Original Article

Atopic dermatitis causes lipid accumulation in the liver of NC/Nga mouse

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Various factors have been reported to influence lipid metabolism and cause metabolic syndrome. However, the influence of allergy on the liver that plays important role of lipid metabolism has not been clarified. The aim of this study was to examine the influence of allergy on lipid metabolism of liver. A model of atopic dermatitis was developed in the NC/Nga mouse using picryl chloride to induce allergy. Lipid metabolism parameters were measured and the mechanism of changes in these parameters was examined using DNA microarray analysis and quantitative reverse transcriptase PCR. Triacylglycerol accumulation was promoted in the liver in the mouse atopic dermatitis model despite reductions in food intake, body weight gain, and serum glucose. As this mechanism, it was thought that atopic dermatitis caused the suppression of fatty acid β-oxidation. These results suggest that atopic dermatitis causes lipid accumulation in the liver.

***Key Words*: allergy, DNA microarray, lipid metabolism, liver, NC/Nga**

Various factors have been reported to influence lipid metabolism and cause metabolic syndrome. For instance, total caloric intake is increased by excessive intake of lipids and this leads to development of obesity and metabolic syndrome.[1] Obesity and metabolic syndrome are also referred to as diseases of longevity or civilization, and include diabetes mellitus, hyperlipidemia and arteriosclerosis.[2,3] To overcome these diseases, the research of the lipid metabolism that is related to the appearance of metabolic syndrome is important. However, the influence of allergy on the liver that plays important role of lipid metabolism has not been clarified.

Allergy is caused by an excessive immune reaction to a certain antigen and may have unpleasant long-term symptoms that include itchy and dry skin in atopic dermatitis,[4] sneezing, runny and blocked nose in rhinitis,[5] and tightness and wheezing in the chest in asthma.[6] Various proinflammatory cytokines [tumor necrosis factor (TNF)-α, etc.] are discharged from the mast cell when developing an allergy.[7] These are related to the sideration and the progress of the allergy symptom. These symptoms cause stress and worsen quality of life.[8–10] It is unclear if an influence of allergy on lipid metabolism is related to the appearance of metabolic syndrome though it is known that obesity and metabolic syndrome promote the allergy symptom.[11] In this study, we examined the influence of allergy on lipid metabolism in the liver of NC/Nga mouse model of atopic dermatitis. This mouse develops atopic dermatitis in a normal environment or with sensitization and induction by an antigen such as 2,4,6-trinitrochlorobenzene (picryl chloride: PiCl).[12–14] We compared lipid metabolism in the allergic mouse with that of a non-allergic mouse (control mouse). Parameters for lipid metabolism in serum and liver were evaluated and lipid metabolism-related gene expression in liver was examined using DNA microarray analysis and quantitative reverse transcriptase PCR (qRT-PCR). The results showed that allergy promotes lipid accumulation in the liver.

Materials and Methods

Materials. PiCl was purchased from Tokyo Kasei Chemical Co. Ltd. Tokyo, Japan). PiCl re-crystallized from 100% ethanol was used to prepare the solutions, which were always prepared just before use and kept shielded from light.[12,15]

Animals. All procedures were performed in accordance with the Animal Experiment Guidelines of Tohoku University. The animal protocol was approved by the Animal Use Committee at Tohoku University.[16] Male NC/Nga mice (5 weeks of age) were obtained from Japan SLC (Hamamatsu, Japan). After acclimatization to a commercial diet (MF; Oriental Yeast, Tokyo, Japan) for 7 week, the mice were divided into two groups, in which they were not sensitized (control group) or sensitized and challenged to develop atopic dermatitis (AD group). The mice were housed 6 per cages with free access to commercial diets and distilled water in a temperature- and humidity-controlled room with light cycles of 12 h on and 12 h off.[17,18] The mice were weighed once a week. Food intake was estimated every second day, always at the same time of the day. At the appropriate time point, scratching behavior of mice was observed. Then, the mice were weighed, anesthetized by diethyl ether and sacrificed by decapitation, and the kidney, liver, skin and serum were collected and stored at −80°C until performance of assays. The pieces of skin from dorsal were fixed in 10% formalin.

