

Supplementary Methods

Cluster derivation

We applied an unsupervised ML approach to develop clinical phenotypes of non-US citizen kidney transplant recipients in the UNOS/OPTN database by conducting unsupervised consensus clustering.^[1] We performed consensus clustering analysis on the whole study population. We initially assessed the distribution and missingness in phenotyping variables. Subsequently, missing data were imputed through multiple imputation using multivariate imputation by chained equations (MICE),^[2] and non-normal data were z-score normalized. Multiple imputation is a widely used approach to estimate variables when data are missing at random. MICE is optimal when less than 30% of a variable's data are missing.^[3-8] All of the extracted variables in our study had missing data $\leq 5\%$ (Table S1). We subsequently applied clustering using the consensus cluster algorithm. The algorithm begins by subsampling a proportion of items and a proportion of features from a data matrix. Each subsample is then partitioned into up to groups (k) by a user-specified clustering algorithm. This process is repeated for a specified number of times. Pairwise consensus values, defined as 'the proportion of clustering runs in which two items are grouped together', are calculated and stored in a consensus matrix (CM) for each cluster. Clustering settings used were as follows: maximum number of clusters, 10; number of iterations, 100; subsampling fraction, 0.8; clustering algorithm, K-means; Euclidean distance).^[1] The number of potential clusters ranges from 2 to 10, to avoid producing an excessive number of clusters that would not be clinical useful. Pairwise consensus values, defined as 'the proportion of clustering runs in which two items are [grouped] together^[1]', are calculated and stored in a CM for each k. Then for each k, a final agglomerative hierarchical consensus clustering using distance of 1-consensus values is completed and pruned to k groups, which are called consensus clusters.

The clustering algorithm is to maximize the potential number of clusters while maintaining high cluster consensus. The optimal number of clusters was determined by examining the CM heat map, cumulative distribution function, cluster-consensus plots with the within-cluster consensus scores, and the proportion of ambiguously clustered pairs (PAC).^[9, 10] The within-cluster consensus score, ranging between 0 and 1, is defined as the average consensus value for all pairs of individuals belonging to the same cluster.^[10] A value closer to one indicates better cluster stability.^[10] PAC, ranging between 0 and 1, is calculated as the proportion of all sample pairs with consensus values falling within the predetermined boundaries.^[9] A value closer to zero indicates better cluster stability.^[9] To examine the cluster profile, we calculated and graphically displayed the standardized mean differences of the variables between each cluster and the overall study population. Calculation of the standardized difference of each parameter used the cutoff of ± 0.3 to show subgroup features with the key features for each cluster.

All cluster derivation analyses were performed using R, version 4.0.3 (RStudio, Inc., Boston, MA; <http://www.rstudio.com/>), with the packages of ConsensusClusterPlus (version 1.46.0)^[10]. We imputed missing data through multivariable imputation by chained equation (MICE) method.^[2] All analyses were two-tailed, and P value < .05 was considered statistically significant.

Table S1. the number and percentages of missing data

	Missing data (total=11,300)
Recipient Age	0 (0)
Recipient male sex	0 (0)
ABO blood group	0 (0)
Body mass index	0 (0)
Kidney retransplant	0 (0)
Kidney donor status	0 (0)
Dialysis duration	83 (1)
Cause of end-stage kidney disease	0 (0)
Comorbidity	
- Diabetes mellitus	0 (0)
- Malignancy	0 (0)
- Peripheral vascular disease	141 (1)
PRA (%)	511 (5)
Positive HCV serostatus	0 (0)
Positive HBs antigen	0 (0)
Positive HIV serostatus	0 (0)
Functional status	298 (3)
Working income	372 (3)
Public insurance	5 (0.0004)
US resident	0 (0)
Undergraduate education or above	419 (4)
Serum albumin	429 (4)
Donor age	0 (0)
Donor male sex	0 (0)
Donor race	0 (0)
History of hypertension in donor	0 (0)
KDPI	0 (0)
HLA mismatch	0 (0)
Cold ischemia time	3 (0.0003)
Kidney on pump	0 (0)
Delay graft function	0 (0)
Allocation type	0 (0)
EBV status	503 (4)
CMV status	0 (0)
Induction immunosuppression	
- Thymoglobulin	0 (0)
- Alemtuzumab	0 (0)
- Basiliximab	0 (0)
- Other	0 (0)
- No induction	0 (0)
Maintenance Immunosuppression	
- Tacrolimus	0 (0)
- Cyclosporine	0 (0)
- Mycophenolate	0 (0)
- Azathioprine	0 (0)
- mTOR inhibitors	0 (0)
- Steroid	0 (0)

Table S2. Country of citizenship of non-US citizen/non-US residents.

