Reference: Immune Functions and Inducible Enzymes

1. Immune Function

The survey examined alterations in the composition of lymphocytes, which are indicators of immune functions, by measuring the proportion of CD4+ T-cells and CD8+ T-cells, which are subsets of T-lymphocytes and the proportion of CD56+ cells, which is an index of natural killer (NK) cells. Measurement was also made of the cell proliferation function when stimulated by PHA and ConA, which are T-lymphocyte growth factors (Table 7-1). The measurements were carried out by SRL, Inc.

No significant difference was observed between regions in CD4+ T-cells and CD8+ T-cells. On the other hand, testing for difference in NK cell activation between A1 regions and B regions in Saitama Prefecture showed that A1 regions were significantly ($p<0.05$) higher, but the values in Saitama Prefecture overall were lower than in other areas. Values in all areas also remained within the normal range. It seemed inappropriate, therefore, to take these up as indicators of exposure.

With respect to cell proliferation function when stimulated by PHA and ConA, the A2 regions in the Saitama Prefecture area returned results with significantly higher levels than the B regions (PHA, $p<0.01$; ConA, $p<0.05$). Reports of animal experiments indicate that dioxins can inhibit T-lymphocyte proliferation, but there have not been any reports that dioxins can accelerate proliferation. The cell proliferation function in A2 regions was also within the normal range. Consequently, this acceleration appears unlikely to be an effect of exposure.

Viewing the three areas in light of results from this survey, no distinct differences were observed among the regions, and it was determined that there was no clear effect on immune function in the residential districts.

No significant relationshops were observed between the concentration of dioxins in the blood and any of the various items under immune function (see Figures 7-1 to 7-7).

2. Inducible Enzymes

Measurements were made of mRNA levels in cytochrome P450 1A1 (CYP1A1), cytochrome P450 1A2 (CYP1A2), and cytochrome P450 1B1 (CYP1B1), which are thought to be affected by minute amounts of dioxins (see Table 7-2). The measurements were carried out by the National Institute for Environmental Studies.

In addition, the induced levels of CYP1A1 were found unreasonably low in many specimens, and these values were not utilized for discussion in the present study.

Among the CYP1A1, CYP1A2, and CYP1B1 molecular species, the greatest difference between regions was observed in CYP1A1 measurements. When the relationship between data on dioxins and inducible enzymes was plotted in graphs, however, no meaningful relationship was observed, and the correlation was not significant. It seems unlikely, therefore, that differences in inducible enzymes were the result of dioxins (see Figures 7-8 to 7-10).

Comparison of inducible enzymes between regions showed a significant difference ($p<0.05$) in CYP1A1 in the Fuchu City area of Hiroshima Prefecture. The levels were not necessarily high in comparison with other areas, however, suggesting that it would be inappropriate to take this as an effect of exposure to dioxins. No significant difference in other inducible enzymes (CYP1A2, CYP1B1) was observed between other regions.

At present there are no standard values for CYP1A1 and other cytochromes, and it will be necessary to further extend knowledge and information about them.

3. Summary

During this fiscal year, experimental measurements were made to determine the effects of low dosages of dioxins on inducible enzymes and alterations in lymphocyte composition, which are indicators of immune function. Comparisons were made between A and B regions in all three survey areas, but no distinct differences were observed in their relation to dioxins between any of the residential districts. Furthermore, no significant correlation was observed between concentrations of dioxins in the blood and any of the items under immune function and inducible enzymes.

Table 7-1. Immune Function

Item	Standard Value	Mean Value, Etc.	Osaka Prefecture Nose Town		Saitama Prefecture			Hiroshima Prefecture Fuchu City	
			A Region	B Region	A1 Region	A2 Region	B Region	A Region	B Region
CD4［%］	25～56	Number of samples	22	15	13	22	13	15	18
		Mean value	45	47	46	44	42	45	43
		Standard deviation	9.4	9.3	7.6	9.5	11	11	7.4
CD8［%］	17～44	Number of samples	22	15	13	22	13	15	18
		Mean value	28	26	25	24	27	26	29
		Standard deviation	7.2	8.1	9.9	7.6	6	8.9	8.6
CD56［%］	10～38	Number of samples	22	15	13	22	13	15	18
		Mean value	18	18	19	19	20	21	24
		Standard deviation	7.5	9.1	6.9	6.8	6.8	9.7	9.3
NK cell activation［%］	18～40	Number of samples	22	15	13	22	13	16	18
		Mean value	53	54	44	31	33	59	51
		Standard deviation	17	16	15	12	15	9.5	17
PHA+［cpm］	26,000～53,000	Number of samples	22	15	13	22	13	15	18
		Mean value	42000	42000	34000	49000	41000	37000	38000
		Standard deviation	7600	11000	13000	9300	7600	11000	9500
CON－A+［cpm］	20,000～48,000	Number of samples	22	15	13	22	13	15	18
		Mean value	33000	37000	25000	43000	36000	32000	32000
		Standard deviation	8600	9000	7000	11000	11000	9600	8800
CONTROL［cpm］	70～700	Number of samples	22	15	13	22	13	15	18
		Mean value	530	620	220	440	780	420	450
		Standard deviation	180	260	78	240	360	240	190

