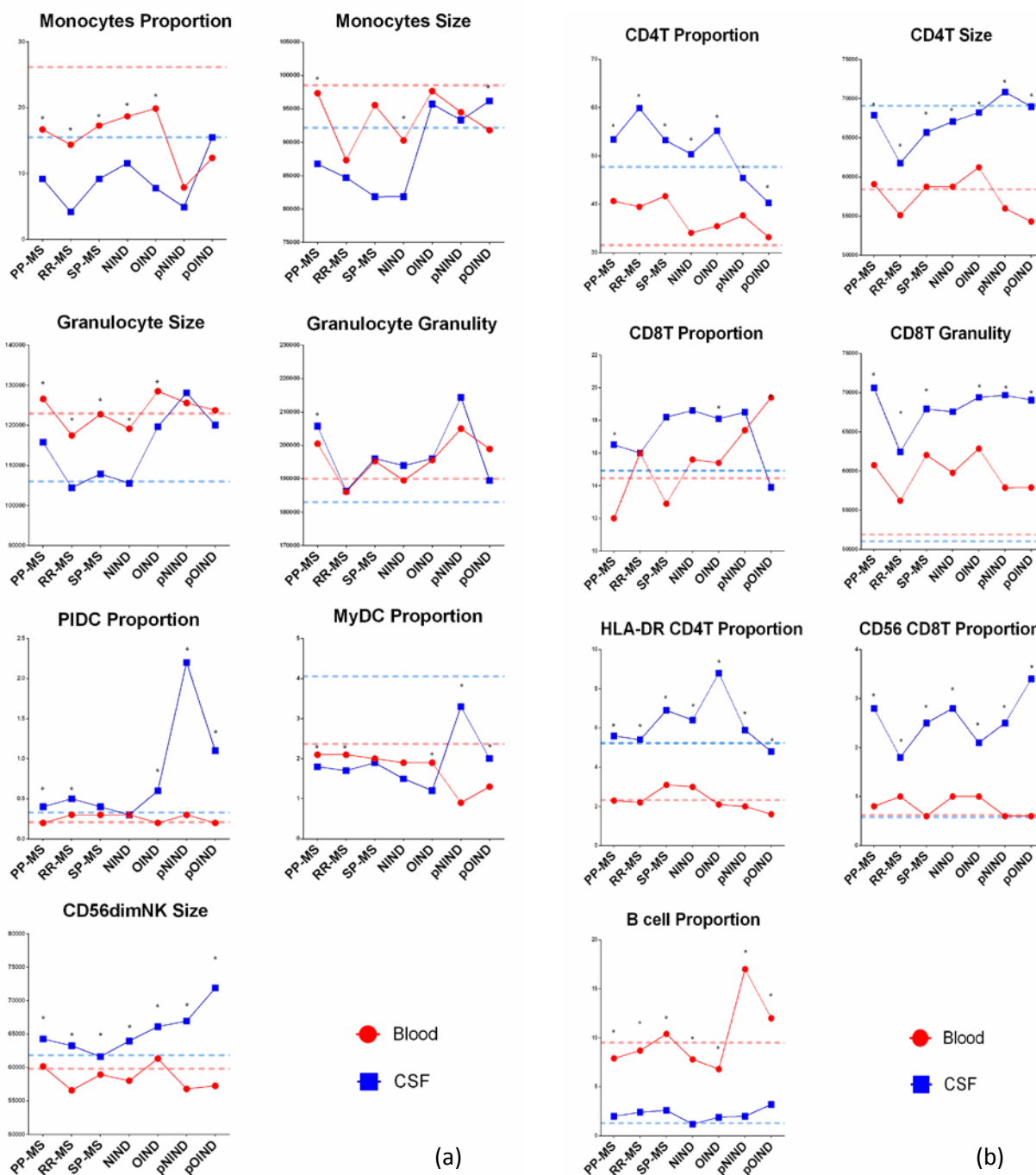
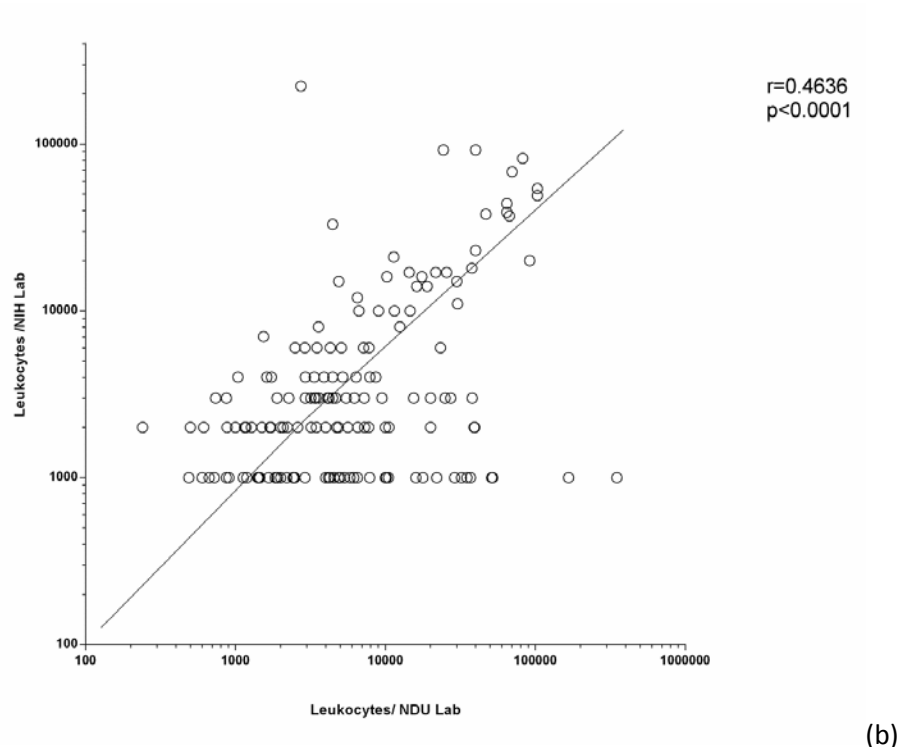
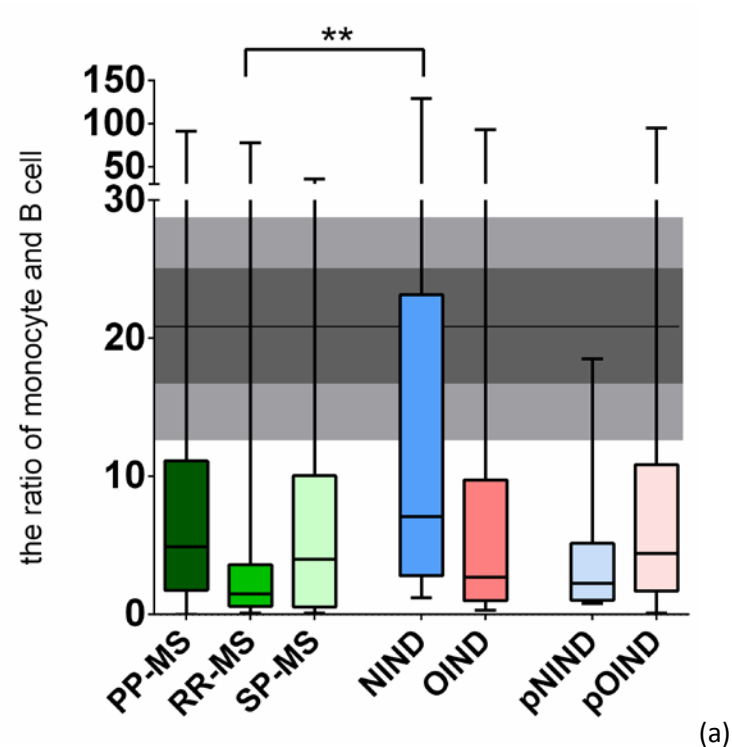


Supplementary figure 1: Gating strategy. Live leukocytes were first identified based on expression of CD45. Mononuclear cells were differentiated from granulocytes based on forward (size) and side scatter (granularity) characteristics. T cells were identified as mononuclear cells expressing CD3, and were further subdivided based on expression of CD4 and CD8 into CD4+ T cells, CD8+ T cells and double negative T cells (DnT). Expression of HLA-DR and CD56 identified proportion of “effector” T cells (HLA-DR+) and “cytotoxic” T cells (CD56+). Monocytes were gated as mononuclear cells that do not express CD3 but express CD14 (and also HLA-DR and intermediate levels of CD45). NK cells were gated as mononuclear cells that do not express CD3, CD14, but express CD56. These were further subdivided into CD56^{dim} and CD56^{bright} NK cells, identified as distinct subpopulations in CD56 mean fluorescent intensity (MFI) histogram. B cells were identified as mononuclear cells that did not express CD3, CD14, CD56, but expressed CD19 (and HLA-DR). Dendritic cells were identified as mononuclear cells that expressed HLA-DR, but lacked expression of lineage markers (CD3, CD4, CD8, CD14, CD19, CD56). They were further subdivided into myeloid DCs (expressing CD11c) and plasmacytoid DCs (expressing CD123). Cells that lacked lineage markers and HLA-DR, but expressed CD123 were gated as basophils.



