Table S1: Sample sizes of 21 tumor types before and after filtering to ensure sufficient mutations per sample.

Cancer[a]	Sample size	Full (# mutations ≥ 6)	FoundationOne (# mutations ≥ 1)	PanCan (# mutations ≥ 1)	TrueSeq (# mutations ≥1)
BLCA	99	99 (100%)	97(98%)	95 (96%)	84 (85%)
BRCA	887	849 (96%)	661 (75%)	647 (73%)	528 (60%)
CARC*	54	53 (98%)	26 (48%)	13 (24%)	10 (19%)
CLL*	158	135 (85%)	79 (50%)	66 (42%)	34 (22%)
CRC	233	233 (100%)	227 (97%)	226 (97%)	219 (94%)
DLBC*	57	55 (96%)	51 (89%)	43 (75%)	31 (54%)
ESO	140	140 (100%)	133 (95%)	125 (89%)	112 (80%)
GBM	291	288 (99%)	247 (85%)	237 (81%)	199 (68%)
HNSC	384	372 (97%)	357 (93%)	347 (90%)	303 (79%)
KIRC	417	414 (99%)	328 (79%)	310 (74%)	220 (53%)
LAML*	194	126 (65%)	132 (68%)	131 (68%)	77 (40%)
LUAD	398	391 (98%)	372 (93%)	359 (90%)	322 (81%)
LUSC	176	176 (100%)	176 (100%)	175 (99%)	158 (90%)
MED*	89	42 (47%)	26 (29%)	24 (27%)	15 (17%)
MEL	118	118 (100%)	117 (99%)	113 (96%)	112 (95%)
MM	204	200 (98%)	157 (77%)	146 (72%)	121(59%)
NB*	75	18 (24.00%)	49 (65%)	61 (81%)	62 (83%)
OV	316	313 (99%)	276 (87%)	281 (89%)	238 (75%)
PRAD*	131	109 (83%)	51 (39%)	45 (34%)	19 (15%)
RHAB*	33	7 (21%)	10 (30%)	4 (12%)	8 (24%)
UCEC	247	247 (100%)	245 (%99)	242 (98%)	229 (93%)
Total	4701	4008[¶]			

*Tumors excluded from NBS analysis due to insufficient mutations or samples

¶Calculated after excluding tumor marked by *

[a]BLCA-Bladder urothelial carcinoma; BRCA-Breast invasive carcinoma; CARC-Carcinoid; CLL-Chronic lymphocytic leukemia; CRC-Colorectal carcinoma; DLBC-Diffuse large B-cell lymphoma; ESO-Esophageal adenocarcinoma; GBM-Glioblastoma multiforme; HNSC-Head and neck squamous cell carcinoma; KIRC-Kidney renal clear cell carcinoma; LAML-Acute myeloid leukemia; LUAD-Lung adenocarcinoma; LUSC-Lung squamous cell carcinoma; MED-Medulloblastoma; MEL-Melanoma; MM-Multiple myeloma; OV-Ovarian serous cystadenocarcinoma; PRAD-Prostate adenocarcinoma; RHAB-Rhabdoid tumor; UCEC-Uterine corpus endometrial carcinoma

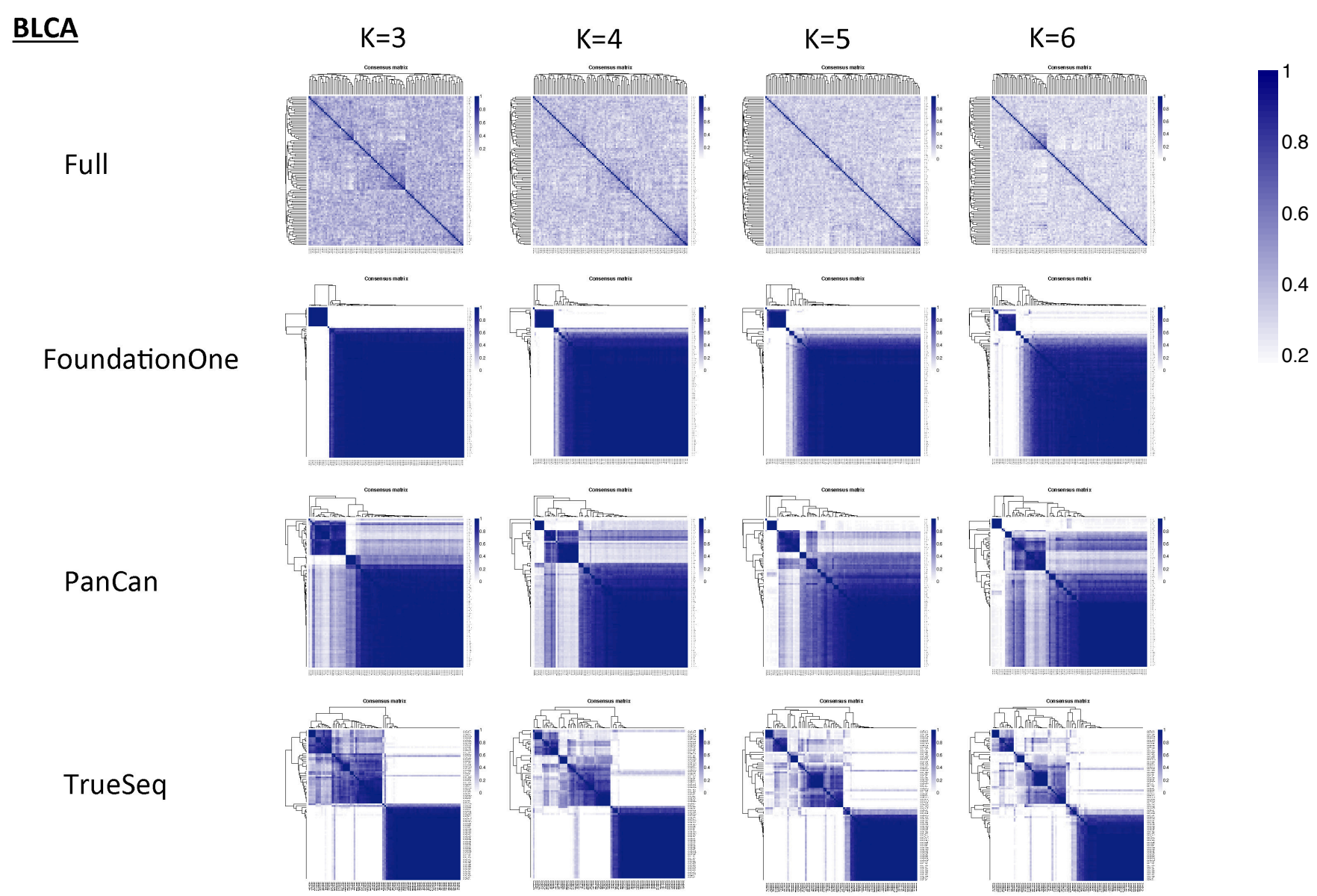

Figure S1: The clustering patterns of BLCA across the four gene sets (Full, FoundationOne, PanCan, and TrueSeq) and rank *K*=3,4,5,6.