Table 7-2. Inducible Enzymes

［copies/ng total RNA］

Item	Mean Value, Etc	Osaka Prefecture Nose Town		Saitama Prefecture			Hiroshima Prefecture Fuchu City	
		A Region	B Region	A1 Region	A2 Region	B Region	A Region	B Region
CYP1A1	Number of samples	16	14	8	22	6	15	11
	Mean value	4900	6300	8200	17000	21000	13000	5400
	Standard deviation	5100	3500	4200	37000	37000	11000	3600
CYP1A2	Number of samples	16	14	8	22	6	15	11
	Mean value	3300	1300	99	36	240	1400	360
	Standard deviation	7100	1800	160	49	410	3400	460
CYP1B1	Number of samples	16	14	8	22	6	15	11
	Mean value	12000	7700	6600	9000	6700	19000	9700
	Standard deviation	7200	7800	3700	7600	3100	21000	5400

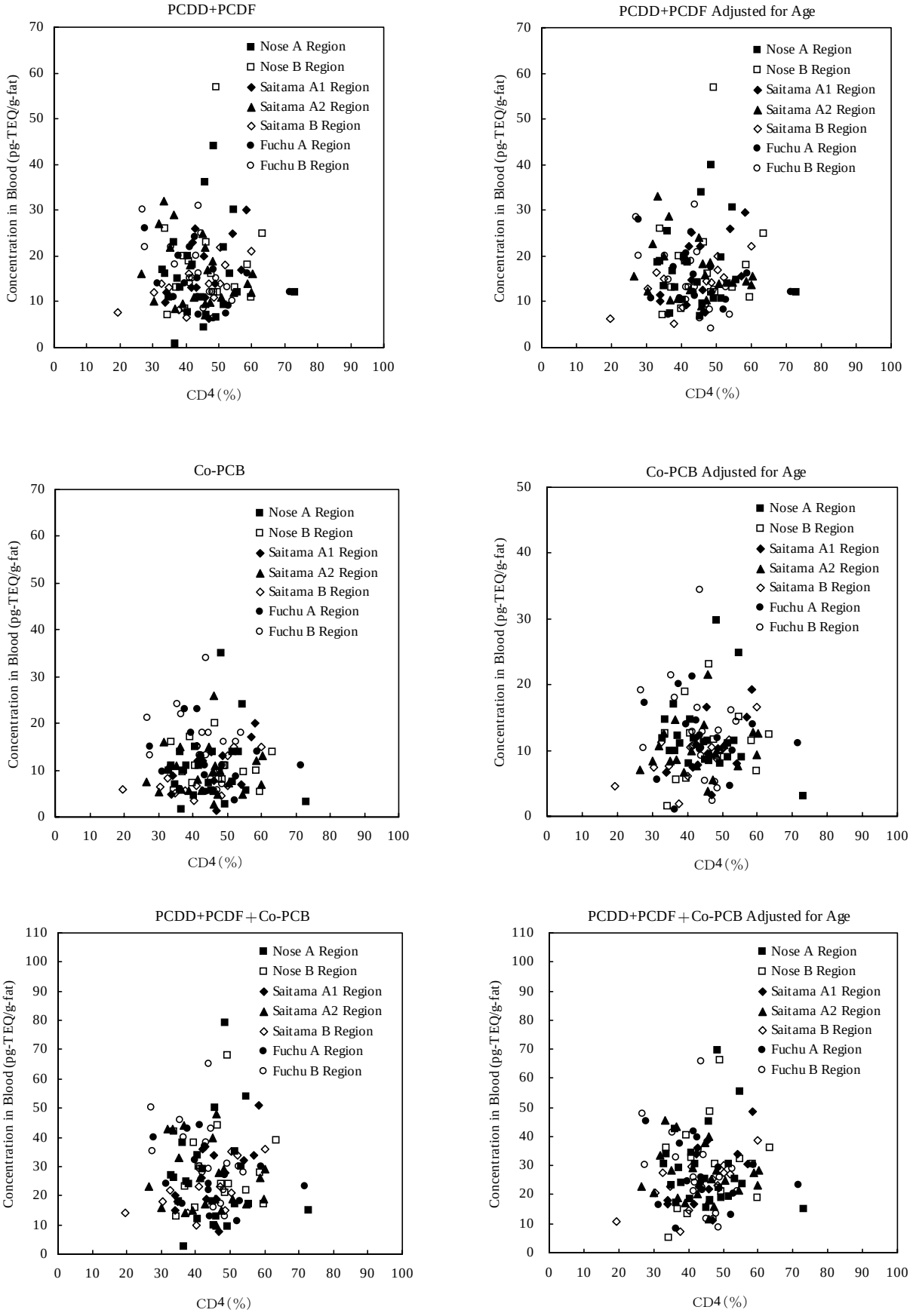

Fig.7-1 Relationship between Concentration in Blood and Health-Related Item (CD4)

