Serum Vaspin Concentrations in Human Obesity and Type 2 Diabetes

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OBJECTIVE—Vaspin was identified as an adipokine with insulin-sensitizing effects, which is predominantly secreted from visceral adipose tissue in a rat model of type 2 diabetes. We have recently shown that vaspin mRNA expression in adipose tissue is related to parameters of obesity and glucose metabolism. However, the regulation of vaspin serum concentrations in human obesity and type 2 diabetes is unknown.

RESEARCH DESIGN AND METHODS—For the measurement of vaspin serum concentrations, we developed an enzyme-linked immunosorbent assay (ELISA). Using this ELISA, we assessed circulating vaspin in a cross-sectional study of 187 subjects with a wide range of obesity, body fat distribution, insulin sensitivity, and glucose tolerance and in 60 individuals with normal glucose tolerance (NGT), impaired glucose tolerance (IGT), or type 2 diabetes before and after a 4-week physical training program.

RESULTS—Vaspin serum concentrations were significantly higher in female compared with male subjects. There was no difference in circulating vaspin between individuals with NGT and type 2 diabetes. In the normal glucose-tolerant group, circulating vaspin significantly correlated with BMI and insulin sensitivity. Moreover, physical training for 4 weeks resulted in significantly increased circulating vaspin levels.

CONCLUSIONS—We found a sexual dimorphism in circulating vaspin. Elevated vaspin serum concentrations are associated with obesity and impaired insulin sensitivity, whereas type 2 diabetes seems to abrogate the correlation between increased circulating vaspin, higher body weight, and decreased insulin sensitivity. Low circulating vaspin correlates with a high fitness level, whereas physical training in untrained individuals causes increased vaspin serum concentrations. ***Diabetes*** **57:372–377, 2008**

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ELISA, enzyme-linked immunosorbent assay; HEK, human embryonic kidney; IGT, impaired glucose tolerance; NGT, normal glucose tolerance; OGTT, oral glucose tolerance test; PAI-1, plasminogen activator inhibitor type 1.

Recently, visceral adipose tissue–derived serpin (vaspin) was identified as a member of serine protease inhibitor family, which was expressed in visceral adipose tissue of Otsuka Long-Evans Tokushima fatty (OLETF) rats at the age when obesity and insulin plasma concentrations reach a peak (1). Vaspin expression was shown to decrease with worsening of diabetes and body weight loss, whereas vaspin serum levels could be normalized by insulin or pioglitazone treatment. Administration of vaspin to obese mice improved glucose tolerance, insulin sensitivity, and altered gene expression of candidate genes for insulin resistance (1). We have recently demonstrated that human vaspin mRNA expression in adipose tissue of obese subjects is fat depot specific but not detectable in lean normal glucose-tolerant individuals (2). We postulated that induction of vaspin mRNA expression in human adipose tissue could represent a compensatory mechanism associated with obesity, severe insulin resistance, and type 2 diabetes (2,3). Taken together, these studies demonstrate that the adipokine vaspin is a novel candidate to link human obesity to its related metabolic alterations.

Until now, no data are available for the regulation of human circulating vaspin. It is unknown whether circulating vaspin is related to measures of obesity, insulin sensitivity, and glucose metabolism. We therefore developed an enzyme-linked immumnosorbent assay (ELISA) for the measurement of human vaspin serum concentrations. To this end, a human vaspin–specific monoclonal antibody was generated, which was then utilized to create a sandwich ELISA. Using this new vaspin ELISA, we sought to determine circulating vaspin in individuals with a wide range of obesity, body fat distribution, insulin sensitivity, and glucose tolerance. In addition, we assessed vaspin serum concentration before and after an intensive 4-week physical training program to test whether vaspin levels are regulated in response to training-associated improvements in body weight and insulin sensitivity.

