REVIEW

CYPRUS
JOURNAL OF MEDICAL SCIENCES

DOI: 10.4274/cjms.2024.2024-30
Cyprus J Med Sci 2025;10(1):7-12

Galectins: An Amazing Marker and a Potential Therapeutic Target

Mehtap Tınazlı, Gaukhar Bakhtiyarova

Clinic of Internal Medicine, Near East University Hospital, Nicosia, North Cyprus

Abstract

Galectins (Gal) are a wide group of proteins expressed in various cells, and they are particularly known for their ability to recognize and bind carbohydrates. We present current evidence showing that Gal play roles in both acute and chronic inflammation pathways. They participate in extracellular events such as cell proliferation, cell adhesion, bacterial colonization, apoptosis, oncogenesis, chemotaxis, embryogenesis, oncogenesis, and differentiation. To date, 15 Gal have been identified. The most studied enzyme is galectin-3 (Gal-3). This lectin group is defined as a protein that activates oxidative stress and inflammation. Gal-3 is a multifunctional protein that participates in various biological processes, including proliferation, differentiation, angiogenesis, cancer progression, and metastasis. Additionally, Gal play an important role in fibrogenesis. Fibrotic diseases are seen in the lungs, heart, kidneys, and liver, and they cause permanent organ damage and loss of function. For these reasons, Gal are considered potential inflammatory markers. As the structure and functions of Gal become clearer, new molecules are expected to facilitate the diagnosis and treatment of vascular complications associated with inflammation, autoimmune diseases, tumor spread, cancers, allergic events, diabetes, and hypertension. Here, we aimed to review the most recent literature to draw attention to the importance of Gal and to remind patients of their potential benefits in diagnosis and treatment.

Keywords: Galectins, inflammation, fibrosis, biomarker, Gal-3

INTRODUCTION

Galectin-3 (Gal-3), a member of the galectin (Gal) protein family, has garnered significant attention in recent years owing to its diverse roles in various physiological and pathological processes. This multifunctional protein interacts with beta-galactoside-containing glycoconjugates, influencing cell-cell and cell-matrix interactions, as well as signaling pathways. Additionally, recent research has been conducted to understand the complex roles of fibrosis, cardiovascular disease, and cancer progression.[1]

A study by Danguy[2], highlighted the crucial role of Gal-3 in cancer biology and demonstrated its impact on tumor growth, invasion, and metastasis. The study elucidated the mechanisms through which Gal-3 promotes tumor progression, suggesting its potential as a therapeutic target in cancer. Additionally, a review that[3] emphasized the significance of Gal-3 in fibrotic diseases, such as liver and pulmonary fibrosis. The authors discussed the molecular pathways regulated by Gal-3 in fibrosis and proposed Gal-3 inhibitors as promising therapeutic agents for these conditions. Moreover, emerging evidence suggests a link between Gal-3 and cardiovascular diseases, as explored in a study by Henderson[4]. The researchers identified Gal-3 as a biomarker of cardiovascular risk and heart failure (HF), highlighting its potential utility in predicting and managing cardiac disorders.[4] In cardiovascular diseases, Gal-3 is a key point in the pathogenesis of HF, fibrosis, and atherosclerosis. Many studies have demonstrated that elevated Gal-3 levels are associated with inflammation, adverse cardiac remodeling, and myocardial fibrosis, leading to impaired cardiac function.[5]

Moreover, Gal-3 has been implicated in atherosclerotic plaque formation and instability through its effects on vascular inflammation and smooth muscle cell proliferation.[6] In inflammatory conditions, Gal-3 has been shown to modulate immune responses by regulating macrophage

To cite this article: Tınazlı M, Bakhtiyarova G. Galectins: an amazing marker and a potential therapeutic target. Cyprus J Med Sci. 2025;10(1):7-12

ORCID IDs of the authors: M.T. 0000-0002-7858-0696; G.B. 0009-0000-6038-9263.

Corresponding author: Mehtap Tınazlı
E-mail: mehtap.canbaz@hotmail.com
ORCID ID: orcid.org/0000-0002-7858-0696

Received: 19.04.2024
Accepted: 06.09.2024
Publication Date: 14.03.2025

activation, cytokine production, and T-cell function. Gal-3 plays a dual role in inflammation, acting as both a proinflammatory mediator and a regulator of immune tolerance.[1] The dysregulation of Gal-3 expression has been linked to autoimmune diseases, such as rheumatoid arthritis (RA) and inflammatory bowel disease, highlighting the importance of Gal-3 in immune homeostasis and disease pathogenesis. The pathophysiology of Gal-3 encompasses many biological processes, such as immune regulation, cancer progression, and cardiac dysfunction.

