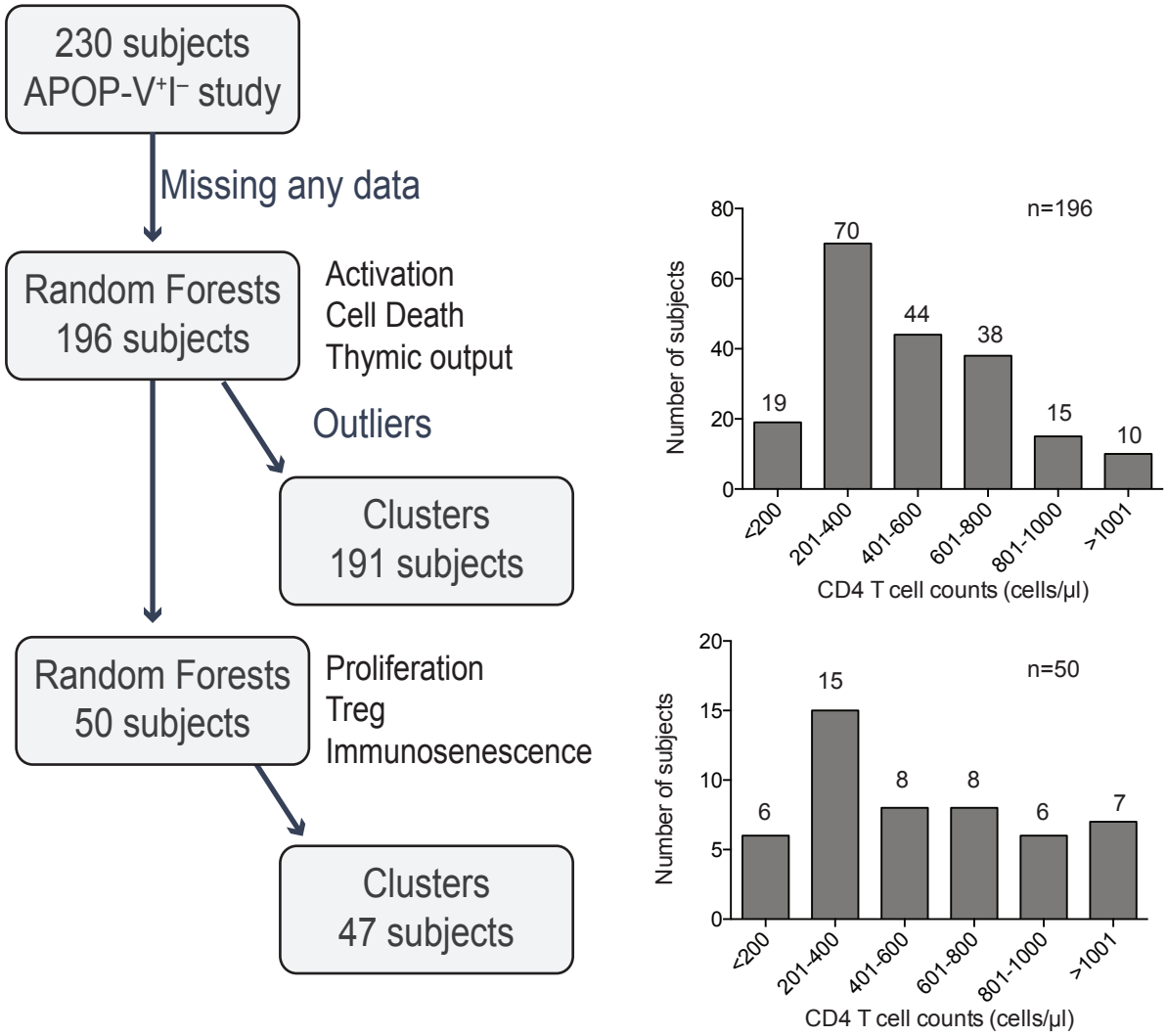
Supplementary Table 1: List of parameters used in this study. Left table shows parameters available for all subjects and right table shows parameters available for a smaller subset of subjects. Parameters are grouped by function.

