INTRODUCTION

Colorectal cancer (CRC) is the third most prevalent cancer in both sexes worldwide. It is the second most common cause of cancer-related mortality in both sexes [1]. It is responsible for 9.4% of newly diagnosed cancer cases in men and 10.1% in women [2]. About 70% of the CRC cases are sporadic, i.e. no familial or genetic contribution can be found [3]. Genetic alterations or genomic re-arrangements can lead to important changes in cells with respect to both their function and the regulation of their proliferation [4]. Genetic derangements include activation of oncogenes (e.g. K-ras); inactivation of tumor suppressor genes (e.g. APC, p53) and DNA mismatch repair genes (e.g. hMSH2, hMLH1); and expression of genes (e.g. COX-2) with an unclear role in tumor formation, but which are considered to take part in the progression of tumor sequence [5]. A thorough understanding of colorectal carcinogenesis requires the elucidation of genetic mechanisms responsible for tumor development.

Galectin-3 is the only chimera galectin in vertebrates, and it has been widely studied. As a 29–35 kDa protein, it is involved in a series of processes in the human body, including cell adhesion, cell activation and chemotraction, cell growth and differentiation, cell cycle, and apoptosis. Galectins are usually devoid of a signal peptide for involvement in the classical secretory pathway. However, galectin-3 has been isolated from...
extracellular space where it binds to a large number of molecules, mainly polyglactosamine-rich molecules found in the extracellular matrix (ECM) or on cell surface. Galectin-3 has a vital function in the modulation of tumor progression in extracellular space [6-8]. It has recently been reported that it is also involved in the Wnt pathway and serves by binding to and promoting beta-catenin translocation into the nucleus [9]. It has also recently been demonstrated that the galectin-3 level is proportional to beta-catenin expression and the amount in colon cancer cells [9,10].

Iacovazzi et al. showed that galectin-3 levels were higher than the control group in well-differentiated colorectal cancers [11]. Immunohistochemical studies have demonstrated that galectin-3 is present in higher amounts in colorectal tissues of metastatic or recurrent cases [12]. Zaia et al. showed that it affects tumor-related survival by inhibiting apoptosis through binding to tumor necrosis factor-related apoptosis-inducing ligand (TRAIL). Mazurek et al. reported findings supporting this information [13]. Animal studies have similarly shown higher galectin-3 expression [14]. Gene expression studies have indicated that the loss of galectin-3 expression is due to epigenetic factors in mucinous colorectal cases. Mahmoud et al. demonstrated that the DNA methylation profile of an LGALS3 promoter was unmethylated in nonmucinous colorectal carcinomas, whereas LGALS3 was aberrantly methylated in mucinous colorectal carcinomas. This has been regarded as important information pointing to differences in the pathogenesis of mucinous-type colorectal cancers [15].

Greco et al. demonstrated that the galectin-3 level was high in adenoma-containing tissues and blood samples of patients with adenomas [16]. Despite being a protein with well-defined functions in blood and tissue, no study has yet explored LGALS3 (galectin-3) gene variations and mutations in colorectal cancers.

About 90% of colorectal cancers are characterized by some somatic mutations in genes taking part in the canonical, or beta-catenin-dependent, Wnt pathway [17]. Although APC is the most commonly mutated Wnt pathway tumor suppressor gene, some CRCs and certain other malignancies have been found to contain germline or somatic mutations in the AXIN1 or AXIN2 genes [18]. AXIN1 is mainly responsible for the assembly of the beta-catenin destruction complex in the Wnt pathway, which serves as an inhibitory step in the expression of Wnt- and beta-catenin-dependent target genes [19]. Alterations of the Wnt pathway are reportedly common in colorectal cancer with microsatellite instability, and AXIN mutations have identified AXIN as one of the genes that plays a role in these alterations [20]. In several studies, elevated levels of nuclear beta-catenin in various human cancers have been demonstrated as a hallmark of active WNT/beta-catenin signaling, while mutations of AXIN gene were significantly less frequent [21].

A genotyping study by Khan et al. conducted in a Kashmiri population revealed a codon D726D (GAT>GAC) variant causing no amino acid change in the first exon of AXIN in cases with colorectal carcinoma [22]. Jin et al. detected 3 silent mutations and 6 missense point mutations in colorectal carcinoma [23]. Formerly known as an AXIN inter-actor in the c-Jun NH(2)-terminal kinase pathway, MAPK is also taken part in the canonical Wnt signaling pathway, where it positively regulates the expression of Wnt target genes [24]. Although there are a number of studies that examined the somatic mutations and functions of the AXIN gene, gene variants have not been studied in detail.

