Machine learning identification of specific changes in myeloid cell phenotype during bloodstream infections

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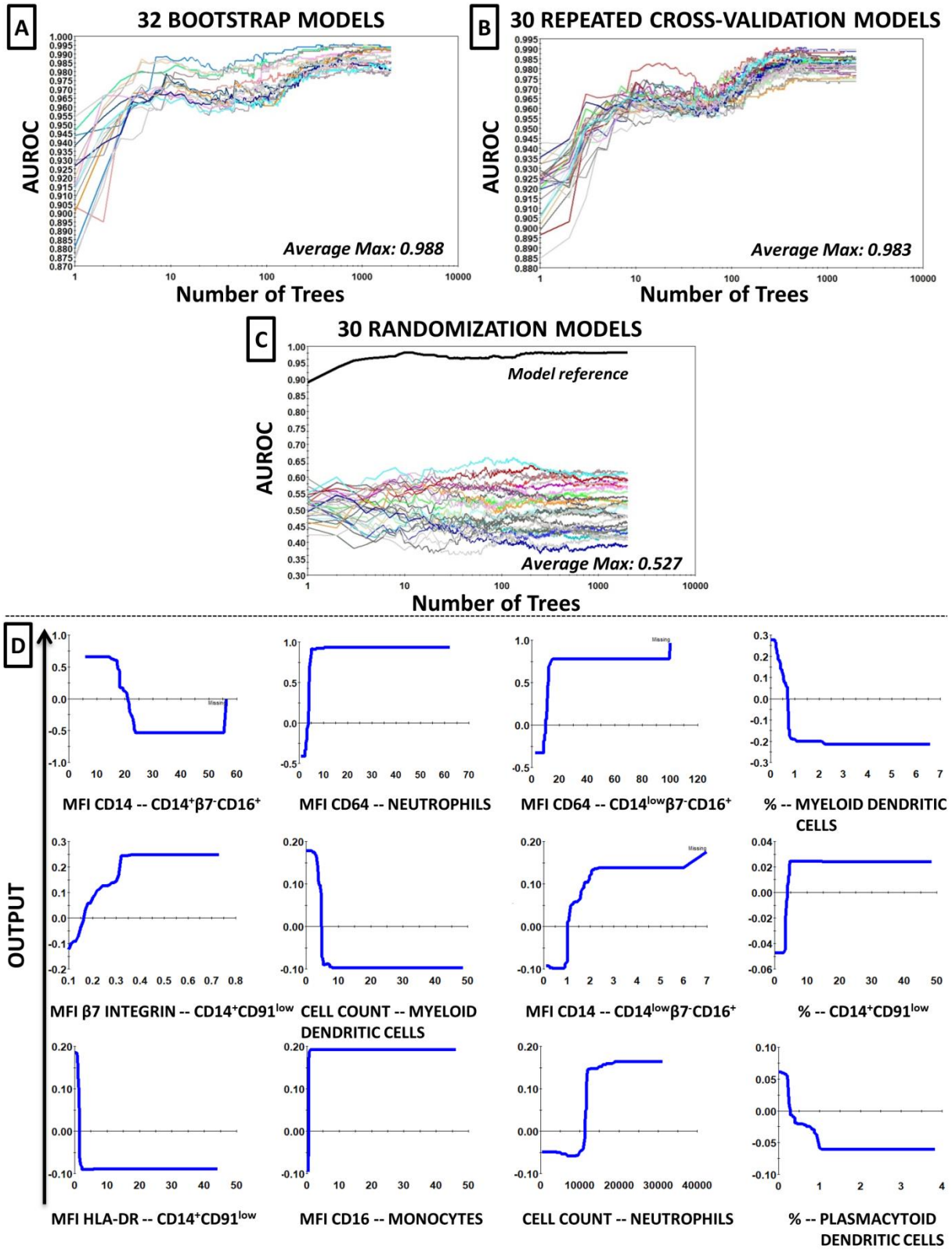
Rank	Importance	Average Log-Likelihood	Predictor
1	100.00	0.04716	MFI CD14 $CD14^{+}\beta7^{-}CD16^{+}$
2	75.54	0.03769	MFI CD64 GRANULOCYTES NEUTROPHILS
3	51.26	0.02829	MFI CD64 $CD14^{low}\beta7^{-}CD16^{+}$
4	12.64	0.01334	% MYELOID DENDRITIC CELLS/MONOCYTES
5	6.87	0.01111	MFI INTEGRIN β7 $CD14^{+}CD91^{low}$
6	3.88	0.00995	CELL COUNT MYELOID DENDRITIC CELLS
7	3.11	0.00965	MFI CD14 $CD14^{low}\beta7^{-}CD16^{+}$
8	2.24	0.00931	% $CD14^{+}CD91^{low}$
9	2.11	0.00926	MFI HLA-DR $CD14^{+}CD91^{low}$
10	2.01	0.00922	MFI CD123 GRANULOCYTES NEUTROPHILS
11	2.01	0.00922	MFI CD16 MONOCYTES
12	1.69	0.00910	CELL COUNT GRANULOCYTES NEUTROPHILS
13	1.64	0.00908	MFI CD14 $CD14^{+}\beta7^{+}CD16^{+}$
14	1.36	0.00897	MFI HLA-DR $CD14^{+}\beta7^{+}CD16^{+}$
15	1.26	0.00893	MFI HLA-DR $CD14^{+}\beta7^{-}CD16^{low}$
16	1.24	0.00892	MFI CD91 $CD14^{+}\beta7^{-}CD16^{-}$
17	1.17	0.00890	MFI CD16 $CD14^{+}\beta7^{+}CD16^{+}$
18	1.11	0.00887	% PLASMACYTOID DENDRITIC CELLS/MONOCYTES
19	1.02	0.00884	MFI CD45 MONOCYTES
20	1.01	0.00883	MFI CD45 GRANULOCYTES NEUTROPHILS
21	0.97	0.00882	MFI CD14 GRANULOCYTES NEUTROPHILS
22	0.93	0.00880	CELL COUNT $CD14^{low}\beta7^{-}CD16^{+}$
23	0.92	0.00880	MFI CD16 $CD14^{+}\beta7^{-}CD16^{+}$
24	0.91	0.00880	MFI INTEGRIN β7 $CD14^{+}B7^{+}CD16^{+}$
25	0.89	0.00879	% $CD14^{+}\beta7^{-}CD16^{+}$
26	0.87	0.00878	MFI CD16 $CD14^{low}\beta7^{-}CD16^{+}$
27	0.85	0.00877	MFI INTEGRIN β7 $CD14^{low}\beta7^{-}CD16^{+}$
28	0.85	0.00877	MFI CD123 $CD14^{+}\beta7^{-}CD16^{+}$
29	0.78	0.00875	CELL COUNT PLASMACYTOID DENDRITIC CELLS/MONOCYTES
30	0.72	0.00872	MFI CD45 $CD14^{+}\beta7^{+}CD16^{-}$
31	0.71	0.00872	MFI CD91 $CD14^{+}\beta7^{-}CD16^{low}$
32	0.70	0.00871	MFI CD91 $CD14^{+}\beta7^{-}CD16^{low}$