Sensitization and challenge. Sensitization and challenge were performed as previously described.[12,15] In brief, the furs of the thoracic and abdominal regions under anaesthetized animals were shaved off with a hair clipper 1 day before the sensitization. Using a micropipette, 150 µl of the sensitizing 5% PiCl solution (PiCl dissolved in a solvent consisting of a mixture of four parts ethanol to one part acetone) was applied to the thoracic and abdominal areas, as well as to the soles of the hind paws. The furs of the back regions under anaesthetized animals were shaved off with a hair clipper 1 day before the challenge. Four days after the sensitization, challenge was performed. A micropipette was used to apply 150 µl of PiCl solution (1% PiCl dissolved in corn oil by heating) to the back and ears. The procedure was repeated once a week for up to 9 weeks.

Skin histology analysis. To observe thickening of the epidermis, each mouse skin was fixed in 10% formalin and embedded in paraffin.[14] Vertical sections (5 µm) were cut, mounted on a glass slide, stained with hematoxylin and eosin, and

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observed using a microscope (BZ-8000; Keyence, Osaka, Japan).

Scratching behavior. Scratching behavior was observed at 17–19 o'clock of the examination day as described previously.[12,15] Before behavioral recording, the mice were put into an acrylic box composed of four cells at least for 1 h for acclimation. Thereafter, their behavior was videotaped for 30 min with any experimenter kept out from the observation room. The playing back of the video served for counting the scratching. The scratching of any regions of the body by the hind paws was counted as spontaneous scratching. Mice rapidly scratched several times for about 1 s and a series of these movements was counted as one bout of scratching.

Biochemical analyses in serum and liver. The lipid compositions in the serum and liver were measured as described previously.[18–20] Triacylglycerol (TG) and total cholesterol (TC) levels in serum and liver, and phospholipid (PL), free fatty acid (FFA), and glucose levels in serum were measured using commercial enzyme kits (Wako Pure Chem., Osaka, Japan) according to the manufacturer's protocol. IgE and insulin levels in serum were determined using ELISA kits (Shibayagi, Shibukawa, Japan).[20] PL levels in liver were determined using the method described by Rouser.[21]

mRNA expression analysis. For DNA microarray analysis and qRT-PCR, total RNA was isolated from liver using an RNeasy Mini Kit (Qiagen, Valencia, CA),[22] eluted with 30 µl RNase-free water, and stored at −80°C until use. DNA microarray analysis (GeneSQUARE, Multiplex Assay DNA Microarray Lifestyle Diseases Gene Expression For Mouse) using the total RNA collected in each group was performed by Kurabo Ind. (Osaka, Japan). To quantify the expression level of genes, the mRNA levels for various genes (Table 1) in liver were determined with a 7300 Real-Time PCR System (Applied Biosystems, Foster City, CA). This system allows real-time quantitative detection of PCR products by measuring the increase in fluorescence caused by binding of SYBR green to double-stranded DNA.[17,18] In brief, cDNA was made using a Ready-To-Go T-Primed First-Strand Kit (Amersham Pharmacia Biotech, NJ) from the total RNA in liver. The cDNA was subjected to PCR amplification using SYBR Premix Ex Taq™ (Perfect Real Time) (Takara Bio, Otsu, Japan) and gene-specific primers (Table 1). The PCR conditions were 95°C for 10 s, and then 95°C for 5 s and 60°C for 31 s over 40 cycles for each gene. Melting curve analysis was performed following each reaction to confirm the presence of only a single reaction product. The threshold cycle (CT) represents the PCR cycle at which an increase in reporter fluorescence above a baseline signal can first be detected. The ratio between the Gapdh content in standard samples and test samples was defined as the normalization factor.

Statistical analysis. Results are expressed as means ± SE. Data were analyzed by Student's t test. A difference was considered to be significant at $p<0.05$.

Results

Appearance of skin lesions and histology. The development of allergy symptoms of atopic dermatitis induced by PiCl was evaluated in male NC/Nga mice (Fig. 1). Dorsal skin lesions and hemorrhage were observed in the AD group (Fig. 1 a and b). The hematoxylin & eosin-stained epidermis in the AD group was very thick compared with that in the control group (Fig. 1 c and d). An increase of scratching behavior and serum IgE level was observed in the AD group (Fig. 1 e and f). These results show that allergy symptoms were induced by PiCl in the AD group.