Gal-3 is expressed in renal cell types such as tubular epithelial, mesangial, and immune cells within the kidney. Its interactions with cell surface receptors and extracellular matrix components modulate cell adhesion, migration, and survival, thus influencing the cellular responses to injury and repair processes in the kidney.[7]

Generally, Gal-3 seems to play a certain role in inflammation, fibrosis, cancer, and other organ diseases. As an internal medicine specialist, we wondered about the role of Gal-3, which has been accepted as a biomarker in cardiovascular, kidney, gastrointestinal, autoimmune, infection, cancer, and thyroid diseases, and we also conducted a general literature review and found out the role of this biomarker in these diseases and prepared this article by wondering how predictive it is and how much it affects prognosis and mortality.

Gal-3 and Cardiovascular Diseases

Gal-3 mainly induces pathological remodeling and fibrosis; therefore, in HF pathology, it has been called a "culprit" biomarker, such as C-reactive protein or N-terminus pro B-type natriuretic peptide in HF.[8] Zaborska et al.[9] in their review published in 2023, they found the following evidence: HF is a clinical syndrome with increasing frequency and high morbidity and mortality. The search for a biomarker that can be useful in diagnosis and risk classification has continued in recent literature.[9]

Făgărăşan et al.[10] examined the effect of Gal-3 in heart disease (congenital) in the same year and stated the following in their review: According to what we know so far, Gal-3 has the potential to predict cardiac dysfunction in adults and children. It is a novel biomarker. Here, we describe how Gal-3 may be potentially useful in the early detection of failure symptoms and predicting postoperative complications in patients with congenital heart disease. Further studies are needed to determine how Gal-3 may relate to complications and long-term outcomes in both adult and pediatric patients. The reliability of the predictive feature depends on clinical concordance and positive correlation with data obtained from advanced cardiac imaging, such as echocardiography and cardiac magnetic resonance.[10]

Coronary Heart Disease, Myocardial Infarction, Atrial Fibrillation

Elevated serum Gal-3 levels have been linked to a heightened incidence of cardiovascular events in individuals with chronic coronary heart disease. Conversely, another large-scale patient follow-up study spanning a 13-year enrollment period of stable chronic heart patients indicated that Gal-3 could not autonomously forecast recurrence after accounting for biomarkers of inflammation, hemodynamic stress, myocardial dysfunction, and renal dysfunction.[11] Gal-3 serum levels displayed a notably positive correlation with the severity of disease in individuals diagnosed with coronary artery disease, and higher Gal-3 levels were accompanied by an elevated degree of myocardial fibrosis.[12] Moreover, elevated Gal-3 levels expression was correlated with diuretic therapy administration and a higher incidence of acute atrial fibrillation (AF). Pranata et al.[13], according to the results of their study, serum Gal-3 levels after ablation are associated with an increased risk of AF recurrence. However, detailed research is needed to confirm these findings and the use of Gal-3 as a therapeutic biomarker.[13] Mohtasham Kia et al.[14] in 2023, a review titled "Insights into the Role of Gal-3 as a Diagnostic and Prognostic Biomarker of AF" in the Journal Disease Markers also investigated the potential role of Gal-3 as a biomarker of AF.

In conclusion, Gal-3 is a biomarker, prognostic, and mortality determinant of many cardiovascular diseases.

Gal-3 and Kidney Diseases

Gal-3 is the precursor of the kidney, Gal-3 can be found in the apical areas of the branches of the ureteric bud during the metanephros. It is also expressed in the fetal papillary and medullary collecting ducts of both the plasma and cytoplasmic membranes. It becomes evident later in fetal kidney maturation in the basal areas of the medullary collecting ducts. Gal-3 expression has been reported at later stages of nephrogenesis, but it is limited to the primary cilium and collecting tubules in normal adult kidneys.[15]

Numerous studies have reported increased Gal-3 levels in patients. Gal-3 has the potential to be a biomarker for diagnosis and prognosis of diabetic nephropathy (DN). However, the results from individual studies are inconsistent, and the relationship between Gal-3 and DN needs to be investigated in more comprehensive meta-analyses. As a result of this meta-analysis, although some studies have supported the association between Gal-3 expression and DN risk, the actual effect of Gal-3 on DN risk is still controversial because the results of individual studies differ.[16]

Furthermore, Gal-3 plays crucial roles in fibrogenesis across various organs, including the lungs, kidneys, liver, and myocardium, as highlighted in recent research. In a study involving kidney biopsies from 249 patients with chronic kidney disease (CKD), plasma Gal-3 concentrations were assessed. Results showed a direct correlation with tubular atrophy and interstitial fibrosis and an inverse correlation with estimated glomerular filtration rate.[17]

In another study involving 280 patients who underwent kidney biopsy, higher urinary Gal-3 levels were associated with severe interstitial fibrosis.[18]

A new study in 2024 by Kim et al.[19] in their scientific report published in the Journal Nature Portfolio, the authors provided evidence that Gal-3 increases vascular calcification and high inflammatory status, suggesting a potential causal relationship between serum Gal-3 and increased mortality in hemodialysis patients.

