J Surg Med. 2019;3(8):564-567.
DOI: 10.28982/josam.602984

Research article
Araştırma makalesi

Journal of Surgery and Medicine
e-ISSN: 2602-2079

# The relationship of serum galectin-3 levels with obesity and insulin resistance

## Serum galektin-3 düzeylerinin obezite ve insulin direnci ile ilişkisi

**Özgür Altun [1], Okan Dikker [2], Murat Akarsu [1],Yücel Arman [1], Şengül Aydın Yoldemir [1], Orkide Kutlu [1], Perihan Özkan Gümüşkaya [1], Tufan Tükek [3]**

**[1] Department of Internal Medicine, Okmeydanı Training and Research Hospital, University of Health Sciences, Istanbul, Turkey**
**[2] Department of Medical Biochemistry, Okmeydanı Training and Research Hospital, University of Health Sciences, Istanbul, Turkey**
**[3] Department of Internal Medicine, Istanbul University, Istanbul, Turkey**

**ORCID ID of the author(s)**
**ÖA: 0000-0003-1810-7490**
**OD: 0000-0002-9153-6139**
**MA: 0000-0002-2675-4252**
**YA: 0000-0002-9584-6644**
**ŞAY: 0000-0003-4236-1181**
**OK: 0000-0002-4402-2231**
**PÖG: 0000-0002-0838-9220**
**TT: 0000-0002-4237-1163**

Corresponding author / Sorumlu yazar:
Okan Dikker
Address / Adres: Darülaceze Caddesi, No: 27, Şişli, İstanbul, Türkiye
e-Mail: okandikker@hotmail.com

Ethics Committee Approval: The present study was approved by the Okmeydanı Training and Research Hospital Ethics Committee (date: 28/8/2018; number: 979).
Etik Kurul Onayı: Bu çalışma, Okmeydanı Eğitim ve Araştırma Hastanesi etik kurulundan onay aldı (tarih: 28/8/2018; sayı: 979).

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Published: 8/14/2019
Yayın Tarihi: 14.08.2019



**Abstract**

Aim: Galectin-3 affects inflammation, cell adhesion, proliferation, differentiation and angiogenesis. Upon examining the pathogenesis of obesity and functions of galectin-3, we thought that galectin-3 may play a significant role in obese patients. This study aims to evaluate the relationship between obesity, insulin resistance and galectin-3 levels.

Methods: Eighty five patients aged between 18-50 years were included in this cross-sectional study. BMI>30 were considered obese, those between 25-30 and 18-25 were considered overweight and normal weight, respectively. Patients with HOMA-IR>2.5 were considered insulin-resistant, and those with <2.5 were evaluated as insulin non-resistant.Galectin-3 levels were measured by Enzyme-linked immunosorbent assay.

Results: Serum galectin-3 levels were significantly higher in obese patients, but not statistically significantly different between those with and without insulin resistance. Galectin-3 levels were also significantly correlated with BMI and total cholesterol levels, but not correlated with HOMA-IR.

Conclusion: In obesity, serum galectin-3 levels may increase to compensate for the inflammation. Our results make it difficult to establish a relationship between insulin resistance and galectin-3.

**Keywords:** Galectin-3, Obesity, Insulin Resistance, Diabetes Mellitus, Metabolic disease

**Öz**

Amaç: Galektin-3, inflamasyon, hücre yapışması, proliferasyonu, farklılaşması ve anjiyogenezi etkiler. Obezitenin patogenezi ve galektin-3'ün fonksiyonlarını incelediğimizde, galektin-3'ün obez hastalarda önemli bir rol oynuyor olabileceğini düşündük. Çalışmamızda obezite ve insülin direnci ile galektin-3 arasındaki ilişkiyi değerlendirmeyi amaçladık.

Yöntemler: 18-50 yaş aralığında erkek ve kadınlardan oluşan 85 olgu bu kesitsel çalışmaya dahil edildi. BMI >30 olan hastalar obez, 25-30 arasında olanlar fazla kilolu, 18-25 arasında olanlar normal kilolu olarak değerlendirildi. HOMA-IR değeri >2,5 olanlar insülin dirençli, <2,5 olanlar ise insülin direnci olmayan hastalar olarak gruplandırıldı. Serum galektin-3 düzeyleri Enzim-bağlı immunosorbent yöntemi ile ölçüldü.

