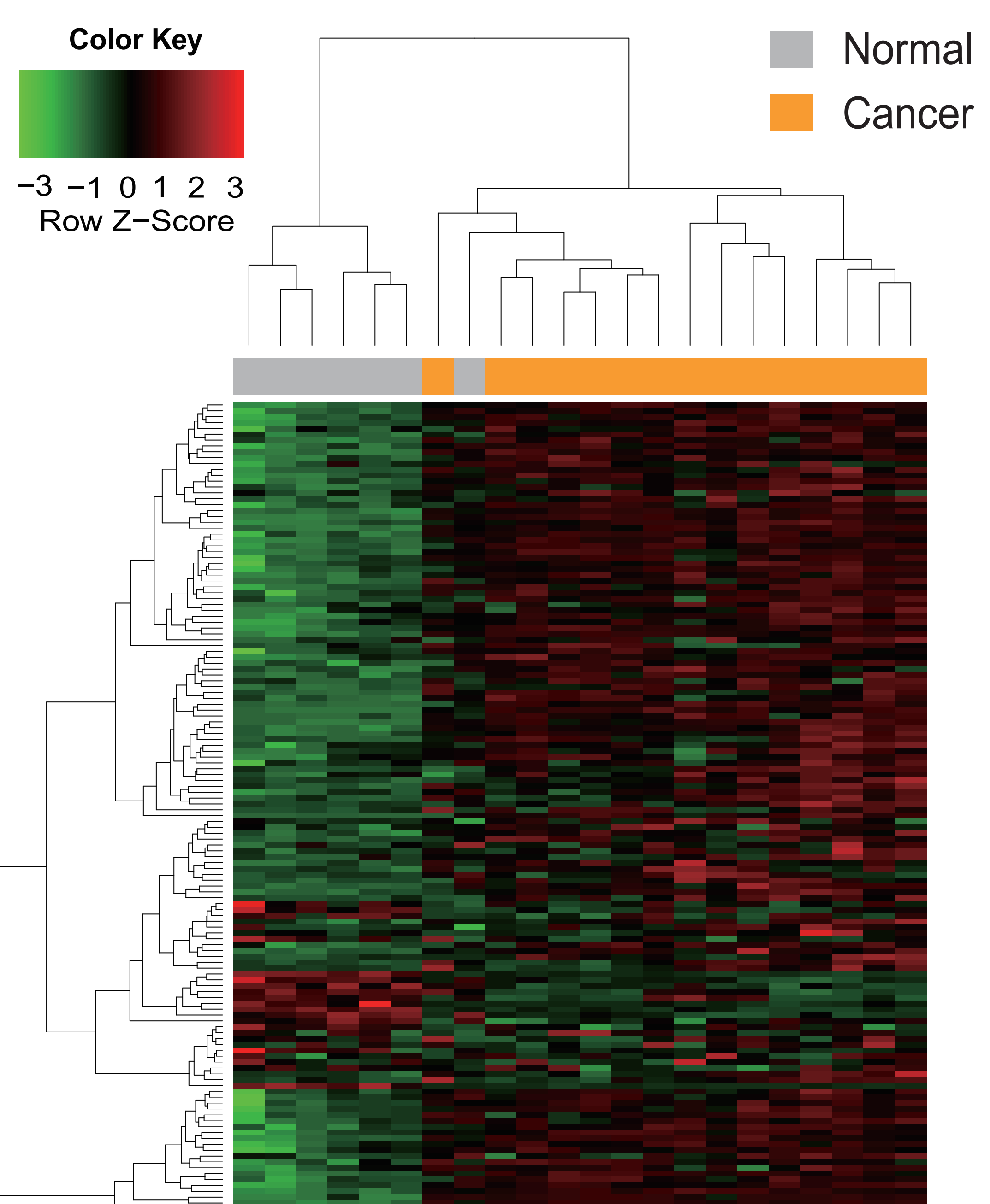