33	0.69	0.00871	MFI CD14 MONOCYTES
34	0.67	0.00870	MFI HLA-DR GRANULOCYTES NEUTROPHILS
35	0.67	0.00870	MFI CD45 $CD14^{+}\beta7^{-}CD16^{-}$
36	0.63	0.00869	MFI HLA-DR $CD14^{+}\beta7^{-}CD16^{+}$
37	0.62	0.00868	MFI CD14 $CD14^{+}\beta7^{-}CD16^{-}$
38	0.60	0.00868	% $CD14^{+}\beta7^{-}CD16^{-}$
39	0.60	0.00868	MFI CD45 $CD14^{low}\beta7^{-}CD16^{+}$
40	0.58	0.00867	MFI CD123 $CD14^{low}\beta7^{-}CD16^{+}$
41	0.57	0.00866	MFI CD64 $CD14^{+}CD91^{low}$
42	0.55	0.00866	MFI CD91 GRANULOCYTES NEUTROPHILS
43	0.54	0.00865	MFI CD91 $CD14^{+}CD91^{low}$
44	0.41	0.00860	MFI CD16 MONONUCLEAR CELLS
45	0.40	0.00860	MFI INTEGRIN β7 MONOCYTES
46	0.40	0.00860	MFI CD91 MONONUCLEAR CELLS
47	0.40	0.00860	MFI CD14 $CD14^{+}\beta7^{-}CD16^{low}$
48	0.39	0.00860	MFI CD64 $CD14^{+}\beta7^{-}CD16^{low}$
49	0.39	0.00860	MFI CD16 $CD14^{+}\beta7^{+}CD16^{-}$
50	0.39	0.00859	MFI CD16 $CD14^{+}CD91^{low}$
51	0.37	0.00859	MFI HLA-DR $CD14^{low}\beta7^{-}CD16^{+}$
52	0.35	0.00858	MFI CD91 $CD14^{+}\beta7^{-}CD16^{+}$
53	0.35	0.00858	MFI CD64 $CD14^{+}\beta7^{-}CD16^{+}$
54	0.33	0.00857	MFI INTEGRIN β7 GRANULOCYTES NEUTROPHILS
55	0.33	0.00857	CELL COUNT $CD14^{+}\beta7^{+}CD16^{+}$
56	0.33	0.00857	% $CD14^{+}\beta7^{+}CD16^{+}$
57	0.31	0.00857	MFI INTEGRIN β7 $CD14^{+}\beta7^{+}CD16^{-}$
58	0.31	0.00856	MFI HLA-DR MONONUCLEAR CELLS
59	0.30	0.00856	MFI CD64 MONONUCLEAR CELLS
60	0.30	0.00856	MFI INTEGRIN β7 $CD14^{+}\beta7^{-}CD16^{+}$
61	0.30	0.00856	MFI CD16 $CD14^{+}\beta7^{-}CD16^{low}$
62	0.29	0.00856	MFI INTEGRIN β7 MONONUCLEAR CELLS
63	0.28	0.00855	MFI CD64 MONOCYTES
64	0.28	0.00855	MFI CD91 $CD14^{+}\beta7^{+}CD16^{-}$
65	0.28	0.00855	MFI CD91 $CD14^{low}\beta7^{-}CD16^{+}$
66	0.27	0.00855	% $CD14^{+}\beta7^{+}CD16^{-}$
67	0.27	0.00855	MFI CD14 MONONUCLEAR CELLS
68	0.26	0.00855	MFI CD16 GRANULOCYTES NEUTROPHILS
69	0.25	0.00854	MFI CD64 $CD14^{+}\beta7^{-}CD16^{-}$