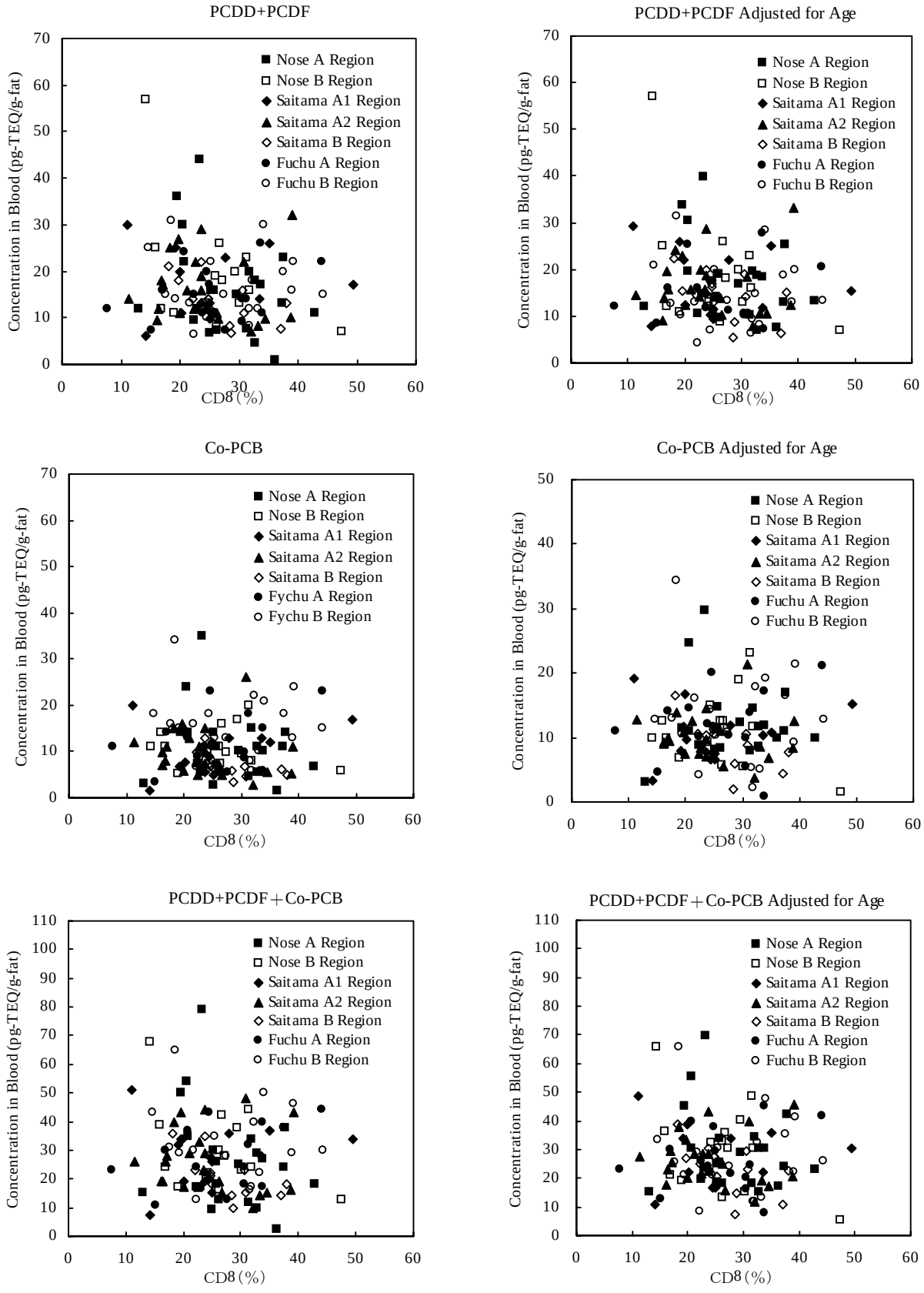

Fig. 7-2 Relationship between Concentration in Blood and Health-Related Item (CD8)