	Parameter	Unit
	Clinical parameters	
1	Time since diagnosis	years
2	Time on ART	years
3	Treatment	PI or NNRTI
4	Drug	Kaletra
		Nevirapine
		ATV
		Efavirenz
		FosApv
		SQV
5	HBV infection	Yes or No
6	HCV infection	Yes or No
7	Detectable VL HCV	Yes or No
8	Age	Years
9	Gender	Male or Female
10	Nadir CD4 T cell count	cells/µl
11	Percentage of CD8	%
12	Absolute CD8 T cell counts	cells/µl
13	Ratio CD4/CD8	-
	Microbial translocation	
14	Soluble CD14	ng/mL
	T-cell cell death	
15	Total CD4 cell death (day 0)	% of CD4 T cells
16	Total CD8 cell death (day 0)	% of CD8 T cells
17	Total CD4 cell death (day 1)	% of CD4 T cells
18	CD4 T cell Necrosi (day 1)	% of CD4 T cells
19	CD4 T cell total apoptosis (day 1)	% of CD4 T cells
20	CD4 T cell intrinsic apoptosis (day 1)	% of CD4 T cells
21	CD4 T cell extrinsic apoptosis (day 1)	% of CD4 T cells
22	Total CD8 cell death (day 1)	% of CD8 T cells
23	CD8 T cell Necrosi (day 1)	% of CD8 T cells
24	CD8 T cell total apoptosis (day 1)	% of CD8 T cells
25	CD8 T cell intrinsic apoptosis (day 1)	% of CD8 T cells
26	CD8 T cell extrinsic apoptosis (day 1)	% of CD8 T cells
	CD4 T cells	
27	$CD45RA^{-}CD31^{+}$	% of CD4 T cells
28	$CD45RA^{+}CD31^{+}$	% of CD4 T cells
29	$CD45RA^{+}CD31^{-}$	% of CD4 T cells
30	$CD45RA^{-}CD31^{-}$	% of CD4 T cells
31	$CD45RA^{-}CD38^{+}$	% of CD4 T cells
32	$CD45RA^{+}CD38^{+}$	% of CD4 T cells
33	$CD45RA^{+}CD38^{-}$	% of CD4 T cells
34	$CD45RA^{-}CD38^{-}$	% of CD4 T cells
35	$CD45RA^{+}$	% of CD4 T cells
36	$CD45RA^{-}$	% of CD4 T cells
37	$CD38^{+}$	% of of CD45RA– CD4 T cells
38	$CD31^{+}$	% of of CD45RA+ CD4 T cells
39	$FAS^{+}PD\text{-}1^{-}$	% of CD4 T cells
40	$FAS^{+}PD\text{-}1^{+}$	% of CD4 T cells
41	$FAS^{-}PD\text{-}1^{+}$	% of CD4 T cells
42	$FAS^{-}PD\text{-}1^{-}$	% of CD4 T cells
43	$FAS^{+}HLA\text{-}DR^{-}$	% of CD4 T cells
44	$FAS^{+}HLA\text{-}DR^{+}$	% of CD4 T cells
45	$FAS^{-}HLA\text{-}DR^{+}$	% of CD4 T cells
46	$FAS^{-}HLA\text{-}DR^{-}$	% of CD4 T cells
47	$PD\text{-}1{+}HLA\text{-}DR^{-}$	% of CD4 T cells
48	$PD\text{-}1{+}HLA\text{-}DR^{+}$	% of CD4 T cells
49	$PD\text{-}1^{-}HLA\text{-}DR^{+}$	% of CD4 T cells
50	$PD\text{-}1^{-}HLA\text{-}DR^{-}$	% of CD4 T cells
51	$HLA\text{-}DR^{+}$	% of CD4 T cells
52	PD-1+	% of CD4 T cells
53	FAS^{+}	% of CD4 T cells
	CD8 T cells	
54	$CD45RA^{-}CD31^{+}$	% of CD8 T cells
55	$CD45RA^{+}CD31^{+}$	% of CD8 T cells
56	$CD45RA^{+}CD31^{-}$	% of CD8 T cells
57	$CD45RA^{-}CD31^{-}$	% of CD8 T cells
58	$CD45RA^{-}CD38^{+}$	% of CD8 T cells
59	$CD45RA^{+}CD38^{+}$	% of CD8 T cells
60	$CD45RA^{+}CD38^{-}$	% of CD8 T cells
61	$CD45RA^{-}CD38^{-}$	% of CD8 T cells
62	$CD45RA^{+}$	% of CD8 T cells
63	$CD45RA^{-}$	% of CD8 T cells
64	$CD38^{+}$	% of of CD45RA– CD8 T cells
65	$CD31^{+}$	% of of CD45RA+ CD8 T cells
66	$FAS^{+}HLA\text{-}DR^{-}$	% of CD8 T cells
67	$FAS^{+}HLA\text{-}DR^{+}$	% of CD8 T cells
68	$FAS^{-}HLA\text{-}DR^{+}$	% of CD8 T cells
69	$FAS^{-}HLA\text{-}DR^{-}$	% of CD8 T cells
70	$HLA\text{-}DR^{+}$	% of CD8 T cells
71	FAS^{+}	% of CD8 T cells
	CMV serology	
72	BIOFLASH CMV IgG	AU/mL
73	BIO-FLASH CMV IgM	AU/mL
74	BIOELISA CMV	OD-COV