Non-US citizen/non-US resident, travel to US for transplant				Non-US citizen/non-US resident, travel to US for reason other than transplant			
Country	All	Cluster 1	Cluster 2	Country	All	Cluster 1	Cluster 2
KUW (Kuwait)	35	32	3	MEX (Mexico)	320	105	215
QAT (Qatar)	22	21	1	ESV (El Salvador)	43	17	26
MEX (Mexico)	17	11	6	IND (India)	21	13	8
SAU (Saudi Arabia)	12	10	2	GTL (Guatemala)	19	5	14
UAE (United Arab Emirates)	12	10	2	CHI (Chile)	14	2	12
BHS (The Bahamas)	9	4	5	HON (Honduras)	13	3	10
BER (Berlin)	8	2	6	DOR (Dominican Republic)	10	3	7
CYI (Cayman Islands)	4	2	2	PHL (Philippines)	9	5	4
IND (India)	4	4	0	BRA (Brazil)	6	4	2
JPN (Japan)	4	0	4	COL (Columbia)	6	4	2
CAN (Canada)	3	1	2	HTI (Haiti)	5	0	5
ECU (Ecuador)	3	2	1	ISR (Israel)	5	5	0
ESV (El Salvador)	3	0	3	CUB (Cuba)	4	2	2
ISR (Israel)	3	2	1	JMC (Jamaica)	4	1	3
JMC (Jamaica)	3	3	0	ECU (Ecuador)	3	1	2
PKT (Pakistan)	3	3	0	KOR (Korea)	3	1	2
ARG (Argentina)	2	2	0	NGA (Nigeria)	3	2	1
GRC (Greece)	2	0	2	SDN (Sudan)	3	1	2
GTL (Guatemala)	2	2	0	BGD (Bangladesh)	2	1	1

HON (Honduras)	2	2	0	BUR (Burma)	2	0	2
HTI (Haiti)	2	0	2	CAM (Cambodia)	2	1	1
NIC (Nicaragua)	2	1	1	ETH (Ethiopia)	2	0	2
PER (Peru)	2	1	1	GHA (Ghana)	2	0	2
PHL (Philippines)	2	1	1	GYA (Guyana)	2	0	2
SAF (South Africa)	2	2	0	PKT (Pakistan)	2	1	1
VEN (Venezuela)	2	1	1	SAU (Saudi Arabia)	2	1	1
BUR (Burma)	1	0	1	SPA (Spain)	2	2	0
CAM (Cambodia)	1	1	0	THL (Thailand)	2	2	0
CHI (Chile)	1	1	0	UKD (United Kingdom)	2	2	0
CSR (Costa Rica)	1	1	0	AGB (Antigua and Barbuda)	1	0	1
CUB (Cuba)	1	0	1	AMN (Armenia)	1	0	1
CVD (Cabo Verde)	1	0	1	ARU (Aruba)	1	0	1
DMK (Denmark)	1	1	0	BEL (Belgium)	1	1	0
DOR (Dominican Republic)	1	0	1	BHS (The Bahamas)	1	0	1
GHA (Ghana)	1	1	0	BOL (Bolivia)	1	1	0
IRN (Iran)	1	0	1	BVI (British Virgin Island)	1	1	0
ITL (Italy)	1	1	0	BZE (Belize)	1	0	1
LEB (Lebanon)	1	1	0	CAN (Canada)	1	0	1
SPA (Spain)	1	1	0	CMR (Comoros)	1	0	1
TDT (Trinidad)	1	1	0	CRS (Cyprus)	1	0	1

