

MAP-kinase mutations and aortic lesions are associated with distribution of circulating monocytes in histiocytosis

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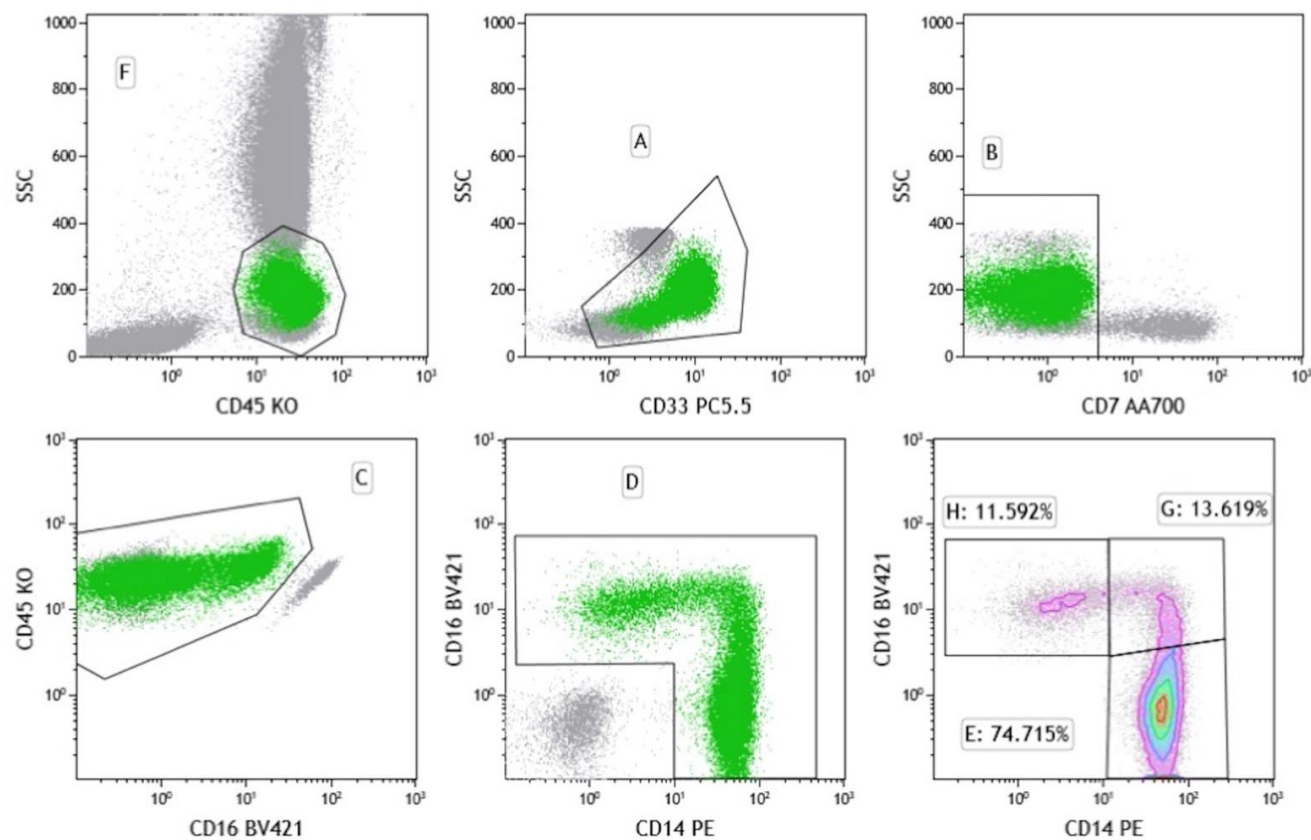
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Supplemental Figure 1: Gating procedure of monocyte subsets by flow cytometry.



Analytic gating of flow cytometry data: monocytes were identified from white blood cells with CD45 (f) and CD33 (a) scattering; after exclusion of T-lymphocytes (b), NK cells (c), residual lymphocytes and basophils (d). Then monocytes were separated on CD14/CD16 scattergram for classical (e), intermediate (g) and non-classical monocytes (h)

Supplementary Table 1: Characteristics of patients with histiocytosis.

Case	Type of histiocytosis	Histiocytosis location	Mutational status	Bone marrow mutation	Monocytes counts	Classical monocytes	Intermediate monocytes	Non classical monocytes
#1	ECD	Mesentery, bone, CNS, peri-renal, heart, vessels	<i>BRAF</i> ^{v600E} c.1799T>A, p.(Val600Glu) <i>KRAS</i> c.437C>T , p(Ala146 Val) <i>TET2</i> c.3622A>T, p.(Lys1208*)	<i>TET2/ZRS2/KRAS/NRAS/BRAF</i>	2,63	96%	3%	1%
#2	ECD	Mesentery, bone, CNS, peri-renal, heart, vessels	<i>BRAF</i> ^{v600E} c.1799T>A, p.(Val600Glu)	<i>TET2/SRSF2/CLB/NRAS</i>	1,60	96%	2%	2%
#3	ECD	Heart, bones, vessels, mesentery, peri-renal	<i>BRAF</i> ^{v600E} c.1799T>A, p.(Val600Glu)	<i>JAK2/TET2/NF1</i>	0,3	96%	3%	1%
#4	ECD	Vessels, bone, sinus	none	none	0,62	92%	7%	1%
#5	ECD	Bone, peri-renal, mesentery	none	<i>TET2</i>	0,27	81%	8%	11%
#6	ECD	Bone, peri-renal, mesentery	none	<i>DNMT3A</i>	0,68	71%	25%	4%
#7	ECD	Bone, heart, vessel, CNS, peri-renal	<i>BRAF</i> ^{v600E} c.1799T>A, p.(Val600Glu)	<i>ASXL1/NF1/TET2/U2AF1</i>	0,6	92%	4%	4%
#8	ECD	Mesentery, peri-renal	none	none	0,43	73%	11,8%	15,2%
#9	ECD	Skin, bone	none	none	0,6	92%	4,9%	3,1%
#10	ECD	Bone, eyes, peri-renal, skin, vessels, CNS	none	none	0,61	82%	8%	10%
#11	ECD	Bone, vessel, peri-renal	none	<i>TET2/SF3B1</i>	0,41	81%	6,5%	12,5%
#12	ECD	Skin, vessels, peri-renal, mesentery	none	none	0,64	92%	4,7%	3,3%
#13	ECD	Mesentery, peri-renal	<i>MAP2K1</i> c.209A>G, p(Lys97Arg)	none	0,68	89%	5,8%	5,2%