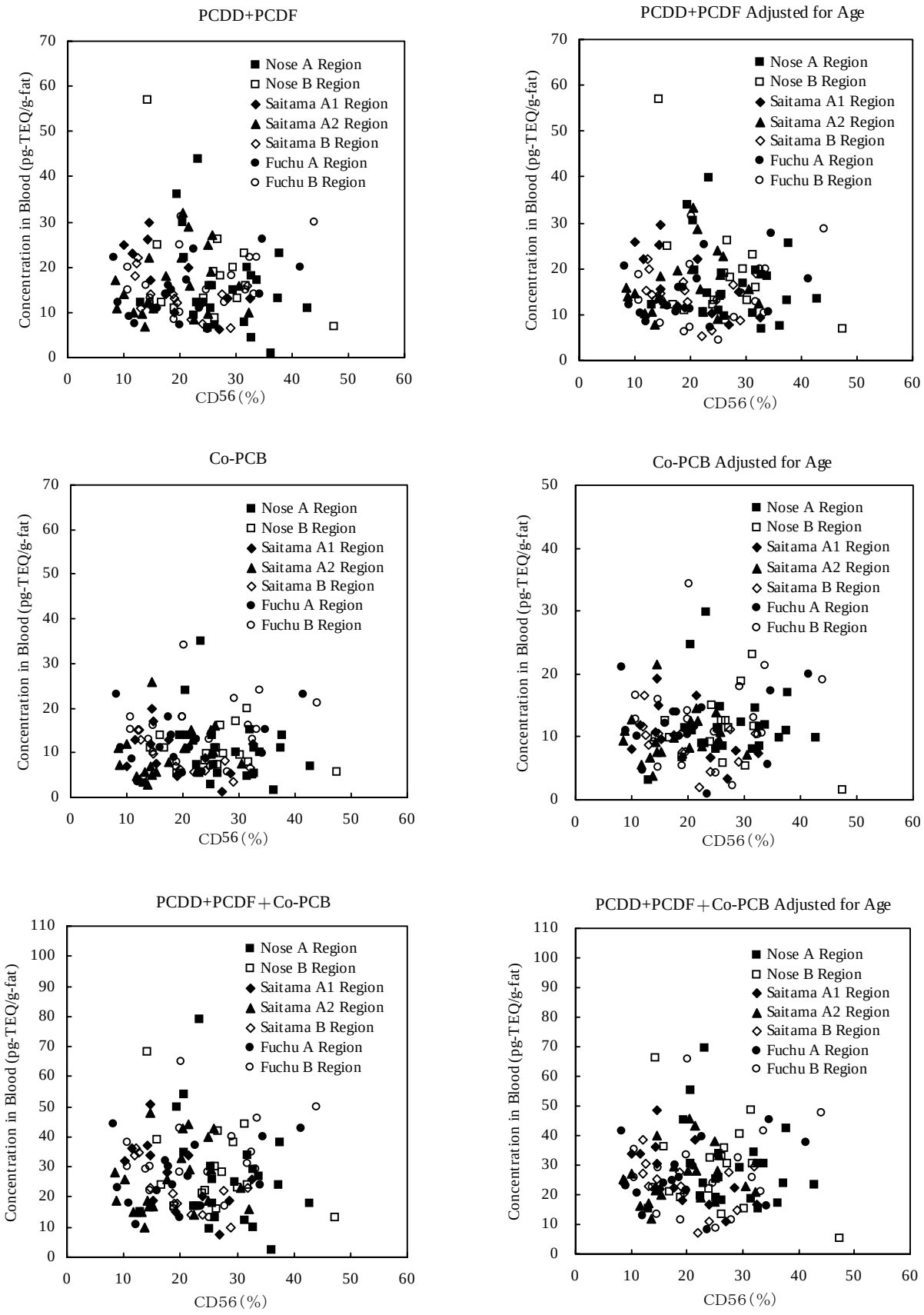

Fig. 7-3 Relationship between Concentration in Blood and Health-Related Item (CD56)