Supplementary figure 2: Diagnosis-specific data for biomarkers that demonstrated significant interaction between sample type and the diagnosis. (a) the innate immune cell: monocyte, granulocyte, myeloid dendritic cell (MyDC), plasmacytoid dendritic cell (PIDC), and CD56dim NK cell; (b) the adaptive immune system: CD4+ T, CD8+ T, HLA-DR+ CD4+ T, CD56+ CD8+ T, and B cell. The biomarker measured in the blood is represented in red color, while the biomarker in CSF is represented by blue color. Statistically-significant differences between blood and CSF for each diagnostic category are highlighted. * $P < 0.01$.



Supplementary figure 3: (a) The ratio of CSF monocytes and CSF B cells in different diagnostic groups. (b) The correlation coefficient between CSF cell counts generated by NIH clinical laboratory, versus Neuroimmunological Diseases Unit (NDU) research laboratory. (3a): Each diagnostic category is represented by one vertical box blot, while data from healthy donors (HD) are depicted as grey shading, with horizontal line representing mean, dark shade of grey representing +/- 1SD and lighter shade of grey representing +/- 2SD of HD cohort. Each box plot shows median, 25-75%-tile and whisker blots represent minimum-maximum-tile for each diagnostic category. *: $P<0.05$, **: $0.01<P<0.005$, ***: $P<0.001$. (3b): Cell count by NIH clinical laboratory was based on unspun CSF sample. In contrast, NDU laboratory based CSF count on spinning on average of 20ml of CSF and re-suspending the cell pellet in 0.4ml of media, achieving 50 fold concentrations.

Supplementary table 1: Age-related changes in the immune subpopulations. To distinguish age-related effects on the immune system from the disease-related effects in pediatric group, the summary of articles describing age-related effects on the immune system in healthy controls is shown in this table (Upper panels: left for proportions and right for absolute numbers). Such data were available only for blood biomarkers. Additionally, correlation coefficients of age with immunophenotyping biomarkers were calculated within each one of three age-homogeneous cohorts in our study. (Pediatric: 0.80-18 years-old, Young adult: 18.00-65.80 years-old and Older adult: 19.80-74.86 year-old). + means positive coefficient (green); - means negative coefficient (light orange), no means no coefficient, and **Bold** signifies $P < 0.0001$.