UKD (United Kingdom)	1	1	0	CYI (Cayman Islands)	1	0	1
ZIM (Zimbabwe)	1	1	0	DMN (Dominica)	1	0	1
Missing	115	85	30	EGY (Egypt)	1	0	1
				GAB (Gabon)	1	1	0
				GER (Germany)	1	1	0
				GRC (Greece)	1	1	0
				GUN (Guyana)	1	0	1
				HKG (Hong Kong)	1	1	0
				ITL (Italy)	1	1	0
				JPN (Japan)	1	0	1
				KEY (Kenya)	1	0	1
				LTV (Latvia)	1	1	0
				MAC (Macau)	1	0	1
				MHI (Marshall Islands)	1	0	1
				MLI (Mali)	1	0	1
				MOR (Morocco)	1	1	0
				MYS (Malaysia)	1	0	1
				NPL (Nepal)	1	1	0
				PER (Peru)	1	1	0
				PLD (Poland)	1	1	0
				QAT (Qatar)	1	1	0
				ROM (Romania)	1	0	1
				RUS (Russia)	1	0	1
				SAF (South Africa)	1	0	1
				SKR (South Korea)	1	1	0
				SNG (Singapore)	1	0	1

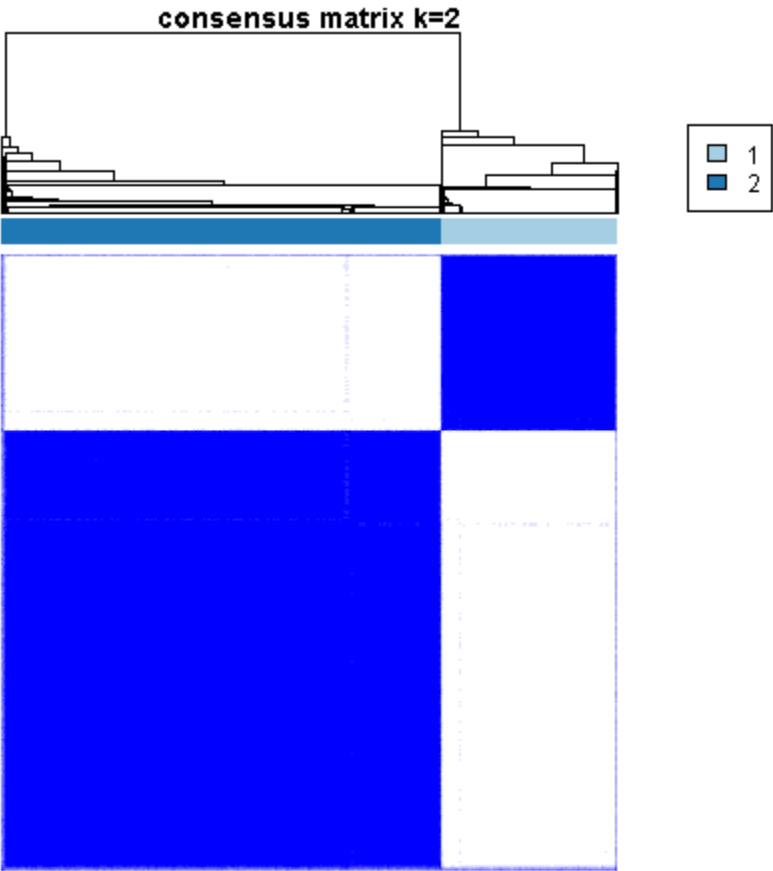
				SOM (Somalia)	1	0	1
				SRB (Serbia)	1	1	0
				STK (Saint Kitts and Nevis)	1	1	0
				STL (Switzerland)	1	1	0
				SYA (Syria)	1	0	1
				TDT (Trinidad)	1	0	1
				TMS (Turkmenistan)	1	0	1
				UAE (United Arab Emirates)	1	1	0
				VEN (Venezuela)	1	1	0
				VTN (Vietnam)	1	0	1
				Missing	434	140	294