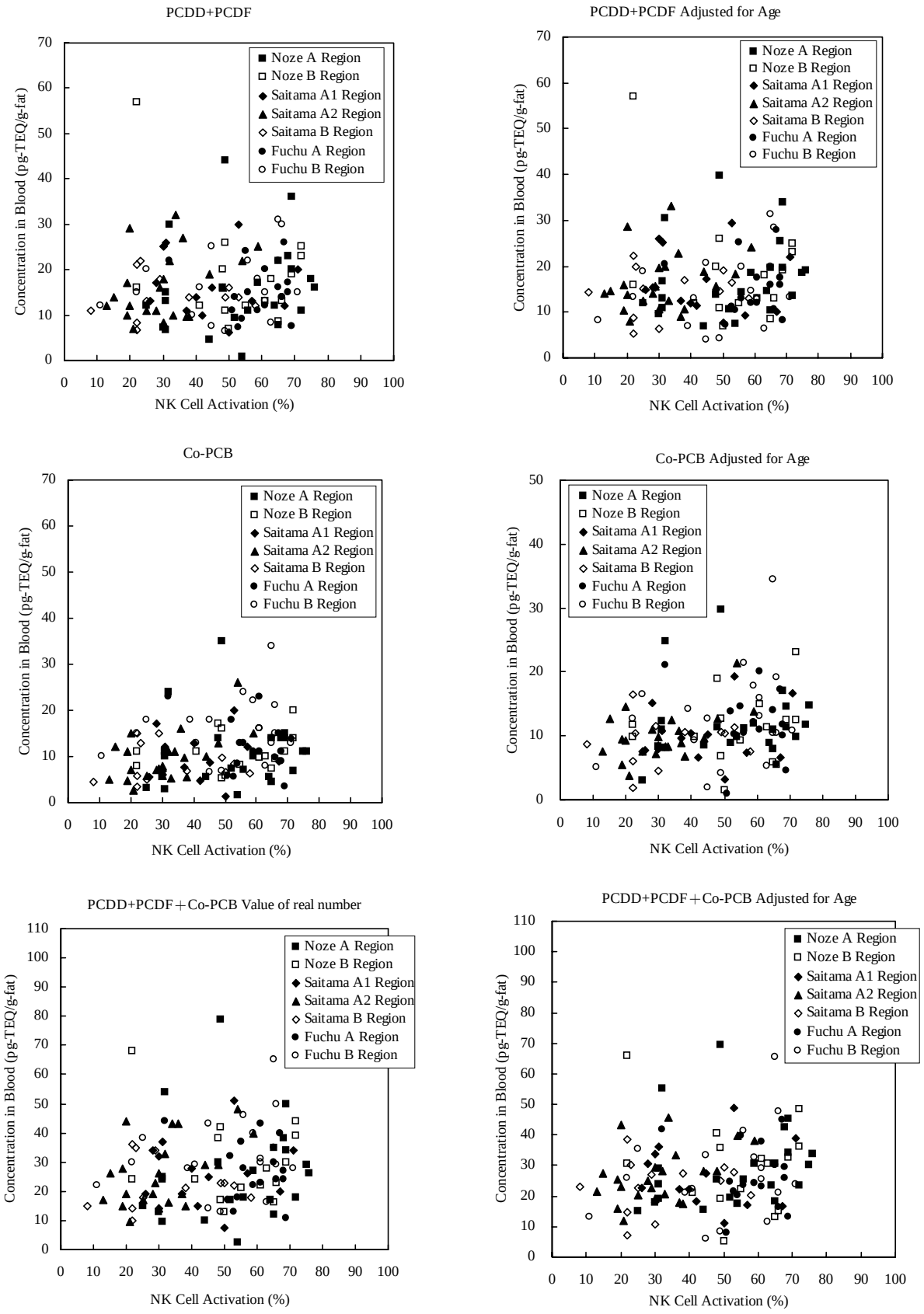

Fig. 7-4 Relationship between Concentration in Blood and Health-Related Item (NK Cell Activation)

