Gender			
Female	41 (30.1%)	56 (41.5%)	0.0689
Male	95 (69.9%)	79 (58.5%)	
Histological Type			
A	11 (8.1%)	18 (13.3%)	<0.001
GBM	106 (77.9%)	49 (36.3%)	
OA	10 (7.4%)	18 (13.3%)	
OD	7 (5.1%)	44 (32.6%)	
PA	2 (1.5%)	6 (4.4%)	
Typeofsurgery			
Completeresection	46 (33.8%)	40 (29.6%)	0.61
Openbiopsy	2 (1.5%)	5 (3.7%)	
Partialresection	72 (52.9%)	71 (52.6%)	
Stereotacticbiopsy	15 (11.0%)	17 (12.6%)	
Missing	1 (0.7%)	2 (1.5%)	
Grade			
1	2 (1.5%)	6 (4.4%)	<0.001
2	3 (2.2%)	20 (14.8%)	
3	25 (18.4%)	60 (44.4%)	
4	106 (77.9%)	49 (36.3%)	

Supplementary Table 4 Clinicopathological information of the patients in TCGA_LGG.

Variables	NEK6 Expression	
	High (N=248)	Low (N=247)
Age (Years)		
Mean (SD)	42.7 (14.1)	43.5 (12.7)
Median [Min, Max]	41.0 [14.0, 87.0]	41.0 [17.0, 75.0]
Gender		
FEMALE	116 (46.8%)	105 (42.5%)
MALE	132 (53.2%)	142 (57.5%)
Histological Type		
Astrocytoma	124 (50.0%)	63 (25.5%)
Oligoastrocytoma	65 (26.2%)	60 (24.3%)
Oligodendroglioma	59 (23.8%)	124 (50.2%)
Race		
AMERICAN INDIAN OR ALASKA NATIVE	1 (0.4%)	0 (0%)
ASIAN	3 (1.2%)	5 (2.0%)
BLACK OR AFRICAN AMERICAN	12 (4.8%)	9 (3.6%)
WHITE	229 (92.3%)	226 (91.5%)
Missing	3 (1.2%)	7 (2.8%)
Radiation Therapy		
NO	34 (13.7%)	84 (34.0%)
YES	69 (27.8%)	70 (28.3%)
Missing	145 (58.5%)	93 (37.7%)
Family History of Cancer		
NO	89 (35.9%)	109 (44.1%)
YES	72 (29.0%)	57 (23.1%)
Missing	87 (35.1%)	81 (32.8%)
Laterality		
Left	116 (46.8%)	125 (50.6%)
Midline	4 (1.6%)	2 (0.8%)
Right	126 (50.8%)	117 (47.4%)
Missing	2 (0.8%)	3 (1.2%)
Idh1 Mutation Found		
NO	20 (8.1%)	13 (5.3%)
YES	25 (10.1%)	66 (26.7%)
Missing	203 (81.9%)	168 (68.0%)
Grade		
G2	99 (39.9%)	139 (56.3%)
G3	148 (59.7%)	108 (43.7%)
Missing	1 (0.4%)	0 (0%)

Supplementary Table 5 Comparing RMST between NEK6 high expression and low expression groups in CGGA_325.

Year	NEK6 High Expression RMST	NEK6 Low Expression RMST	Estimation	LCI
1	9.893200891	11.07254683	-1.17935	-1.80292
2	14.91854922	20.51977188	-5.60122	-7.22644
3	18.23657117	29.15592751	-10.9194	-13.5734
4	20.26800058	37.00093557	-16.7329	-20.3243
5	21.65435637	44.54468169	-22.8903	-27.4059
6	22.73012955	51.87428988	-29.1442	-34.5873
7	23.69165101	58.64740085	-34.9557	-41.3138
8	24.63597642	64.69981195	-40.0638	-47.3295
9	25.51809627	70.58959146	-45.0715	-53.2678
10	26.19711121	76.09000309	-49.8929	-58.969
11	26.87162936	81.29092816	-54.4193	-64.3892
12	27.54614751	86.46550124	-58.9194	-69.8237

Abbreviations: RMST, restricted mean survival time; LCI, lower limit of 95% confidence interval; UCI, upper limit of 95% confidence interval.

Supplementary Table 6 Comparing RMST between NEK6 high expression and low expression groups in CGGA_693.

Year	NEK6 High Expression RMST	NEK6 Low Expression RMST	Estimation	LCI
1	10.12278319	11.45155199	-1.32877	-1.70763
2	16.3974278	21.0465714	-4.64914	-5.72257
3	20.9430994	29.4528507	-8.50975	-10.3181
4	24.76166628	36.92228551	-12.1606	-14.7272
5	28.10402247	43.98720622	-15.8832	-19.223
6	31.17669404	50.54757367	-19.3709	-23.4944
7	34.11060293	56.617435	-22.5068	-27.429
8	36.87758253	62.02849892	-25.1509	-30.8683
9	39.46193861	66.91033396	-27.4484	-33.98
10	41.68906774	71.54611932	-29.8571	-37.2573
11	43.57495128	76.18190467	-32.607	-40.9527
12	45.38154543	80.81769003	-35.4361	-44.8305

Abbreviations: RMST, restricted mean survival time; LCI, lower limit of 95% confidence interval; UCI, upper limit of 95% confidence interval.

Supplementary Table 7 Comparing RMST between NEK6 high expression and low expression groups in GSE16011.