70	0.25	0.00854	% $CD14^{low}\beta7^{-}CD16^{+}$
71	0.24	0.00854	CELL COUNT $CD14^{+}\beta7^{+}CD16^{-}$
72	0.23	0.00853	MFI CD64 $CD14^{+}\beta7^{+}CD16^{-}$
73	0.23	0.00853	MFI CD14 $CD14^{+}\beta7^{+}CD16^{-}$
74	0.21	0.00853	MFI CD45 $CD14^{+}\beta7^{-}CD16^{low}$
75	0.21	0.00853	CELL COUNT LYMHOCYTES
76	0.20	0.00852	MFI CD14 $CD14^{+}CD91^{low}$
77	0.20	0.00852	MFI CD45 $CD14^{+}\beta7^{-}CD16^{+}$
78	0.20	0.00852	% $CD14^{+}\beta7^{-}CD16^{low}$
79	0.19	0.00852	MFI CD123 $CD14^{+}\beta7^{-}CD16^{-}$
80	0.18	0.00851	CELL COUNT $CD14^{+}\beta7^{-}CD16^{-}$
81	0.17	0.00851	CELL COUNT $CD14^{+}CD91^{low}$
82	0.16	0.00850	MFI CD64 $CD14^{+}\beta7^{+}CD16^{+}$
83	0.14	0.00850	MFI HLA-DR $CD14^{+}\beta7^{+}CD16^{-}$
84	0.14	0.00850	CELL COUNT MONOCYTES
85	0.13	0.00849	MFI CD91 $CD14^{+}\beta7^{+}CD16^{+}$
86	0.12	0.00849	MFI CD123 $CD14^{+}\beta7^{+}CD16^{+}$
87	0.12	0.00849	MFI CD123 $CD14^{+}\beta7^{+}CD16^{-}$
88	0.12	0.00849	MFI CD91 MONOCYTES
89	0.11	0.00848	MFI CD16 $CD14^{+}\beta7^{-}CD16^{-}$
90	0.10	0.00848	CELL COUNT $CD14^{+}\beta7^{-}CD16^{low}$
91	0.10	0.00848	MFI CD45 $CD14^{+}\beta7^{+}CD16^{+}$
92	0.10	0.00848	MFI CD45 MONONUCLEAR CELLS
93	0.08	0.00847	MFI HLA-DR MONOCYTES
94	0.06	0.00847	MFI HLA-DR $CD14^{+}\beta7^{-}CD16^{-}$
95	0.06	0.00847	CELL COUNT $CD14^{+}\beta7^{-}CD16^{+}$
96	0.05	0.00846	MFI CD123 $CD14^{+}CD91^{low}$
97	0.03	0.00846	MFI INTEGRIN β7 $CD14^{+}\beta7^{-}CD16^{low}$
98	0.03	0.00846	MFI CD123 MONOCYTES
99	0.03	0.00845	MFI CD123 MONONUCLEAR CELLS
100	0.02	0.00845	MFI CD123 $CD14^{+}\beta7^{-}CD16^{low}$
101	0	0.00844	MFI INTEGRIN β7 $CD14^{+}\beta7^{-}CD16^{-}$