RESEARCH DESIGN AND METHODS

Cross-sectional study. A total of 187 Caucasian men (n = 89) and women (n = 98) were selected among ~700 subjects recruited in the context of a study on insulin resistance at the Department of Medicine, University of Leipzig, to represent a wide range of obesity, insulin sensitivity, and glucose tolerance. The age ranged from 17 to 79 years and BMI from 19.6 to 61.5 kg/m^2. Subjects were subsequently divided into groups of normal glucose tolerance (NGT), impaired glucose tolerance (IGT), and type 2 diabetes on the basis of a 75-g oral glucose tolerance test (OGTT) according to American Diabetes Association criteria (4). Subjects with NGT were defined by a fasting plasma glucose <6.0 mmol/l and a 120-min plasma glucose <7.8 mmol/l. Subjects with IGT were defined by a fasting plasma glucose <6.0mmol/l and a 120-min plasma glucose >7.8 and <11.1 mmol/l. Subjects with type 2 diabetes were

TABLE 1
Anthropometric and metabolic characteristics of the study groups

	Male subjects (n = 89)		Female subjects (n = 98)	
	NGT	Type 2 diabetes	NGT	Type 2 diabetes
n	36	53	18	80
Age (years)	39 ± 19*†	62 ± 7	56 ± 16*	62 ± 8.4
BMI (kg/m^2)	24.2 ± 5.0*†	35 ± 6.1	28.0 ± 7.3*	34.2 ± 6.3
Body fat (%)	22.2 ± 6.0*†	31.4 ± 5.2†	30.1 ± 8.2*	40.3 ± 6.1
A1C (%)	5.7 ± 1.1*	6.6 ± 1.0	5.6 ± 1.6*	6.5 ± 1.0
Fasting blood glucose (mmol/l)	5.6 ± 1.1*	7.4 ± 2.1	5.6 ± 1.2*	7.2 ± 2.0
Free fatty acids (mmol/l)	0.36 ± 0.11*	0.55 ± 0.25	0.38 ± 0.20*	0.53 ± 0.23
Total cholesterol (mmol/l)	4.4 ± 0.8*†	5.0 ± 1.0†	5.2 ± 1.2*	5.9 ± 1.0
HDL cholesterol (mmol/l)	1.3 ± 0.3†	1.1 ± 0.2†	1.6 ± 0.5	1.4 ± 0.3
LDL cholesterol (mmol/l)	2.7 ± 0.7*†	3.4 ± 1.0†	3.0 ± 0.6*	3.8 ± 0.9

Data are means ± SD. *$P < 0.05$ for patients with type 2 diabetes vs. normal glucose-tolerant individuals. †$P < 0.05$ for difference between male and female subjects within the normal glucose-tolerant or type 2 diabetic group.

defined by a fasting plasma glucose >7.0 mmol/l and/or a 120-min OGTT glucose >11.1 mmol/l. Subjects with IGT (n = 20) were included into the interventional study, whereas only individuals with NGT and type 2 diabetes were included into the cross-sectional study. All subjects fulfilled the following inclusion criteria: *1*) absence of any acute or chronic inflammatory disease as determined by a leukocyte count >7,000 Gpt/l, C-reactive protein > 5.0 mg/dl or clinical signs of infection, *2*) undetectable antibodies against glutamic acid decarboxylase, *3*) no medical history of hypertension (i.e., systolic blood pressure was <140 mmHg and diastolic blood pressure was <85 mmHg, *4*) no clinical evidence of either cardiovascular or peripheral artery disease, *5*) no thyroid dysfunction, *6*) no alcohol or drug abuse, and *7*) no pregnancy. The study was approved by the ethics committee of the University of Leipzig. All subjects gave written informed consent before taking part in the study.

Interventional study. A total of 60 subjects with NGT (n = 20; 9 male and 11 female subjects), IGT (n = 20; 9 male and 11 female subjects), and type 2 diabetes (n = 20; 11 male and 9 female subjects) were enrolled in 60 min of supervised physical training sessions 3 days per week as described previously (5). In brief, each training session included 20 min of biking or running, 20 min of swimming, and 20 min of warming-up/cooling-down periods. All subjects completed a graded bicycle ergometer test to volitional exhaustion and had maximal oxygen uptake measured with an automated open-circuit gas analysis system at baseline and after 4 weeks of training. The highest oxygen uptake per min reached was defined as the maximal oxygen uptake (Vo_{2max}), and subjects subsequently trained at their individual submaximal heart rate defined as 70–80% of the individual maximal heart rate during the bicycle ergometer test. At baseline and after 4 weeks of training (48 h after the last training session), blood samples were obtained in the fasting state and measurements of anthropometric parameters were performed.

