Effects of Donor Age on Frequency of Sister Chromatid Exchanges and Accumulation of Dioxins and Related Chemicals in Healthy Japanese

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Introduction

The ability to induce sister chromatid exchanges (SCEs) is a well-known property of many DNA-damaging agents [1]. So, analysis of SCEs rates has been proposed to be a sensitive indicator of DNA damage [2].

Human bodies have been already contaminated with highly toxic organochlorine compounds such as polychlorinated dibenzo-*p*-dioxins (PCDDs), polychlorinated dibenzofurans (PCDFs) and coplanar polychlorinated biphenyls (Co-PCBs) [3,4] and their age-related increase was observed in the adipose tissue of Japanese people [3]. It also has been demonstrated that these chemicals can induce SCEs in cultured human lymphocytes in vitro [5,6]. Therefore, in this study, we investigated whether the *in vivo* exposure to these chemicals could enhance SCE frequency in cultured lymphocyte obtained from healthy Japanese, and the frequency of SCEs and the contamination levels of PCDDs, PCDFs and Co-PCBs in the blood and sebum would be altered with donor age.

Materials and Methods

In September, 1994 to October, 1995, 60 to 80 ml of the peripheral blood and sebum of the face were individually obtained from 39 healthy volunteers (25 males and 14 females, mean age : 44.3 years old and the range : 20~64 years old) and the concentrations of PCDDs, PCDFs and Co-PCBs were determined in those samples by the methods previously reported [4,7]. Frequencies of SCEs in the lymphocytes of individual whole-blood cultures were counted and analyzed as described before [5,6].

Pearson correlation coefficients between two variables interested were computed and the statistical significance was evaluated by Fisher's test.

Results

1) Correlation between frequency of SCEs and Donor Age

Mean frequency of SCEs in the control (solvent, DMSO, treated) cultures was 10.1/cell and the range 7.9~14.1/cell and the mean SCE frequency in the 7,8-benzoflavone (ANF), $8x10^{-5}$M treated cultures was 13.6/cell and the range 10.2~17.8/cell. We observed statistically significant positive correlation between the SCE rate in the control culture ($r=0.42$, $p=0.007$) or in the ANF treated culture ($r=0.55$, $p=0.0002$) and donor age. The relationship between SCEs frequency in the control culture and donor age is indicated in Fig.1.

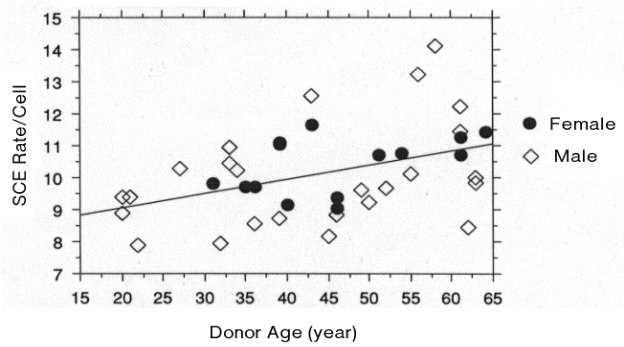

Fig.1. Positive correlation between the SCE frequency in the control culture and donor age ($r=0.42$, $p=0.007$)

2) Correlation between the concentration of PCDDs, PCDFs and Co-PCBs in the blood and sebum and donor age

Respective mean total concentrations of PCDDs, PCDFs and Co-PCBs as 2,3,7,8-tetrachlorodibenzo-*p*-dioxin toxic equivalent (2,3,7,8-TCDD TEQ) value on the fat weight basis in the blood and sebum were 37.6 and 30.7 pg/g, so the mean level in the sebum was somewhat lower than that in the blood. Ranges of their total concentrations in the blood and sebum were 8~80 pg/g and 7~78 pg/g, respectively. Statistically significant positive correlation was observed between donor age and their total levels in the blood ($r=0.32$, $p=0.06$) or sebum ($r=0.52$, $p=0.002$). Fig.2 shows the relationship between their total levels in the blood and donor age.

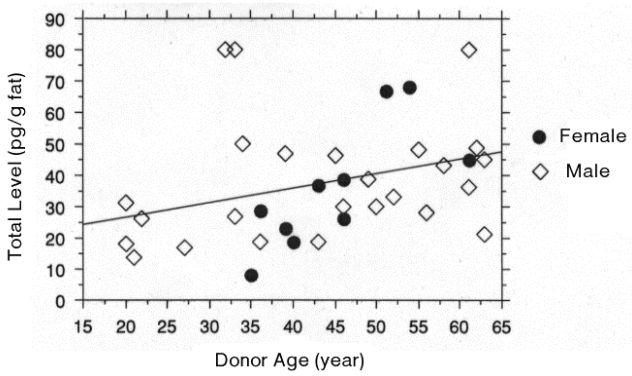

Fig.2. Positive correlation between the total concentration of PCDDs, PCDFs and Co-PCBs as 2,3,7,8-TCDD TEQ on the fat weight basis in the blood and donor age (r=0.32, p=0.06)

3) Correlation between the SCE frequency and the concentration of PCDDs, PCDFs and Co-PCBs

It was examined whether the SCE rate in the blood lymphocyte was influenced with the contamination levels of PCDDs, PCDFs and Co-PCBs in the blood and sebum or not. Neither the SCE frequency in the control culture nor that in the ANF treated one was changed significantly with the toxic chemical levels as 2,3,7,8-TCDD TEQ values in the blood and sebum. The relationship between the SCE rates in the control culture and their total concentrations in the sebum is given in Fig.3.

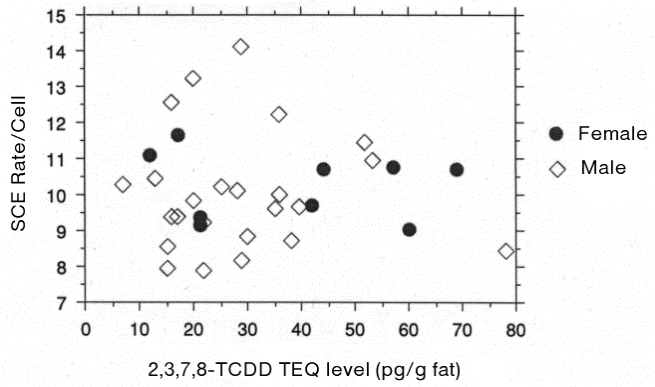

Fig.3. Relationship between the SCE frequency in the control culture and total concentration of PCDDs, PCDFs and Co-PCBs as 2,3,7,8-TCDD TEQ value in the sebum of face (r=-0.025, p=0.89)

Discussion

Since the accumulation of mutation load is one of the causes of aging, and since the mutation frequency in human lymphocyte increases with age [8], in general, increasing frequency of SCEs in relation to aging seemed to be understandable. There are, however, the majority of earlier studies reported 1975 to 1984 indicate that aging does not significantly affect the baseline frequency of SCEs, namely, in control culture. In contrast, many of the studies also strongly suggest that the level of baseline SCE is certainly low in young individuals as compared to that of older ones, which is in accordance with our present study. In our investigation, not only in the control culture, but also in the ANF treated culture, frequency of SCEs is significantly increased with age-dependent manner.

The variation in general hormonal ststus with age of the individual may also contribute to this phenomenon. Therefore, in this context, PCDDs, PCDFs and Co-PCBs, which have been considered endocrine disruptors, that is, environmental hormones, are expected to influence the SCE formation. Age-dependent increase in their contamination levels in the blood and sebum of face was observed in this study. They, however, did not change the frequency of SCEs in either the control culture or the ANF treated culture.

References

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