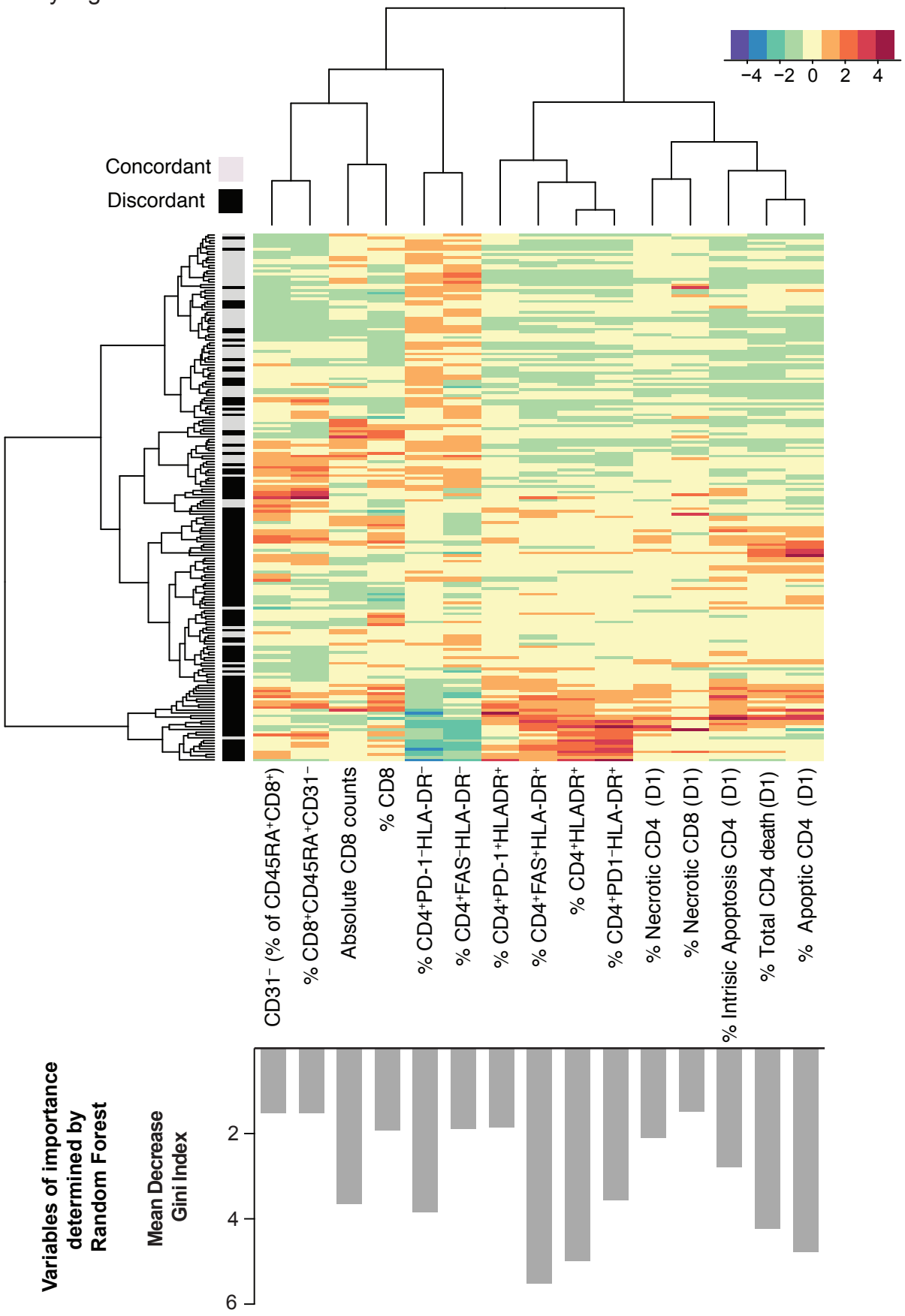
	Parameter	Unit
	CD4 T cells	
75	Naïve	% of CD4 T cells
76	Central memory	% of CD4 T cells
77	Transitional memory	% of CD4 T cells
78	Effector	% of CD4 T cells
79	$CD27^{-}CD45RA^{-}CCR7^{+}$	% of CD4 T cells
80	$CD27^{-}CD45RA^{+}CCR7^{+}$	% of CD4 T cells
81	$CD27^{-}CD45RA^{-}CCR7^{-}$	% of CD4 T cells
82	Effector memory	% of CD4 T cells
83	TEMRA	% of CD4 T cells
84	$CD57^{+}$	% of CD4 T cells
85	$CD57^{+}$	% of naïve CD4 T cells
86	$CD57^{+}$	% of central memory CD4 T cells
87	$CD57^{+}$	% of transitional memory CD4 T cells
88	$CD57^{+}$	% of effector memory CD4 T cells
89	Naïve	% of CD8 T cells
90	Central memory	% of CD8 T cells
91	Transitional memory	% of CD8 T cells
92	Effector	% of CD8 T cells
93	$CD27^{-}CD45RA^{-}CCR7^{+}$	% of CD8 T cells
94	$CD27^{-}CD45RA^{+}CCR7^{+}$	% of CD8 T cells
95	$CD27^{-}CD45RA^{-}CCR7^{-}$	% of CD8 T cells
96	$CD27^{-}CD45RA{+}CCR7^{-}$	% of CD8 T cells
97	Revertant	% of CD8 T cells
98	$CD57^{+}$	% of CD8 T cells
99	$CD57^{+}$	% of naïve CD8 T cells