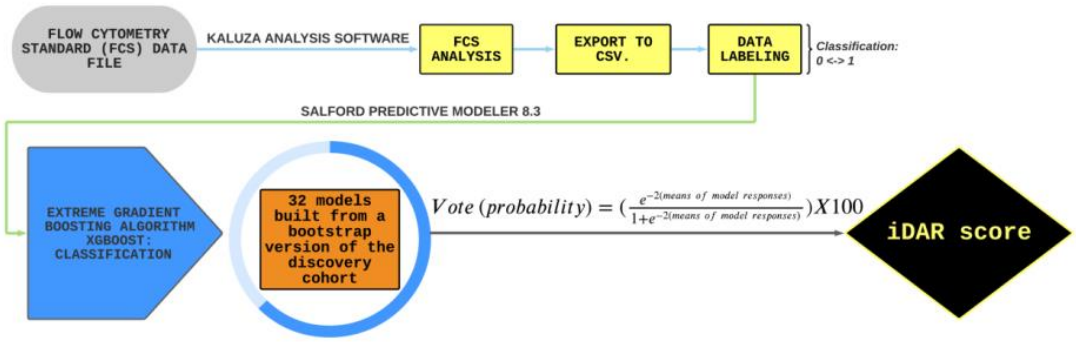
Appendix 1. List of features used within iDAR algorithm.



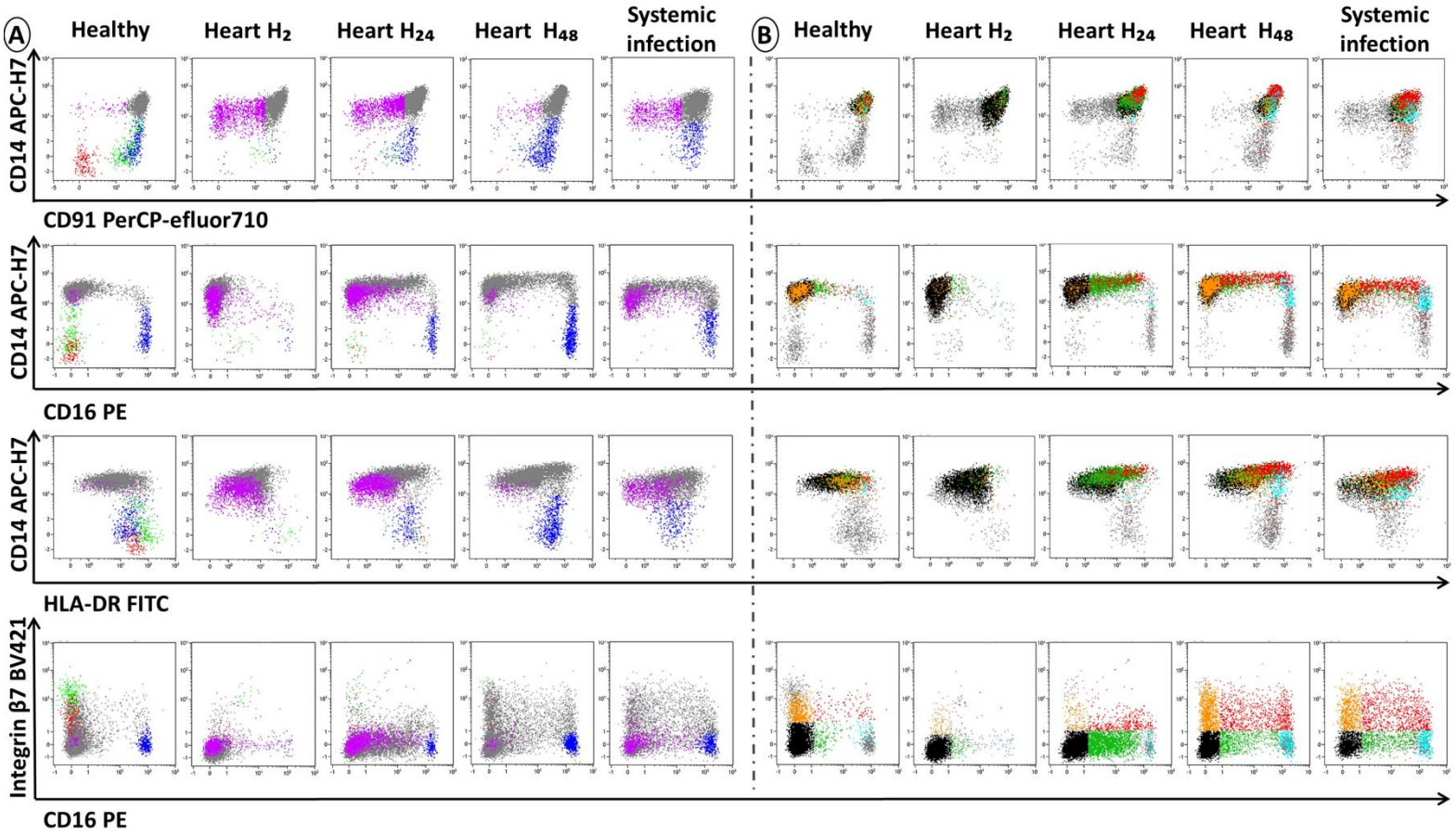
Appendix 2. Chart curves showing modelling performance for 32 bootstrap (A), 30 random seeds repeated cross-validation (B) and 30 target shuffle models (C). In (D), partial dependence plots for the top 12 variables with the variable importance scores as measured by XGBoost.