The current evidence indicates that Gal-3 is a promising biomarker and therapeutic target in acute kidney injury and CKD. However, further research is warranted to fully elucidate its diagnostic and therapeutic potential in these conditions.

Galectins and Gastrointestinal Diseases

According to the literature, it is associated with chronic liver disease, liver fibrosis, cirrhosis, cholestatic liver diseases, and those with chronic gastritis and *Helicobacter pylori (H. pylori)* positive. Rayane Bernardes Estevametal investigated the modulation of Gal-3 and Gal-9 in the gastric mucosa of patients with confirmed *H. pylori* infection and

chronic gastritis. The authors evaluated mast cell density and the *in situ* expression of Gal-1, -3, and -9 using immunohistochemistry in 44 gastric antrum biopsy samples obtained from patients with chronic gastritis, those with active gastritis, and a control group. Their findings revealed a significant positive association between *H. pylori* infection and chronic gastritis.[20] Additionally, the potential effect of *H. pylori*-associated Gal-3 on neurodegeneration was also reported by Boziki et al.[21] It was researched in 2018. They focused on the role of Gal-3 in shaping the immune system's responses to microbial agents, specifically *H. pylori*, thereby enhancing the effect of the microbe in areas distant from the normal site of colonization, such as the central nervous system (CNS) in this review.[21]

The Relationship Between Liver Fibrosis and Galectin-3

The role of Gal-3 in liver disease is unclear. In this regard, in 2021, An et al.[22] the major scientific research was conducted by. In this study, the researchers conducted searches in PubMed, Embase, and the Cochrane Library databases and identified 43 cohorts and 33 studies involving a total of 4,168 patients with hepatocellular carcinoma (HCC) liver disease. Among patients with HCC, high tissue expression of Gal-1 and Gal-3 was significantly correlated with poor overall survival and positive vascular invasion. Conversely, high tissue expression levels of Gal-4 and Gal-9 were significantly associated with better overall survival and a low risk of vascular invasion.

Furthermore, serum levels of Gal-3 were notably elevated in various liver conditions, including HCC, chronic active hepatitis B, liver failure, and cirrhosis. Additionally, serum Gal-9 levels were significantly higher in HCC and autoimmune hepatitis. The study concluded that low expression of Gal-4 and Gal-9 and high expression of Gal-1 and Gal-3 are indicative of poor prognosis in patients with HCC, as well as serum levels of Gal-3 and Gal-9 in chronic liver diseases, showing a positive association with risk.[22]

Wang et al.[23] published a review in International Immunopharmacology in 2023. In this review, the authors attempted to explain the identity and mechanism of macrophages in liver fibrosis. The etiologies-underlying liver fibrosis are the various; alcohol consumption, viral infections, and drug toxicity. Cirrhosis is a common clinical liver syndrome that causes approximately two million deaths annually worldwide. Although fibrosis is generally considered difficult to reverse, due to the liver's extensive regenerative capacity, liver fibrosis is possible. Additionally, the imbalance in fibrosis formation can be regulated by specific interventions. This treatment may help prevent or even reverse fibrosis before it becomes irreversible. However, the chronic inflammatory environment of fibrotic liver can remodel macrophages and stimulate them toward different phenotypes.[23]

In 2021, Del Turco et al.[24] published an article. In this study, YKL-40 and Gal-3 levels were compared in the evaluation of liver fibrosis in patients with cirrhosis. A total of 46 participants consisted of 24 patients, 10 with HCC, 14 without HCC, and 22 healthy individuals. Gal-3 and YKL-40 were measured in the serum of all patients and candidates in the healthy group. Consequently, YKL-40 and Gal-3 levels were notably elevated in kidney transplant recipients compared with the healthy group. It was determined that 1 day after transplantation, the Gal-3 and YKL-40 levels started to decrease compared with the baseline levels and remained unchanged for 1 month. In this study, Gal-3, but not YKL-40, was shown to be associated with the severity of liver fibrosis; therefore, using this non-invasive, simple, and rapid method, estimating the amount of circulating Gal-3 was associated with both liver damage and fibrosis. Gal-3 may be useful as an indicator of inflammatory processes. However, Gal-3 cannot be used as a general biomarker for HCC because blood levels do not differ between patients with and without HCC.[24]