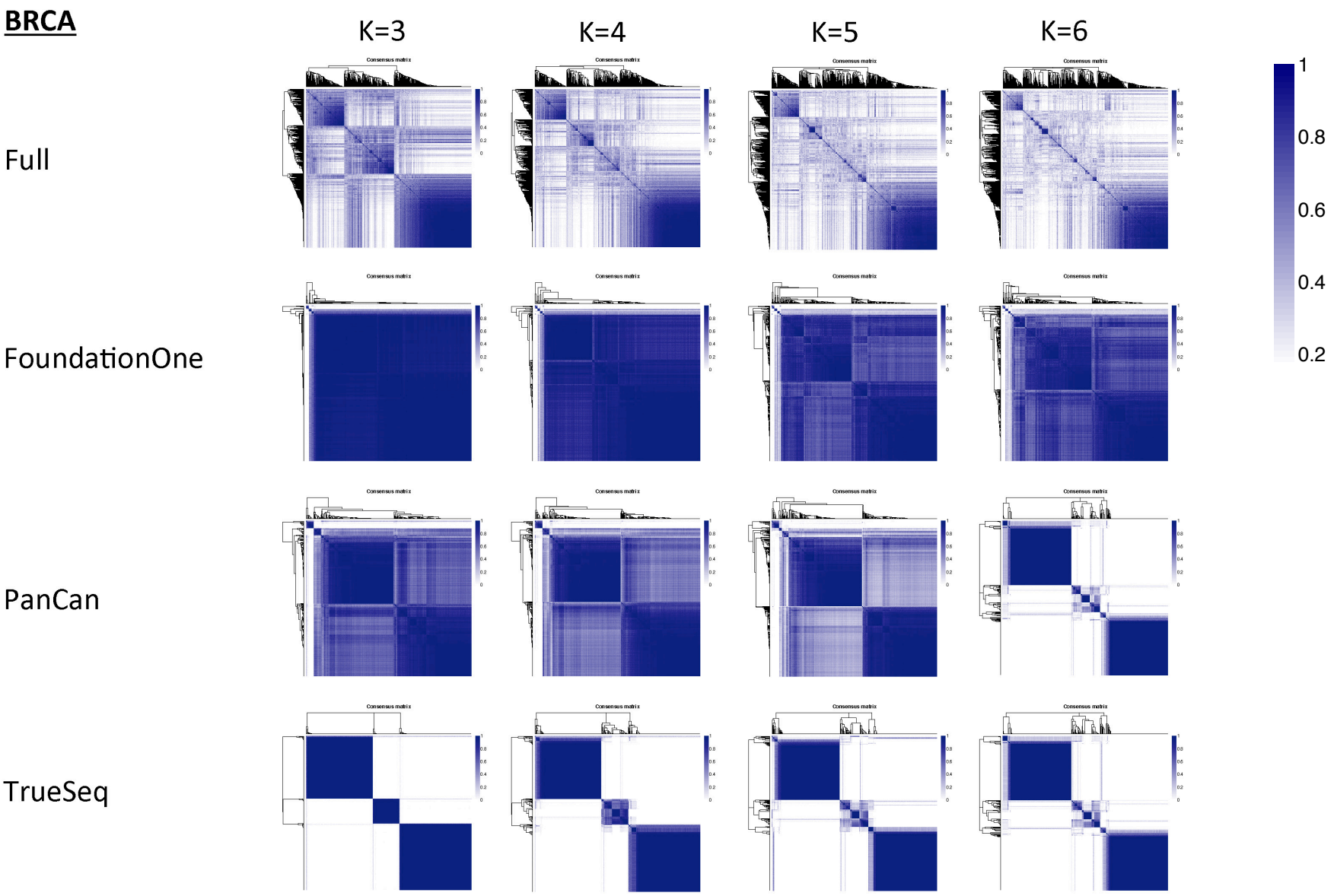

Figure S2: The clustering patterns of BRCA across the four gene sets (Full, FoundationOne, PanCan, and TrueSeq) and rank *K*=3,4,5,6.

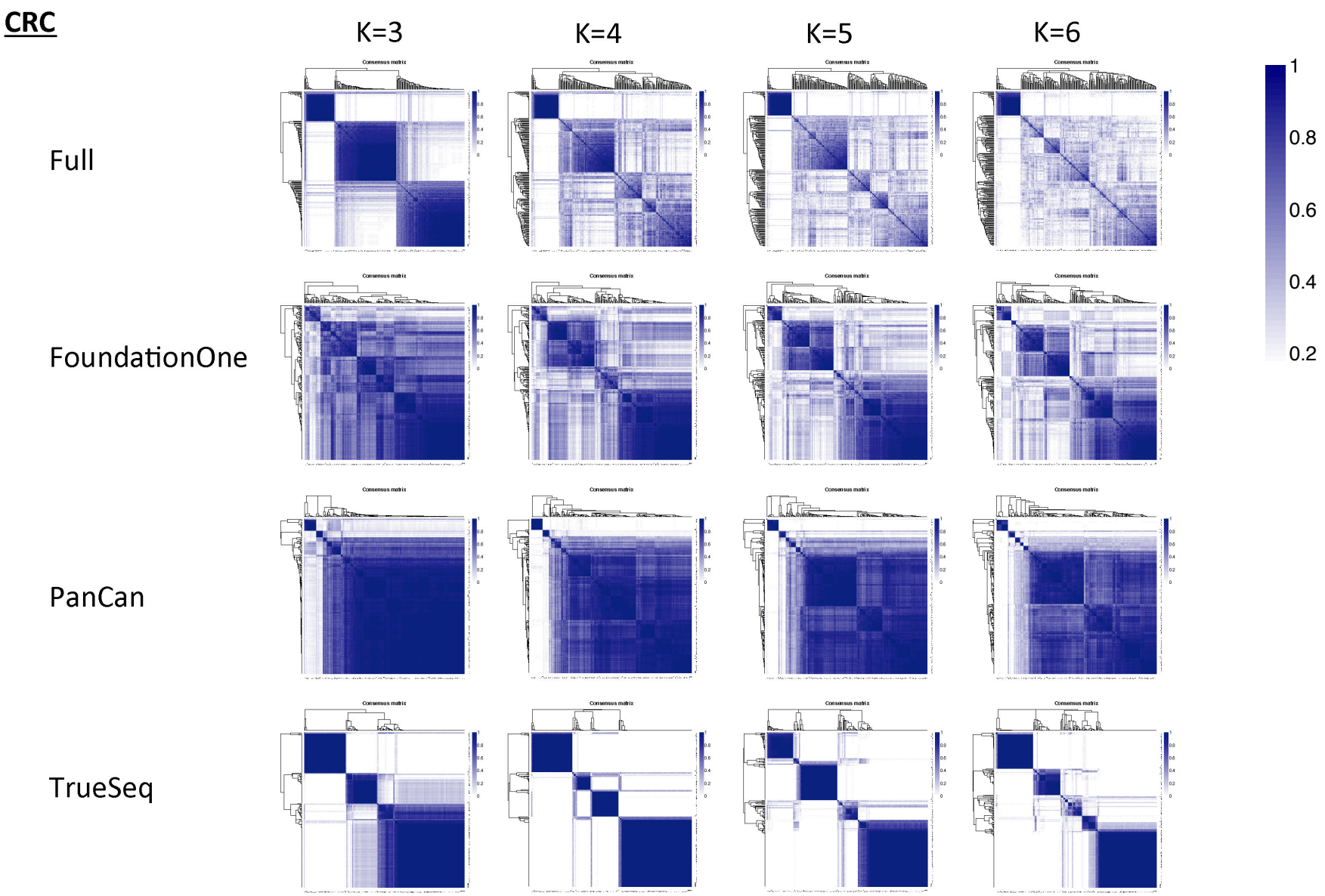

Figure S3: The clustering patterns of CRC across the four gene sets (Full, FoundationOne, PanCan, and TrueSeq) and rank *K*=3,4,5,6.

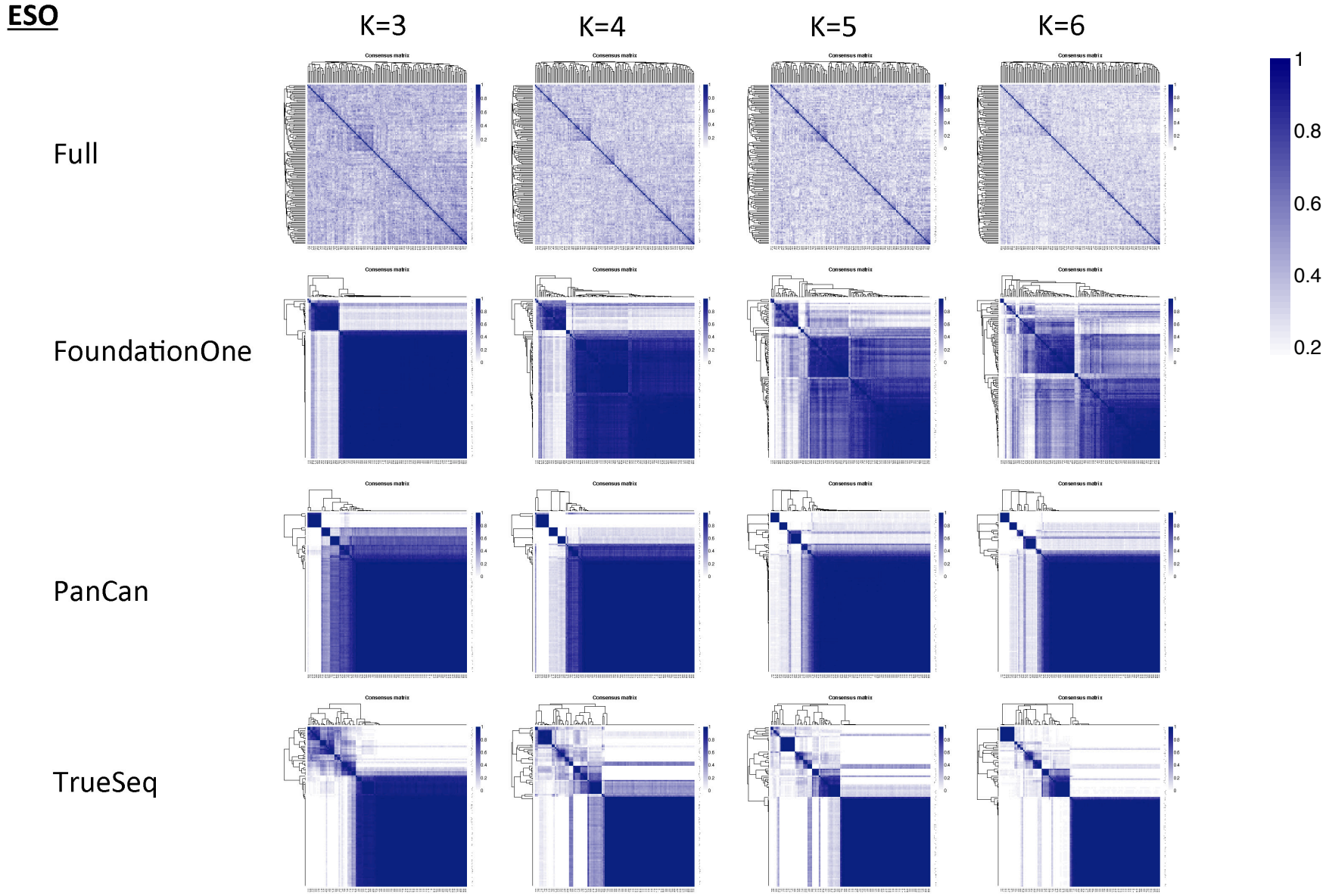

Figure S4: The clustering patterns of ESO across the four gene sets (Full, FoundationOne, PanCan, and TrueSeq) and rank *K*=3,4,5,6.