Assays, measures of body fat content, and OGTT. All baseline blood samples were collected between 8 and 10 A.M., after an overnight fast. Plasma insulin was measured with an enzyme immunometric assay for the IMMULITE automated analyzer (Diagnostic Products, Los Angeles, CA). BMI was calculated as weight in kilorgams divided by square of height in meters. Waist and hip circumferences were measured and waist-to-hip ratio was calculated. Percentage body fat was measured by dual-energy X-ray absorptiometry. Three days before the OGTT, patients documented a high-carbohydrate diet in diet protocols. The OGTT was performed after an overnight fast with 75 g standardized glucose solution (Glucodex Solution; Merieux, Montreal, Canada). Venous blood samples were taken at 0, 60, and 120 min for measurements of plasma glucose concentrations. Insulin sensitivity was assessed with the euglycemic-hyperinsulinemic clamp method (6,7).

Vaspin ELISA development and measurement of vaspin serum concentrations. The gene-encoding human vaspin was amplified from the human visceral fat cDNA library by PCR. While the human embryonic kidney (HEK) 293 cell–expressed vaspin was used for recombinant human vaspin, standard *E. coli*–expressed vaspin was used as an immunogen for generating human vaspin-specific monoclonal and polyclonal Abs. For making recombinant vaspin proteins in HEK293 cells and *E. coli*, the portion of the gene-encompassing presumed mature polypeptides, Leu^{21} through Lys^{414}, was amplified and digested with appropriate restriction enzymes and then cloned into both pAGNF (AdipoGen, Seoul, Korea) and pET21a (Novagen, Madison, WI). pAGNF is an in-house eukaryotic vector whose expression is driven by the cytomegalovirus early promoter and secretion is facilitated by the plasminogen activator inhibitor type I (PAI-1) leader peptide. A FLAG tag is incorporated at the mature human vaspin peptide. The proteins, FLAG- and His-tagged forms, were purified through anti-FLAG and Ni- Sepharose column, respectively. Endotoxin was removed through two–consecutive column chromatography using Detoxigel (Pierce, Rockford, IL). Polyclonal and monoclonal Abs were produced by immunizing rabbits and BALB/c mice, respectively, with recombinant His-tagged human Vaspin according to general protocols. Corresponding immunoglobulin fractions were prepared from serum and ascites. FLAG-tagged vaspin was used for ELISA standard. A DNA sequence encoding mature peptide of human vaspin (NP_776249, amino acid Leu^{21} through Lys^{414}) was tagged with FLAG(DYKDDDDK) at the NH_2-terminus. This recombinant protein was used for formulating standard proteins at a variety of dilutions (see online appendix Tables [available at http://dx.doi.org/10.2337/db07-1045]). A sandwich ELISA format was designed with the use of a pair of monoclonal and polyclonal Abs. A total of 100 μl of the human serum in 1:5 dilutions was applied to each well, which had been coated by 5 μg/ml of a human vaspin–specific monoclonal Ab and was incubated at 37°C for 1 h followed by washing three times with PBS with 0.05% Tween-20. A total of 100 μl of human vaspin polyclonal antibody at 5 mg/ml was added per well. The secondary antibody reaction was performed at 37°C for 1 h, followed by washing three times with PBS with 0.05% Tween-20. Colorimetric reaction was conducted for 20 min with the use of horseradish peroxidase–conjugated streptavidin (Zymed, South San Francisco, CA) diluted 1:1,000 in PBS and 2,2′-azino-bis(2-ethylbenzothiazoline-6-sulfonic acid) (Pierce) as substrate. The optical density was measured at 450 nm; its sensitivity was 12 pg/ml. While the degree of precision of the ELISA system in terms of coefficient of variance (%) of intra-assay was between 1 and 3.8% (online appendix Table 1), that of interassays was between 3 and 9% (online appendix Table 2). Spike recovery (online appendix Table 3) and linearity (online appendix Table 4) were in a range of 90–107% and 100–109%, respectively. Specificity was determined using human adiponectin retinol-binding protein 4, visfatin, PAI-1, tumor necrosis factor-α, resistin-like-molecule-β, fatty acid–binding protein 4, angiopoietin-like protein 6, glutathione peroxidase 3, and mouse resistin (online appendix Table 5).