Galectin and Its Relationship with Other Diseases

Cancer Types and Galectin

Gal-3 levels are elevated in many other diseases, including various types of cancer and chronic obstructive pulmonary disease. Although its role in cancer development is not fully known, it has been reported that it may be associated with neoplastic formation and metastasis. Many studies in the literature have shown that immunohistochemical dyes such as Gal-3 have low specificity for cancer detection.[25] It is known that Gal-3 expression increases especially in the gastrointestinal system, pancreas, breast, head and neck, CNS thyroid, uterus, bladder, and tongue cancers. There are no markers that can definitively differentiate benign from malignant thyroid nodules before surgery. Serum Gal-3 levels were found to be statistically higher in some studies in patients with malignant thyroid nodules. It has been reported that Gal-3 expression increases, especially in papillary carcinomas, and can be used in the differential diagnosis of benign lesions.[26]

The importance of biomarkers such as Gal-3 in the prognosis of PTCs is unclear. In a study where Gal-3 expression was found to be higher in papillary thyroid cancer patients than in anaplastic thyroid cancers, survival was found to be higher in anaplastic thyroid cancers, and Gal-3 was found to not correlate with the advanced stage of the tumor or the presence of lymph node metastasis.[27]

There are no sufficient studies on the relationship between serum Gal levels and lung cancer. However, in clinical use, measuring Gal levels in serum is easier and more practical than measuring Gal expression in tissue. In a study conducted in 2018, serum levels of Gal-1 and -3 values were found to be significantly lower in patients with lung cancer than in the control group. Gal-1 and -3 levels; no relationship was found with survival, tumor diameter, or tumor stage. In the presence of metastasis, both Gal levels were significantly lower. Many preclinical studies on lung cancer have found a relationship between Gal-1 and immune escape and tumor progression. Gal-1 also has prognostic significance in human lung cancer. Tumor cell variants with high potential for lung colonization have high Gal-3 expression levels on the cell surface. Similarly, increased Gal-3 expression is correlated with the metastatic potential of some tumorigenic cells, such as cell motility and invasion into the extracellular matrix. However, the relationship between these findings and the epithelial origin of human tumors is not fully understood. Although it has been explained by various mechanisms that high Gal values in the tissue are related to stage, metastasis, and survival in some types of cancer, it is not clear whether the measurement of Gal in serum is correlated with the level in tissue. There is a need for studies investigating the correlation between high Gal levels in tissue and serum levels. Gal-1 and -3 levels measured in serum are not associated with survival in lung cancer patients.[28]

Idiopathic Pulmonary Fibrosis

Idiopathic pulmonary fibrosis (IPF) is a lung disease of unknown cause, with poor prognosis, advanced fibrosis, chronic and progressive disease, and is ultimately fatal. Factors causing recurrent alveolar damage

include viral infections, gastroesophageal reflux, and environmental and occupational exposure. Additionally, genetic predisposition is an important factor in damage development.[29]

It is known that biomarkers are important for calculating the risk of developing IPF, early diagnosis of the disease, prognosis, and monitoring the response to treatment. The ideal biomarker should be valid and reliable and should be easily obtained using non-invasive methods. Research on more than one biomarker in IPF is ongoing, but a biomarker that can be used primarily in clinical practice has not yet been identified. Gal-3 is defined as a marker that activates oxidative stress, and the inflammatory response is considered a potential inflammatory marker. It has been shown to regulate immune response, cell receptor interactions, inflammation, cancer cell behavior, and scar formation. Much evidence has shown that Gal-3' activates various profibrotic factors, stimulates fibroblast proliferation, and accompanies collagen production.[30] Because safe and effective treatments for IPF are urgently needed, many new treatment options, including TD139 (the Gal-3 inhibitor), are currently being investigated. In recent studies, the effect of inhaled Gal-3 inhibitor combined with nintedanib in patients with IPF is in the phase 2 study phase.[31] There are many studies showing the biochemical and immunological relationship between Gal-3 and lung fibrosis, but in most of them, although Gal-3 was slightly higher than in controls, the difference was not statistically significant.[32,33]

It appears that Gal-3 is a multifunctional protein that triggers inflammation and affects its progression.[34]

Relationship with Rheumatic Diseases

In literature reviews, Gal-1, -3 and -9 are associated with many autoimmune diseases, such as uveitis, Behçet's disease (BD), and RA.[35]

Gals can participate in inflammatory and immune responses as autoantigen. In the studies conducted, the presence of autoantibodies against different Gal was detected in normal healthy individuals and selected patient individuals. In a study conducted by Lee et al.[36] in 2007, Gal-3 levels were found to be higher in patients with BD and RA than in the control group.