100	$CD57^{+}$	% of central memory CD8 T cells
101	$CD57^{+}$	% of transitional memory CD8 T cells
102	$CD57^{+}$	% of effector memory CD8 T cells
103	$CD57^{+}$	% of revertant CD8 T cells
104	$Ki67^{+}$	% of CD4 T cells
105	$Ki67^{+}$	% of CD4 non-Treg cells
106	Treg classic ($CD25^{hi}FOXP3^{+}$)	% of CD4 T cells
107	$Ki67^{+}$	% of CD4 Treg classic
108	Treg Natural	% of CD4 T cells
109	Treg Effector	% of CD4 Treg natural
110	Treg $CD25^{hi}CD127^{low}$	% of CD4 T cells
111	Treg $CD25^{bright}$	% of CD4 T cells
112	$Ki67^{+}$	% of CD4 Treg $CD25^{bright}$
113	Treg $CD25^{low}$	% of CD4 T cells
114	$Ki67^{+}$	% of CD4 Treg $CD25^{low}$
115	Treg $CD25^{Bright}FOXP3^{Bright}$	% of CD4 T cells
116	$Ki67^{+}$	% of CD4 Treg $CD25^{bright}FOXP3^{bright}$
117	Treg $CD25^{low}FOXP3^{low}$	% of CD4 T cells
118	$Ki67^{+}$	% of CD4 Treg $CD25^{low}FOXP3^{low}$
119	$Ki67^{+}$	% of CD8 T cells
120	$Ki67^{+}$	% of CD8 non-Treg cells
121	Treg classic ($CD25^{hi}FOXP3^{+}$)	% of CD8 T cells
122	$Ki67^{+}$	% of CD8 Treg classic