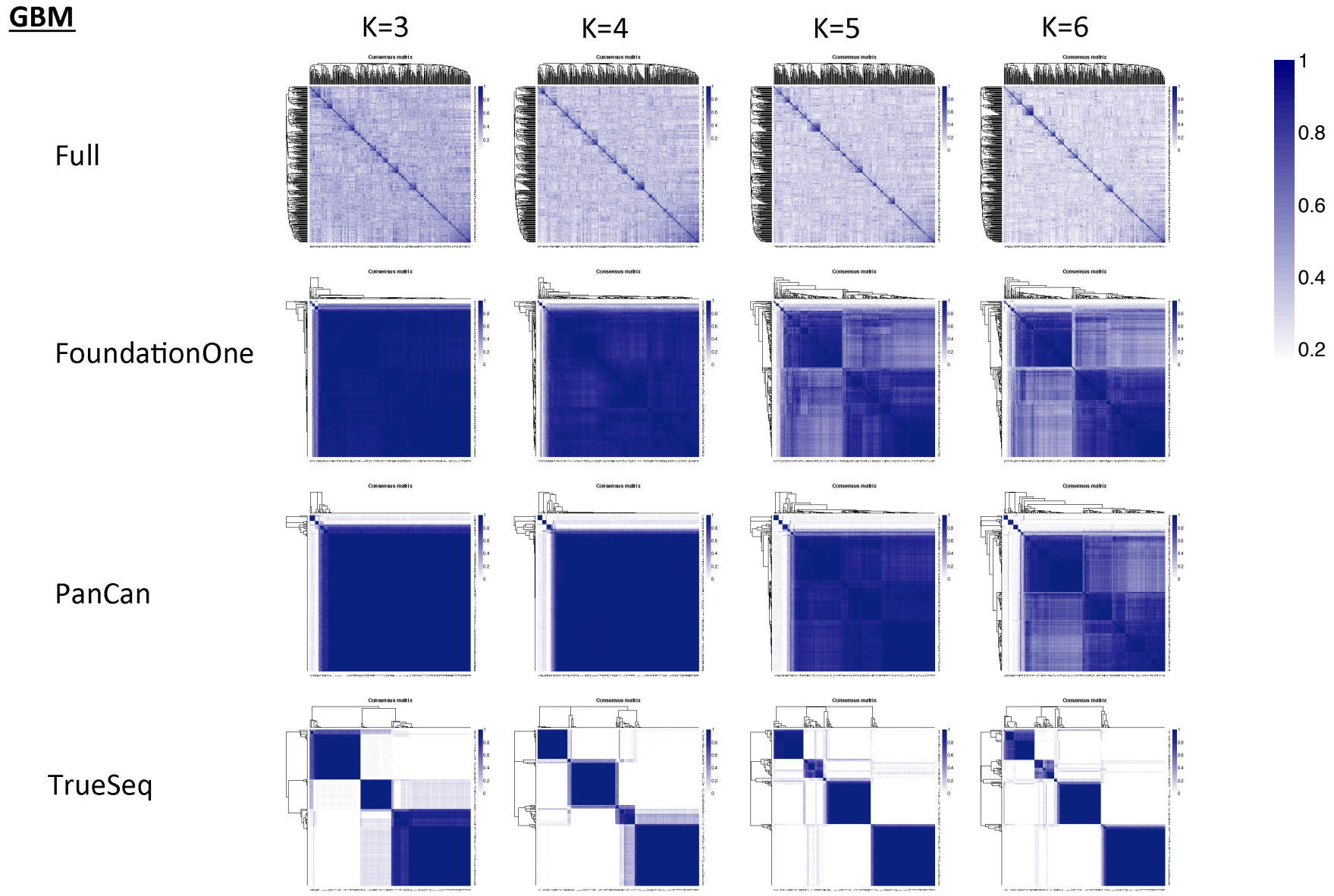

Figure S5: The clustering patterns of GBM across the four gene sets (Full, FoundationOne, PanCan, and TrueSeq) and rank *K*=3,4,5,6.

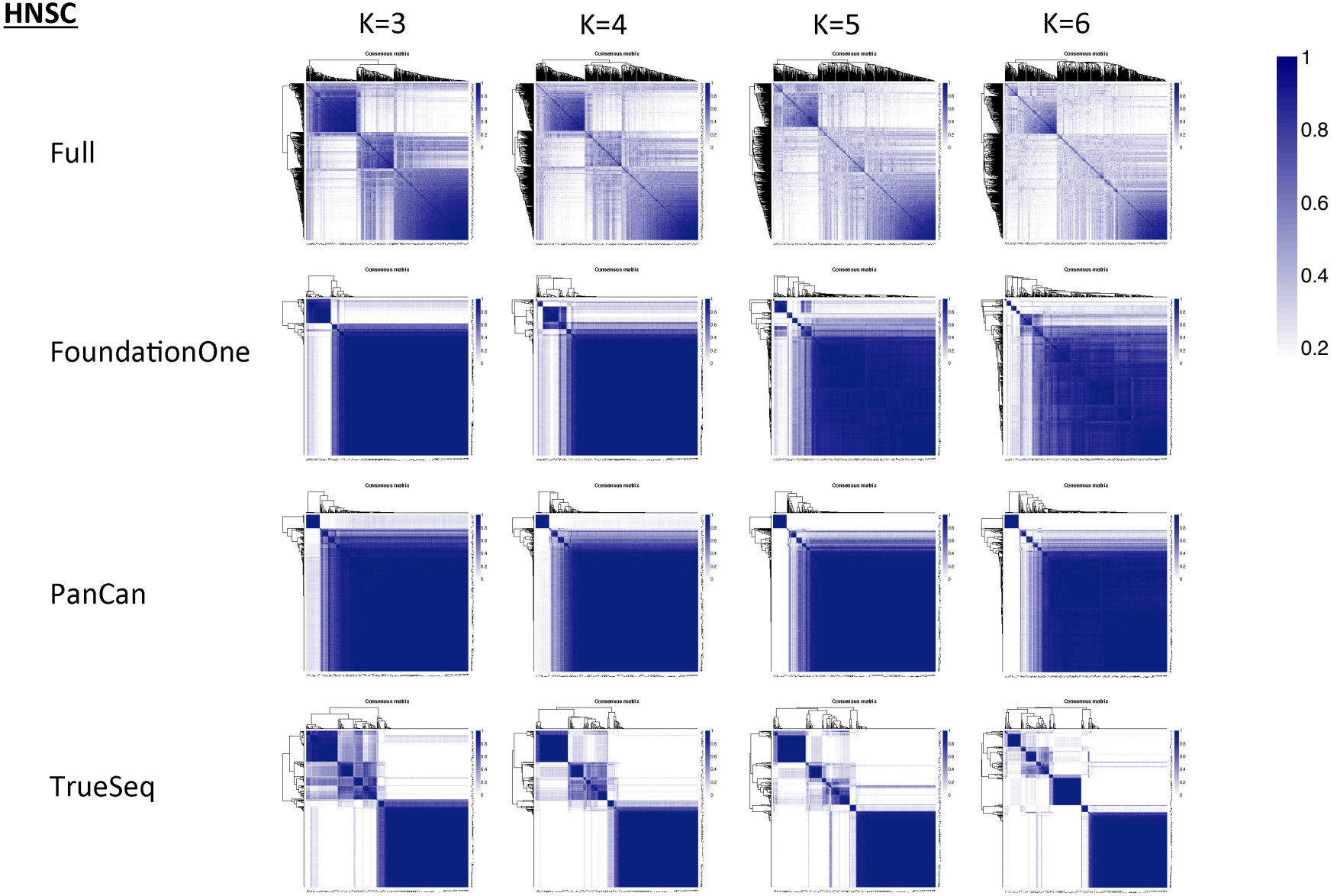

Figure S6: The clustering patterns of HNSC across the four gene sets (Full, FoundationOne, PanCan, and TrueSeq) and rank *K*=3,4,5,6.