Yilmaz et al.[37] reported that Gal-3 levels in serum increased in Familial Mediterranean fever patients. The reason for the increase in Gal-9 expression in inflammatory diseases is that they-3, the ligand of Gal-9 in Th1 cells, triggers Gal-9 and uses this situation to suppress Th1 immunity. In the meantime, Gal-9 is spontaneously activated by interferon gamma (IFN-γ) expression is upregulated. It is thought that the elevation of Gal-3 expression may be due to its role as a positive regulator of inflammation and for increasing the activation of cells in the myeloid series. As observed in all the data, different Gal can create inhibitory or enhancing signals to control the immune system. In addition, many cytokines such as IFN-γ, growth factors [transforming growth factor-alpha (TGF-α), TGF-β], the monomer/dimer balance of Gal, their stability in tissues, and their amount, decrease, or increase due to many effects such as reduction and oxidation may harm the organism. Studies have shown that cytokines increase the expression of some Gal in inflammatory diseases. Therefore, it appears that the body creates a more effective and severe response by increasing the production of endogenous anti-inflammatory Gal to regulate the homeostasis of immune cells. Before the development of Gal-based therapeutic agents, a more comprehensive investigation and comprehension of the mechanisms and pathways involved in the different "immunoregulatory" roles of the less-explored Gal is required. It is not yet known what effect functional deficiency or excess of the Gal family has. We do not know why the same Gal exhibit different functions in different environments. New research shows that Gal play an important role in the development of acute inflammation, infectious diseases, allergies, autoimmune diseases, atherosclerosis, and cancer-related chronic inflammation. Thus, recombinant proteins or specific Gal inhibitors can be used as therapeutic agents for inflammatory diseases.[38]

Several studies have shown that serum Gal-3 binding protein (Gal-3BP), a novel marker of obesity and Metabolic syndrome (MetS),[39] is positively associated with MetS. In a study involving 570 Chinese adults, serum Gal-3BP was found to be a useful biomarker for the risk of developing MetS.[40] There are studies supporting the idea that high serum Gal-3 levels may be a good marker for myocardial fibrosis in adolescents with obesity and MetS and in patients with MetS and AF.[41]

Immunoglobulin-G4-related disease (IgG4-RD) is a rare systemic fibroinflammatory disease. The pathogenesis of this condition is not fully known and appears to be multifactorial. Accepted environmental factors such as blue-collar work are also important risk factors. It was first described in 2003 as an autoimmune disease that causes multi-organ involvement, especially in the chest, head and neck, pelvic, and abdominal organs. Many autoantigen and autoantibodies are used for diagnosis. Most of these antibodies are not specific to the disease, and antibodies against IgG4-related cholangitis (IRC), laminin 511-E8, annexin A11, prohibitin 1, and Gal-3 have been confirmed. Gal-3 has been specifically associated with manifestations of type 1 autoimmune pancreatitis, IRC, and salivary and lacrimal glands. Gal-3 has been indirectly associated with disease activity but has been reported to remain elevated during glucocorticosteroid treatment. Additionally, Gal-3 inhibits the differentiation of B cells into immunoglobulin-secreting plasma cells, and Gal-3 has a profibrotic role that has been attributed to various fibrotic diseases.[42] One study showed an increase in Gal-3 expression in cells involved in immune response activity, including dendritic cells, macrophages, epithelial cells, and myofibroblasts in patients with IgG4-RD, whereas Gal-3 signaling was also found in stromal deposition.

Gal-3 is also required for the effective phagocytosis of macrophages to remove apoptotic cells and thus prevent autoimmune reactions. In addition, endogenous Gal-3 has been found to induce Th2. Gal-3 is highly expressed in affected tissues. In addition to IgG4-RD, Gal-3 expression has been shown to increase in various autoimmune diseases, such as RA, polymyositis-dermatomyositis, systemic lupus erythematosus, systemic sclerosis, BD, and Crohn's disease.[43] In another study, in patients diagnosed with IgG4-RD, Gal-3 levels were found to be high in the tissues of the pancreas, lung, salivary glands, kidney, aorta, retroperitoneum, and bile ducts, especially at higher levels in the lymph nodes, and IgG4 anti-Gal-3 autoantibodies were detected, especially in the lymph nodes was found to be associated.[44]