Bulgular: Fazla kilolu ve normal kilolulara göre serum galektin-3 düzeyleri obezlerde daha yüksek düzeylerde idi. Fazla kilolu ve normal kilolular arasında serum galektin-3 düzeyleri anlamlı farklı değildi. İnsülin direnci olan ve olmayan grup arasında galektin-3 düzeyleri arasında herhangi bir fark görülmedi. Galektin-3 düzeyleri BMI ve total kolesterol ile korele iken, HOMA-IR ile arasında anlamlı bir korelasyon saptanmadı.

Sonuç: Obez hastaların serum galektin-3 seviyeleri, diğer gruplara oranla anlamlı olarak daha yüksek saptandı. Obezitedeki inflamatuvar süreçte kompensasyon amacı ile koruyucu etki göstermek üzere galektin-3 düzeylerinin arttığını düşünmekteyiz. Ancak, bulgularımız insülin direnci ve HOMA-IR ile serum galektin-3 düzeyleri arasında bir ilişki kurmayı güçleştirmektedir.

**Anahtar kelimeler:** Galektin-3, Obezite, İnsülin Direnci, Diabetes Mellitus, Metabolik hastalık

**How to cite / Atıf için:** Altun Ö, Dikker O, Akarsu M, Arman Y, Yoldemir ŞA, Kutlu O, Gümüşkaya PÖ, Tükek T. The relationship of serum galectin-3 levels with obesity and insulin resistance. J Surg Med. 2019;3(8):564-567.

## Introduction

Galectin-3 is a member of the soluble beta-galactoside binding lectin family and affects cell adhesion, proliferation, differentiation, inflammation and angiogenesis [1]. Galectin-3 activity depends on its cellular localization. While extracellular galectin-3 stimulates apoptosis, intracellular galectin-3 in inhibits it [2]. Galectin-3 is expressed in a wide variety of cells, especially in macrophages and adipocytes. Recombinant galectin-3 induces pre-adipocyte proliferation in vitro [3].

Being overweight is associated with increased number of macrophages in dysfunctional adipocytes and the adipose tissue [4]. In addition to impaired lipid storage in excess weight, the release of adipokines and inflammatory cytokines is increased, which explains the low-grade systemic inflammation in overweight patients [2]. Although epidemiological studies have determined the relationship between visceral fat mass and metabolic disorders such as insulin resistance and obesity, the pathophysiological mechanisms are not clear [5]. Obesity is a chronic pro-inflammatory condition characterized by increased lipids and adipose tissue, which causes ectopic fat accumulation in different tissues, and increased pro-inflammatory cytokine levels [6]. It is also an important factor in the pathogenesis of type 2 diabetes mellitus [7].

When we examined the pathogenesis of obesity and the functions of galectin-3, we thought that galectin-3 may play an important role in these patients. This study aims to evaluate the relationship between obesity, insulin resistance and galectin-3 levels.

## Materials and methods

This study was approved by the Local Ethics Committee and performed in accordance with the principles of Declaration of Helsinki. A total of 85 patients (18-50 years old, male and female) who were admitted to our internal medicine outpatient clinic between August 2018 and October 2018 were included in the study. Patients complying with the inclusion criteria were informed by the researchers. After obtaining informed consent form from the volunteers, detailed history of participants were taken. BMI was calculated by division of weight (kg) to the square of the height (m). Patients with BMI> 30 kg/m$^2$ were considered obese, those between 25 and 30 kg/m$^2$ were overweight, and those between 18 and 25 kg/m$^2$ were evaluated as normal weight. For the determining insulin resistance, HOMA-IR was calculated according to the formula: fasting insulin (uIU/mL) x fasting glucose (mg/dL) /405. Patients with HOMA-IR> 2.5 were considered insulin resistant.

Patients with a history of chronic disease, malignancy, diabetes mellitus, pregnant women, steroid users and immobilized patients were not included in the study. One more additional tube of blood was obtained from the volunteers during routine laboratory investigations. After resting for 20 minutes at room temperature, samples were centrifuged for 10 minutes on 4000 rpm and obtained sera were preserved at -80 °C. Galectin-3, glucose, urea, creatinine, cholesterol, triglyceride, HDL-cholesterol, LDL-cholesterol and insulin levels of patients were measured.

