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Association between food consumption and serum aryl hydrocarbon receptor ligand activity among middle-aged Korean adults

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ABSTRACT

BACKGROUND/OBJECTIVES: The diet is an important route of exposure to endocrine-disrupting chemicals (EDCs). However, few studies have investigated the association between dietary intake and EDC exposure levels among Koreans. In an earlier study, we showed that the bioactivity of serum aryl hydrocarbon receptor ligands (AhRLs) could be a surrogate biomarker to indicate exposure to EDCs and that they inhibit mitochondrial function. We also found that the mitochondria-inhibiting substances (MIS) in serum ascertained by intracellular adenosine triphosphate (MIS-ATP) and reactive oxygen species (MIS-ROS) levels could be biomarkers of exposure to EDCs, as they showed a strong correlation with AhRL and the levels of EDCs in the blood. Here, we investigated the association between the consumption of specific foods and surrogate serum biomarkers for EDCs, namely AhRL, MIS-ATP, and MIS-ROS, among middle-aged Korean adults.
SUBJECTS/METHODS: A total of 1,466 participants aged 45–76 yrs from the Ansung cohort of the Korean Genome and Epidemiology Study were included. Food consumption, including that of meat, fish, vegetables, and fruits, was measured using a semiquantitative food frequency questionnaire.
RESULTS: Fish intake was positively associated with AhRL ($\beta = 0.0035$, $P = 0.0166$), whereas cruciferous vegetable intake was negatively associated with AhRL ($\beta = -0.0007$, $P = 0.0488$). Cruciferous vegetable intake was positively associated with the MIS-ATP levels ($\beta = 0.0051$, $P = 0.0420$). A higher intake of fish was significantly associated with an increased risk of high AhRL (tertile: odds ratio [OR], 1.49; 95% confidence intervals (CIs), 1.08–2.06; P for trend = 0.0305). In addition, the second-highest tertile of cruciferous vegetable intake had lower odds of high AhRL than the lowest tertile (OR, 0.73; 95% CIs, 0.54–0.97), although no significant linear trend was observed.
CONCLUSION: Consumption of different types of foods may be differentially associated with EDC exposure in middle-aged Korean adults.

Keywords: Diet; endocrine disruptors; AH receptor; fishes; vegetables

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Conflict of Interest
The authors declare no potential conflicts of interests.

Author Contributions
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INTRODUCTION

Exposure to environmental chemical pollutants has received significant attention due to their role in the pathogenesis of metabolic diseases [1-3]. Previous systematic reviews have reported that exposure to endocrine-disrupting chemicals (EDCs) is associated with an increased risk of obesity and type 2 diabetes [1,4]. Although EDCs are heterogeneous, many EDCs contain ligands that interact with the aryl hydrocarbon receptor (AhR). Thus, serum AhR ligand (AhRL) bioactivity has been used as a surrogate biomarker for screening EDCs, such as dioxins [5,6]. In our previous observational studies, we have shown that AhRL and mitochondria-inhibiting substances (MIS) in serum, ascertained by AhR transactivation activity, and the levels of intracellular adenosine triphosphate (MIS-ATP) and reactive oxygen species (MIS-ROS) production could be biomarkers of exposure to EDCs, as they showed a strong correlation with the blood levels of EDCs [7,8]. Furthermore, we found that serum AhRL and MIS-ROS levels were positively associated with the risk of diabetes, including gestational diabetes, whereas MIS-ATP showed an inverse association with the diabetes risk in the Korean population [8-10].

Diet is an important route of exposure to EDCs, and the concentration of chemical environmental pollutants in the body may vary depending on the individual's diet. Foods such as meat, fish, and dairy products are easily contaminated with EDCs, and grains, vegetables, and fruits can be contaminated by EDCs through several pathways such as the use of chemical fertilizers and pesticides, root uptake from contaminated soil, and food preparation (*e.g.*, processing, packaging, and storage) [11,12].

Specific compounds abundant in cruciferous vegetables, including broccoli, cabbage, and cauliflower, may regulate AhR activity through indole-3-carbinol [13-15]. Further, flavonoids such as galangin, quercetin, kaempferol, and resveratrol function as dietary antagonists to inhibit AhR activation [15]. These findings suggest that the association between diet and EDC exposure may vary depending on the dietary components.

While several pathways are involved in the exposure to dietary EDC, epidemiologic studies on the association between dietary intake and EDCs in the Korean population are limited. Therefore, in the present study, we aimed to examine the association between food consumption and surrogate EDC biomarkers in middle-aged Korean adults.