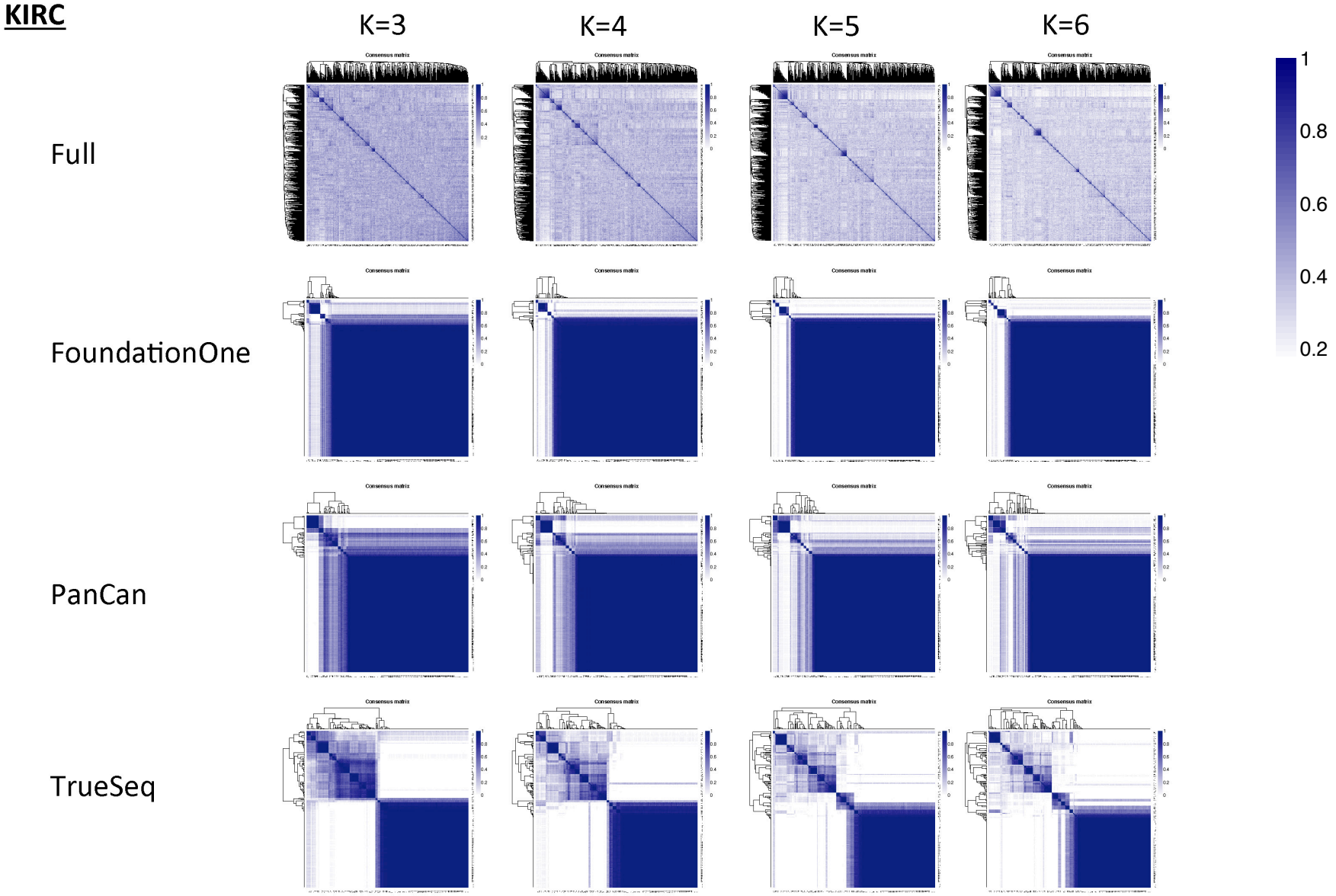

Figure S7: The clustering patterns of KIRC across the four gene sets (Full, FoundationOne, PanCan, and TrueSeq) and rank *K*=3,4,5,6.

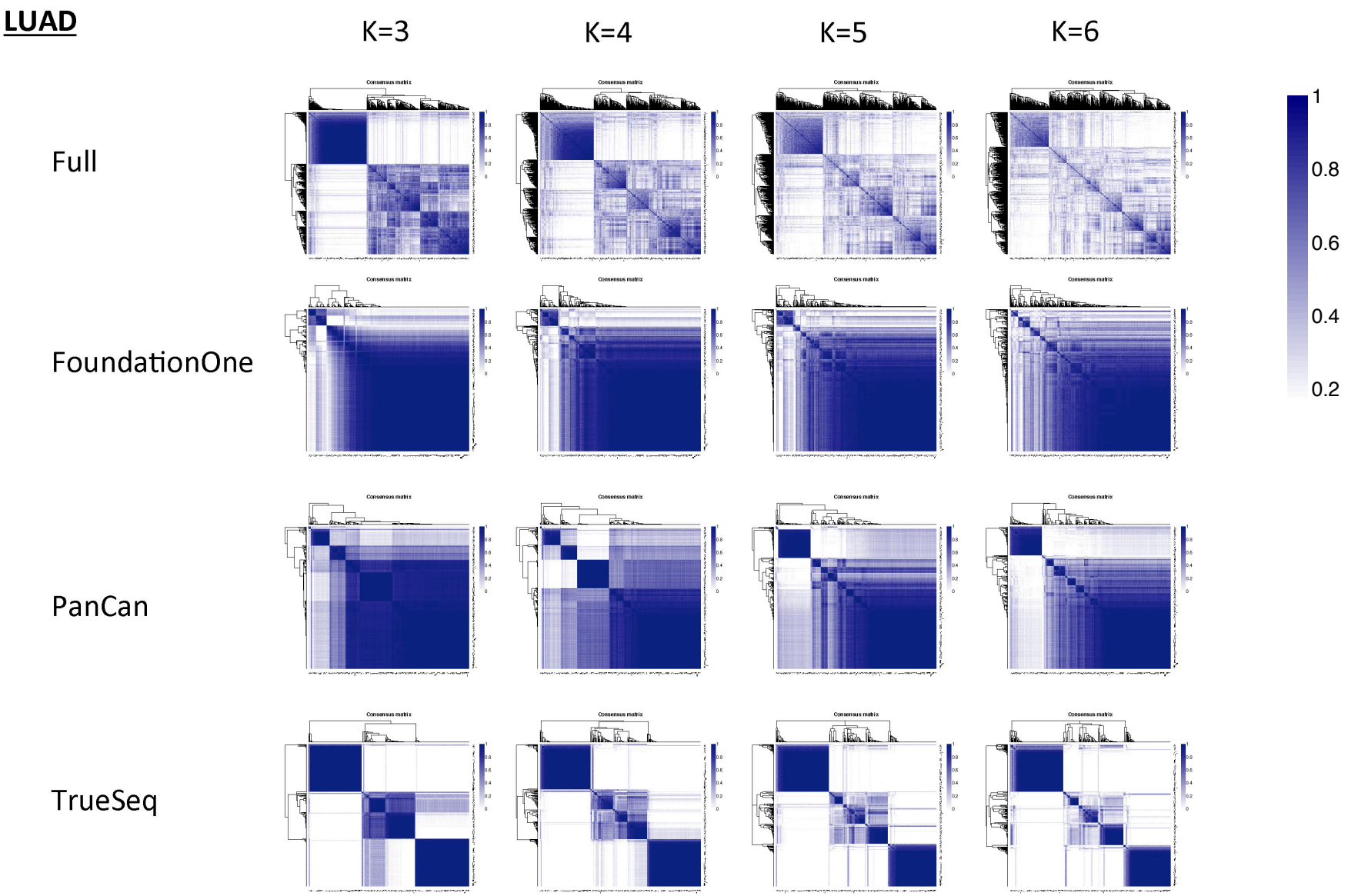

Figure S8: The clustering patterns of LUAD across the four gene sets (Full, FoundationOne, PanCan, and TrueSeq) and rank *K*=3,4,5,6.