**Measurements of galectin-3 and performance characteristics of the assay**

On the day of analysis, the sera were left to thaw at room temperature. Enzyme-Linked Immuno Sorbent Assay (ELISA) kits (Human Galectin-3 ELISA, eBioscience, Lot No: 125631001) were usedfor the measurement of serum Galectin-3 levels. The analytical (linear) measurement range was 0.47 - 30 ng/mL for galectin-3. The minimal detection limit was 0.29 ng/mL. The reported intraassay and interassay CV's were <12 % and <10 %, respectively.

**Statistical analysis**

IBM SPSS version 20.0 (SPSS Inc, Chicago Illinois) was used for statistical analysis. The normal distribution of the parameters was analyzed with the Shapiro Wilk test. In addition to using descriptive statistics (mean, standard deviation, frequency) for the comparison of the quantitative data of parameters with a normal distribution, One Way Anova test was used in intergroup comparisons; Tukey's HSD test and Tamhane's T2 tests were used for determining the differing group. For non-normally distributed parameters, Kruskal Wallis test was used in intergroup comparisons and Mann Whitney U test in determining the differing group. Student-t test was utilized in comparing normally distributed parameters between two groups, and Mann Whitney U test was used for comparing the non-normally distributed parameters between two groups. The correlation between galectin-3 levels and other parameters was evaluated by non-parametric Spearman test. $P$<0.05 was considered statistically significant.

## Results

The demographic and laboratory data of obese and non-obese groups are summarized in Table 1. Serum galectin-3 levels and BMI were found to be statistically significantly higher in obese patients compared to the non-obese group ($P$=0.003 and $P$<0.001, respectively). Other parameters were not statistically different between the two groups.

The demographic and laboratory data of study groups are summarized in Table 2. Serum galectin-3 levels were significantly higher in obese patients than the control and overweight groups ($P$=0.015 and $P$<0.001, respectively), but there was no significant difference between normal and overweight groups ($P$=0.977). Urea, creatinine, total cholesterol, HDL-cholesterol and LDL-cholesterol levels of the 3 groups were similar ($P$>0.05).

The results of correlation analysis between galectin-3 levels and other parameters are summarized in Table 3. A positive correlation was determined between galectin-3 levels, BMI and total cholesterol levels in all participants ($P$=0.002, r=0.337 and $P$=0.042, r=0.220, respectively).

The demographic and laboratory data of patients with or without insulin resistance are summarized in Table 4. Serum galectin-3 levels, age, HbA1c, creatinine, total cholesterol and LDL-cholesterol levels were not different between groups with and without insulin resistance ($P$>0.05).

Table 1: Demographic and laboratory data of obese and non-obese patients

| | BMI<30 (n=39) Mean (SD) | BMI>30 (n=46) Mean (SD) | *P*-value |
|---|---|---|---|
| Galectin-3 (ng/mL) | 23.4 (23.9) | 38 (20.1) | 0.003 |
| Age (Years) | 44.3 (9) | 46 (10.4) | 0.276 |
| HOMA-IR | 3.4 (3.7) | 4.2 (2.5) | 0.246 |
| BMI (Kg/m$^2$) | 26 (2.7) | 35 (3.7) | <0.001 |
| Fasting insulin (µIU/mL) | 14.3 (13.9) | 17.4 (10) | 0.246 |
| Fasting glucose (mg/dL) | 92 (12) | 96 (12) | 0.125 |
| HbA1c (%) | 5.6 (0.4) | 5.7 (0.3) | 0.834 |
| Urea (mg/dL) | 24.2 (6.8) | 24.6 (7.7) | 0.839 |
| Creatinine (mg/dL) | 0.77 (0.13) | 0.79 (0.47) | 0.778 |
| Total Cholesterol (mg/dL) | 189 (37) | 200 (47) | 0.269 |
| LDL-Cholesterol (mg/dL) | 114 (35) | 122 (44) | 0.370 |
| HDL-Cholesterol (mg/dL) | 46.8 (12.6) | 46.6 (10.1) | 0.929 |
| Triglyceride (mg/dL) | 142 (104) | 153 (92) | 0.621 |