Effects of allergy on growth parameters. The effects of allergy on growth parameters are shown in Table 2. Final body weight, body weight gain, and food intake in the AD group were significantly lower than those in the control group. Liver and kidney weights did not differ significantly between the two groups. These results suggest that allergy decreased food intake and suppressed the growth of NC/Nga mice.

Effects of allergy on lipid metabolism. Lipid metabolism parameters in serum and liver were determined to examine the effects of allergy (Table 3). The liver TG, TC, and PL levels in the AD group were 176%, 108%, and 96% of the respective levels in

Table 1. Nucleotide sequences of gene-specific primers used for qRT-PCR

Genbank ID	Gene Name	Sequences of primers (5' to 3')	
		Forward	Reverse
NM_031884	Abcg5	AGGGCCTCACATCAACAGAG	GCTGACGCTGTAGGACACAT
NM_015729	Acox1	TCCAGACTTCCAACATGAGGA	CTGGGCGTAGGTGCCAATTA
NM_007434	Akt2	ACGTGGTGAATACATCAAGACC	GCTACAGAGAAATTGTTCAGGGG
NM_007527	Bax	TGAAGACAGGGGCCTTTTTG	AATTCGCCGGAGACACTCG
NM_007643	Cd36	ATGGGCTGTGATCGGAACTG	GTCTTCCCAATAAGCATGTCTCC
NM_007669	Cdkn1a	CGAGAACGGTGGAACTTTGAC	CAGGGCTCAGGTAGACCTTG
NM_009949	Cpt2	CCTGCTCGCTCAGGATAAACA	GTGTCTTCAGAAACCGCACTG
NM_007824	Cyp7a1	GGGATTGCTGTGGTAGTGAGC	GGTATGGAATCAACCCGTTGTC
NM_007988	Fas	CCTGGATAGCATTCCGAACCTG	TTCACAGCCTGGGGTCATCTTTGC
NM_008061	G6pc	CGACTCGCTATCTCCAAGTGA	GTTGAACCAGTCTCCGACCA
NM_008062	G6pdx	TGGGTCCACCACTGCCACTTTTG	ATTGGGCTGCACACGGATGACCA
NM_008084	Gapdh	AGGTCGGTGTGAACGGATTTG	TGTAGACCATGTAGTTGAGGTCA
AK079302	Hmgcr	AGCTTGCCCGAATTGTATGTG	TCTGTTGTGAACCATGTGACTTC
NM_017370	Hp	GCTATGTGGAGCACTTGGTTC	CACCCATTGCTTCTCGTCGTT
NM_008341	Igfbp1	ATCAGCCCATCCTGTGGAAC	TGCAGCTAATCTCTCTAGCACTT
NM_133748	Insig2	GGAGTCACCTCGGCCTAAAAA	CAAGTTCAACACTAATGCCAGGA
NM_010700	Ldlr	TGACTCAGACGAACAAGGCTG	ATCTAGGCAATCTCGGTCTCC
NM_013839	Lxrα	CTCAATGCCTGATGTTTCTCCT	TCCAACCCTATCCCTAAAGCAA
NM_010786	Mdm2	TGTCTGTGTCTACCGAGGGTG	TCCAACGGACTTTAACAACTTCA
NM_008615	Me1	GTCGTCAAGGCTATTGTGGTAA	GCCGTGTAAAGGGCCAGTT
NM_011640	p53	GCGTAAACGCTTCGAGATGTT	TTTTTATGGCGGGAAGTAGACTG
NM_011144	Pparα	AGAGCCCCATCTGTCCTCTC	ACTGGTAGTCTGCAAAACCAAA
NM_011480	Srebp1	GGAGACATCGCAAACAAGC	TGAGGTTCCAAAGCAGACTG
AF374267	Srebp2	GCAGCAACGGGACCATTCT	CCCCATGACTAAGTCCTTCAACT