Supplementary Figure 1



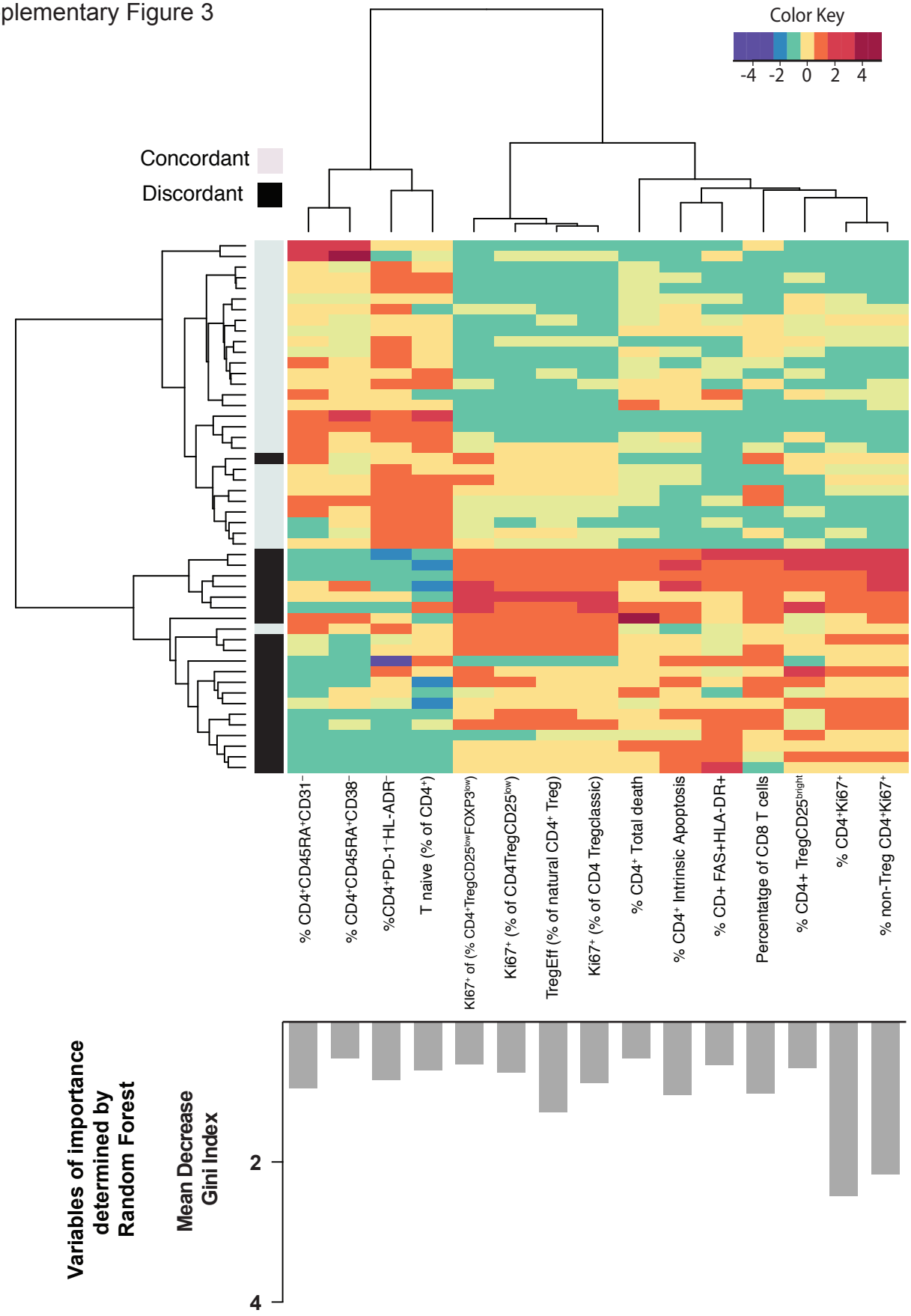
Supplementary Figure 1. Analysis strategy. The figure shows the starting cohort (references 19 and 20). Random forest approach classification was performed with 196 individuals with a complete dataset (see supplementary Table 1). The distribution of the different CD4 T-cell counts strata is shown for this subset. Hierarchical clustering and heatmaps were analyzed in a subgroup of 191 subjects after removal of outliers. In a subgroup of subjects, additional Treg, T-cell differentiation and proliferation parameters were analyzed (n=50). Strata according to CD4 T-cell counts is also shown for this subset.

