

Table S1: Frequency of PF4/heparin-specific B cells in normal human PBMCs

Donors	#1	#2	#3	#4	#5	#6	#7	#8	#9	#10	#11	#12	#13	#14	#15	#16
B cell percentage in PBMCs	8.6	1.3	4.4	8.5	8.8	4.5	2.3	3.4	2.7	2.7	4.5	3.5	1.4	5.4	5.1	4.9
Number of PF4/heparin-specific B cells per thousand PBMC B cells	1.0	0.4	0.3	0.6	0.5	0.2	0.3	1.0	0.1	0.5	0.2	0.4	0.7	0.4	0.3	0.8

The frequency of B cells in human PBMCs that produce PF4/heparin-specific antibodies was estimated by the MPN analysis of limiting dilution 96-well cultures containing a 5-fold serial dilution of PBMCs. PBMCs ( $1 \times 10^5$  or  $2 \times 10^4$ ) from normal donor were cultured in 0.2 ml of RPMI 1640 containing 10% FBS, 1% sodium pyruvate, 1% nonessential amino acids, 0.5% L-glutamine, 50  $\mu$ M 2-mercaptoethanol, 100 U/ml penicillin, and 100  $\mu$ g/ml streptomycin in 96-well round-bottomed microplates. For polyclonal activation of B cells, the cells were stimulated with CpG (3  $\mu$ g/ml), Zysorbin (1:10,000 dilutions), and Lectin (100 ng/ml) from pokeweed. The percentage of B cells in the PBMCs was determined by FACS analysis after CD19 staining and the number of B cells in each well was calculated. Twenty four to 36 wells were set up for each dilution of PBMCs from an individual donor. After 6-7 days of culture, supernatants were collected and tested for PF4/heparin-specific antibody production. For the MPN estimation, one assumption is that whenever a well has one or more PF4/heparin-specific B cells among the PBMCs, PF4/heparin antibodies produced in this well upon *in vitro* stimulation can be detected by the ELISA assay. With this assumption, the minimum frequency of PF4/heparin-specific B cells in PBMCs was calculated by the binomial theorem. Based on the theorem, the formula for calculating the minimum frequency of PF4/heparin-specific B cells in human PBMC B cells is:  $P = 1 - (1 - X)^{1/N}$ . In this formula, P is the frequency of PF4/heparin-specific B cells in human PBMC B cells, X is the fraction of 24 or 36 wells with the same dilution of PBMCs that tested positive for PF4/heparin-specific antibodies, and N is the number of B cells in each well.