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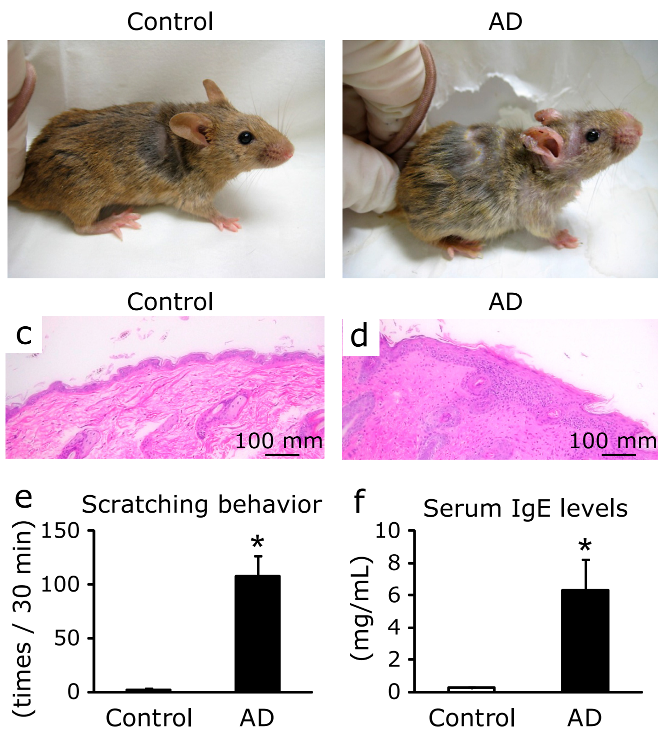

Fig. 1. The appearance of skin lesion on control mice (a) and AD mice (b). Severe dermatitis with hemorrhage, edema, erosion and dryness appears in the ears, neck and dorsal skin were observed in AD mice. Hematoxylin-eosin staining of paraffin-embedded sections (3–5 μm thick) from skin biopsies of control mice (c, $\times$10) and AD mice (d, $\times$10). Note the thickening of the epidermis in D compared with C. The results shown are representative of 6 mice in each group. The scratching behavior (e) and the serum IgE levels (f) on control mice and AD mice. Values are means $\pm$ SE, $n = 6$. *Significantly different at $p<0.05$ from control mice.

Table 2. Effects of allergy on growth parameters in NC/Nga mice

	Control	AD
Body weight (g)		
Initial	26.2 ± 0.5	26.2 ± 0.5
Final	29.9 ± 0.5	28.1 ± 0.4*
Gain	3.99 ± 0.28	1.96 ± 0.27*
Food intake (g/day)	4.51 ± 0.07	4.2 ± 0.07*
Tissue weight (g/100 g body weight)		
Liver	4.32 ± 0.05	4.3 ± 0.01
Kidney	1.51 ± 0.03	1.54 ± 0.04

Values are means $\pm$ SE, $n = 6$. *Significantly different at $p<0.05$ from control mice.

the control group, with TG, TC and PL showing significant changes. These results suggest that allergy influenced lipid metabolism and promoted lipid accumulation in the liver. The serum levels of glucose and TG in the AD group were 83% and 85% of the respective levels in the control group, showed a significant decrease in glucose. There were no significant differences in serum TG, TC, PL, FFA and insulin levels between the two groups. These results suggest that allergy influenced sugar metabolism and reduced the serum glucose level.

Effects of allergy on expression of mRNA for lipid metabolism-related genes. The above results show that substantial changes in lipid metabolism occur with allergy in NC/Nga mice. To examine the mechanism underlying these effects, allergia-related changes in mRNA expression for 334 genes related to lipid and sugar metabolism were examined using DNA microarray analysis of liver samples from NC/Nga mice. Genes with a change in mRNA expression over 1.5 fold are shown in Table 4. Increased mRNA levels with allergy were found for Igfbp1, which is involved in insulin signaling; Cdkn1a, which promotes cell cycle arrest and lipid accumulation; G6pc, which promotes gluconeogenesis; Insig2, which regulates biosynthesis of sterols and is involved in insulin signaling; and Hp, which is involved in host defense in the liver of NC/Nga mice. Decreased mRNA levels were found for Akt2, which are involved in insulin signaling; Acox1 and Pparα, which promotes catabolism of fatty acids; and Cyp7a1, which promotes catabolism of sterols. To confirm these results, the mRNA levels of selected genes were measured by qRT-PCR (Table 4). The mRNA levels of Igfbp1, Cdkn1a, Insig2, Hp, Acox1, Pparα and Cyp7a1 showed changes that were consistent with the results of DNA microarray analysis.