Year	NEK6 High Expression RMST	NEK6 Low Expression RMST	Estimation	LCI
1	8.119478549	10.57747123	-2.45799	-3.30566
2	10.97092956	18.93829454	-7.96736	-9.80993
3	12.37518467	25.81991698	-13.4447	-16.2426
4	13.10152352	31.49029351	-18.3888	-22.0409
5	13.74106716	36.28090048	-22.5398	-27.0635
6	14.3806108	40.51058978	-26.13	-31.5404
7	15.02015444	44.09561788	-29.0755	-35.3398
8	15.65969808	47.2022893	-31.5426	-38.6415
9	16.29924172	49.81378851	-33.5145	-41.4093
10	16.89273822	51.97600953	-35.0833	-43.7163
11	17.19204465	53.75528498	-36.5632	-45.793
12	17.4478621	55.23522744	-37.7874	-47.5684

Abbreviations: RMST, restricted mean survival time; LCI, lower limit of 95% confidence interval; UCI, upper limit of 95% confidence interval.

Supplementary Table 8 Comparing RMST between NEK6 high expression and low expression groups in TCGA_LGG.

Year	NEK6 High Expression RMST	NEK6 Low Expression RMST	Estimation	LCI
1	11.55150997	11.8581403	-0.30663	-0.56571
2	21.59145374	23.39173975	-1.80029	-2.61817
3	30.24600933	34.17152087	-3.92551	-5.53248
4	38.01930896	43.83803661	-5.81873	-8.42899
5	44.7228815	52.71461241	-7.99173	-11.7966
6	50.50900372	61.01412597	-10.5051	-15.6711
7	55.51347114	68.74209999	-13.2286	-19.8832
8	59.95952121	76.13245787	-16.1729	-24.4451
9	63.67839097	82.69666085	-19.0183	-28.9241
10	66.76741282	89.17541522	-22.408	-34.0557
11	69.55916479	95.10864232	-25.5495	-39.0163
12	71.42963861	100.3369553	-28.9073	-44.0284
13	72.74021106	104.0191271	-31.2789	-47.8643
14	73.85691184	106.6509665	-32.7941	-50.7972
15	74.97361263	108.4031227	-33.4295	-52.7552

Abbreviations: RMST, restricted mean survival time; LCI, lower limit of 95% confidence interval; UCI, upper limit of 95% confidence interval.

Supplementary Table 9 Correspondence between ID and description of GO terms.

	ID	Description
CGGA_325	GO:0001819	positive regulation of cytokine production
	GO:0042060	wound healing
	GO:0043410	positive regulation of MAPK cascade
	GO:0030198	extracellular matrix organization
	GO:0043062	extracellular structure organization
	GO:0045229	external encapsulating structure organization
	GO:0051960	regulation of nervous system development
	GO:0002253	activation of immune response
	GO:0034329	cell junction assembly
	GO:0050867	positive regulation of cell activation
	GO:1903037	regulation of leukocyte cell-cell adhesion
	GO:0061564	axon development
CGGA_693	GO:0002460	adaptive immune response based on somatic recombination of immune receptors built from immunoglobulin superfamily domains
	GO:0022409	positive regulation of cell-cell adhesion
	GO:0070661	leukocyte proliferation
	GO:0001667	ameboid-type cell migration
	GO:1902105	regulation of leukocyte differentiation
	GO:0003002	regionalization
	GO:0099177	regulation of trans-synaptic signaling
	GO:0007264	small GTPase mediated signal transduction
	GO:0050804	modulation of chemical synaptic transmission
	GO:0050808	synapse organization
	GO:0051051	negative regulation of transport
	GO:0032943	mononuclear cell proliferation
GSE_16011	GO:0042730	fibrinolysis
	GO:0099174	regulation of presynapse organization
	GO:1905606	regulation of presynapse assembly
	GO:0085029	extracellular matrix assembly
	GO:0031295	T cell costimulation
	GO:1902622	regulation of neutrophil migration
	GO:0002455	humoral immune response mediated by circulating immunoglobulin
	GO:0001774	microglial cell activation
	GO:0031294	lymphocyte costimulation
	GO:0010043	response to zinc ion
	GO:0043114	regulation of vascular permeability
	GO:0061028	establishment of endothelial barrier
TCGA_LGG	GO:0009954	proximal/distal pattern formation
	GO:0032689	negative regulation of type II interferon production
	GO:0042088	T-helper 1 type immune response
	GO:0043277	apoptotic cell clearance
	GO:0006911	phagocytosis/engulfment
	GO:0001914	regulation of T cell mediated cytotoxicity
	GO:0046638	positive regulation of alpha-beta T cell differentiation
	GO:0006584	catecholamine metabolic process
	GO:0009712	catechol-containing compound metabolic process
	GO:0061900	glial cell activation
	GO:0002707	negative regulation of lymphocyte mediated immunity
	GO:0010718	positive regulation of epithelial to mesenchymal transition

Supplementary Table 10 Comparing RMST between NEK6 high expression and low expression groups in ZN_Glioma.

Year	NEK6 High Expression RMST	NEK6 Low Expression RMST	Estimation	LCI
1	11.73684211	12	-0.26316	-0.65683
2	21.44736842	23.93157895	-2.48421	-4.78033
3	30.04766286	35.3	-5.25234	-9.85622
4	37.13636364	45.75894737	-8.62258	-15.9353
5	37.48969452	51.59	-14.1003	-22.8988

Abbreviations: RMST, restricted mean survival time; LCI, lower limit of 95% confidence interval; UCI, upper limit of 95% confidence interval.