BMI: Body-Mass Index, HDL-cholesterol: High density lipoprotein- cholesterol, HOMA-IR: Homeostatic model of assessment- insulin resistance, LDL-cholesterol: Low density lipoprotein- cholesterol, SD: Standard deviation

Table 2: Demographic and laboratory data of study participants

| | A BMI <25 (n:16) | B BMI:25-30 (n:23) | C BMI>30 (n:46) | Comparison of A-B *P*-value | Comparison of B-C *P*-value | Comparison of A-C *P*-value |
|---|---|---|---|---|---|---|
| Galectin-3 (ng/mL) | 25.6 (28.4) | 21.9 (20.7) | 28 (20.1) | 0.977 | <0.001 | 0.015 |
| HOMA-IR | 1.5 (0.4) | 4.7 (4.4) | 4.2 (2.5) | 0.001 | 0.869 | <0.001 |
| BMI (Kg/m$^2$) | 23.2 (1.5) | 28 (1.1) | 35 (37) | <0.001 | <0.001 | <0.001 |
| Age (Years) | 40.6 (4.9) | 46.8 (10.4) | 46 (10.4) | 0.069 | 0.848 | 0.026 |
| Insulin(µIU/mL) | 7.3 (2.5) | 19.2 (16.4) | 17.4 (10) | 0.001 | 0.919 | <0.001 |
| Glucose(mg/dL) | 85 (10) | 97 (11) | 96 (10) | 0.001 | 0.584 | 0.0014 |
| HbA1c (%) | 5.6 (0.2) | 5.8 (0.4) | 5.7 (12) | 0.001 | 0.107 | 0.015 |
| Urea (mg/dL) | 24.6 (7.3) | 24 (6.5) | 24.6 (7.7) | 0.786 | 0.760 | 0.981 |
| Creatinine (mg/dL) | 0.78 (0.16) | 0.78 (0.12) | 0.8 (0.5) | 0.597 | 0.512 | 0.358 |
| TotaLcholesterol (mg/dL) | 185.8 (32) | 192 (41) | 200 (47) | 0.909 | 0.745 | 0.299 |
| LDL-cholesterol (mg/dL) | 114 (35.9) | 114 (36.6) | 122 (44) | 0.940 | 0.606 | 0.645 |
| HDL-cholesterol (mg/dL) | 49.6 (10.9) | 44.8 (13.5) | 46.6 (10.1) | 0.184 | 0.369 | 0.454 |
| Triglyceride(mg/dL) | 106 (48) | 168 (124) | 153 (92) | 0.081 | 0.980 | 0.034 |

A: Normal weight group, B: Overweight group, C: Obese group. BMI: Body-Mass Index, HDL-cholesterol: High density lipoprotein- cholesterol, HOMA-IR: Homeostatic model of assessment- insulin resistance, LDL-cholesterol: Low density lipoprotein- cholesterol

Table 3: Correlation between galectin-3 levels and other parameters

| | | BMI | Fasting glucose | Fasting insulin | HbA1c | HOMA-IR | Total Cholesterol | LDL-Cholesterol |
|---|---|---|---|---|---|---|---|---|
| Galectin -3 | r | 0.337 | 0.066 | 0.039 | 0.018 | 0.037 | 0.220 | 0.209 |
| | *P*-value | 0.002 | 0.548 | 0.724 | 0.868 | 0.734 | 0.042 | 0.055 |
| | n | 85 | 85 | 85 | 85 | 85 | 85 | 85 |

Table 4: Demographic and laboratory data in subgroups with or without insulin resistance

| | HOMA-IR<2.5 (n:36) Mean (SD) | HOMA-IR >2.5 (n:49) Mean (SD) | *P*-value |
|---|---|---|---|
| Galectin-3 (ng/mL) | 33.6 (22.1) | 28.4 (23.8) | 0.294 |
| HOMA-IR | 1.6 (0.5) | 5.4 (3.2) | <0.001 |
| Age (Years) | 28.8 (6.3) | 33.6 (22.1) | 0.005 |
| BMI (Kg/m$^2$) | 42.7 (8.9) | 46.67 (10.6) | 0.075 |
| Insulin (µIU/mL) | 7.5 (2.6) | 22.3 (12.2) | <0.001 |
| Glucose (mg/dL) | 87 (9.8) | 99 (12.6) | <0.001 |
| HbA1c (%) | 5.6 (0.4) | 57 (0.4) | 0.297 |
| Urea (mg/dL) | 22.4 (7.1) | 25.7 (7.4) | 0.039 |
| Creatinine (mg/dL) | 0.78 (0.51) | 0.77 (0.17) | 0.891 |
| Total Cholesterol (mg/dL) | 194 (44) | 195 (43) | 0.891 |
| HDL-Cholesterol (mg/dL) | 50 (10.7) | 43.8 (10.7) | 0.005 |
| Triglyceride (mg/dL) | 118 (64) | 170 (112) | 0.015 |
| LDL-Cholesterol (mg/dL) | 117 (44) | 120 (38) | 0.727 |