	Literature (%)	NDU data (%)				Literature (Abs)	NDU data (Abs)				Reference	
		All	Pediatric	Younger	Older		All	Pediatric	Younger	Older		
blood	CD3	--	-0.10	0.22	-0.24	0.00	--	-0.33	-0.37	0.07	0.00	Wallach, Jacques. 2004
	CD4T	-	0.14	-0.11	0.03	-0.02	--	-0.23	-0.41	0.10	-0.01	Wallach, Jacques. 2004; Lemster et al., 2013
	HLA-DR CD4T		0.29	0.14	0.26	-0.14		-0.10	-0.35	0.19	-0.09	
	CD56 CD4T	+	0.12	-0.07	0.03	0.07		-0.09	-0.25	0.07	0.12	
	CD8	-	-0.28	0.40	-0.11	-0.01	--	-0.42	-0.18	0.02	0.02	Wallach, Jacques. 2004; Lemster et al., 2013
	HLA-DR CD8T		0.21	0.03	0.26	-0.02		0.05	-0.08	0.22	0.02	
	CD56 CD8T	+	0.10	-0.15	0.13	0.09		-0.11	-0.46	0.03	0.15	Lemster et al., 2013
	Tdn		-0.36	0.26	-0.06	-0.08		-0.41	0.09	0.01	-0.03	
	CD56dimNK	+	0.07	-0.11	0.29	0.12	+	-0.11	-0.21	0.21	0.11	Solana et al., 2012
	CD56briNK	-	0.00	-0.25	0.11	0.04	-	-0.25	-0.37	0.08	0.08	Solana et al., 2012
	Mono	-	0.28	0.02	0.10	0.05	--	-0.02	-0.47	0.14	0.09	Wallach, Jacques. 2004
	B	-	-0.31	-0.21	0.02	-0.19	--	-0.25	-0.13	0.11	-0.04	Wallach, Jacques. 2004
	PIDC	no	0.10	-0.11	0.23	0.08	no	-0.16	-0.13	0.10	0.14	Solana et al., 2012
	MyDC	no	0.34	0.25	0.29	0.25	no	0.03	-0.24	0.33	0.27	Solana et al., 2012
	Basophil	-	0.19	0.04	0.13	0.14	-	0.04	-0.04	0.08	0.00	Wallach, Jacques. 2004
	Granulocyte	+	0.24	0.23	-0.01	-0.13	++	-0.03	-0.09	-0.01	-0.19	Wallach, Jacques. 2004
	Tc	CD3	N/A	0.14	0.19	-0.09	-0.17	N/A	-0.33	-0.04	-0.04	-0.19
CD4T		N/A	0.21	0.18	0.10	-0.14	N/A	-0.30	-0.10	-0.02	-0.19	
HLA-DR CD4T		N/A	0.19	0.11	0.19	-0.15	N/A	-0.20	0.30	-0.01	-0.17	
CD56 CD4T		N/A	0.06	0.07	0.11	0.04	N/A	-0.27	-0.23	-0.05	-0.13	
CD8		N/A	0.15	-0.18	0.05	0.00	N/A	-0.35	0.02	-0.07	-0.21	
HLA-DR CD8T		N/A	0.19	-0.11	0.07	-0.04	N/A	-0.22	0.26	-0.10	-0.14	
CD56 CD8T		N/A	0.01	-0.32	0.33	-0.04	N/A	-0.32	-0.06	0.15	-0.16	
Tdn		N/A	-0.37	-0.31	-0.11	0.08	N/A	-0.39	0.04	-0.13	0.01	
CD56dimNK		N/A	-0.07	-0.53	0.16	0.08	N/A	-0.35	-0.01	0.07	-0.11	
CD56briNK		N/A	0.12	-0.05	0.30	0.07	N/A	-0.18	0.26	0.07	-0.08	
Mono		N/A	0.10	-0.17	0.09	0.20	N/A	-0.18	-0.06	0.08	0.05	
B		N/A	-0.11	-0.10	-0.19	-0.05	N/A	-0.33	0.21	-0.23	-0.17	
PIDC		N/A	-0.17	-0.24	0.12	0.13	N/A	-0.29	-0.17	0.13	-0.07	+ : positive coefficient (green)
MyDC		N/A	0.02	-0.12	0.27	0.22	N/A	-0.24	-0.13	0.20	0.05	- : negative coefficient (light orange)
Basophil		N/A	-0.09	-0.01	-0.02	0.04	N/A	-0.24	-0.09	0.10	-0.13	no: no coefficient
Granulocyte		N/A	0.05	-0.11	0.18	0.05	N/A	-0.25	-0.32	0.17	-0.12	Bold: P<0.001