Table S2. Proportion of clusters according to the regions

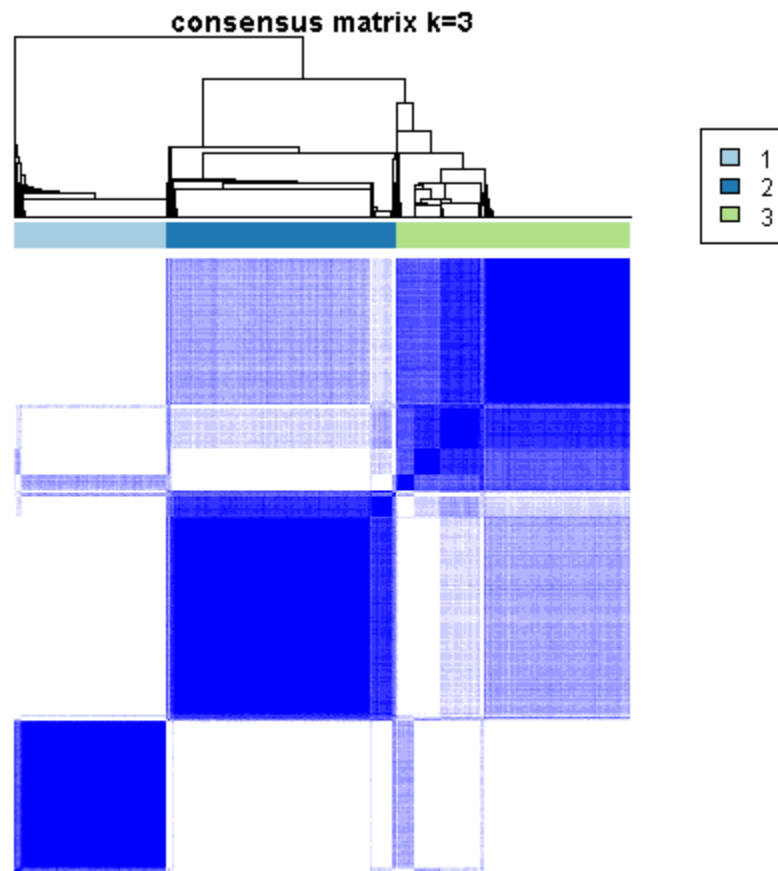
Region	N	Cluster 1	Cluster 2
1	474	137 (29)	337 (71)
2	797	298 (37)	499 (63)
3	831	220 (26)	611 (74)
4	1213	353 (29)	860 (71)
5	45776	1079 (24)	3497 (76)
6	417	90 (22)	327 (78)
7	816	341 (42)	475 (58)
8	329	85 (26)	244 (74)
9	1362	481 (35)	881 (65)
10	239	96 (40)	143 (60)
11	246	46 (19)	200 (81)
Total	11300	3226 (29)	8074 (71)

Reported as n (%)

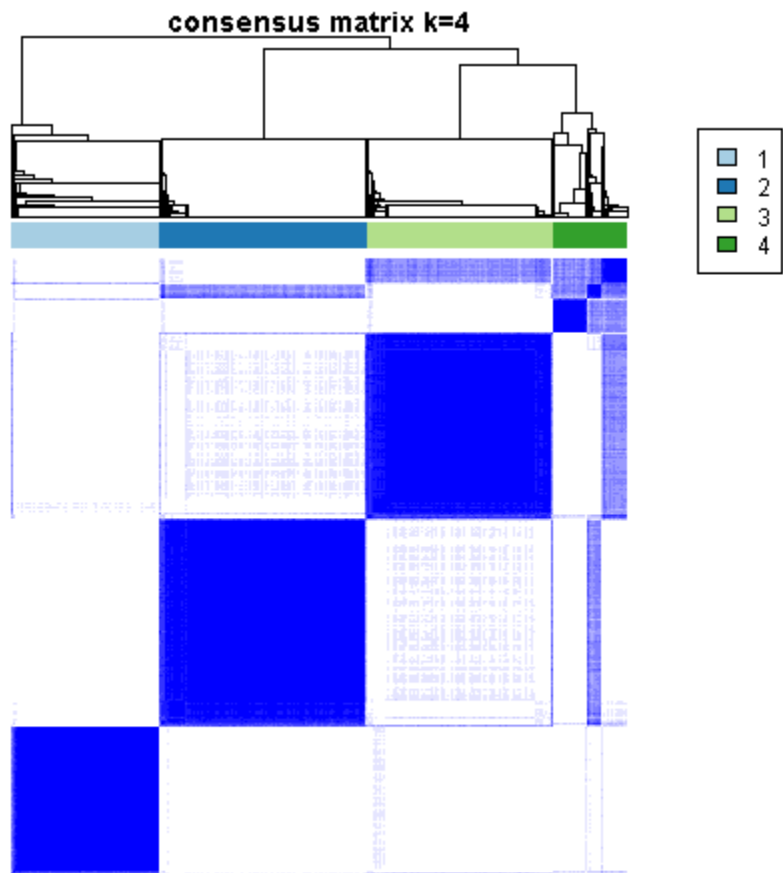
Supplementary Figure S1. Consensus matrix heat map ($k = 2$) depicting consensus values on a white to blue color scale of each cluster