SUBJECTS AND METHODS

Study design and participants

This study is part of the Ansung cohort of the Korean Genome and Epidemiology Study (KoGES), which is a community-based prospective study. The Ansung cohort comprised 5,018 middle-aged adults aged 40–69 yrs enrolled in 2001–2002 and subjected to a biennial follow-up. Details of the KoGES were reported by Kim and Han in an earlier publication [16]. Serum samples from 1,466 participants who responded to a semi-quantitative food frequency questionnaire (SQFFQ) were used for the surrogate serum biomarker assays in 2008. This study was approved by the Institutional Review Board of the Korea Disease Control and Prevention Agency, formerly the Korea Centers for Disease Control and Prevention and Eulji University Hospital (EMCS 2019-05-008). Written informed consent was obtained from all participants.

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Dietary assessment

Food consumption between 2005 and 2006 was assessed using a 106-item SQFFQ. The FFQ surveys were conducted twice in KoGES (2001–2002 and 2005–2006). Data from the later collection period 2005 to 2006 were used despite the time gap between the FFQ survey and serum collection. The meat, fish, vegetable, and fruit intakes were measured in grams per day based on the consumption frequency per day and serving size of each food item. Meat included red meat, processed meat, and poultry, while fish included fish and shellfish. Since salted/pickled vegetables were included in the vegetables, the intake of non-starchy, unsalted vegetables was estimated based on the total vegetable intake. The intake of cruciferous vegetables such as cabbage, radish, lettuce, kale, and broccoli was also assessed, and salted vegetables made with cruciferous vegetables were included. The total energy intake was calculated based on the seventh edition of the Korean Food Composition Table [17].

Surrogate serum biomarker assay

The AhRL bioactivity assay was performed using pGL4-DRE-luc (puromycin+)/pRL-mTK double-positive stable cells and heat-inactivated serum samples [8]. This assay is similar to the chemical-activated luciferase gene expression assay, except that the former uses different recombinant cell lines and includes an organic solvent extraction-free sample preparation method. The intra- and inter-assay coefficients of variation of AhRL were less than 5.0%. MIS-ATP and MIS-ROS assays were conducted to evaluate the levels of the serum mitochondrial inhibitors. Briefly, in a 96-well plate, pRL-mTK-transfected mouse Hepa1c1c7 cells (5×10^4 cells/well) were treated with 10 μL heat-inactivated serum samples for 48 h. The ATP content was measured using the CellTiter-Glo® luciferase kit (Promega, Madison, WI, USA), and the output was normalized to Renilla luciferase activity. The ROS level was determined using 5-(and-6)-chloromethyl-2′,7′-dichlorodihydrofuorescein diacetate and acetyl ester (CM-H_2DCFDA; Molecular Probes, Eugene, OR, USA). Both MIS-ATP and MIS-ROS were expressed as percentages of charcoal-stripped serum-treated controls. The intra- and inter-assay coefficients of variation for these methods were less than 6.0%. All cell-based assays were performed in duplicate using blinded samples.

Measurement of other variables

Sociodemographic variables, including age, sex, and education, as well as lifestyle variables, including exercise, smoking, and alcohol consumption, were collected using a self-administered questionnaire. Education level was classified as 'elementary school or lower,' 'middle school,' 'high school,' and 'college or higher.' Exercise was defined as "yes" if the subject regularly engaged in exercise that was intense enough to raise a sweat. Smoking status and alcohol consumption were categorized as none, former or current.

Statistical analysis

Pearson's correlation coefficients between the surrogate serum biomarkers for EDCs and food consumption were measured after adjusting for age and total energy intake. Multiple linear regression analysis was performed to examine the association between the surrogate serum biomarkers for EDCs and food consumption, including food consumption variables, age, sex, education, body mass index (BMI), fasting blood glucose, triglycerides, alcohol consumption, and smoking. Participants were grouped into tertiles according to their food intake (meat, fish, vegetables, and fruits), and multiple logistic regression analysis was used to estimate the odds ratio (OR) and 95% confidence interval (CI) of high AhRL and low MIS-ATP. The lowest tertile of food consumption was used as the reference group. High AhRL was defined as ≥ 2.7 pM and low MIS-ATP was defined as ≤ 88.1%, according to a previous study

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[8]. The *P*-value for the linear trend was calculated using the median value of each tertile of food consumption. All statistical analyses were performed using SAS (version 9.4; SAS Institute, Cary, NC, USA), and all statistical tests were 2-sided (α = 0.05).