Supplementary Figure 2



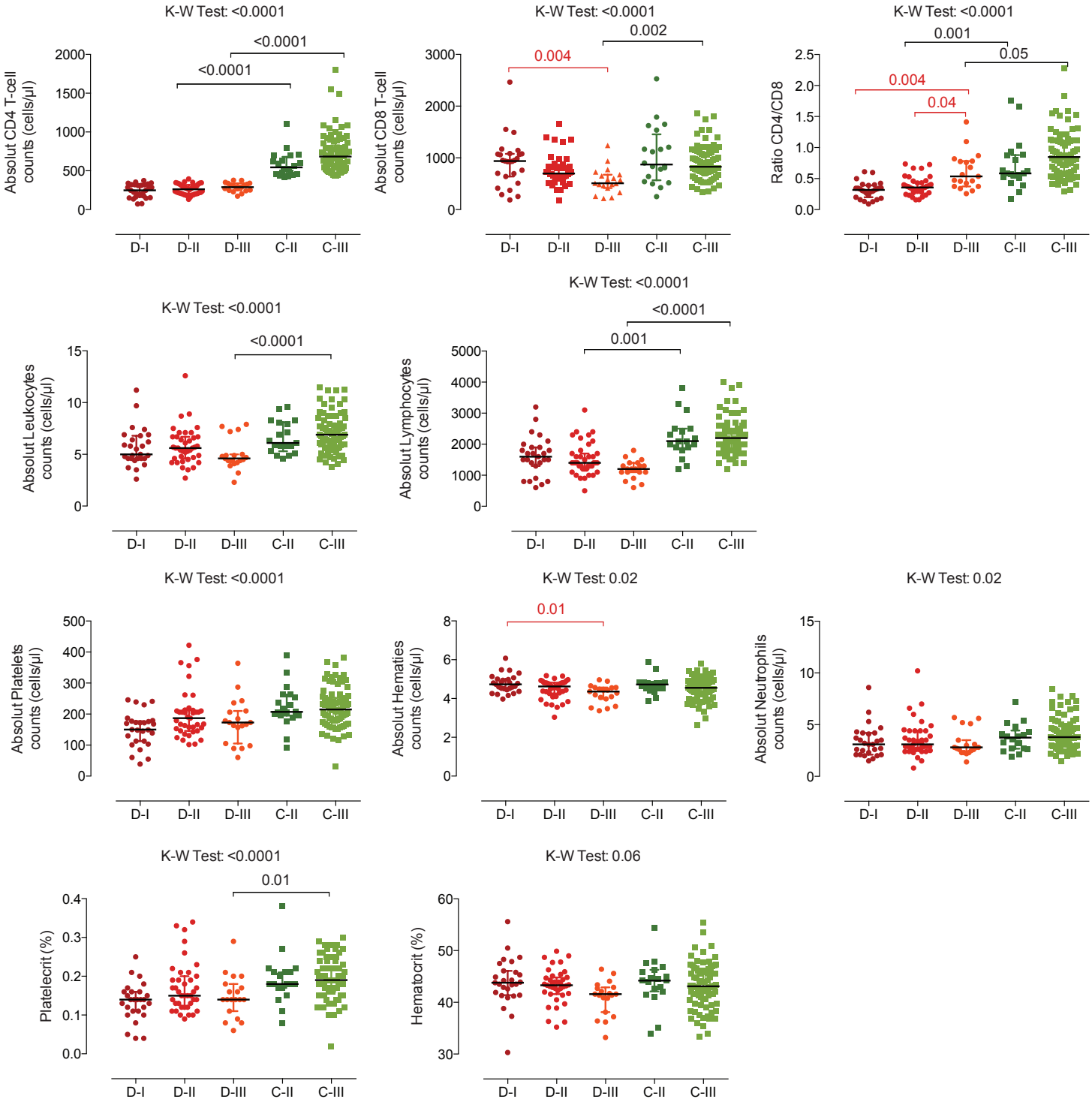
Supplementary Figure 2. Clustering of subjects according to variables of importance of the ΔCD4 T-cell count value 350 cells/μL. Heatmap of 191 individuals generated using relevant parameters for classification shown in Figure 2. The output heatmap shows one small group of mostly immunodiscordant individuals (Group I) and a major group of intermingled immunodiscordant and immunoconcordant individuals. Color key is shown in the upper right side and Gini index for each variable is shown in the lower histogram.