The aim of our study was to investigate the relationship between the gene variants of AXIN1 (rs214250) and galectin-3 (rs4644 and rs4652) genes and histopathological factors, and to determine the effect of genotype and haplotype on serum galectin-3 levels.

**MATERIALS AND METHODS**

**Patients**

Our study included a total of 236 patients with histopathological and demographic data, of whom 119 (42 women and 77 men) had colorectal cancer and 117 were healthy controls. The mean age of the colorectal cancer patients and the control group were 60.98 ± 13.3 and 56.2 ± 11.35 years, respectively. The demographic data is shown on Table 1.

**Genotyping**

All patients gave written informed consent. Istanbul University Ethics Committee approved the study. The peripheral blood samples were drawn into ethylenediaminetetraacetic acid (EDTA)-containing glass tubes. The salting-out process was used to obtain DNA material from peripheral circulating lymphocytes. Afterwards, polymerase chain reaction (PCR) restriction fragment length polymorphism (RFLP) methods were utilized to genotype rs4644 and rs4652 variants of the LGALS3 gene. For genotyping the rs214250 variant of the

**TABLE 1. Demographic and medical history information**

| Parameter                       | Controls (n=117) | Patients (n=119) |
|---------------------------------|-----------------|-----------------|
| Female, n (%)                   | 52 (44.4)       | 42 (35.3)       |
| Male, n (%)                     | 65 (55.6)       | 77 (64.7)       |
| Average age                     | 56.2 ± 11.35    | 60.98 ± 13.3    |
| Median age                      | 55.5 ± 3.69     | 57.9 ± 5.80     |
| Family history of cancer        |                 |                 |
| Available (%)                   | 0 (0)           | 5 (4.2)         |
| Not available (%)               | 117 (100)       | 114 (95.8)      |
| Consumption of Alcohol          |                 |                 |
| Positive (%)                    | 0 (0)           | 4 (3.4)         |
| Negative (%)                    | 117 (100)       | 115 (96.6)      |
| Smoking                         |                 |                 |
| Positive (%)                    | 0 (0)           | 9 (7.6)         |
| Negative (%)                    | 117 (100)       | 110 (92.4)      |
AXIN1 gene, the ASO (allele specific oligonucleotide)-PCR method was used. PCR amplification was achieved using the following primers: Forward (wild-type): 5’- GAG GAC GCC GAT CCA TCG -3’ and Reverse: 5’- GGA TGC TCT CAG GGT TCT -3’ and Reverse: 5’- AAG GAA TGC CAT CTC ACC AG -3’. For the PCR process of all variants, the PCR conditions were set as follows: 95°C for 5 min followed by 35 cycles of 95°C for 30 s, 60°C for 30 s, 72°C for 45 s, and a final extension of 72°C for 10 min. PCR product was studied in agarose gel electrophoresis in 148 bp for AXIN1 genotyping. The PCR product containing LGALS3 gene rs4644 variant was treated at 37°C for 3 hours. The enzymatic restriction yielded restriction products of 201 bp for CC genotype, 204 bp, 170 bp, 51 bp for CA genotype, and 170 bp, 31 bp for AA genotype. The PCR product containing LGALS3 gene rs4652 variant was treated by BsaW1 enzyme at 60°C for 3 hours. The enzymatic restriction yielded restriction products of 201 bp for CC genotype, 201 bp, 134 bp, 67 bp for CA genotype, and 134 bp, 67 bp for AA genotype. PCR-RFLP and ASO PCR conditions of analysis of LGALS3 and AXIN1 variants are shown in Table 2.

Elisa

The enzyme-linked immunosorbent assay (ELISA) method was used to measure the galectin-3 level from the whole blood samples. The 96-well microplates were read at 450nm wavelength using Vivid Vision Microplate Reader (ALKA Tecnologia, São Paulo, Brazil).

Statistical analysis

Statistical analyses of the study data were done with the SPSS 11.0 software (SPSS Inc., Chicago, IL, USA). The two groups were compared by Chi square test and Fisher test with respect to differences of genotype and allelic frequency. Student’s t test was used to compare the demographic variables of the two groups. The inter-group differences of ELISA results were analyzed with Kruskal-Wallis Test.

RESULTS

The demographic data are presented on Table 1. Genotypes of all genes were determined by gel band patterns (Figures 1 and 2). The distribution of the genotypes pertaining to the rs214250 variant of the AXIN1 gene, the rs4644 variant of the LGALS3 gene, and the rs4652 variant of the LGALS3 gene were shown in Table 3.

No significant differences were found between the colorectal cancer and control groups with regard to genotype distribution and allelic frequencies for the rs214250 variant of the AXIN1 gene (p=0.05). In contrast, the C allele was significantly more common (92.6%, 63 patients) in the advanced tumor stage (T3+T4) than in the early tumor stage (73.7%, 14 patients) in the rs214250 variant of the AXIN1 gene (p=0.022, OR: 1.257 (0.953-1.659)).