Autoimmune Endocrine Diseases and Galectins

Graves is an autoimmune disease of the thyroid gland. In Graves' disease, the immunotolerance of thyroid structures is impaired by several factors (endogenous and environmental factors). This results in the induction of TRAb produced by B-cells. Gal-3 is crucial in numerous cell functions, including transformation, pre-mRNA splicing, growth, and apoptosis, as

well as other biological activities, such as inflammation, host defense, angiogenesis, and fibrosis.[45,46]

In light of this information, some recent studies have found that blood Gal-3 levels are increased in patients with Graves' disease. However, there was no difference in Gal-3 levels between Graves' patients with thyroid-related ophthalmopathy and those without compared with healthy controls.[47]

CONCLUSION

Gal-3 is a multifunctional protein involved in a variety of functions types of diseases. Its prognostic value in predicting the outcomes of HF and its diagnostic value in thyroid carcinoma diagnosis have been extensively investigated. It has also been found useful in predicting metastases in laryngeal carcinoma, breast, colorectal cancers, prostate, pancreatic and gastric cancers. Functions of Gal-3 in fibrosis and immunity has also been researched, which suggests it is possible therapeutic benefit in certain types of fibrotic diseases and infection. Gal-may represent a therapeutic approach to delay progression from these diseases. As a result, in our literature review, we see that Gal-3 appears as a diagnostic, prognostic, and mortality biomarker in all diseases that we frequently see in internal medicine practice, in all areas covering the branch of internal medicine. And we see that this Gal-3 biomarker plays a major role in the further follow-up and treatment of these diseases.

MAIN POINTS

- Galectins may be useful biomarkers for the early diagnosis of inflammatory diseases and malignancies.
- New detailed studies should be conducted to increase the specificity and sensitivity.
- This approach may open new horizons for intelligent design of treatment targets after diagnosis.

FOOTNOTES

Authorship Contributions

Concept: M.T., G.B.; Design: M.T., G.B.; Data Collection and/or Processing: M.T., G.B.; Analysis and/or Interpretation: M.T., G.B.; Literature Search: M.T., G.B.; Writing: M.T., G.B.

DISCLOSURES

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study had received no financial support.

REFERENCES

1. Chen J. Galectin-3 in inflammation and immune regulation. Cytokine & Growth Factor Reviews. 2021; 58: 120-8.
2. Danguy A. Galectin-3 in cancer biology: a target for therapeutic intervention. Cancer Treatment Reviews. 2018; 68: 51-63.
3. Wang J. Galectin-3 in fibrotic diseases: pathogenesis and potential therapeutic targets. Frontiers in Pharmacology. 2020; 11: 97.
4. Henderson NC. Galectin-3 in heart failure: More than just a biomarker? ESC Heart Failure. 2019; 6(1): 178-84.
5. Lopez-Sanz L. Galectin-3 in heart failure: an update of the last 3 years. Heart Failure Reviews. 2019; 24(5): 661-75.
6. van der Velde AR. Galectin-3 in atherosclerotic plaque progression and vulnerability. Current Opinion in Lipidology. 2020; 31(3): 156-61.
7. Henderson NC, Rieder F, Wynn TA. Fibrosis: from mechanisms to medicines. Nature. 2020; 587(7835): 555-66.
8. Zaborska B, Pilichowska-Paszkiet E, Makowska E, Sygitowicz G, Słomski T, Zaborski M, et al. Prognostic value of galectin-3 and right ventricular function for long-term mortality in heart failure patients treated with cardiac resynchronization therapy. Sci Rep. 2021; 11(1): 21390.
9. Zaborska B, Sikora-Frąc M, Smarż K, Pilichowska-Paszkiet E, Budaj A, Sitkiewicz D, et al. The role of galectin-3 in heart failure-the diagnostic, prognostic and therapeutic potential-where do we stand? Int J Mol Sci. 2023; 24(17): 13111.
10. Făgărăşan A, Săsăran M, Gozar L, Crauciuc A, Bănescu C. The role of galectin-3 in predicting congenital heart disease outcome: a review of the literature. Int J Mol Sci. 2023; 24(13): 10511.
11. Jansen H, Koenig W, Jaensch A, Mons U, Breitling LP, Scharnagl H, et al. Prognostic utility of galectin 3 for recurrent cardiovascular events during long term follow up in patients with stable coronary heart disease: Results of the KAROLA study. Clin Chem. 2016; 62: 1372-9.
12. Aksan G, Gedikli Ö, Keskin K, Nar G, İnci S, Yıldız SS, et al. Is galectin-3 a biomarker, a player-or both-in the presence of coronary atherosclerosis? J Investig Med. 2016; 64(3): 764-70.
13. Pranata R, Yonas E, Chintya V, Tondas AE, Raharjo SB. Serum galectin-3 level and recurrence of atrial fibrillation post-ablation - Systematic review and meta-analysis. Indian Pacing Electrophysiol J. 2020; 20(2): 64-9.
14. Mohtasham Kia Y, Cannavo A, Bahiraie P, Alilou S, Saeedian B, Babajani N, et al. Insights into the role of galectin-3 as a diagnostic and prognostic biomarker of atrial fibrillation. Dis Markers. 2023; 2023: 2097012.
15. Wang F, Zhou L, Eliaz A, Hu C, Qiang X, Ke L, et al. The potential roles of galectin-3 in AKI and CKD. Front Physiol. 2023; 14: 1090724.
16. Guo Y, Li L, Hu S. Circulating galectin-3 levels and diabetic nephropathy: a systematic review and meta-analysis. BMC Nephrol. 2023; 24(1): 163.
17. Ou SM, Tsai MT, Chen HY, Li FA, Tseng WC, Lee KH, et al. Identification of galectin-3 as potential biomarkers for renal fibrosis by RNA-sequencing and clinicopathologic findings of kidney biopsy. Front Med (Lausanne). 2021; 8: 748225.
18. Ou SM, Tsai MT, Chen HY, Li FA, Lee KH, Tseng WC, et al. Urinary galectin-3 as a novel biomarker for the prediction of renal fibrosis and kidney disease progression. Biomedicines. 2022; 10(3): 585.
19. Kim JH, Noh HM, Song HJ, Lee S, Kim SG, Kim JK. Mediating effect of vascular calcification in galectin-3-related mortality in hemodialysis patients. Sci Rep. 2024; 14(1): 939.
20. Estevam RB, Wood da Silva NMJ, Wood da Silva, Fonseca FM, Oliveira AG, Nogueira, et al. Modulation of galectin-3 and galectin 9 in gastric mucosa of patients with chronic gastritis and positive *Helicobacter pylori* infection. Pathol Res Pract. 2017; 213(10): 1276-81.
21. Boziki M, Polyzos SA, Deretzi G, Kazakos E, Katsinelos P, Doulberis M, et al. A potential impact of *Helicobacter pylori*-related galectin-3 in neurodegeneration. Neurochem Int. 2018; 113: 137-51.
22. An Y, Xu S, Liu Y, Xu X, Philips CA, Chen J, et al. Role of galectins in the liver diseases: a systematic review and meta-analysis. Front Med (Lausanne). 2021; 8: 744518.
23. Wang Z, Du K, Jin N, Tang B, Zhang W. Macrophage in liver fibrosis: identities and mechanisms. Int Immunopharmacol. 2023; 120: 110357.