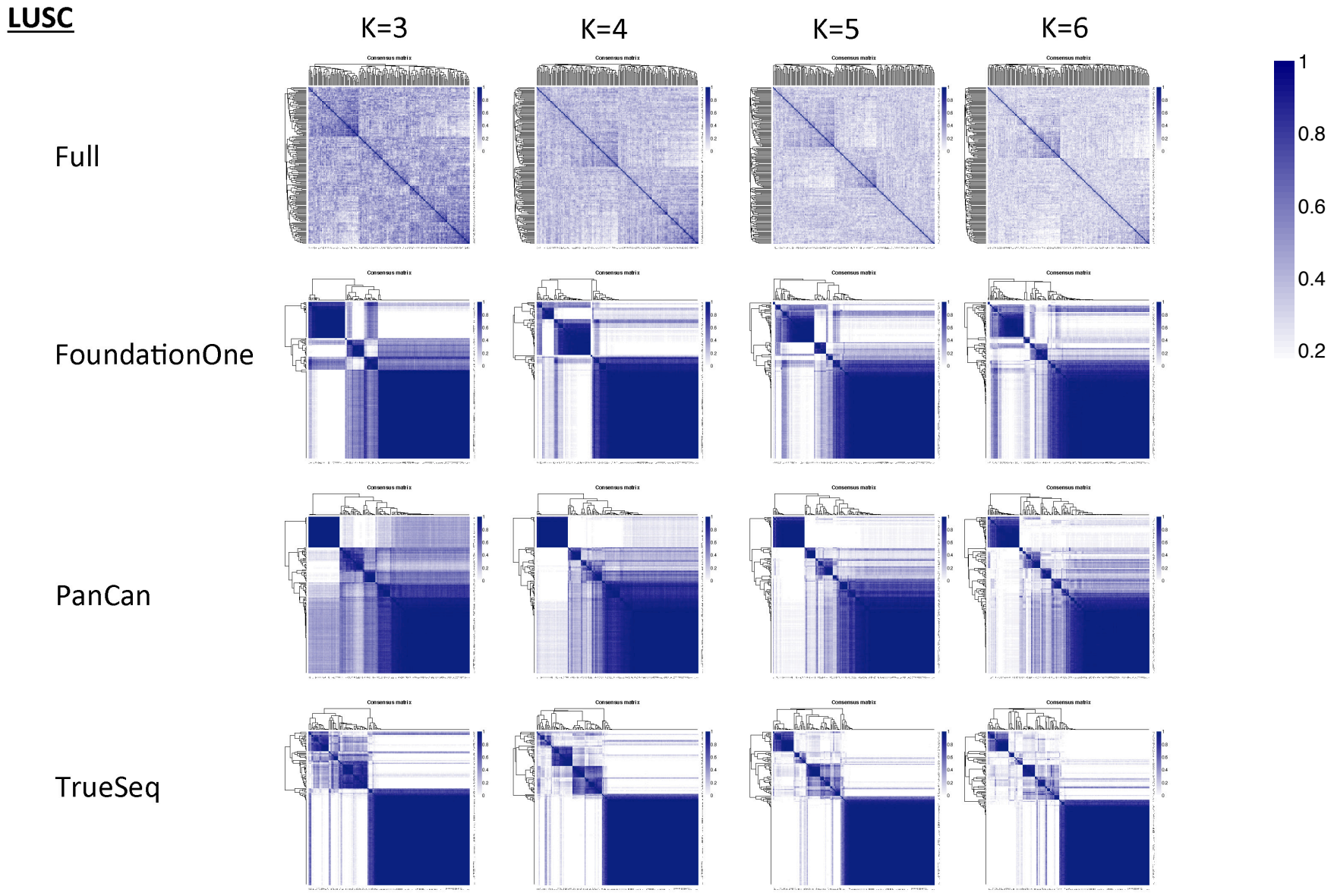

Figure S9: The clustering patterns of LUSC across the four gene sets (Full, FoundationOne, PanCan, and TrueSeq) and rank *K*=3,4,5,6.

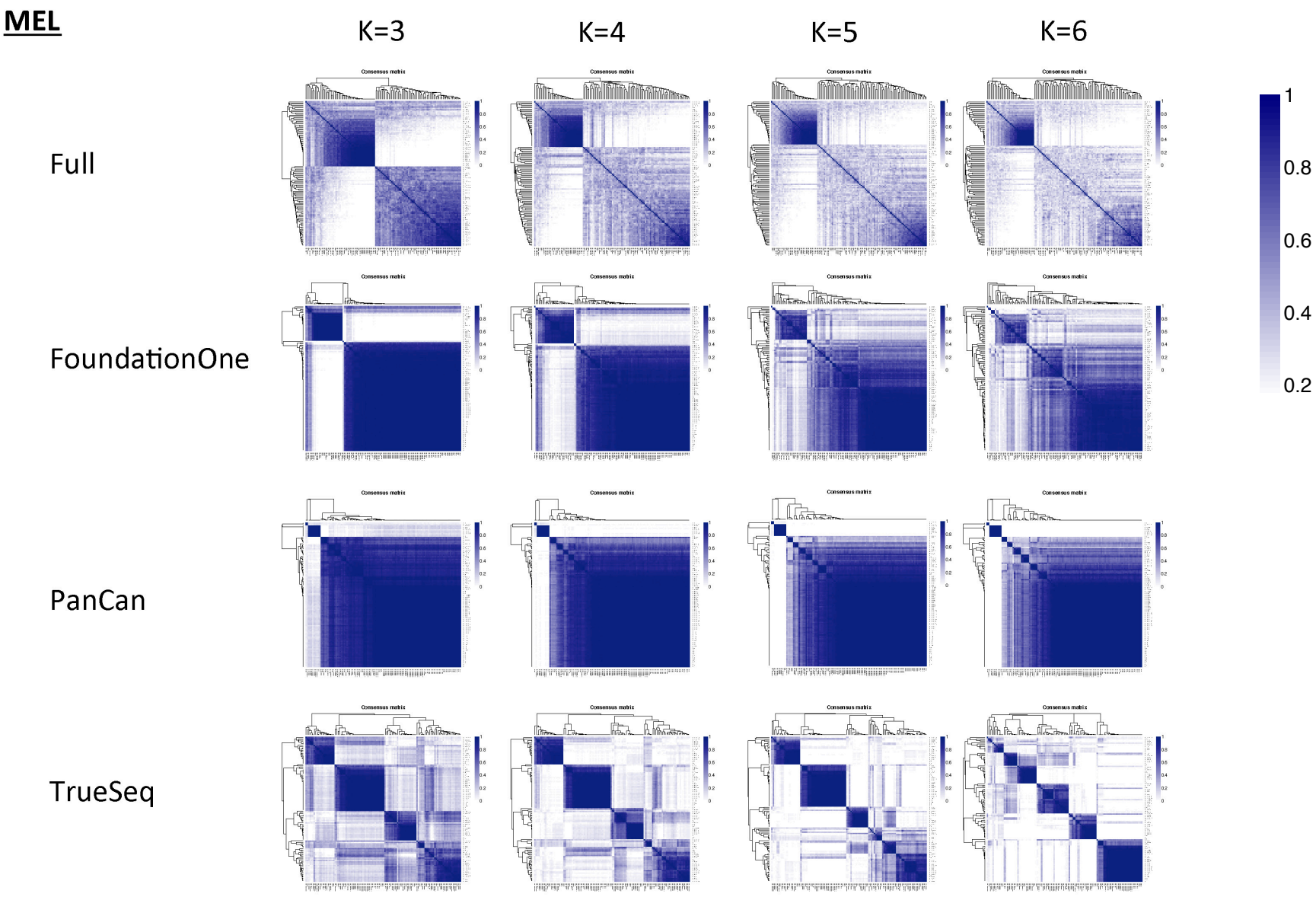

Figure S10: The clustering patterns of MEL across the four gene sets (Full, FoundationOne, PanCan, and TrueSeq) and rank *K*=3,4,5,6.