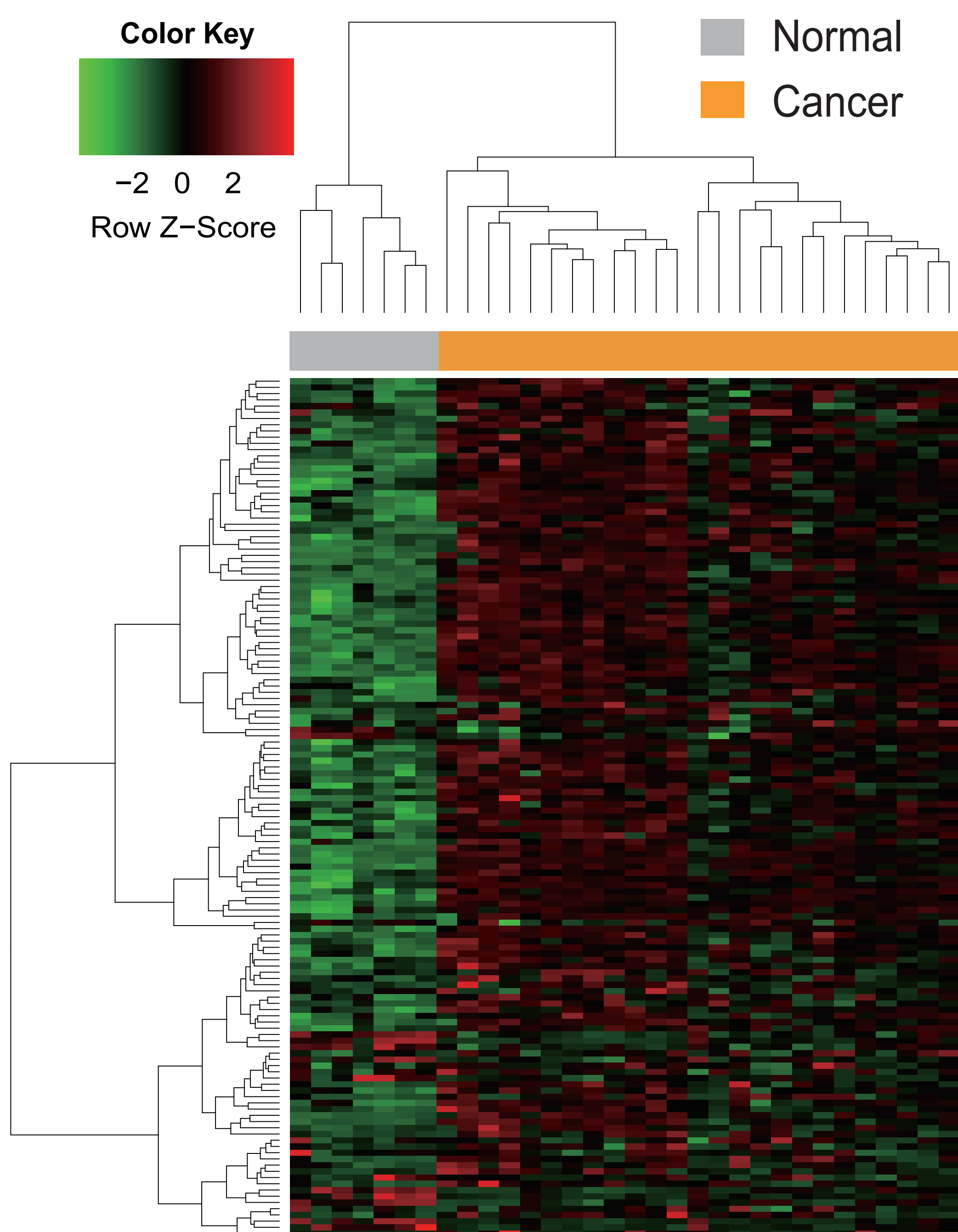