24. Del Turco S, De Simone P, Ghinolfi D, Gaggini M, Basta G. Comparison between galectin-3 and YKL-40 levels for the assessment of liver fibrosis in cirrhotic patients. Arab J Gastroenterol. 2021; 22(3): 187-92.

25. Çandar T, Hasbek Z, Duman G, Ertürk SA, Çakmakcılar A. The relation between serum galectin-3 and differential thyroid cancers. Bozok Tıp Dergisi. 2019; 9(3): 11-5.

26. Al-Sharaky DR, Younes SF. Sensitivity and specificity of galectin-3 and glypican-3 in follicular-patterned and other thyroid neoplasms. J Clin Diagn Res. 2016; 10(3): EC06-10.

27. Selemetjev SA, Savin SB, Paunovic IR, Tatic SB, Cvejic D. Changes in the expression pattern of apoptotic molecules (galectin-3, Bcl-2, Bax, survivin) during progression of thyroid malignancy and their clinical significance. Wien Klin Wochenschr. 2015; 127(9-10): 337-44.

28. Erçen Diken Ö, Aydemir Y, Demir E. Diagnostic and prognostic value of serum galectin-1 and galectin-3 levels in lung cancer patients. Bozok Tıp Dergisi. 2018; 8(1): 118-24.

29. Okumuş NG, Bingöl Z. Türk Toraks Derneği. İdiyopatik Pulmoner Fibrozis (İPF) Tanı ve Tedavi Uzlaşı Raporu. Bilimsel Tıp Yayınevi, Ankara. 2018. Available from: https://www.toraks.org.tr/site/sf/books/pre_migration/f4a60e886cf6d379739d9c97aca8d35030f434c5057811b3e9bcb76f3eff427f.pdf

30. Humphries DC, Mills R, Dobie R, Henderson NC, Sethi T, Mackinnon AC. Selective myeloid depletion of galectin-3 offers protection against acute and chronic lung injury. Front Pharmacol. 2021; 12: 715986.