Supplementary Figure 3

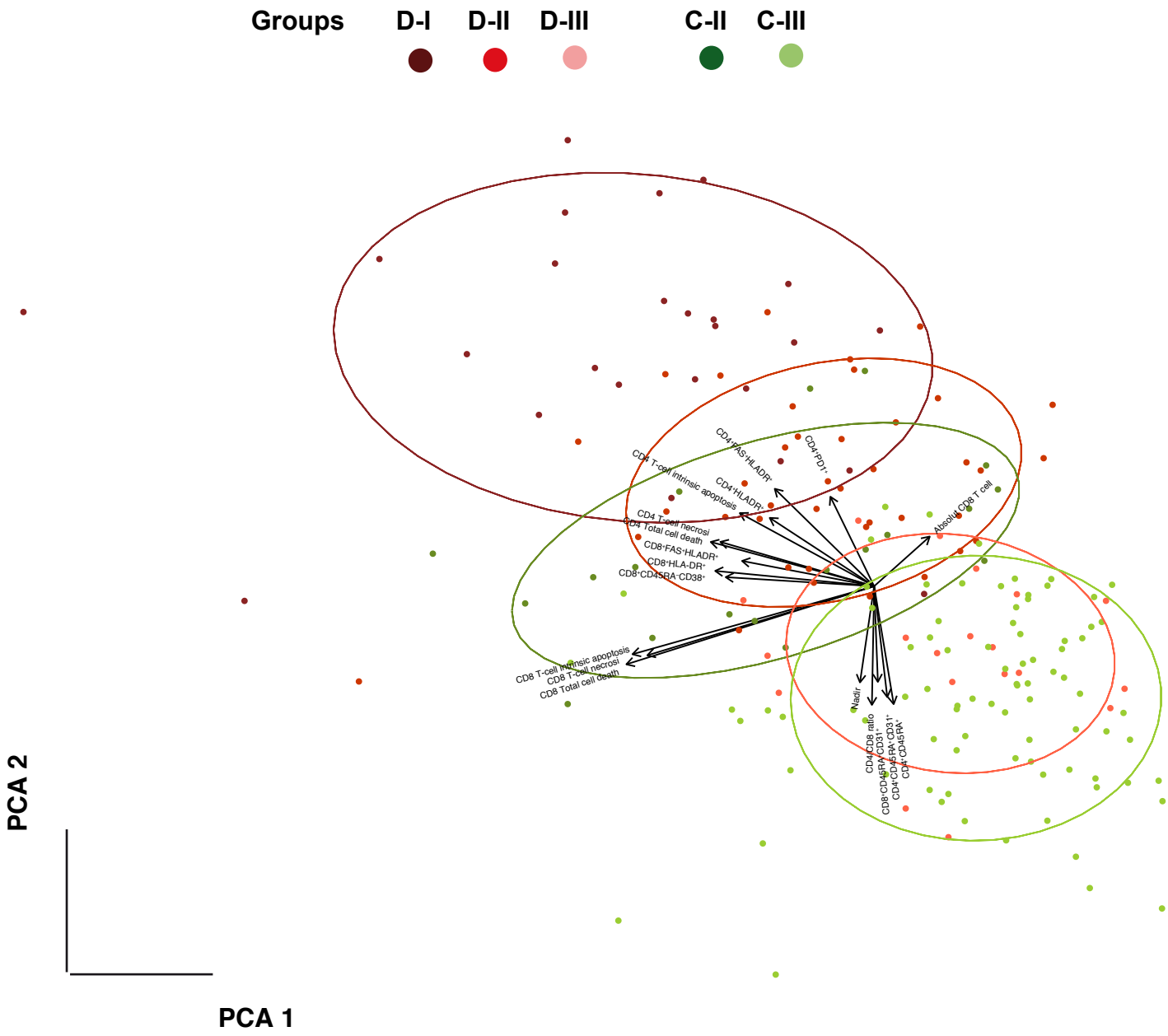


Supplementary Figure 3. Clustering of subjects according to variables of importance obtained from Treg, proliferation and differentiation data for a CD4 T-cell count cutoff 400 cells/μL. Heatmap of 49 individuals generated from activation, cell death, thymic output, Treg, proliferation, differentiation and immunosenescence data shows a clear segregation of immunodiscordant and immunoconcordant individuals. Color key is shown in the upper right side and Gini index for each variable is shown in the lower histogram.