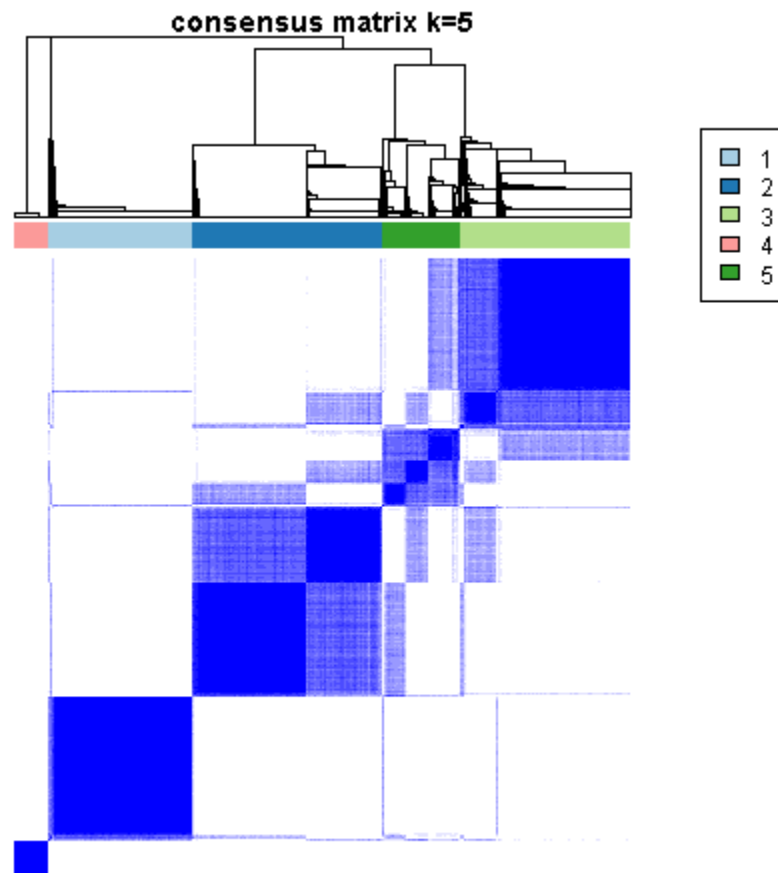
Supplementary Figure S2. Consensus matrix heat map ($k = 3$) depicting consensus values on a white to blue color scale of each cluster



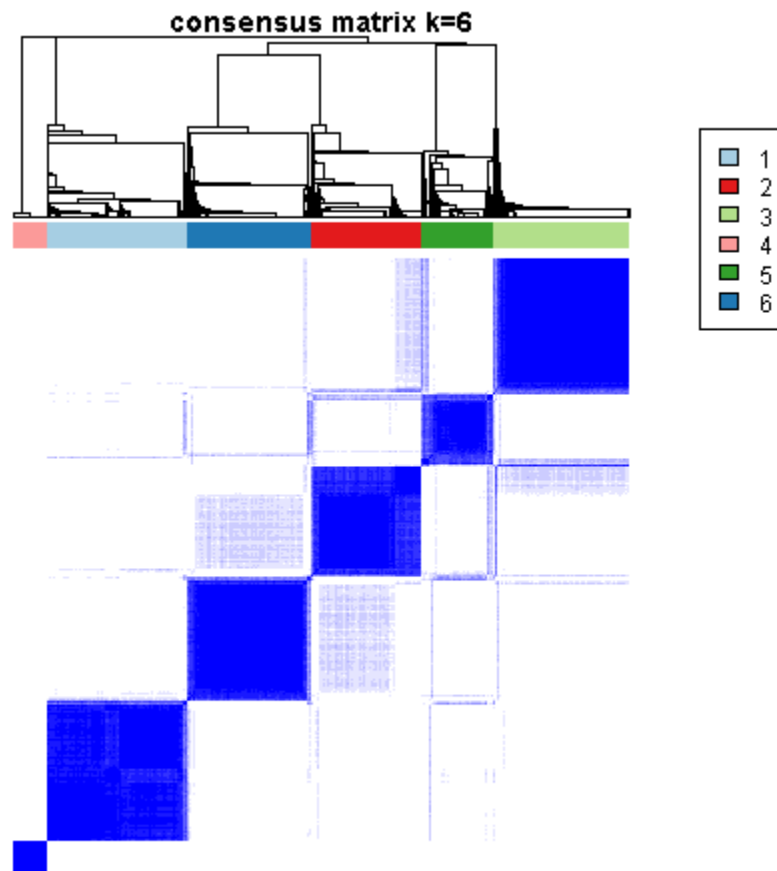
Supplementary Figure S3. Consensus matrix heat map ($k = 4$) depicting consensus values on a white to blue color scale of each cluster