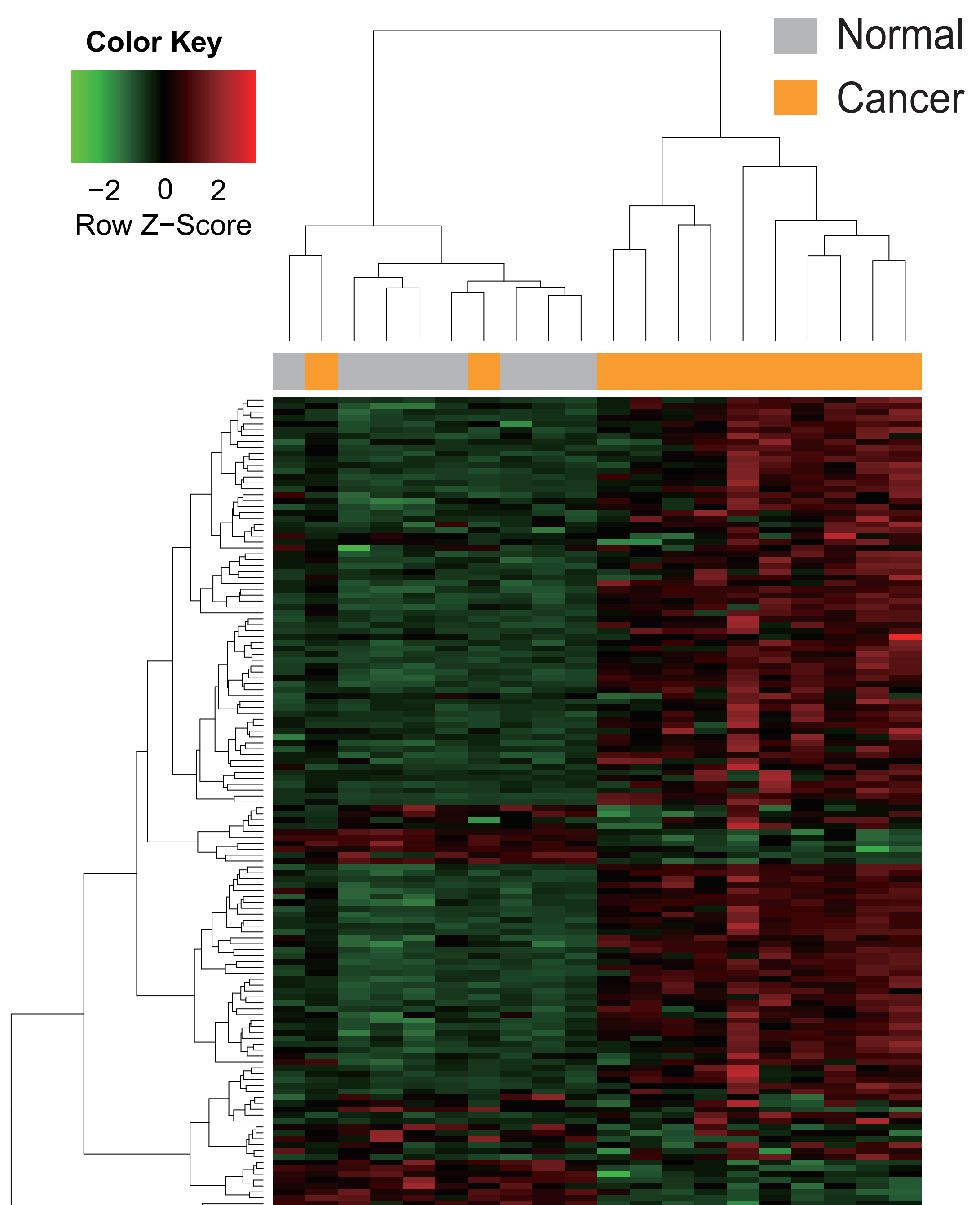
(A)