RESULTS

General characteristics of study participants

The general characteristics of the participants are listed in **Table 1**. The mean age was 60.6 ± 8.4 yrs, and 55.3% of the participants were female. Most participants attended elementary school or less (50.5%) and did not perform regular exercise (68.3%). Among the participants, 16.3% and 43.1% were current smokers and alcohol consumers, respectively. The mean total energy intake was 1,699.5 kcal, and BMI was 24.3 kg/m^2. The average AhRL, MIS-ATP, and MIS-ROS levels were 2.68 pM, 89.3%, and 115.9%, respectively.

Association between food consumption and surrogate serum biomarkers for endocrine-disrupting chemicals

After adjustment for age and total energy intake, the AhRL level was positively correlated with fish intake (r = 0.054, $P < 0.05$) and negatively associated with cruciferous vegetables

Table 1. General characteristics of the study participants

Characteristics	Total (n = 1,466)
Age (yrs)	60.6 ± 8.4
Sex	
Male	656 (44.8)
Female	810 (55.3)
Education	
Elementary school or less	740 (50.5)
Middle school	321 (21.9)
High school	331 (22.6)
College or more	73 (5.0)
Exercise	
Yes	464 (31.7)
No	1,001 (68.3)
Smoking	
Never	953 (65.1)
Former	273 (18.6)
Current	239 (16.3)
Alcohol consumption	
Never	742 (50.7)
Former	92 (6.3)
Current	631 (43.1)
Energy intake (kcal/day)	1,699.5 ± 564.3
Macronutrient intake (% of energy)	
Fat	12.6 ± 5.8
Protein	12.9 ± 2.6
Carbohydrate	74.4 ± 7.9
BMI (kg/m^2)	24.3 ± 3.2
Fasting glucose (mg/DL)	102.6 ± 30.5
Triglycerides (mg/DL)	139.4 ± 85.0
AhRL (TCDDeq, pM)	2.68 ± 1.83
MIS-ATP (%)	89.3 ± 12.8
MIS-ROS (%)	115.9 ± 15.5

Values are presented as mean ± SD or number (%).
BMI, body mass index; AhRL, aryl hydrocarbon receptor ligand; TCDDeq, 2,3,7,8-tetrachlorodibenzodioxin equivalents; MIS, mitochondria-inhibiting substances; ATP, adenosine triphosphate; ROS, reactive oxygen species.

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Table 2. Pearson's correlation coefficient between surrogate serum biomarkers for endocrine-disrupting chemicals and food consumption

Food consumption (g/day)	AhRL (TCDDeq, pM)	MIS-ROS (%)	MIS-ATP (%)
Meat	0.016	0.040	0.018
Fish	0.054*	0.036	0.031
Vegetables	−0.045	0.054*	−0.002
Non-starchy, unsalted vegetables	−0.002	0.070*	−0.017
Cruciferous vegetables	−0.062*	0.043	0.028
Fruits	0.021	0.017	−0.025
Grains	0.016	−0.038	−0.014

Adjusted for age and total energy intake.
AhRL, aryl hydrocarbon receptor ligand; TCDDeq, 2,3,7,8-tetrachlorodibenzodioxin equivalents; MIS, mitochondria-inhibiting substances; ROS, reactive oxygen species; ATP, adenosine triphosphate.
*$P < 0.05$.

Table 3. Multiple linear regression analysis between surrogate serum biomarkers for endocrine-disrupting chemicals and food consumption

Food consumption (g/day)	AhRL (TCDDeq, pM)			MIS-ROS (%)			MIS-ATP (%)		
	β	SE	*P*-value	β	SE	*P*-value	β	SE	*P*-value
Meat	0.0000***	0.0010	0.9969	0.0070	0.0094	0.4561	0.0034	0.0077	0.6564
Fish	0.0035	0.0015	0.0166	0.0065	0.0131	0.6194	0.0154	0.0108	0.1547
Non-starchy, unsalted vegetables[1)]	0.0008	0.0005	0.1436	0.0090	0.0047	0.0565	−0.0066	0.0039	0.0935
Cruciferous vegetables	−0.0007	0.0003	0.0488	0.0044	0.0031	0.1486	0.0051	0.0025	0.0420
Other vegetables[2)]	−0.0012	0.0010	0.2164	−0.0078	0.0088	0.3717	−0.0140	0.0072	0.0528
Fruits	0.0006	0.0003	0.0663	0.0018	0.0030	0.5519	−0.0034	0.0025	0.1638
Grains	0.0004	0.0004	0.3363	−0.0013	0.0037	0.7214	−0.0015	0.0030	0.6209
Adjusted R^2		0.1973			0.0928			0.0875	