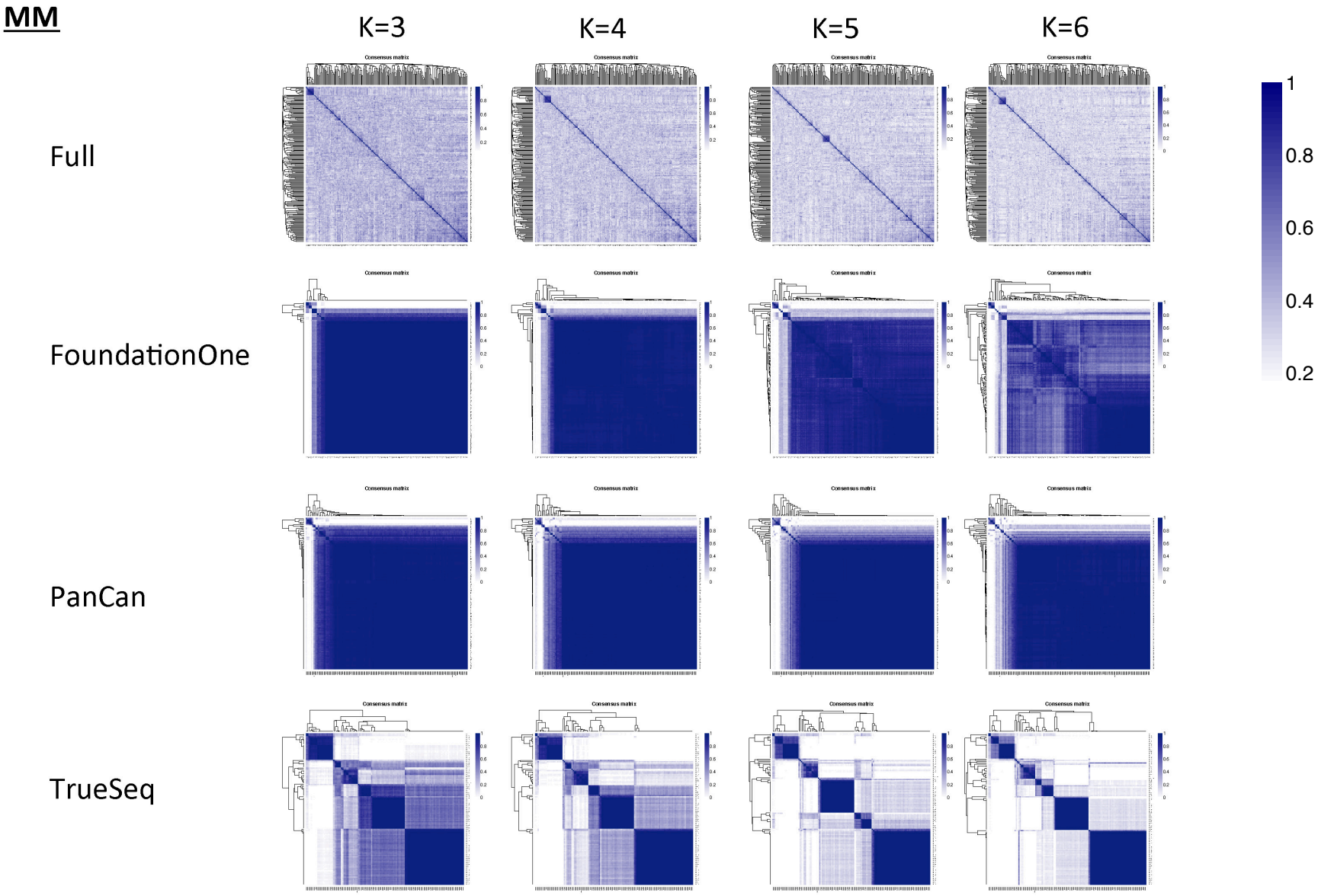

Figure S11: The clustering patterns of MM across the four gene sets (Full, FoundationOne, PanCan, and TrueSeq) and rank *K*=3,4,5,6.

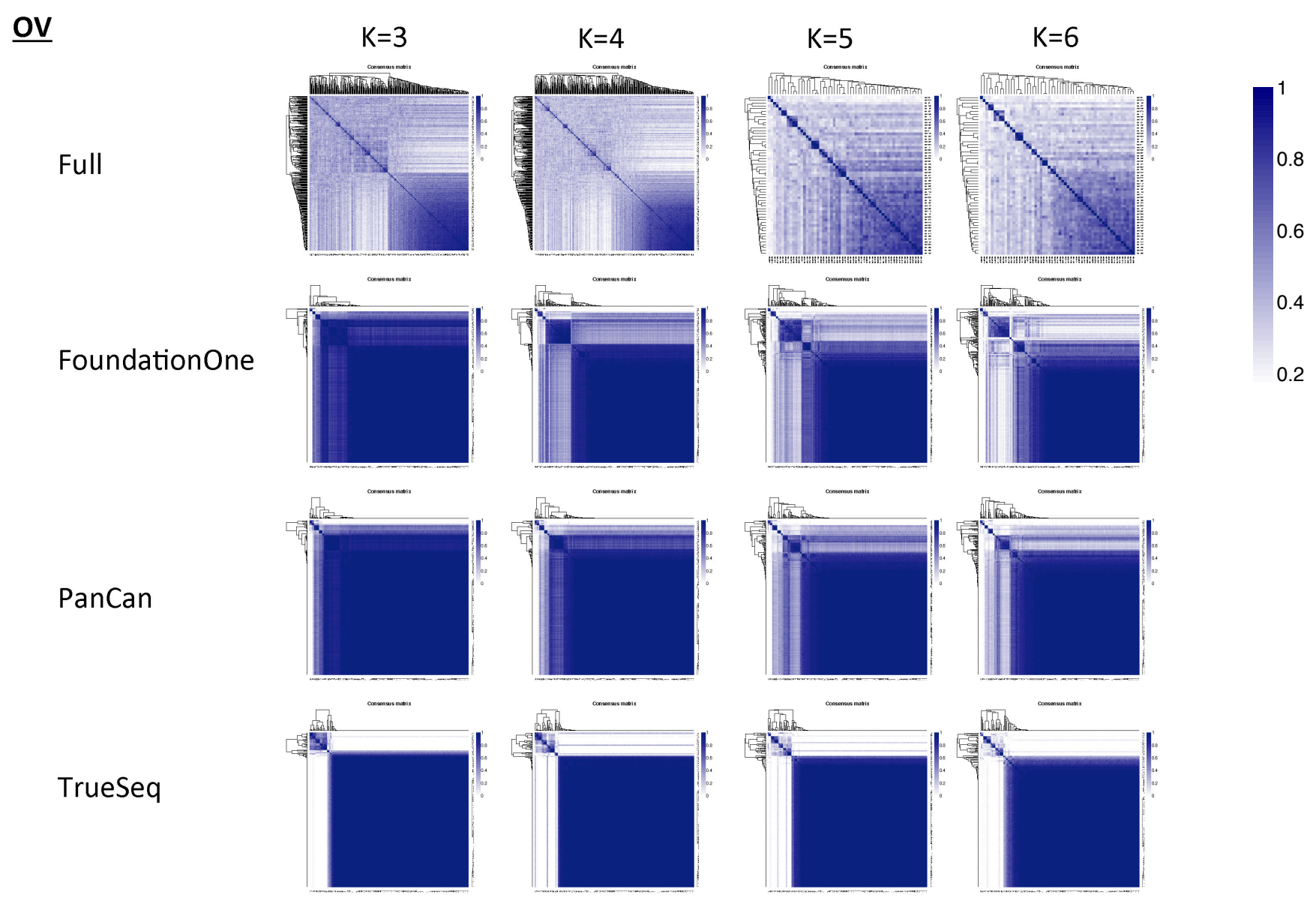

Figure S12: The clustering patterns of OV across the four gene sets (Full, FoundationOne, PanCan, and TrueSeq) and rank *K*=3,4,5,6.