Table 3. Effects of allergy on lipid and sugar metabolism parameters in serum and liver of NC/Nga mice

	Control	AD
Serum		
TG (mg/dL)	112.4 ± 5.9	95.6 ± 5.4
TC (mg/dL)	71.2 ± 3.7	75.3 ± 4.6
PL (mg/dL)	140.4 ± 4	145.2 ± 8.5
FFA (mEq/L)	1.3 ± 0.14	1.16 ± 0.11
Glucose (mg/dL)	187.5 ± 5	154.9 ± 10.3*
Insulin (ng/mL)	0.204 ± 0.018	0.216 ± 0.031
Liver		
TG (mg/g)	4.57 ± 0.3	8.05 ± 0.88*
TC (mg/g)	3.09 ± 0.04	3.32 ± 0.07*
PL (mg/g)	35.9 ± 0.24	34.1 ± 0.32*

Values are means $\pm$ SE, $n = 6$. *Significantly different at $p<0.05$ from control mice.

The mRNA expression levels for various genes related to lipid metabolism were also examined (Table 5). Expression of mRNA for p53, which induces Cdkn1a, did not change significantly, but the level of mRNA for Bax, which is induced by p53, increased and that for Mdm2, which promotes degradation of p53, decreased with allergy. These results suggest that activation of p53 pathway induces Cdkn1a and promotes lipid accumulation in the liver of NC/Nga mice under allergy. Among fatty acid catabolism-related genes, the levels of mRNA for Cpt2, which promote fatty acid β-oxidation, were decreased by allergy. These results suggest that allergy causes cell cycle arrest, decreases fatty acid catabolism, and promotes lipid accumulation in the liver of NC/Nga mice. In contrast, there were no significant differences in mRNA levels for Srebp1, Fas, Me1, G6pdx, Ldlr, and Cd36, which are also involved in lipid metabolism. These results suggest that allergy doesn't influence the fatty acid synthesis.

Among the cholesterol metabolism-related genes, there were no significant changes in mRNA levels for Hmgcr, Srebp2, Abcg5, and Lxrα, which are also involved in cholesterol metabolism. These results suggest that allergy decreases expression of mRNA for Cyp7a1, which promotes cholesterol catabolism, thus causing cholesterol accumulation in the liver of NC/Nga mice.

Discussion

In this study, we induced allergy in NC/Nga mice through development of PiCl-induced atopic dermatitis (Fig. 1).[12–15] Food intake, body weight gain, and serum glucose were reduced by allergy (Tables 2 and 3), but TG accumulation was promoted in the liver (Table 3). The mechanism of this unusual phenomenon

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Table 4. The change in liver mRNA expression of lipid and sugar metabolism-related genes that were increased or decreased by allergy measured using DNA microarray and qRT-PCR assay

Gene Name	DNA microarray	qRT-PCR		Gene function
	Fold vs control	Control	AD	
Igfbp1	4.17	1 ± 0.2	4.2 ± 1.2*	insulin signal
Cdkn1a	2.71	1 ± 0.2	2.7 ± 0.7*	cell cycle arrest
G6pc	1.95	1 ± 0	1.4 ± 0.3	gluconeogenesis
Insig2	1.85	1 ± 0.1	2 ± 0.3*	sterol synthesis regulation
Hp	1.54	1 ± 0.1	2.2 ± 0.3*	immune/defense response
Akt2	0.37	1 ± 0.1	1.1 ± 0.1	insulin signal
Acox1	0.45	1 ± 0.1	0.7 ± 0.1*	fatty acid β-oxidation
Pparα	0.5	1 ± 0.1	0.5 ± 0.1*	lipid metabolism
Cyp7a1	0.67	1 ± 0.1	0.6 ± 0.1*	sterol metabolism

Values are expressed as a ratio of control and presented as means ± SE, $n = 6$. *Significantly different at $p<0.05$ from control mice.