Statistical analyses. Data are shown as means ± SE, unless stated otherwise. Before statistical analysis, nonnormally distributed parameters were logarithmically transformed to approximate a normal distribution. The following statistical tests were used: paired Student's t test, χ quadrate test, and Pearson's simple correlation. Linear relationships were assessed by least-square regression analysis. Statistical analysis was performed using SPSS version 12.0 (Chicago, IL). P values <0.05 were considered to be statistically significant.

RESULTS

Development and validation of a novel vaspin ELISA. The current ELISA system was made possible by a human vaspin–specific monoclonal antibody. We could not measure serum vaspin from mouse or rat sera using this assay (data not shown). No cross-reactivity was observed with the use of a number of classical or new adipokines. Since vaspin seems to be a serpin member, we were interested in examining cross-reactivity with PAI-1, which turned out to be negative. Due to its high sensitivity (12 pg/ml), we were able to observe a certain range of serum vaspin levels from

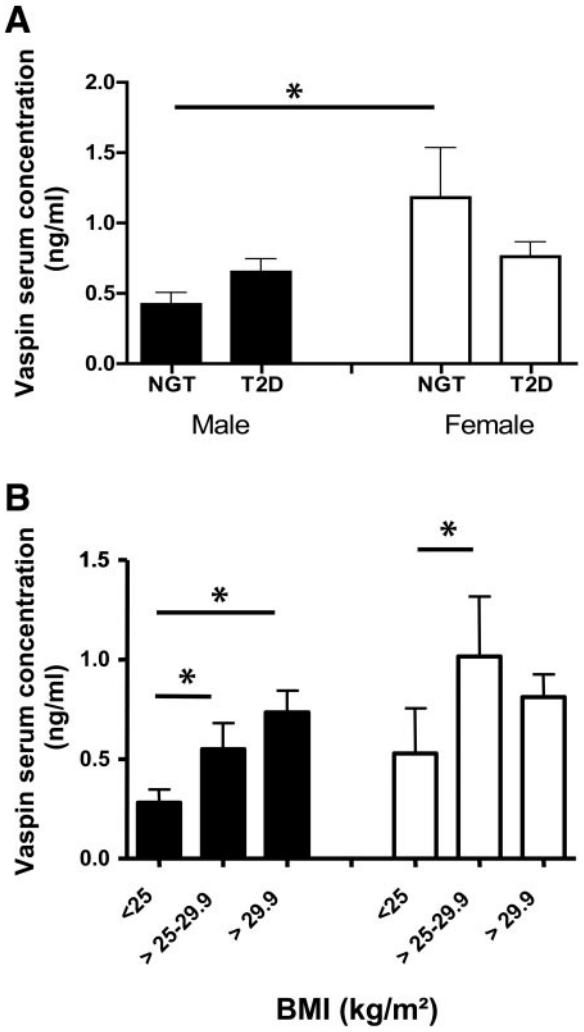

FIG. 1. Vaspin serum concentrations in normal glucose tolerant (NGT) individuals and patients with type 2 diabetes (T2D). *A*: Circulating vaspin in male subjects (n = 36) and female subjects (n = 18) with NGT and in male subjects (n = 53) and female subjects (n = 80) with type 2 diabetes. *B*: Vaspin serum concentrations in lean (BMI <25 kg/m^2; male subjects n = 16; female subjects n = 19), overweight (BMI >25–29.9 kg/m^2; male subjects n = 46; female subjects n = 32), and obese (BMI >30 kg/m^2; male subjects n = 29; female subjects n = 45) subjects. Data are means ± SE. *P < 0.05 between groups. ■, male subjects; □, female subjects.

all the sera we tested. A narrow range (1–9%) of coefficient of variation of inter- and intra-assays and sufficient degree of recovery and linearity (100–109%) strengthened reliability of this system (online appendix Tables 1–5).