BMI: Body-Mass Index, HDL-cholesterol: High density lipoprotein- cholesterol, HOMA-IR: Homeostatic model of assessment- insulin resistance, LDL-cholesterol: Low density lipoprotein- cholesterol, SD: Standard deviation (17 patients with insulin resistance were overweight and 32 were obese. Of the patients without insulin resistance, 16 were normal weight, 6 were overweight, and 14 were obese.)

## Discussion

In our study, serum galectin-3 levels of obese patients were higher compared to the overweight and normal weight groups. Increased levels of this molecule in obese patients werereported in previous studies as well [8-11]. Since most of the studies were experimental animal studies, being a clinical study that used international classifications in patient grouping, our study has brought a different perspective to the subject. In the first study regarding this topic, Weigert et al. [8] classified patients into normal weight (BMI <25), obese (BMI >25) and those with type 2 diabetes mellitus, and reported high serum galectin-3 levels in obese and type 2 diabetic patients. They also included overweight patients in the obese group and there were also non-obese patients with type 2 diabetes mellitus. According to internationally accepted criteria, we selected the obese group as BMI> 30 kg/m$^2$to for a more specific definition.

Galectin-3 levels were higher in the obese group. In our study, we did not find any significant difference between normal and overweight groups. In addition, we found a positive correlation between galectin-3, BMI and total cholesterol levels. There are various opinions about why the level of galectin-3 increases in obese patients. Krautbauer et al. [10] reported that adiponectin down regulates adipocyte and monocyte galectin-3 protein and impaired adiponectin activity in obesity causes elevations in galectin-3 levels. Reduced adiponectin levels have been reported in obese patients [12]. Therefore, galectin-3 levels may increase in obesity, since the inhibitory effect on galectin-3 is eliminated in adiponectin deficiency. Also, high IL-6 levels in obesity may increase levels of galectin-3 [11]. Jung-Hwan et al. [13] reported that high galectin-3 levels were associated with obesity, and that galectin-3 interacts directly with peroxisome proliferator-activated receptor (PPAR) -gamma and regulates the expression and transcriptional activation of PPAR-gamma. (PPAR) –gamma, a receptor located in nucleus, has a key role in lipid metabolism. It is activated by the PPAR-gamma ligands, binds to the PPAR-gamma response element, and increases the expression of target genes. Galectin-3 has been reported to be involved in adipogenesis by direct PPAR-gamma regulation.

There is no consensus about the roles galectin-3 in the body. Galectin-3 has been reported to play a protective role against inflammation in different models. Rhodes et al. [14] showed increased expression of galectin-3 in visceral adipose tissue and subcutaneous adipose tissue in mice with high fat diet-induced obesity. In dietary-associated atherosclerosis and diabetes-associated renal injury models, galectin-3 deficient mice were found to have increased inflammation [15]. These data suggest that galectin-3 plays a protective role in metabolic complications and inflammation associated with obesity [15-17].Galectin-3 binds to advanced glycation end products (AGE) and stimulates their degradation. Since AGE accumulate in long-lasting proteins and cause tissue damage associated with the severity of diabetic complications, we believe that high levels of galectin-3 may be protective [18].