Table 2. PCR-RFLP and ASO-PCR conditions of LGALS3 and AXIN1 variants analysis

| Gene   | Primer (forward)       | Primer (reverse)       | Annealing temperature | PCR product size | RFLP Enzyme | PCR RFLP (fragment size) |
|--------|------------------------|------------------------|-----------------------|------------------|-------------|-------------------------|
| LGALS3 | 5’- TTA TCC TGG         | 5’- AAG GAA TGC        | 60°C                  | 201 bp           | StyI        | 201 bp, 170 bp, 31 bp   |
| (Rs4644)| ACA GGC ACC TC -3’     | CAT CTC ACC AG -3’    |                       |                  |             |                         |
| LGALS3 | 5’- TTA TCC TGG         | 5’- AAG GAA TGC        | 60°C                  | 201 bp           | BsaW1       | 134 bp, 67 bp           |
| (Rs4652)| ACA GGC ACC TC -3’     | CAT CTC ACC AG -3’    |                       |                  |             |                         |

| Gene   | Primer (common)        | Primer (wild type)     | Primer (mutant type)  | PCR product size | Annealing temperature (°C) |
|--------|------------------------|------------------------|-----------------------|------------------|---------------------------|
| AXIN1  | 5’- GGA TGC TCT        | 5’- GAG GAC GCC        | 5’- GAG GAC GCC       | 148 bp           | 60°C                      |
| (Rs214250)| CAG GGT TCT -3’      | GAT CCA TCG -3’        | GAT CCA TCA -3’       |                  |                           |

Figure 1. PCR-RFLP agarose gel electrophoresis of Rs4644 variant of LGALS3 gene. M: marker; Lane 1 and 7: 2A, 2B; Lane 2: 1A, 1B; Lane 3: 3A; Lane 4: 3B in patients and control groups.

Figure 2. ASO-PCR agarose gel electrophoresis of Rs214250 variant of AXIN1 gene. M: marker; C allele: 1A, 2A, 3A; T allele: 1B, 2B, 3B in patients and control groups.
TABLE 3. The distribution of Axin rs214250, Gal3 rs4644 and Gal3 rs4652 alleles in patients and controls

| Genotypes and alleles | Patients n(%) | Controls n(%) | p-value |
|-----------------------|---------------|---------------|---------|
| Axin rs214250         |               |               |         |
| CC                    | 74 (62.2)     | 77 (65.8)     | 0.260   |
| CT                    | 33 (27.7)     | 23 (19.7)     |         |
| TT                    | 12 (10.1)     | 17 (14.5)     |         |
| C allele              | 181 (76.1)    | 177 (75.6)    | 0.917   |
| T allele              | 57 (23.9)     | 57 (24.4)     |         |
| Gal3 rs4644           |               |               |         |
| CC                    | 62 (52.1)     | 61 (52.1)     | 0.026   |
| CA                    | 52 (43.7)     | 40 (34.2)     |         |
| AA                    | 5 (4.2)       | 16 (13.7)     |         |
| C allele              | 176 (74)      | 162 (69.2)    | 0.25    |
| A allele              | 62 (26)       | 72 (30.8)     |         |
| Gal3 rs4652           |               |               |         |
| AA                    | 46 (38.7)     | 48 (41)       | 0.039   |
| AC                    | 65 (54.6)     | 50 (42.7)     |         |
| CC                    | 8 (6.7)       | 19 (16.2)     |         |
| A allele              | 157 (66)      | 146 (62.4)    | 0.418   |
| C allele              | 81 (34)       | 88 (37.6)     |         |