Adjusted for age, sex, education, body mass index, fasting blood glucose, triglycerides, alcohol consumption, and smoking.
[1)]Some cruciferous vegetables were excluded from the linear regression analysis.
[2)]Other vegetables included starchy vegetables and salted vegetables, which were not prepared with cruciferous vegetables.
AhRL, aryl hydrocarbon receptor ligand; TCDDeq, 2,3,7,8-tetrachlorodibenzodioxin equivalents; MIS, mitochondria-inhibiting substances; ATP, adenosine triphosphate; ROS, reactive oxygen species.
***$P < 0.0001$ for all models.

(r = −0.062, $P < 0.05$), and the intake of vegetables (r = 0.054) and non-starchy, unsalted vegetables (r = 0.070) was positively associated with ROS (**Table 2**). In a multiple linear regression model (**Table 3**), the AhRL level was positively associated with fish intake and negatively associated with cruciferous vegetable intake (adjusted R^2 = 0.1973). The MIS-ATP level was positively associated with cruciferous vegetable intake (adjusted R^2 = 0.0875), whereas no significant association was found between food consumption and the MIS-ROS level.

Association between food consumption and high AhRL and low MIS-ATP

Table 4 shows the multivariable-adjusted ORs and 95% CIs of high AhRL and low MIS-ATP according to the tertiles of food consumption. A higher intake of fish was associated with an increased risk of high AhRL (highest tertile: OR, 1.49; 95% CI, 1.08–2.06; *P* for trend= 0.0305). In the second tertile, the intake of cruciferous vegetables had a 27% decreased risk of high AhRL compared to the lowest tertile (OR, 0.73; 95% CI, 0.54–0.97), although no significant linear trend was observed. On the other hand, food consumption was not significantly associated with low MIS-ATP.

In a stratified analysis by sex and obesity status, the significant associations between fish and cruciferous vegetable intake and high AhRL were attenuated (**Table 5**). However, the intake of meat had an increased OR of high AhRL (OR, 1.56; 95% CI, 1.02–2.38) in the normal weight group of the second tertile. Meanwhile, the intake of non-starchy, unsalted vegetables had a decreased OR of high AhRL (OR, 0.61; 95% CI, 0.40–0.92), compared to the lowest tertile.

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Table 4. Odds ratios and 95% confidence intervals of high AhRL and low MIS-ATP according to the food consumption

Food consumption	No.	Median (g/day)	High AhRL	Low MIS-ATP
Meat				
Tertile 1	487	7.5	1.00	1.00
Tertile 2	490	26.4	1.21 (0.90–1.62)	1.04 (0.79–1.36)
Tertile 3	489	75.1	0.99 (0.71–1.38)	1.15 (0.84–1.56)
P for trend			0.6518	0.3641
Fish				
Tertile 1	488	5.3	1.00	1.00
Tertile 2	489	16.0	1.34 (1.00–1.79)	1.13 (0.87–1.48)
Tertile 3	489	41.4	1.49 (1.08–2.06)	1.26 (0.93–1.69)
P for trend			0.0305	0.1505
Non-starchy, unsalted vegetables				
Tertile 1	488	33.7	1.00	1.00
Tertile 2	489	88.6	0.92 (0.69–1.23)	1.07 (0.82–1.40)
Tertile 3	489	190.0	0.83 (0.61–1.15)	1.07 (0.80–1.42)
P for trend			0.2636	0.7062
Cruciferous vegetables				
Tertile 1	488	55.5	1.00	1.00
Tertile 2	489	159.0	0.73 (0.54–0.97)	0.96 (0.74–1.25)
Tertile 3	489	310.7	0.87 (0.65–1.17)	1.01 (0.77–1.33)
P for trend			0.4964	0.8913
Fruits				
Tertile 1	488	19.0	1.00	1.00
Tertile 2	489	69.7	1.09 (0.82–1.46)	1.06 (0.81–1.38)
Tertile 3	489	208.1	1.02 (0.75–1.39)	1.07 (0.81–1.42)
P for trend			0.9540	0.6935

Adjusted for age, sex, education, body mass index, fasting blood glucose, triglycerides, alcohol consumption, smoking, and total energy intake. *P* for trend was calculated using the median value of each tertile.
AhRL, aryl hydrocarbon receptor ligand; MIS, mitochondria-inhibiting substances; ATP, adenosine triphosphate.