Table 5. Effects of allergy on mRNA expression of lipid metabolism-related genes of NC/Nga mice

Gene name	Control	AD	Gene function
p53	1 ± 0.1	0.9 ± 0	apoptosis, cell cycle arrest
Mdm2	1 ± 0.1	0.6 ± 0.0*	proteasome, degradation of p53
Bax	1 ± 0	1.4 ± 0.1*	apoptosis, target of p53
Srebp1	1 ± 0.1	1.5 ± 0.2	fatty acid biosynthesis
Fas	1 ± 0.1	0.9 ± 0.1	
Me1	1 ± 0.1	1 ± 0.2	
G6pdx	1 ± 0.1	1.4 ± 0.2	
Cpt2	1 ± 0.1	0.6 ± 0.1*	fatty acid β-oxidation
Ldlr	1 ± 0	1 ± 0.1	lipoprotein uptake
Cd36	1 ± 0.2	1.6 ± 0.3	fatty acid uptake
Hmgcr	1 ± 0.1	0.9 ± 0.1	cholesterol biosynthesis
Srebp2	1 ± 0.1	1.1 ± 0.1	
Lxrα	1 ± 0.1	1.3 ± 0.1	cholesterol metabolism
Abcg5	1 ± 0.1	1.1 ± 0	cholesterol transporter

The expressions were measured using qRT-PCR assay. Values are expressed as a ratio of control and presented as means ± SE, $n = 6$. *Significantly different at $p<0.05$ from control mice.

was examined in detail using DNA microarray analysis and qRT-PCR. The results suggested that the mechanism involved cell cycle arrest induced by upregulation of Cdkn1a and a decrease of fatty acid β-oxdation induced by downregulation of PPARα, Acox1 and Cpt2 (Tables 4 and 5). These results are the first to show that allergy has a major influence on lipid metabolism. Therefore, allergy not only gave the unpleasant symptom but also disturbed the lipid metabolism, and the possibility of leading to fatty liver was suggested.

Cdkn1a induced by p53 causes cell cycle arrest,[23] which then promotes lipid accumulation in cells. Expression of mRNA for Cdkn1a and activation of p53 is elevated in mice with fatty liver[24] and Bax is induced by activation of p53 and Mdm2 inactivates p53.[25] Although the level of mRNA for p53 was unchanged by allergy, the upregulation of p53 target genes such as Cdkn1a and Bax and downregulation of Mdm2, which degrades p53, suggest that p53 was activated. Bax induces apoptosis[25] and Cdkn1a and Igfbp1 block this induction of apoptosis.[26,27] Since mRNA levels for Bax, Cdkn1a, and Igfbp1 were all increased by allergy (Tables 4 and 5), it is possible that apoptosis induction by Bax was blocked by Cdkn1a and Igfbp1.

Allergy also reduced the mRNA levels for PPARα, Acox1 and Cpt2 and suppressed fatty acid β-oxidation. Mice deficient in PPARα Acox1 and Cpt2 develop hepatic steatosis[28] and in our study the mRNA levels for PPARα Acox1 and Cpt2 were significantly lower in the AD group (Table 5). In contrast, allergy didn't influence the fatty acid synthesis (Table 5). Overall, our results are consistent with changes in gene expression that induce TG accumulation in the liver.

Allergy also increased the cholesterol level in the liver (Table 3). Cyp7a1 promotes cholesterol catabolism in the liver[29] and therefore the increase in cholesterol may have been caused by downregulation of Cyp7a1 (Table 4).