Vaspin serum concentrations in the cross-sectional study. Anthropometric and metabolic characteristics of 187 individuals in the cross-sectional study are summarized in Table 1. Vaspin serum concentrations ranged from 0.1 to 6.74 ng/ml. In normal glucose-tolerant subjects, circulating vaspin was significantly higher in female compared with male subjects, whereas no sex differences have been found in subjects with type 2 diabetes (Fig. 1*A*). Vaspin levels were 1.5-fold higher in female subjects with NGT compared with type 2 diabetes (Fig. 1*A*). However, this difference was not statistically significant (P = 0.085). In male subjects, circulating vaspin was not different between NGT and type 2 diabetes (Fig. 1*A*). We further investigated a subgroup of competitive sportsmen (n = 30) as a model for the long-term effects of physical training

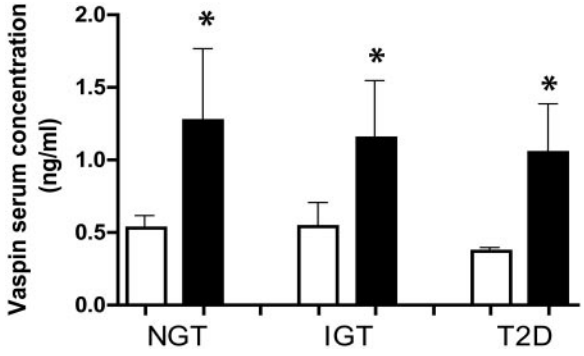

FIG. 2. Effect of 4 weeks of an intensive exercise program on vaspin serum concentrations in normal glucose tolerant (NGT) individuals and patients with IGT or type 2 diabetes (T2D). Circulating vaspin in groups of NGT (n = 20), IGT (n = 20), and type 2 diabetes (n = 20). Data are means ± SE. *P < 0.05 between baseline and after 4 weeks of intensive physical training. □, basal; ■, after training.

on vaspin concentrations. The definition of competitive sportsmen was based on training protocols, demonstrating that this subgroup performed at least 3 h of exercise in track and fields on 6 consecutive days per week in the context of a local sports club. Competitive sportsmen have significantly lower serum vaspin concentrations (0.28 ± 0.07 ng/ml) compared with lean normal glucose-tolerant control subjects (0.77 ± 0.42 ng/ml).This effect could be due to significantly lower BMI in competitive sportsmen (22.5 ± 0.7 kg/m^2) compared with normal glucose-tolerant control subjects (24.2 ± 1.6 kg/m^2). To further elucidate whether differences in total body fat mass explain different vaspin serum concentrations, we performed a subgroup analysis of normal glucose-tolerant male subjects with a BMI of 26 kg/m^2 with either <20% (n = 10) or >20% (n = 10) body fat. Individuals with <20% body fat had significantly lower vaspin serum concentration (0.19 + 0.05 ng/ml) than BMI-matched subjects with >20% body fat (0.36 + 0.1 ng/ml). Vaspin serum concentrations were significantly lower in lean compared with overweight and/or obese male and female subjects (Fig. 1*B*). Moreover, in normal glucose-tolerant subjects circulating vaspin correlates with BMI (r = 0.27, P = 0.03) and BMI-adjusted glucose infusion rate during the steady state of an euglycemic-hyperinsulinemic clamp (r = −0.25, P = 0.035). BMI-adjusted correlation between circulating vaspin and glucose infusion rate remained significant after additional adjusting for age and sex (r = −0.21, P = 0.046). Interestingly, correlation between circulating vaspin, BMI, and insulin sensitivity was not confirmed in patients with type 2 diabetes. The lack of correlation between vaspin and BMI was observed independently of diabetes therapy by either diet/exercise or metformin. Only in male normal glucose-tolerant, but not type 2 diabetic, subjects was vaspin serum concentration significantly correlated with systolic blood pressure (r = −0.5, P = 0.02) and total cholesterol (r = −0.61, P = 0.003). However, these correlations did not remain significant after adjusting for BMI.