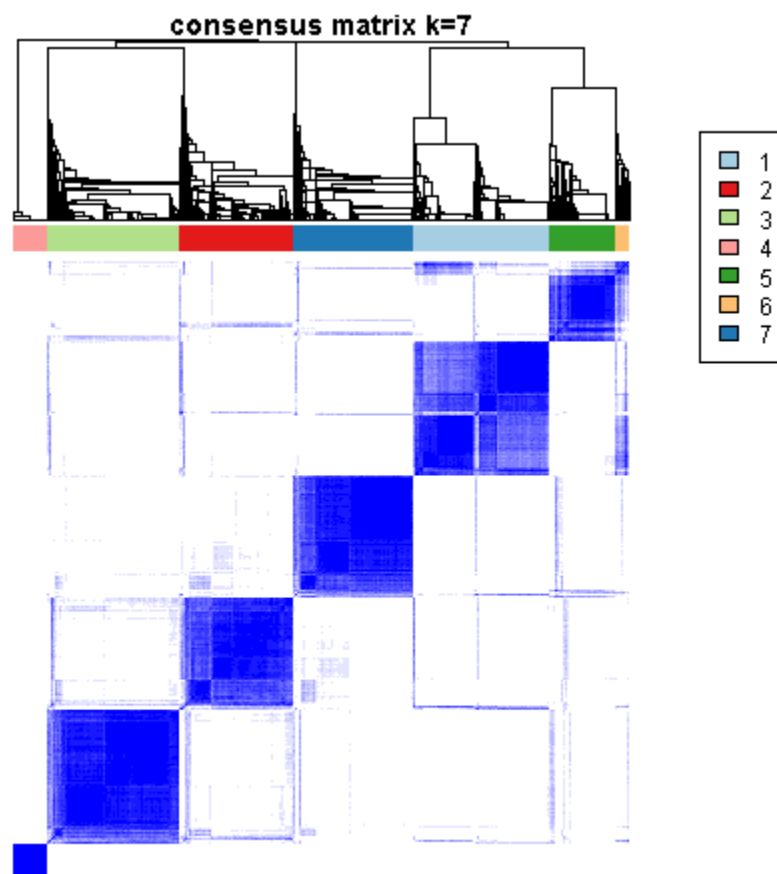
Supplementary Figure S4. Consensus matrix heat map ($k = 5$) depicting consensus values on a white to blue color scale of each cluster



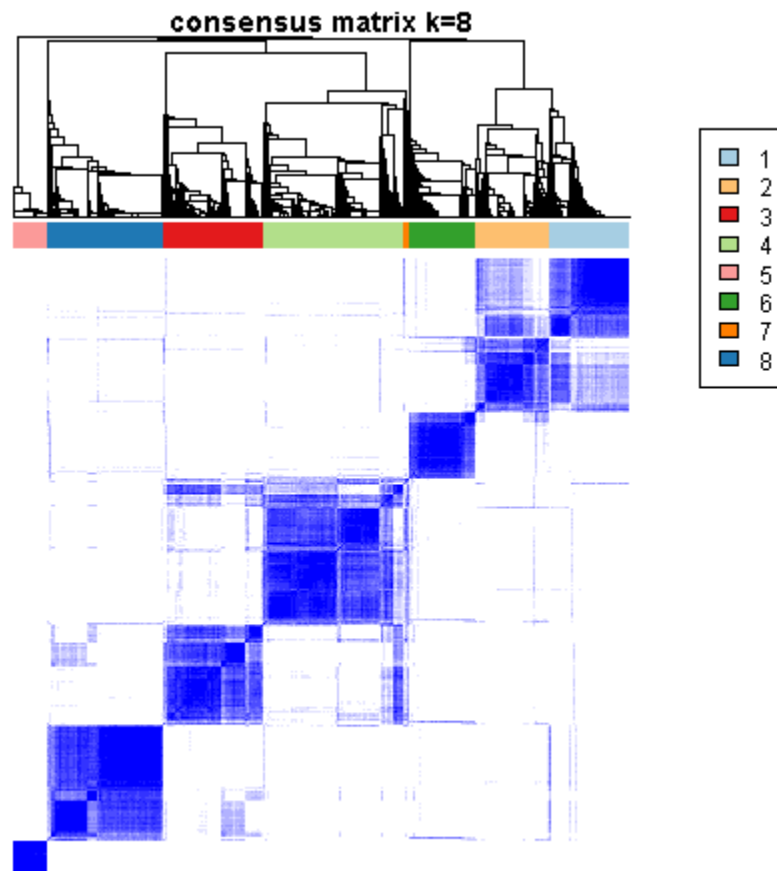
Supplementary Figure S5. Consensus matrix heat map ($k = 6$) depicting consensus values on a white to blue color scale of each cluster