Supplementary Figure 4



Supplementary Figure 5



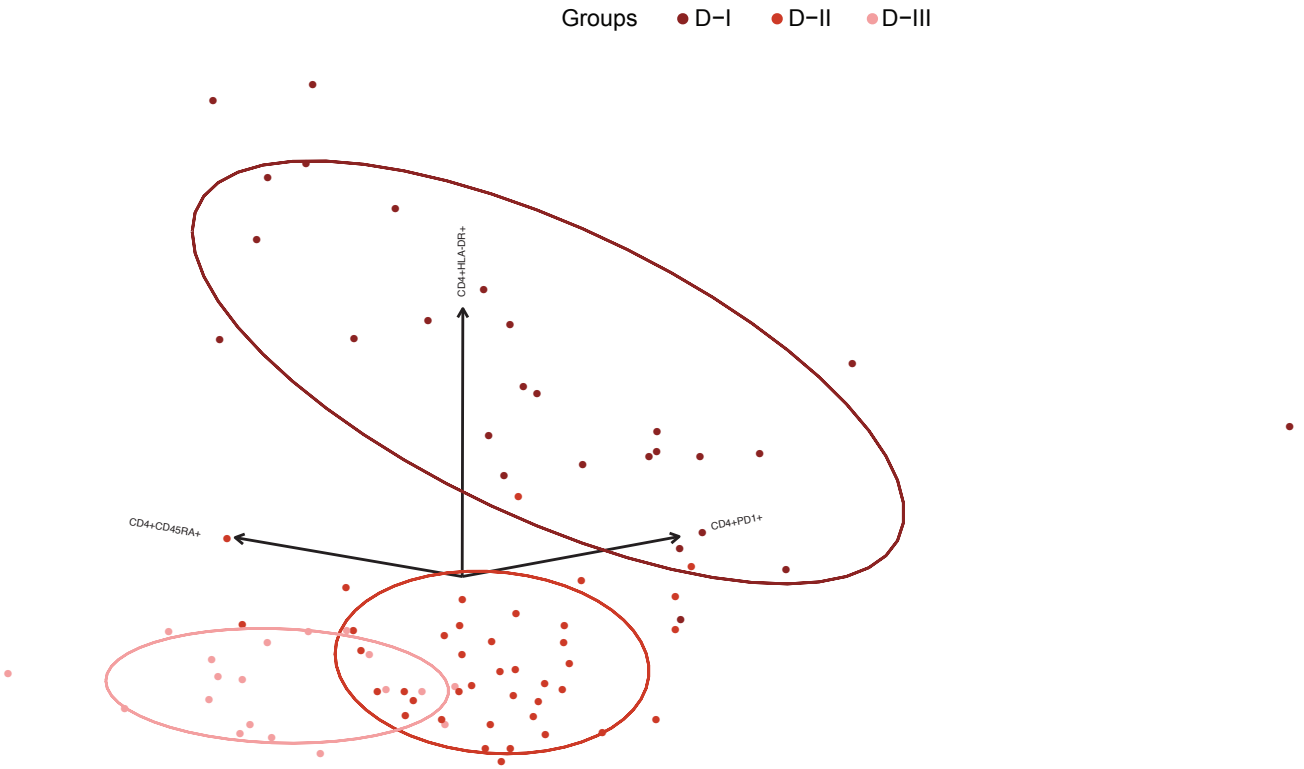
Supplementary Figure 4. PCA analysis of thymic output, cell death and activation data in CD4 and CD8 T cells. Data were standardized and a varimax rotation was performed on the two first components. Before rotation, the first two components accounted for 48% of the overall variability. Ellipses for each group represent a multivariate Normal contour at the 68% of confidence level (corresponding to a distance of one standard deviation from the mean). Colors represent the groups of previous clustering results

Supplementary Figure 6

A

	D-I	D-II	D-III	Classification error
D-I	**26**	1	0	0.037
D-II	3	**29**	8	0.275
D-III	0	4	**15**	0.210

B



Supplementary Figure 5. Simplified classification of immunodiscordant subjects. The following parameters: frequency of $CD4^+CD45RA^+$, $CD4^+HLA\text{-}DR^+$ and $CD4^+PD\text{-}1^+$ cells were selected according to differences among immunodiscordant subgroups in order to establish a simplified classification algorithm. (A). Confusion matrix to assess the ability of this simple classification algorithm to segregate D-I, D-II and D-III individuals. (B). PCA analysis of this classification. Ellipses for each group represent a multivariate Normal contour at the 68% of confidence level (corresponding to a distance of one standard deviation from the mean). Colors represent the groups of previous clustering results