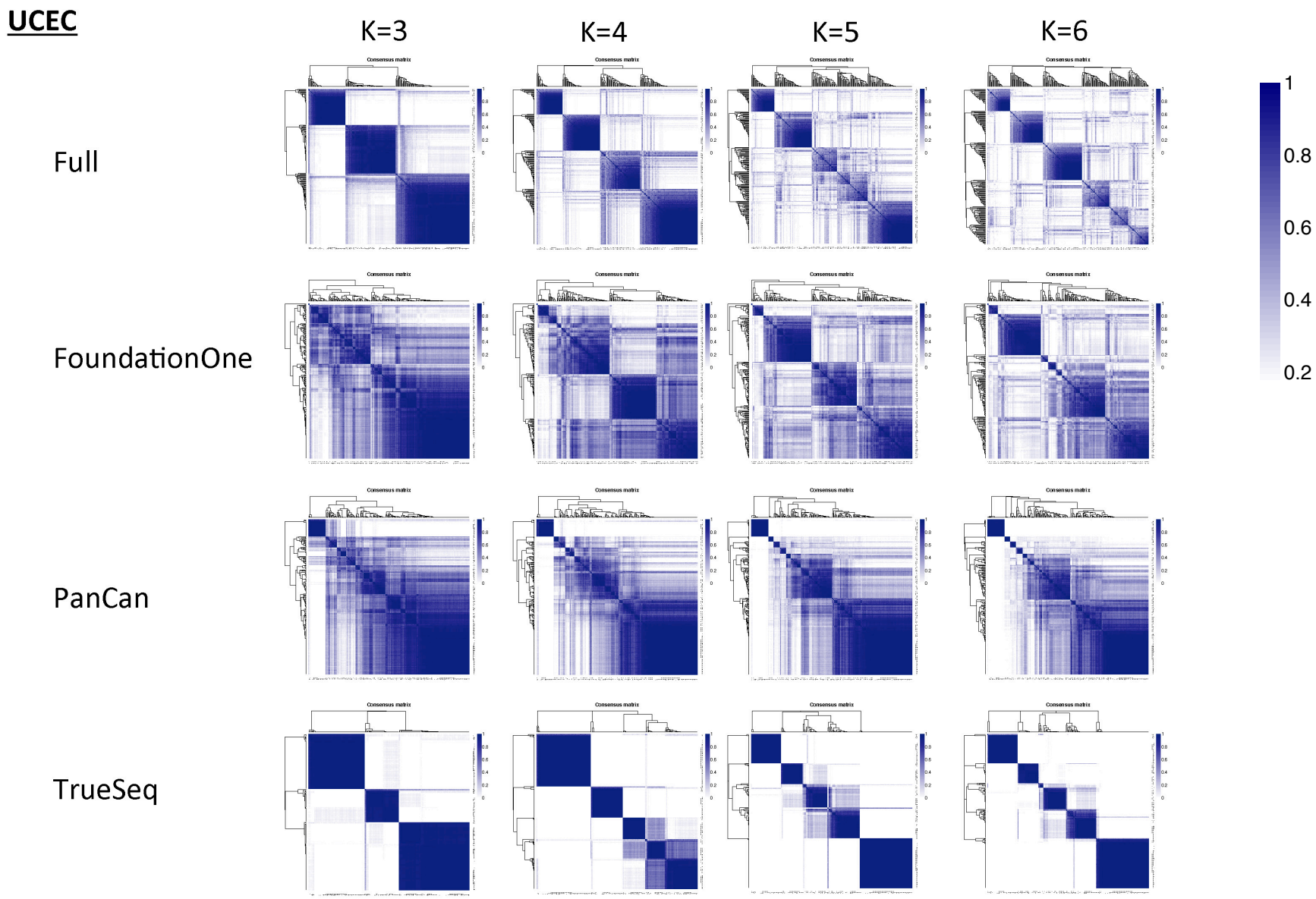

Figure S13: The clustering patterns of UCEC across the four gene sets (Full, FoundationOne, PanCan, and TrueSeq) and rank *K*=3,4,5,6.

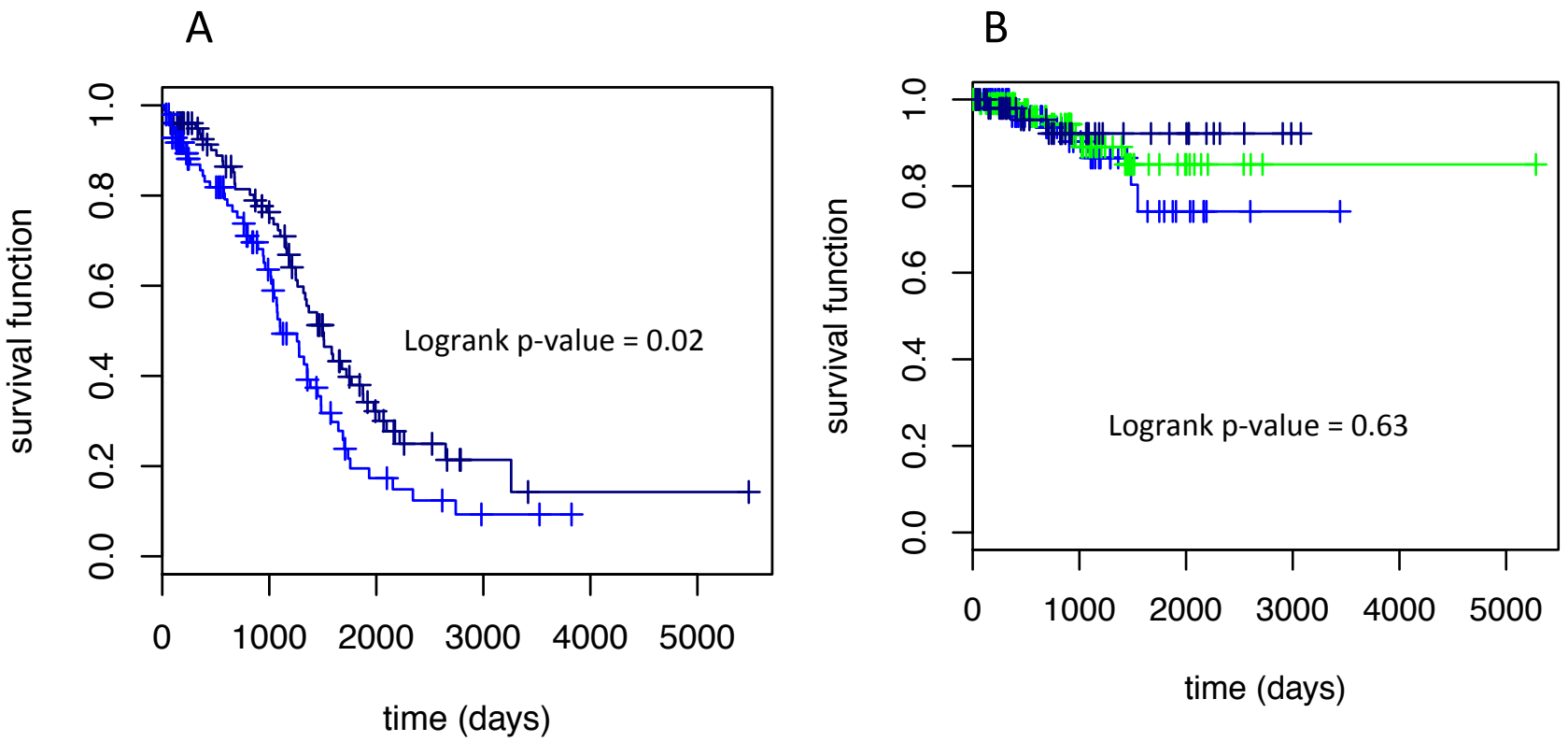

Figure S14: NBS subtypes using the Full dataset and the associations with survival for three cancers, OV (A) and UCEC (B).

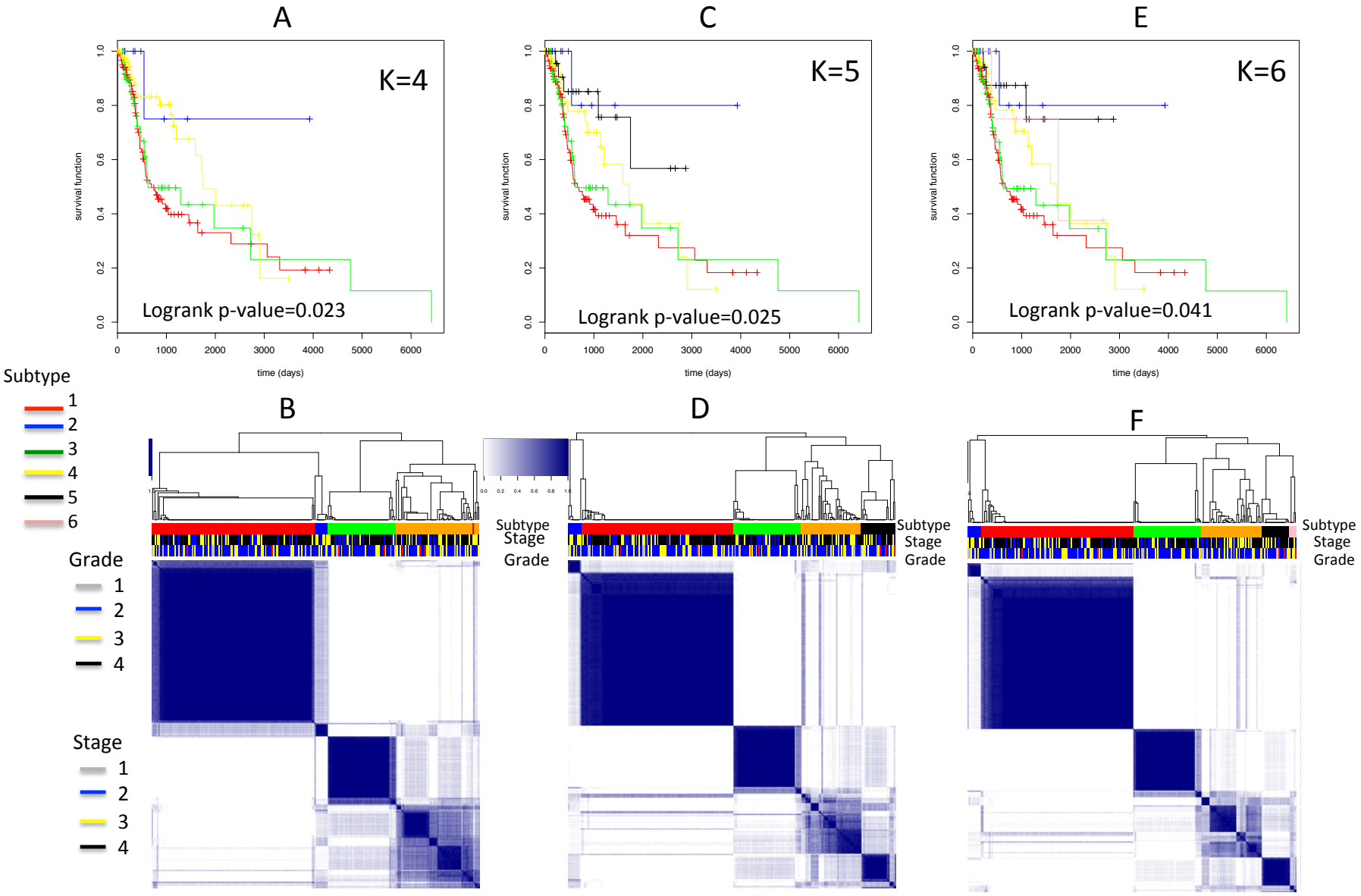

Figure S15: Subtypes associated with survival across different rank *K*'s for HNSC based on the TrueSeq panel. The sample subtype assignments for K=4,5,6, display an approximate nesting structure.