Vaspin serum concentrations in response to 4 weeks of intensive exercise training. A total of 60 Caucasian men and women completed a 4-week training program and were studied after being divided into subjects with NGT (n = 20), IGT (n = 20), glucose tolerance, or type 2 diabetes (n = 20), as previously described (5). The training effect was confirmed by a significant improvement in $V\text{O}_{2\text{max}}$ in all groups. As determined by matched

TABLE 2
Multivariate linear regression analysis of changes in different parameters as predictors of increased vaspin serum concentration in response to a 4-week intensive physical training program ($n = 60$)

	ΔVaspin serum concentration	
	β-Coefficient	*P* value
Model 1		
Age	−0.08	0.4
Sex	0.09	0.2
ΔBMI	**−0.56**	**<0.001**
Model 2		
Age	−0.05	0.5
Sex	0.07	0.3
ΔBMI	**−0.38**	**<0.001**
ΔGlucose infusion rate*	**0.29**	**0.003**
Model 3		
Age	−0.05	0.5
Sex	0.07	0.3
ΔBMI	**−0.32**	**<0.001**
ΔVo_{2max}	**0.3**	**0.001**

Significant correlations are shown in bold. *Glucose infusion rate during the steady state of a euglycemic-hyperinsulinemic clamp. Δ, change of parameter.

paired *t* test ($P < 0.05$), all subjects had a significant increase in $V_{O_{2max}}$ after the training period. Four weeks of physical training resulted in significant decreases in BMI, waist-to-hip ratio, and percent body fat in all glucose tolerance groups and insulin sensitivity significantly improved in the impaired glucose-tolerant and type 2 diabetic groups (5).

Vaspin serum concentration significantly increased approximately twofold in subgroups of normal glucose-tolerant, impaired glucose-tolerant, and type 2 diabetic subjects (Fig. 2) in response the 4-week training program. There was a significant correlation between change in vaspin serum concentrations and change in $V_{O_{2max}}$ ($r = 0.6$, $P = 0.004$) after the training program. Multivariate linear regression analyses revealed that reduced BMI, improved insulin sensitivity, and increased fitness level ($V_{O_{2max}}$) are predictors of increased vaspin serum concentrations after training (Table 2). However, long-term intensive physical training in competitive sportsmen was associated with significantly lower vaspin serum concentrations.

DISCUSSION

Increased visceral adipose tissue mass is associated with higher prevalence of insulin resistance, type 2 diabetes, and the risk of cardiovascular disease (rev. in 8–10). Visceral fat depot–specific secretion of adipokines may, at least in part, explain the adverse effects of intra-abdominal fat accumulation. Such fat depot differences in protein or mRNA expression have been reported for several adipokines, including leptin (11,12), PAI-1 (13), retinol binding protein 4 (14), and interleukin-6 (15). Vaspin was isolated from visceral adipose tissue of OLETF rats (1), a model of human type 2 diabetes that shares common components of the human metabolic syndrome, including abdominal obesity, insulin resistance, hypertension, and dyslipidemia (16). Administration of recombinant vaspin was shown to improve glucose tolerance and insulin sensitivity in obese mice and normalized altered expression of genes relevant to insulin resistance (1). We have recently shown that vaspin mRNA expression was more frequently detectable in human visceral compared with subcutaneous fat (2). We hypothesize that increased vaspin secretion might represent a compensatory mechanism in response to decreased insulin sensitivity or impairment of glucose metabolism. We therefore sought to provide new mechanistic insight into the relationship between vaspin serum concentrations and obesity or its associated metabolic disorders.

We developed an ELISA for the measurement of human serum vaspin concentrations. A general pitfall of developing an ELISA is the choice of proper standard that resembles the analyte of interest in body fluids in terms of protein conformation, as well as posttranslational modification. In this sense, expression of recombinant human vaspin in HEK293 cells seems to be more appropriate than in *E. coli*. Moreover, this HEK293 cell–derived human vaspin was able to augment glucose uptake in human primary adipocytes (B.-S.Y., N.K., J.K., N.L., J.W.P., E.-S.S., K.R., A.O., M.F., M.S., M.B., unpublished observations), which is reminiscent of the prior observation that in vivo administration of recombinant vaspin ameliorated hyperglycemia (1). Thus, we believe that the current human vaspin ELISA system can be readily used for the measurement of human serum vaspin.