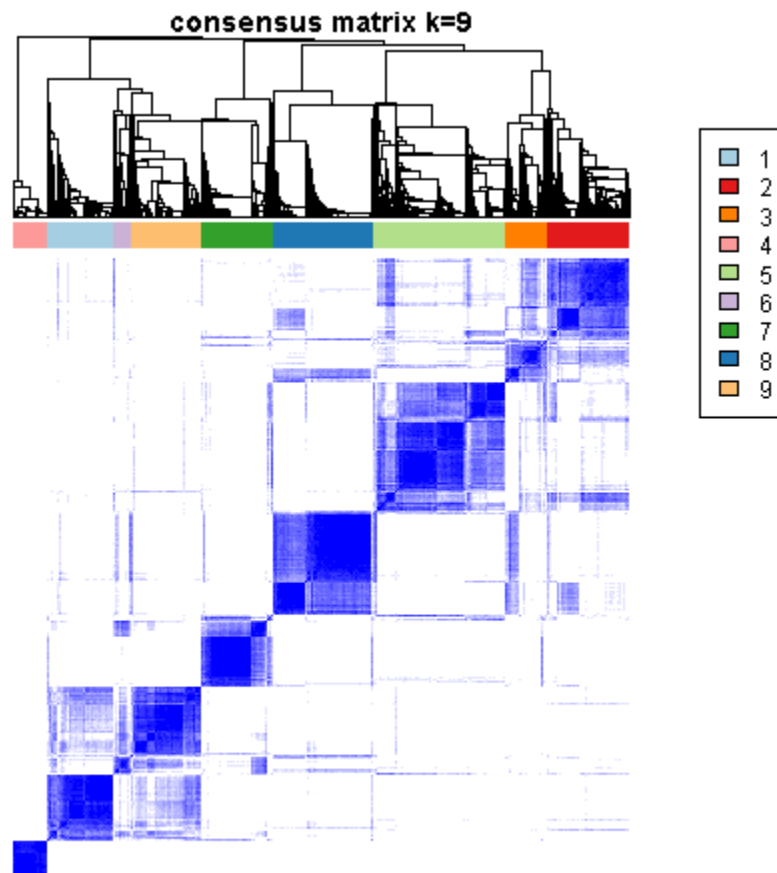
Supplementary Figure S6. Consensus matrix heat map ($k = 7$) depicting consensus values on a white to blue color scale of each cluster



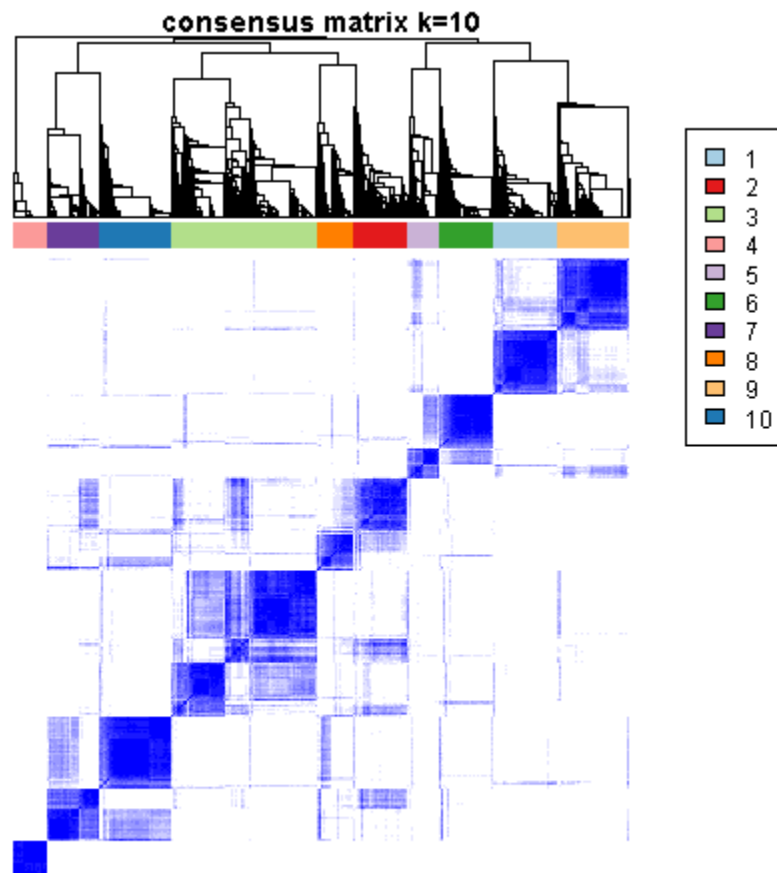
Supplementary Figure S7. Consensus matrix heat map ($k = 8$) depicting consensus values on a white to blue color scale of each cluster