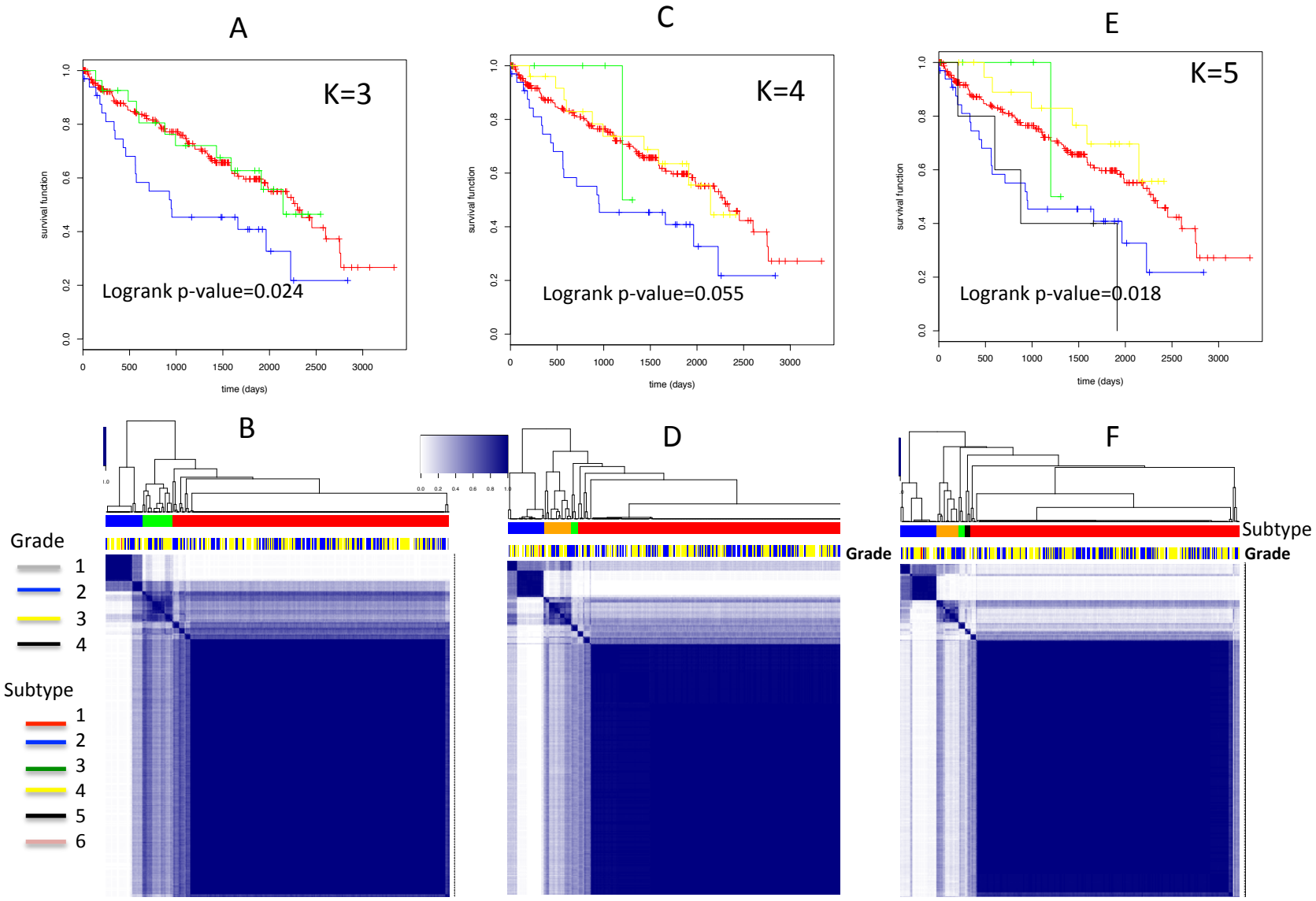

Figure S16: Subtypes associated with survival across different rank *K*'s for KIRC based on the PanCan panel. The sample subtype assignments for K=3,4,5, display an approximate nesting structure.

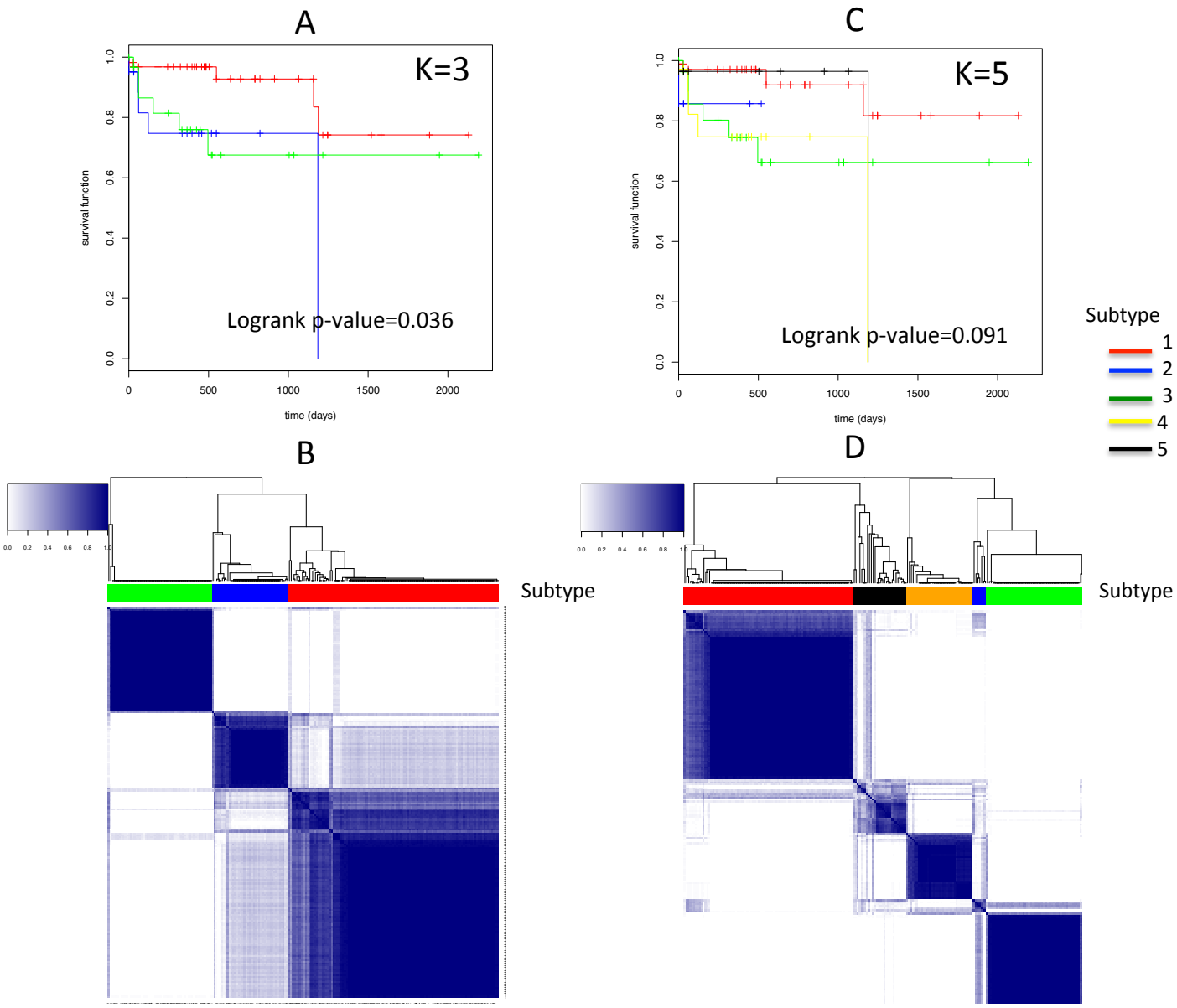

Figure S17: Subtypes associated with survival across different rank *K*'s for CRC based on the TrueSeq panel. The sample subtype assignments for K=3,5, display an approximate nesting structure.