The serum glucose level was also decreased by allergy (Table 3). Two mechanisms may underlie this phenomenon. First, a decrease in food intake may have been caused by allergy (Table 2), since it has been shown that stress decreases food intake.[30,31] Second, the changes in lipid metabolism may have influenced sugar metabolism, since reduced glycogen storage in liver causes increased fatty acid β-oxidation and gluconeogenesis to maintain energy homeostasis.[32,33] The serum glucose level is maintained by gluconeogenesis, but is suppressed as β-oxidation is suppressed.[34,35] A decrease in serum glucose also occurs in PPARα knockout mice during fasting.[32] We found that fatty acid β-oxidation was suppressed in the AD group (Table 5) and this may be related to the low serum glucose level. A decrease in serum glucose is normally accompanied by a decrease in serum insulin,[36] but we did not find a significant change in serum insulin (Table 3). Expression of mRNA for Igfbp1 and Insig2 are suppressed by insulin,[37,38] but the mRNA levels for these genes

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were increased in the AD group (Table 4). Since insulin was unable to suppress Igfbp1 and Insig2 expression, insulin resistance may be caused by allergy in the liver.

Allergic disease such as atopic dermatitis, rhinitis, and asthma cause considerable stress.[39] Stress has various influences on regulation of biological processes, but the detailed mechanisms are unclear. Stress not only causes mental defects[40] but influences pathological conditions such as metabolic syndrome,[41] cardiovascular diseases,[42] cancer,[43] eating disorder,[44] and asthma.[39] Thus, reduction of stress is important for improvement of quality of life in modern society. Various types of stress have been reported to influence lipid and sugar metabolism and cause metabolic syndrome.[41,45] Hence, the stress that allergy induced might have caused the phenomenon of this study though the influence of allergia-induced stress on lipid metabolism has not been known. In addition, we think as follows about the reason why fatty acid β-oxidation system is inhibited by atopic dermatitis. TNF-α that is the proinflammatory cytokine is secreted from the mast cell when becoming atopic dermatitis.[7] TNF-α reaches the liver through the blood vessel, activates p53 and Cdkn1a in cells, and causes the apoptosis and the cell cycle arrest.[46,47] The oxidative stress in the cell rises when the apoptosis and the cell cycle arrest are induced.[46] And, the oxidative stress inhibits fatty acid β-oxidation system of the liver.[48,49] Therefore, it was thought that atopic dermatitis inhibited fatty acid β-oxidation.

In this study, we considered these phenomena only by the mRNA level. In our past research, mRNA level of fatty acid β-oxidation system enzyme showed the tendency to look like the enzymatic activity well.[49] In this study, it was thought that not only mRNA level of β-oxidation system enzyme but also the enzymatic activity decreases also. However, it will be necessary to confirm these in the future because the enzymatic activity is not measured.

In this study, we found that allergy disrupts lipid and sugar metabolism in the liver. These changes can lead to metabolic syndrome, which emphasizes the importance of reduction of allergy for improvement of quality of life. Therefore, further studies of the effects of allergy are needed to address this problem.

Acknowledgment

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Abbreviations

Abcg5	ATP-binding cassette, subfamily G, member 5
Acox1	acyl-Coenzyme A oxidase 1, palmitoyl
AD	atopic dermatitis
Akt2	thymoma viral proto-oncogene 2
Bax	Bcl2-associated X protein
Cd36	CD36 antigen
Cdkn1a	cyclin-dependent kinase inhibitor 1A
Cpt2	carnitine palmitoyltransferase 2
Cyp7a1	cytochrome P450, family 7, subfamily a, polypeptide 1
Fas	fatty acid synthase
FFA	free fatty acid
G6pc	glucose-6-phosphatase, catalytic
G6pdx	glucose-6-phosphate dehydrogenase X-linked
Gapdh	glyceraldehyde-3-phosphate dehydrogenase
Hmgcr	3-hydroxy-3-methylglutaryl-Coenzyme A reductase
Hp	haptoglobin
Igfbp1	insulin-like growth factor binding protein 1
Insig2	insulin induced gene 2
Ldlr	low density lipoprotein receptor
Lxrα	nuclear receptor subfamily 1, group H, member 3
Mdm2	transformed mouse 3T3 cell double minute 2
Me1	malic enzyme, supernatant
p53	transformation related protein 53
PiCl	picryl chloride
PL	phospholipid
Pparα	peroxisome proliferator activated receptor alpha
qRT-PCR	quantitative reverse transcriptase PCR
Srebp1	sterol regulatory element binding factor 1
Srebp2	sterol regulatory element binding protein 2
TC	total cholesterol
TG	triacylglycerol
TNF	tumor necrosis factor-α

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