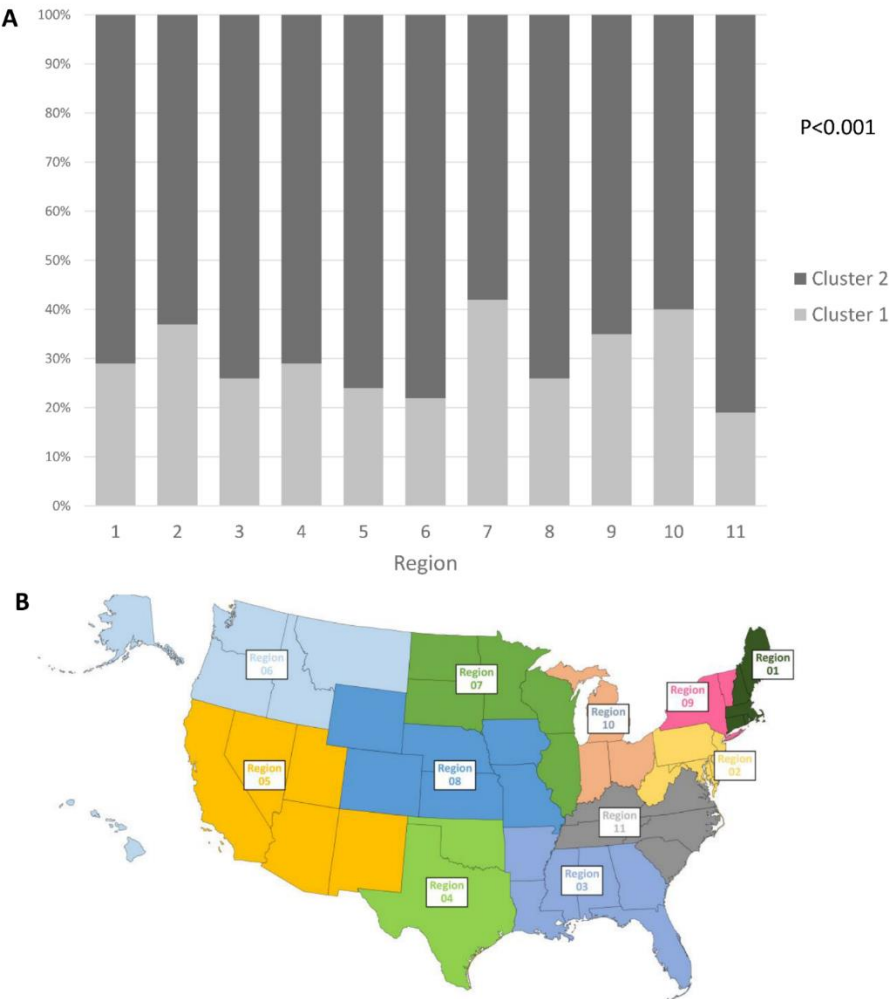
Supplementary Figure S8. Consensus matrix heat map ($k = 9$) depicting consensus values on a white to blue color scale of each cluster



Supplementary Figure S9. Consensus matrix heat map ($k = 10$) depicting consensus values on a white to blue color scale of each cluster



Supplementary Figure S10. A. Proportion of clusters according to the regions. **B.** OPTN regions.



References

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