Despite the apparent association of elevated galectin-3 levels with obesity, the relationship between insulin resistance and galectin-3 appears to be contradictory. Obesity-related insulin resistance is a characteristic precursor of type 2 diabetes mellitus. There are studies reporting that various molecules such as galectin-3 may be associated with insulin resistance and BMI. Li et al. [19] reported that galectin-3-knockout mice, in which circulating galectin-3 levels were reduced, needed more insulin when exposed to a high-fat diet or aging; galectin-3 was upregulated in obesity, and defined that it as a pro-inflammatory molecule which may cause insulin resistance. In the same study, a negative correlation between galectin-3 and HOMA-IR was reported. Baek et al. [20] also found that galectin-3 deficient mice were insulin-sensitive. In contrast, Pang et al. [16] reported that there was no difference in the insulin sensitivity of galectin-3 deficient mice. Darrow and Shohet [21] reported hyperglycemia with reduced plasma insulin levels in galectin-3 deficient mice indicating beta-cell dysfunction without a change in insulin sensitivity. Ohkura et al. [22] reported that galectin-3 was associated with decreased plasma insulin levels and insulin sensitivity in type 2 diabetics, but not with BMI. Galectin-3 was

also reported to inhibit insulin signals with a mechanism that directly binds the insulin-receptor [23]. Yılmaz et al. [24] reported high levels of galectin in patients with diabetes and pre-diabetes, possibly leading to diabetes and complications. Karlsen et al. [25] reported that overproduction of galectin-3 inhibited beta cell damage caused by the cytotoxic effects of interleukin-1 beta.

In our study, we found statistically insignificant differences in serum galectin-3 levels between groups with and without insulin resistance. We found insulin levels to be significantly higher in obese and overweight groups than control group. No correlation was found between galectin-3 levels, insulin and HOMA-IR in both the obese and non-obese groups. Therefore, we did not detect a relationship between insulin resistance and serum galectin-3 levels. Since there are contradictory results in the literature, more studies are warranted.

**Limitations**

There are some limitations of our study. First, the sample size could have been larger. Secondly, inflammatory cytokine levels were not studied in the sera.

**Conclusion**

We believe that galectin-3 levels are increased in obese patients for protective purposes, to compensate for the inflammatory process in obesity. Our results make it difficult to establish a relationship between insulin resistance and galectin-3. We believe that galectin-3 is an important molecule in monitoring treatment outcomes of metabolic diseases.