(B)



(C)



(D)

Supplementary table 1. Definition of 12 topological algorithms

Algorithm	explanation
Clustering Coefficient	The global clustering coefficient is based on triplets of nodes. A triplet is three nodes that are connected by either two (open triplet) or three (closed triplet) undirected ties. A triangle graph therefore includes three closed triplets, one centered on each of the nodes (n.b. this means the three triplets in a triangle come from overlapping selections of nodes). The global clustering coefficient is the number of closed triplets (or 3 x triangles) over the total number of triplets (both open and closed).
We assume that a biological network $G = (V, E)$ is an undirected network, where V is the collection of nodes within the network and E is the edge set. We can use another notation $G = (V(G), E(G))$ to represent a network, where $V(G)$ is the collection of nodes in a network G , and $E(G)$ is the collection of edges in a network G . For a set S , we use $ S $ to denote its cardinality (i.e. the number of elements in the set). Local based method only considers the direct neighborhood of a vertex. Given a node v , $N(v)$ denotes the collections of its neighbors.	
Degree method (Deg)	$Deg(v) = N(v) $
Maximum Neighborhood Component (MNC)	$MNC(v) = V(MC(v)) $ where $MC(v)$ is a maximum connected component of the $G[N(v)]$ and $G[N(v)]$ is the induced subgraph of G by $N(v)$.
Density of Maximum Neighborhood Component (DMNC)	$DMNC(v) = E(MC(v)) / V(MC(v)) ^\epsilon$ where $\epsilon = 1.7$.
Maximal Clique Centrality (MCC)	Given a node v , the MCC of v is defined as $MCC(v) = \sum_{C \in S(v)} (C - 1)!$, where $S(v)$ is the collection of maximal cliques which contain v , and $(C - 1)!$ is the product of all positive integers less than $ C $. If there is no edge between the neighbors of the node v , then $MCC(v)$ is equal to its degree.
The length of a shortest path between nodes u and v is denoted as $dist(u, v)$. Let $C(v)$ be the component which contains node v .	
Closeness (Clo)	$Clo(v) = \sum_{w \in V} \frac{1}{dist(v, w)}$
EcCentricity (EC)	$EC(v) = \frac{ V(C(v)) }{ V } \times \frac{1}{\max\{dist(v, w): w \in C(v)\}}$
Radiality (Rad)	$Rad(v) = \frac{ V(C(v)) }{ V } \times \frac{\sum_{w \in C(v)} (\Delta_{C(v)} + 1 - dist(v, w))}{\max\{dist(v, w): w \in C(v)\}}$ where $\Delta_{C(v)}$ is the maximum distance between any two vertices of the component $C(v)$.
BottleNeck (BN)	Let T_s be a shortest path tree rooted at node s . $BN(v) = \sum_{s \in V} p_s(v)$ where $p_s(v) = 1$ if more than $ V(T_s) /4$ paths from node s to other nodes in T_s meet at the vertex v ; otherwise $p_s(v) = 0$.
Stress (Str)	$Sre(v) = \sum_{s \neq t \neq v \in C(v)} \sigma_{st}(v)$, where $\sigma_{st}(v)$ is the number of shortest paths from node s to node t which use the node v .

Betweenness (BC)

$BC(v) = \sum_{s \neq t \neq v \in C(v)} \frac{\sigma_{st}(v)}{\sigma_{st}}$, where σ_{st} is the number of shortest paths from node s to node t .

Edge Percolated
Component (EPC)

Given a threshold ($0 \leq \text{the threshold} \leq 1$), we create 1000 reduced networks by assigning a random number between 0 and 1 to every edge and remove edges if their associated random numbers are less than the threshold. Let the G_k be the reduced network generated at the k th time reduced process. If nodes u and v are connected in G_k , set δ_{vt}^k to be 1; otherwise $\delta_{vt}^k = 0$. For a node v in G , $EPC(v)$ is defined as