Table 5. Odds ratios and 95% confidence intervals of high AhRL according to food consumption stratified by sex and obesity status

Food consumption	Sex		Obese status	
	Male (n = 656)	Female (n = 810)	Normal (n = 766)	Obese (n = 542)
Meat				
Tertile 1	1.00	1.00	1.00	1.00
Tertile 2	1.02 (0.66–1.58)	1.01 (0.68–1.50)	1.56 (1.02–2.38)	0.91 (0.57–1.46)
Tertile 3	1.30 (0.80–2.11)	0.92 (0.59–1.43)	0.90 (0.55–1.46)	1.02 (0.60–1.75)
Fish				
Tertile 1				
Tertile 2	1.27 (0.82–1.97)	1.45 (0.97–2.15)	1.42 (0.93–2.15)	1.43 (0.89–2.31)
Tertile 3	1.47 (0.92–2.37)	1.54 (0.98–2.42)	1.37 (0.87–2.16)	1.65 (0.97–2.80)
Non-starchy, unsalted vegetables				
Tertile 1	1.00	1.00	1.00	1.00
Tertile 2	0.93 (0.61–1.43)	0.90 (0.61–1.33)	0.61 (0.40–0.92)	1.58 (0.99–2.51)
Tertile 3	0.92 (0.58–1.46)	0.85 (0.55–1.32)	0.72 (0.46–1.13)	0.91 (0.54–1.51)
Cruciferous vegetables				
Tertile 1	1.00	1.00	1.00	1.00
Tertile 2	0.80 (0.52–1.24)	0.68 (0.46–1.01)	0.77 (0.51–1.18)	0.73 (0.46–1.16)
Tertile 3	0.96 (0.62–1.49)	0.80 (0.53–1.18)	0.75 (0.49–1.16)	1.08 (0.68–1.72)
Fruits				
Tertile 1	1.00	1.00	1.00	1.00
Tertile 2	0.91 (0.60–1.40)	0.99 (0.67–1.46)	1.22 (0.81–1.83)	1.15 (0.72–1.83)
Tertile 3	0.85 (0.55–1.33)	1.03 (0.68–1.56)	0.86 (0.54–1.36)	1.54 (0.95–2.51)

Adjusted for age, sex (for obesity-stratified analysis), body mass index (for sex-stratified analysis), education, fasting blood glucose, triglycerides, alcohol consumption, smoking, and total energy intake. Obese was defined as body mass index ≥ 25 kg/m^2 for the participants who maintained the same weight status from 2005 to 2008 (n = 1,308).
AhRL, aryl hydrocarbon receptor ligand.

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DISCUSSION

This study found that several foods were differentially associated with serum AhRL. After adjusting for confounding variables, fish intake was positively associated with AhRL, while cruciferous vegetable intake was negatively associated with AhRL. Furthermore, the cruciferous vegetable intake was positively associated with the MIS-ATP level, although no significant association was found with low MIS-ATP levels using multiple logistic regression analysis. Meat and fruit intake were not significantly associated with these serum EDC biomarkers. These findings suggest that the serum levels of AhRL and MIS-ATP might be useful in the evaluation of exposure to EDCs in foods.

However, the concentration of serum EDCs may not accurately represent the level of exposure to EDCs, and an assessment of the level of dietary exposure to EDCs is challenging [10,11]. The present study used serum AhRL, MIS-ROS, and MIS-ATP as surrogate biomarkers for EDCs. Most EDCs, including persistent organic pollutants (POPs), increase AhR bioactivity and could lead to the mitochondrial dysfunction of cells in which mitochondrial ROS production increases and ATP production decreases [10,18]. AhR has also been reported to mediate the toxic effects of heavy metals such as mercury and cadmium [19-21]. Therefore, our study findings derived from an epidemiologic study may be a significant addition to previous findings wherein it was shown that AhR activity can be regulated by dietary components [13,15,22].