#14	LCH	Bone, skin, endocrine, lung	none	none	0,45	98%	1,5%	0,5%
#15	LCH	lung	none	none	0,58	92%	4%	4%
#16	LCH	Lung, endocrine, bone	none	none	0,75	83%	8%	9%
#17	LCH	Bone , lung , endocrine	<i>BRAF</i> ^{V600E} c.1799T>A,p.(Val600Glu	none	0,68	90%	4%	6%
#18	LCH	lung	none	none	0,37	79%	16,2%	4,8%
#19	LCH	lung	none	none	0,51	85%	7,2%	7,8%
#20	LCH	CNS, brain, endocrine	none	<i>DNMT3A/ASXL1</i>	0,39	88%	9,3%	2,7%
#21	LCH	Bone, liver, skin, endocrine	<i>BRAF</i> ^{V600E} c.1457_1471del,p.(486_490del) <i>DNMT3A</i> c.1742G>C,p.(Trp581Ser)	none	0,88	85%	13%	2%
#22	LCH/ECD	Bone, lung, skin, vessels	<i>BRAF</i> ^{V600E} c.1799T>A,p.(Val600Glu	<i>KRAS/SH2B3/SRSF2/TET2</i>	3,32	94%	5%	1%
#23	L group	Bone	none	none	0,48	73%	15,4%	11,6%
#24	ICH	skin	<i>TET2</i> c.270C>T , p.(Gln904Ter) <i>ASXL1</i> c.1773C>A,p.(Tyr591Ter) <i>SRSF2</i> c.284C>A, p.(Pro95His)	<i>ASXL1/TET2/SRSF2</i>	1,23	89%	8,3%	2,7%
#25	ICH	skin	none	none	0,4	85%	8,3%	6,7%
#26	RDD	Peri-renal	<i>MAP2K1</i> c.395C>T, p(Ala132Val)	<i>TET2,ASXL1,DNMT3A,JAK2</i>	0,51	83%	5%	11%
#27	RDD	Skin, bone, eyes, vessels	<i>MAP2K1</i> c.395C>T, p(Ala132Val)		0,61	97%	2%	1%
#28	RDD	bone	none	none	0,66	92%	4%	4%
#29	RDD	Skin, lymph node	none	none	0,5	87%	5%	8%
#30	XJG	skin	none	none	0,58	87%	8%	5%

#31	XJG	skin	none		0,91	88%	4,9%	7,1%
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CNS: central nervous system. ECD: Erdheim-Chester Disease. LCH: Langerhans cell histiocytosis. RDD: Rosai Dorfman disease. ICH: indeterminate cell histiocytosis. CNS: central nervous system

Supplementary Table 2: Main characteristics of patients with histiocytosis, giant cell arteritis and healthy donors.

	Histiocytosis (n=31)	GCA (n=21)	HD (n=21)	P value
Age at dosage (years)	62 [44-71]*	76 [66-81]	73 [57-82]	0.0027
Hemoglobin (g/dL)	12.6 [11.5-14]*	11 [10.2-12]°	13.6 [12.6-14.4]	<0.0001
White count cell (G/l)	7.4 [5.2-8.9]	9.6 [6.6-11] °	5.6 [4.7-6.8]	0.0004
Neutrophils(G/l)	4.4 [3.4-5.9] *	6.7 [4.6-8.2] °	3.2 [2.7-4.1]	<0.0001
Lymphocyte (G/l)	1.6 [1.1-2.0]	1.5 [1.2-1.7]	1.6 [1.0-2.1]	0.5838
Total monocytes (G/l)	0.58 [0.43-0.66] *	0.71 [0.61-0.87] °	0.49 [0.36-0.62]	0.0008
Classical monocytes %	88% [83-92.7]	85.7% [74.2-91.8]	85.9% [77.5-89.8]	0.1419
Intermediate monocytes%	5.8% [4-8] *	7.8% [5.8-16]	6.6% [4.4-13.3]	0.0473
Non-classical monocytes %	4 %[2-8]	4.2% [1.6-6.8] °	6.1% [4.3-10]	0.0103
C –reactive protein (mg/L)	4 [3.7-11.5] *^	75.7[46-99.5] °	2.9[2.9-2.9]	<0.0001

P value is the result of the result of Kruskal Wallis test. * p<0.05 histiocytosis vs GCA. ° p<0.05 GCA vs HD. ^ p<0.005 histiocytosis vs HD. All quantitative data are expressed by median with interquartile range [IQR].