$$EPC(v) = \frac{1}{|V|} \sum_{k=1}^{1000} \sum_{t \in V} \delta_{vt}^k.$$

Supplementary table 2. Analysis gene ontology and KEGG pathway by KOBAS 3.0

Term	Database	ID	Gene number	Gene entrzed ID	P-Value
ECM-receptor interaction (ranked 1)	KEGG PATHWAY	hsa04512	7	3914 7057 3909 6385 6382 3673 3918	2.76×10^{-8}
Focal adhesion (ranked 2)	KEGG PATHWAY	hsa04510	6	3914 3909 7057 3673 3918 4233	9.30×10^{-5}
Proteoglycans in cancer (ranked 3)	KEGG PATHWAY	hsa05205	6	3710 7057 6385 6382 3673 4233	9.80×10^{-5}
Mucin type O-Glycan biosynthesis (ranked 4)	KEGG PATHWAY	hsa00512	3	11227 56913 55808	2.24×10^{-4}
PI3K-Akt signaling pathway (ranked 5)	KEGG PATHWAY	hsa04151	7	3914 3909 1946 7057 3918 3673 4233	2.24×10^{-4}
cell migration (ranked 60)	Gene Ontology	GO:0016477	29	10276 706 57402 55612 3909 6385 2195 5337 6382 3673 10103 5584 6286 79148 7057 7262 23767 54443 80005 3958 634 8754 55359 1948 306 3728 102 4233 6374	1.42×10^{-16}
cell adhesion (ranked 91)	Gene Ontology	GO:0007155	26	10276 137075 55612 3909 7057 6385 10232 3958 2195 10551 3673 1739 1948 1946 6281 23767 51208 3959 3914 634 8754 27242 3918 3728 102 1048	4.97×10^{-12}
cell-cell adhesion (ranked 264)	Gene Ontology	GO:0098609	13	1739 1948 1048 634 8754 137075 1946 27242 23767 3958 3728 2195 51208	1.33×10^{-5}
extracellular matrix disassembly (ranked 429)	Gene Ontology	GO:0022617	4	102 3914 3909 3918	2.90×10^{-4}
hemidesmosome assembly (ranked 275)	Gene Ontology	GO:0031581	3	3914 3909 3918	1.79×10^{-5}
extracellular exosome (ranked 53)	Gene Ontology	GO:0070062	46	6590 114569 706 57402 8743 79098 7057 6385 79838 2195 6382 9052 23446 10103 1739 5584 6286 6558 6281 5315 124220 65108 3959 3958 634 2810 8754 3934 79083 26 306 3909 26509 3728 102 9045 3880 1728 6277 11254 1048 5349 5268 10903 1510 822	7.67×10^{-20}
plasma membrane (ranked 45)	Gene Ontology	GO:0005886	64	25924 114569 54843 3710 3775 10276 1946 57402 8743 6281 6385 10232 3958 2195 5337 11343 3673 9052 23446 10103 1739 5584 152831 54933 9833 6286 6558 7057 5315 23767 2157 51208 9462 113146 65108 27242 6382 5023 137075 634 8754 55612 55359 2706 26 306 26509 3728 160851 102 4233 3783 3880 6277 11254 1048 5349 5445 26031 55450 688 8853 2537 1948	6.19×10^{-23}

bicellular tight junction (ranked 227)	Gene Ontology	GO:0005923	6	1739 5584 137075 26 51208 1894	3.50×10^{-6}
focal adhesion (ranked 169)	Gene Ontology	GO:0005925	11	2274 1948 8754 55612 6385 23767 3728 2195 6382 102 3673	1.61×10^{-7}
cell-cell adherens junction (ranked 2592)	Gene Ontology	GO:0005913	1	3728	1.76×10^{-1}
laminin binding (ranked 239)	Gene Ontology	GO:0043236	4	8754 3673 3958 7057	5.86×10^{-6}
protein homodimerization activity (ranked 178)	Gene Ontology	GO:0042803	14	26 1048 634 6277 23767 11343 7153 6281 1894 3728 10551 102 23281 1510	2.72×10^{-7}
protein phosphatase binding (ranked 343)	Gene Ontology	GO:0019903	5	634 3783 4233 3728 4751	7.74×10^{-5}
calcium ion binding (ranked 203)	Gene Ontology	GO:0005509	13	26 54843 3710 6277 388743 9833 6286 57402 79148 7057 306 6281 2195	1.09×10^{-6}

Note: The term of gene ontology is ranked in brackets by KOBAS when they are ranked in top 15 by DAVID analysis. The term of KEGG pathway is ranked in brackets by KOBAS when they are ranked in top 5 by DAVID analysis.