The study participants with the highest fish intake had a 49% increased risk of high AhRL compared to those with the lowest fish intake, suggesting that high fish consumption may increase the risk of exposure to EDCs. Fish and shellfish have been recommended as good nutritional sources of protein and essential fatty acids, including eicosapentaenoic acid and docosahexaenoic acid [23-25]. However, they are also major sources of heavy metals such as mercury and POPs, including organochlorine pesticides, polychlorinated biphenyls, and polybrominated diphenyl ethers [11,26,27,28]. EDCs, including POPs and mercury, may be present in high concentrations in the food chain, leading to high EDC concentrations in predators and large fish [29]. Hence, in the United States (US), the Food and Drug Administration and Environmental Protection Agency have provided a chart to help people choose which fish to eat and avoid based on mercury levels [27]. Although a few studies have measured EDCs in fish from several areas in the US, Korea, and Pakistan [28,30,31], the EDC contents in various fish have not been well investigated, compared to mercury. Due to the limited fish items in the FFQ, evaluating associations with specific types of fish was difficult. Further prospective studies in a large Korean population are needed to examine the consumption of various types of fish and their exposure to EDCs based on the biomarker levels.

Asian populations tend to consume more fish than Western populations [32,33]. Recently, Jeon *et al.* [34] measured the serum concentrations of major POPs in Korean adults who participated in the Korean National Environmental Health Survey Cycle 3 (2015–2017). The levels of most POPs were high among participants living in coastal areas and with frequent fish consumption, which is consistent with our findings. Considering the health benefits of fish, a systematic risk-benefit analysis is required to establish fish consumption guidelines for Koreans.

Unlike fish, cruciferous vegetables such as cabbage, radish, and broccoli showed a negative association with serum AhRL, which is consistent with previous studies [13-15]. Cruciferous vegetables are rich in indoles, which are a significant class of dietary AhR ligands, and

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include indole-3-carbinole, indole-3-acetonitrile, 3,3′-diindolylmethane, and indolo(3,4) bicarbazole [12,20]. In the present study, a linear decreasing trend was not observed in the association between consumption of cruciferous vegetables and the risk of high AhRL. Although this finding cannot be completely explained in this study, the limited cruciferous vegetable items on the list and the inclusion of salted cruciferous vegetables as important parts of the Korean traditional diet (*e.g.*, kimchi) might be partly related to the attenuation of the negative association. Nonetheless, this finding indicates that a high intake of cruciferous vegetables may confer protective effects against exposure to EDCs.

In this study, meat and fruit consumption was not significantly associated with serum EDC biomarkers. EDCs can accumulate in the fatty tissues of living organisms, and high-fat animal foods are easily contaminated by EDCs [11,35]. However, fish usually have higher EDC concentrations compared to other food groups [11,36], and a previous study reported that meat is not the major food group responsible for exposure to environmental organic pollutants [37]. In addition, the fact that the study participants were middle-aged and generally consumed high levels of carbohydrates from rice and other grains rather than meat [38] might also be related to the nonsignificant relationship observed between meat and EDC biomarkers.

The flavonoids in fruits and vegetables are known to have inhibitory effects on AhR activity [15,22]. However, fruits can be contaminated by EDCs during production and processing. Thus, the possibility of masking the adverse effects of EDC exposure through the beneficial effects of flavonoids cannot be ruled out [12]. Further studies are needed to elucidate the underlying mechanisms between flavonoids and EDCs in humans.

This study had several limitations. First, because the SQFFQ was not conducted in every follow-up survey, there was a time interval between the times the SQFFQ survey and serum collection were conducted. However, the SQFFQ is known to be a useful tool for assessing long-term regular food intake. Second, due to the limited number of items on the SQFFQ, specific and accurate categorization of food groups was difficult. For example, few large-sized fish items such as tuna were included, and only canned tuna was on the list. In addition, several cruciferous vegetables were combined with other vegetables. Third, the relatively small sample size may attenuate the statistical significance of the association between food consumption and EDC biomarkers. Lastly, although the total energy intake was adjusted in the model as a confounding variable, potential bias related to the association between food intake and the exposure level of EDCs cannot be ruled out. Despite these limitations, to the best of our knowledge, this is the first study to investigate the relationship between food consumption and EDC biomarkers in the adult Korean population.

In conclusion, serum AhRL and MIS-ATP, which are EDC biomarkers, were associated with fish and cruciferous vegetable intake in middle-aged Korean adults. A high fish intake was associated with a higher AhRL, whereas a high cruciferous vegetable intake was associated with a lower AhRL and a higher MIS-ATP. These findings suggest that consumption of different types of foods might be differentially associated with EDC exposure, and further prospective studies in the Korean population are required to investigate the role of specific foods and other dietary components in exposure to environmental pollutants and to develop dietary recommendations to reduce EDC exposure.

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