In this study, we demonstrate a sexual dimorphism in vaspin serum concentrations with ~2.5-fold–higher levels in normal glucose-tolerant female compared with male subjects. Sex differences with higher serum concentrations in female subjects have been demonstrated for the adipokines leptin (17,18) and adiponectin (19). Inhibitory effects of androgens on leptin and adiponectin expression are likely (20). However, whether androgens modulate vaspin expression needs to be investigated in further studies. Interestingly, these sex differences were abrogated in type 2 diabetic patients, suggesting that metabolic alterations in type 2 diabetes, including chronic hyperglycemia and decreased insulin sensitivity, modulate vaspin serum concentrations. Lean individuals have significantly lower circulating vaspin levels compared with both overweight and obese subjects. This result supports our previous finding that adipose vaspin mRNA expression was absent in lean normal glucose-tolerant individuals (2). Moreover, we found a significant correlation between vaspin serum concentrations, BMI, and insulin sensitivity. In accordance with our previous report that subcutaneous vaspin mRNA expression negatively, and independently of percent body fat, correlates with glucose infusion rate (2), we found an age-, sex-, and BMI-independent significant negative correlation between circulating vaspin and glucose infusion rate during a clamp. Surprisingly, vaspin serum concentrations were lower in lean subjects but increased with weight loss associated with the physical training program. The most likely explanation for this paradox is that vaspin serum concentration is differentially regulated in the resting state and after exercise. Similar to our observations for vaspin serum concentrations, interleukin-6 is increased during and after exercise, whereas in the resting state elevated circulating interleukin-6 correlates with increased BMI and decreased insulin sensitivity (21). Moreover, elevated vaspin concentrations after 4 weeks of intensive physical training might represent a transient adaptation mechanism because competitive sportsmen with long-term physical training had significantly lower vaspin serum concentration than untrained age- and BMI-matched control subjects. The potential

mechanisms, which underly elevated circulating vaspin, requires further investigation, with more sophisticated methods. Especially the identification of the protease substrate for the induction of the protease inhibitor vaspin might help to elucidate the regulation of vaspin gene expression. For another protease inhibitor, PAI-1, fat depot–specific expression differences have been reported (13), as well as relationships between PAI-1 and BMI (22), insulin sensitivity (22), diet, and physical training (23,24). These results, together with our data on circulating vaspin, suggest that protease inhibitors either play a causative role in the development of obesity and metabolic disorders or that they are at least biomarkers for these diseases. It is noteworthy that elevated serum concentrations of another serpin adipokine, pigment epithelium-derived factor, which is a strong inhibitor of angiogenesis, have been found in patients with type 2 diabetes (25). Moreover, in an analogous manner to relationships between circulating vaspin and anthropometric parameters in our study, circulating pigment epithelium-derived factor has been previously shown to be strongly associated with BMI and parameters of the metabolic syndrome (26).

In analogy to the abrogated sex differences in patients with type 2 diabetes, there was no correlation between circulating vaspin and BMI in patients with type 2 diabetes. This suggests a dysregulation of vaspin secretion in patients with type 2 diabetes. We cannot exclude that diet and metformin therapy of type 2 diabetes might contribute to the lack of association between increased circulating vaspin and obesity. Further studies are necessary to elucidate the mechanisms mediating these changes in vaspin regulation in patients with type 2 diabetes.

Independent of sex and glucose tolerance group, 4 weeks of physical exercise lead to increased vaspin serum concentrations. Elevated vaspin levels are associated with decreased BMI but also with improvement in insulin sensitivity and in fitness level. Insulin-sensitizing effects of vaspin on adipose tissue have been reported in mice (1). It is therefore tempting to speculate that increased vaspin serum concentrations contribute to the insulin-sensitizing effects of physical activity. Further studies are needed to define whether vaspin plays a causal role in this relationship. However, our data suggest vaspin as a circulating biomarker for interventions, which improve insulin sensitivity.

In conclusion, our data suggest that vaspin represents a new biomarker for obesity and impaired insulin sensitivity. Elevated circulating vaspin during the first weeks of physical training in untrained individuals could mediate the improvement of insulin resistance in response to exercise, whereas high fitness level correlates with low vaspin serum concentrations.

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