## References


1. Dumic J, Dabelic S, Flögel M. Galektin-3: an open-ended story. Biochim Biophys Acta. 2006;1760:616–35.
2. Rasouli N, Kern PA. Adipocytokines and the metabolic complications of obesity. J Clin Endocrinol Metab. 2008;93:64–73.
3. Kiwaki K, Novak CM, Hsu DK, Liu FT, Levine JA. Galektin-3 stimulates preadipocyte proliferation and is upregulated in growing adipose tissue. Obesity. 2007;15:32–9.
4. Zeyda M, Farmer D, Todoric J, Aszmann O, Speiser M, Gyori G, et al. Human adipose tissue macrophages are of an anti-inflammatory phenotype but capable of excessive pro-inflammatory mediator production. Int J Obes. 2007;31:1420–8.
5. Demerath EW, Reed D, Rogers N, Sun SS, Lee M, Choh AC, et al. Visceral adiposity and its anatomical distribution as predictors of the metabolic syndrome and cardiometabolic risk factor levels. Am J Clin Nutr. 2008;88:1263–71.
6. Martinez-Martinez E, Cachofeiro V, Rousseau E, Alvarez V, Calvier L, Fernandez- Celis A, et al. Interleukin-33/ST2 system attenuates aldosterone-induced adipogenesis and inflammation. Mol Cell Endocrinol. 2015;411:20-7.
7. Makki K, Froguel P, Wolowczuk I. Adipose tissue in obesity-related inflammation and insulin resistance: cells, cytokines, and chemokines. ISRN Inflamm. 2013;139239.
8. Weigert J, Neumeier M, Wanninger J, Bauer S, Farkas S, Scherer MN, et al. Serum galektin-3 is elevated in obesity and negatively correlates with glycosylated hemoglobin in type 2 diabetes. J Clin Endocrinol Metab. 2010;95:1404-11.
9. de Boer RA, van Veldhuisen DJ, Gansevoort RT, Muller Kobold AC, van Gilst WH, Hillege HL, et al. The fibrosis marker galektin-3 and outcome in the general population. J Intern Med. 2012;272:55–64.
10. Krautbauer S, Eisinger K, Hader Y, Buechler C. Free fatty acids and IL-6 induce adipocyte galectin-3 which is increased in white and brown adipose tissues of obese mice. Cytokine. 2014;69:263–71.
11. Pang J, Nguyen VT, Rhodes DH, Sullivan ME, Braunschweig C, Fantuzzi G. Relationship of galektin-3 with obesity, IL-6, and CRP in women. J Endocrinol Invest. 2016;12:1435-43.
12. Buechler C, Wanninger J, Neumeier M. Adiponectin, a key adipokine in obesity related liver diseases. World J Gastroenterol. 2011;17:2801–11.
13. Jung-Hwan B, Seok-Jun K, HyeokGu K, Hyun-Woo L, Jung-Hoon K, Kyung H, et al. Galektin-3 Activates PPAR_ and Supports White Adipose Tissue Formation and High-Fat Diet-Induced Obesity. Endocrinology.2015;156:147–56.
14. Rhodes DH, Pini M, Castellanos KJ, Montero-Melendez T, Cooper D, Perretti M,et al. Adipose tissue-specific modulation of galectin expression in lean and obese mice: evidence for regulatory function. Obesity.2013;21:310–9.
15. Pejnovic NN, Pantic JM, Jovanovic IP, Radosavljevic GD, Djukic A, Arsenijevic NN, et al. Galektin-3 is a regulator of metaflammation in adipose tissue and pancreatic islets. Adipocyte. 2013;2:266–71.
16. Pang J, Rhodes DH, Pini M, Akasheh RT, Castellanos KJ, Cabay RJ, et al. Increased adiposity, dysregulated glucose metabolism and systemic inflammation in Galektin-3 KO mice. PloS One. 2013;8:e57915.
17. Pejnovic N, Pantic J, Jovanovic I, Radosavljevic G, Milovanovic M, Nikolic I, et al. Galektin-3 deficiency accelerates high-fat diet induced obesity and amplifies inflammation in adipose tissue and pancreatic islets. Diabetes. 2013;62:1932–44.
18. Zhu W, Sano H, Nagai R, Fukuhara K, Miyazaki A, Horiuchi S. The role of galectin-3 in endocytosis of advanced glycation end products and modified low density lipoproteins. Biochem Biophys Res Commun. 2001;280:1183–8.
19. Li P, Liu S, Lu M, Bandyopadhyay G, Oh D, Imamura T, et al. Hematopoietic-derived galektin-3 causes cellular and systemic insulin resistance. Cell. 2016;167:973–84.
20. Baek JH, Kim SJ, Kang HG, Lee HW, Kim JH, Hwang KA, et al. Galektin-3 activates PPAR and supports white adipose tissue formation and high-fat diet induced obesity. Endocrinology. 2015;156:147–56.
21. Darrow AL, Shohet RV. Galektin-3 deficiency exacerbates hyperglycemia and the endothelial response to diabetes. Cardiovasc Diabetol. 2015;14:73.
22. Ohkura T, Fujioka Y, Nakanishi R, Shiochi H, Sumi K, Yamamoto N, et al. Low serum galektin-3 concentrations are associated with insulin resistance in patients with type 2 diabetes mellitus. Diabetol Metab Syndr. 2014;6:106.
23. Li P, Oh DY, Bandyopadhyay G, Lagakos WS, Talukdar S, Osborn O, et al. LTB4 promotes insulin resistance in obese mice by acting on macrophages, hepatocytes and myocytes. Nat Med. 2015;21:239.
24. Yilmaz H, Cakmak M, Inan O, Darcin T, Akcay A. Increased levels of galectin‐3 were associated with prediabetes and diabetes: new risk factor? J Endocrinol Invest. 2015;38:527–33.
25. Karlsen AE, Storling ZM, Sparre T, Larsen MR, Mahmood A, Storling J, et al. Immune-mediated beta-cell destruction in vitro and in vivo—a pivotal role for galektin-3. Biochem Biophys Res Commun. 2006;344:406–15.


This paper has been checked for language accuracy by JOSAM editors.
The National Library of Medicine (NLM) citation style guide has been used in this paper.

Suggested citation: Patrias K. Citing medicine: the NLM style guide for authors, editors, and publishers [Internet]. 2nd ed. Wendling DL, technical editor. Bethesda (MD): National Library of Medicine (US); 2007-[updated 2015 Oct 2; cited Year Month Day]. Available from: http://www.nlm.nih.gov/citingmedicine