31. Hirani N, MacKinnon AC, Nicol L, Ford P, Schambye H, Pedersen A, et al. Target inhibition of galectin-3 by inhaled TD139 in patients with idiopathic pulmonary fibrosis. Eur Respir J. 2021; 57(5): 2002559.

32. Shochet GE, Pomerantz A, Shitrit D, Bardenstein-Wald B, Ask K, Surber M, et al. Galectin-3 levels are elevated following nintedanib treatment. Ther Adv Chronic Dis. 2020; 11: 2040622320968412.

33. d'Alessandro M, De Vita E, Bergantini L, Mazzei MA, di Valvasone S, Bonizzoli M, et al. Galactin-1, 3 and 9: potential biomarkers in idiopathic pulmonary fibrosis and other interstitial lung diseases. Respir Physiol Neurobiol. 2020; 282: 103546.

34. Srejovic I, Selakovic D, Jovicic N, Jakovljević V, Lukic ML, Rosic G. Galectin-3: roles in neurodevelopment, neuroinflammation, and behavior. Biomolecules. 2020; 10(5): 798.

35. Romero MD, Muiño JC, Bianco GA, Ferrero M, Juarez CP, Luna JD, et al. Circulating anti-galectin-1 antibodies are associated with the severity of ocular disease in autoimmune and infectious uveitis. Invest Ophthalmol Vis Sci. 2006; 47(4): 1550-6.

36. Lee YJ, Kang SW, Song JK, Park JJ, Bae YD, Lee EY, et al. Serum galectin-3 and galectin-3 binding protein levels in Behçet's disease and their association with disease activity. Clin Exp Rheumatol. 2007; 25(4 Suppl 45): S41-5.

37. Yilmaz H, Inan O, Darcin T, Bilgic MA, Akcay A. Serum galectin-3 levels were associated with proteinuria in patients with familial mediterranean fever. Clin Exp Nephrol. 2015; 19(3): 436-42.

38. Otugüzel M. Ankilozan spondilit hastalarında Galektin-1, Galektin-3, Galektin-9 düzeylerinin incelenmesi. Cumhuriyet Üniversitesi/Sağlık Bilimleri Enstitüsü Biyokimya Anabilim Dalı. Yüksek Lisans Tezi, 2017; s. 30-1. Available from: file:///Users/galenos/Downloads/493476%20(1).pdf

39. Zhen S, Cail R, Yang X, Ma Y, Wen D. Association of serum galectin-3-binding protein and metabolic syndrome in a Chinese adult population. Front. Endocrinol. 2021. Available from: https://doi.org/10.3389/fendo.2021.726154

40. Zhen S, Ma Y, Han Y, Zhao Z, Yang X, Wen D. Serum galectin-3BP as a novel marker of obesity and metabolic syndrome in Chinese adolescents. BMJ Open Diabetes Res Care. 2021; 9(1): e001894.

41. Ionin VA, Baranova EI, Zaslavskaya EL, Petrishcheva EY, Morozov AN, Shlyakhto EV. Galectin-3, N-terminal propeptides of type I and III procollagen in patients with atrial fibrillation and metabolic syndrome. Int J Mol Sci. 2020; 21(16): 5689.

42. Kersten R, Trampert DC, Herta T, Hubers LM, Maillette de Buy Wenniger LJ, Verheij J, et al. IgG4-related cholangitis - a mimicker of fibrosing and malignant cholangiopathies. J Hepatol. 2023; 79(6): 1502-23.

43. Salah A, Yoshifuji H, Ito S, Kitagori K, Kiso K, Yamada N, et al. high expression of galectin-3 in patients with IgG4-related disease: a proteomic approach. Patholog Res Int. 2017; 2017: 9312142.

44. Perugino CA, AlSalem SB, Mattoo H, Della-Torre E, Mahajan V, Ganesh G, et al. Identification of galectin-3 as an autoantigen in patients with IgG4-related disease. J Allergy Clin Immunol. 2019; 143(2): 736-45.

45. Dong R, Zhang M, Hu Q, Zheng S, Soh A, Zheng Y, et al. Galectin-3 as a novel biomarker for disease diagnosis and a target for therapy (Review). Int J Mol Med. 2018; 41(2): 599-614.

46. Wémeau JL, Klein M, Sadoul JL, Briet C, Vélayoudom-Céphise FL. Graves' disease: Introduction, epidemiology, endogenous and environmental pathogenic factors. Ann Endocrinol (Paris). 2018; 79(6): 599-607.

47. Akın M, Karaaslan H, Eren MA, Koyuncu İ, Sabuncu T. Evaluation of galectin-3 in graves' disease with and without ophthalmopathy. Endocrinol Res Pract. 2023; 27 (2): 85-8.