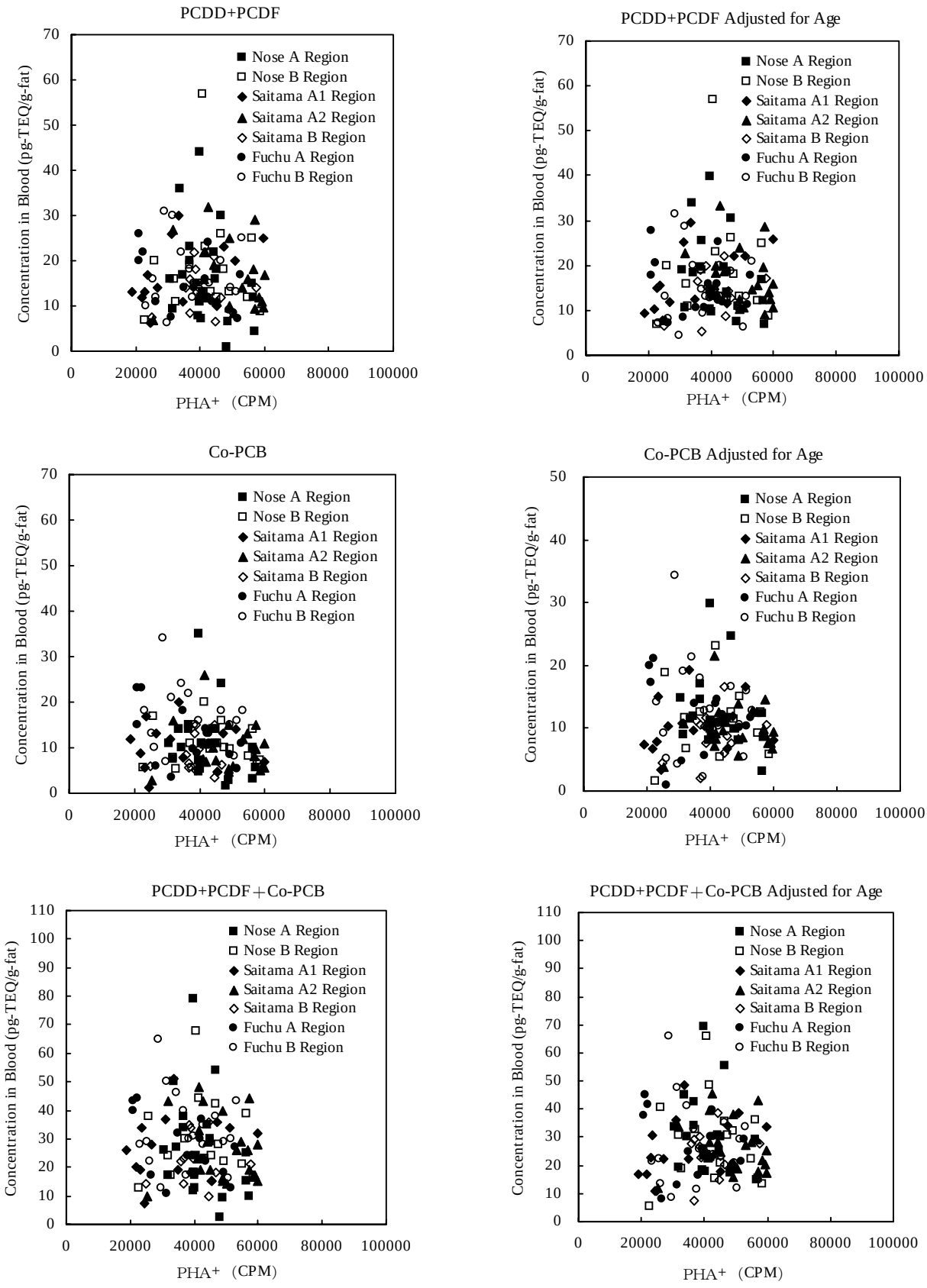

Fig. 7-5 Relationship between Concentration in Blood and Health-Related Item (PHA+)