Model Building	TOP 10 VARIABLES IMPORTANCE SCORE VIA RANDOMIZATION TEST --- RVIS
-30 REPEATED CROSS-VALIDATION RUNS WITH DIFFERENT SEEDS AUROC = 0.98 -30 RANDOMIZED CLASSIFICATION AUROC = 0.58 -32 PARAMETRIC BOOTSTRAP AUROC = 0.988 Specificity = 98 Sensitivity = 92 Threshold = 0.24 PARAMETERS : SUBSAMPLE --- 0.5 LEARNRATE --- 0.001 TERMINAL NODE PER TREE --- 6 PREDICTORS PER TREE --- ALL PREDICTORS IN MODEL --- ALL HESSIAN --- 1 LOSS FUNCTION --- CLASSIFICATION BINARY Newton split search : L_0, L_1, L_2 --- 0 NO INFECTION (Probability %) MEAN --- 0.16 MEDIAN --- 0.07 MIN --- 0.01 MAX --- 3.8 VARIANCE --- 0.17 STANDARD DEVIATION --- 0.41 STANDARD ERROR --- 0.03 BLOODSTREAM INFECTION (Probability of positive blood culture %) MEAN --- 98 MEDIAN --- 99.8 MIN --- 62.9 MAX --- 100 VARIANCE --- 46 STANDARD DEVIATION --- 6.8 STANDARD ERROR --- 0.88	⊕ MFI CD14 $CD14^{+}\beta7^{-}CD16^{+}$ --- 100 ⊕ MFI CD64 GRANULOCYTES NEUTROPHILS --- 69 ⊕ MFI CD64 $CD14^{low}\beta7^{-}CD16^{+}$ --- 45 ⊕ % MYELOID DENDRITIC CELLS/MONOCYTES --- 12 ⊕ MFI INTEGRIN β7 $CD14^{+}CD91^{low}$ --- 6 ⊕ CELL COUNT MYELOID DENDRITIC CELLS --- 3.5 ⊕ MFI CD14 $CD14^{low}\beta7^{-}CD16^{+}$ --- 2.8 ⊕ % $CD14^{+}CD91^{low}$ --- 2.4 ⊕ MFI HLA-DR $CD14^{+}CD91^{low}$ --- 1.9 ⊕ MFI CD16 MONOCYTES --- 1.9

Appendix 3. The statistics of the randomization classification model, the repeated cross validation runs and the bootstrap are given. The model report includes the parameters used as well as the results of the cross-validation along the first 10 scores of variable importance.



Appendix 4. iDAR construction flowchart.



Appendix 5. Representative flow cytometry bivariate plots of CD14, CD16, CD91, HLA-DR and integrin β7 expression markers are shown for healthy, heart surgery at H_2, H_{24}, H_{48} and positive blood culture patients. Myeloid populations reported are: plasmacytoid dendritic cells (A; red), myeloid dendritic cells (A; green), $CD14^{low}$ $\beta7^{-}CD16^{+}$ non-classical monocytes (A; blue), $CD14^{+}CD91^{low}$ (A; pink), $CD14^{+}\beta7^{-}CD16^{-}$ (B; black), $CD14^{+}\beta7^{-}CD16^{low}$ (B; green), $CD14^{+}\beta7^{-}CD16^{+}$ (B; azure), $CD14^{+}\beta7^{+}CD16^{-}$ (B; orange) and $CD14^{+}\beta7^{+}CD16^{+}$ cells (B; red).