TABLE 4. Clinical and histopathological data of colorectal cancer patients

| Histopathological criteria | Galeklin3 rs: 4644, n (%) | Galeklin3 rs: 4652, n (%) | AXIN, n (%) |
|----------------------------|-----------------|-----------------|-------------|
|                            | CC   | CA  | AA  | CC   | CA  | AA  | CC   | CC   | CT  | TT  |
| Gender                     |      |     |     |      |     |     |      |      |     |     |
| Female                     | 21 (50) | 20 (47.6) | 1 (2.4) | 15 (35.7) | 27 (64.3) | 0 (0) | 23 (54.8) | 15 (35.7) | 4 (9.5) |
| Male                       | 41 (53.2) | 32 (41.6) | 4 (5.2) | 31 (40.3) | 38 (49.4) | 8 (10.6) | 51 (66.2) | 18 (23.4) | 8 (10.4) |
| T stage                    |      |     |     |      |     |     |      |      |     |     |
| T3+T4                      | 32 (47.1) | 34 (50) | 2 (2.9) | 25 (36.8) | 38 (55.9) | 5 (7.4) | 46 (67.6) | 17 (25) | 5 (7.4) |
| T1+T2                      | 10 (52.6) | 7 (36.8) | 2 (10.5) | 7 (36.8) | 10 (52.6) | 2 (10.5) | 9 (42.4) | 5 (26.3) | 5 (26.3) |
| N stage                    |      |     |     |      |     |     |      |      |     |     |
| N1+N2+N3                   | 23 (52.3) | 18 (40.9) | 3 (6.8) | 18 (40.9) | 22 (50) | 4 (9.1) | 27 (61.4) | 11 (25) | 6 (13.6) |
| N0                         | 19 (44.2) | 23 (53.5) | 1 (2.3) | 14 (32.6) | 26 (63.7) | 3 (7) | 28 (65.1) | 11 (25.6) | 4 (9.3) |
| M stage                    |      |     |     |      |     |     |      |      |     |     |
| M1                         | 10 (55.6) | 7 (38.9) | 1 (5.6) | 7 (38.9) | 10 (55.6) | 1 (5.6) | 9850 | 6 (33.3) | 3 (16.7) |
| M0                         | 32 (45.7) | 35 (50) | 3 (4.3) | 25 (35.7) | 39 (55.7) | 6 (8.6) | 47 (67.1) | 16 (22.9) | 7 (10) |
| Angio-lymphatic invasion   |      |     |     |      |     |     |      |      |     |     |
| Positive                   | 15 (55.6) | 11 (40.7) | 1 (3.7) | 9 (33.3) | 16 (59.3) | 2 (7.4) | 14 (51.9) | 8 (29.6) | 5 (18.5) |
| Negative                   | 25 (43.9) | 29 (50.9) | 3 (5.3) | 21 (36.8) | 31 (54.4) | 5 (8.8) | 38 (66.7) | 14 (24.6) | 5 (8.8) |
| Perineural invasion        |      |     |     |      |     |     |      |      |     |     |
| Positive                   | 11 (37.9) | 17 (58.6) | 1 (3.4) | 8 (27.6) | 20 (69) | 1 (3.4) | 19 (65.5) | 8 (27.6) | 2 (6.9) |
| Negative                   | 30 (52.6) | 24 (42.1) | 3 (5.3) | 23 (40.4) | 28 (49.1) | 6 (10.5) | 35 (61) | 14 (24.6) | 8 (14) |
| Differentiation            |      |     |     |      |     |     |      |      |     |     |
| Low                        | 6 (66.7) | 3 (33.3) | 0 (0) | 5 (55.6) | 4 (44.4) | 0 (0) | 4 (44.4) | 4 (44.4) | 1 (11.1) |
| Medium-High                | 17 (45.9) | 17 (45.9) | 3 (8.1) | 13 (35.1) | 17 (45.9) | 7 (18.9) | 23 (62.2) | 9 (24.3) | 5 (13.5) |
| Mucinous component         |      |     |     |      |     |     |      |      |     |     |
| Mucinous Ca                | 7 (87.5) | 1 (12.5) | 0 (0) | 4 (50) | 3 (37.5) | 1 (12.5) | 5 (62.5) | 2 (25) | 1 (12.5) |
| Non-Mucinous Ca            | 35 (44.3) | 40 (50.6) | 4 (5.1) | 28 (35.4) | 45 (57) | 6 (7.6) | 50 (63.3) | 20 (25.3) | 9 (11.4) |

DISCUSSION

Colorectal cancer, the third most prevalent cancer worldwide, has become a major public health problem with an excess of 1.2 million new cases each year [26]. In the majority of CRC cases, there is no identifiable family history or genetic risk factors.
alterations, and the disease is largely sporadic. It has recently become clearer that CRC is a heterogeneous malignancy where prognosis and (targeted) treatment response in a given patient are largely dependent on molecular, as well as genetic properties, of the tumor [25, 26]. Unfortunately, there is still insufficient information about the molecular pathology of CRC.

The canonical Wnt pathway is responsible for the determination of cell fate at the developmental stages and in adult cellular homeostasis, and its dysregulation is responsible for a variety of malignant disorders [27]. The canonical Wnt pathway conveys extracellular Wnt signals into the cell nucleus by affecting levels and localization of β-catenin. The formation of β-catenin destruction complex involves the AXIN1, and AXIN2 proteins [28]. Previous studies have shown that LGALS3 plays a role in the Wnt/β-catenin pathway and is involved in cell migration and invasion, with its levels proportional to β-catenin in different cancer types [29,30].

In colorectal cancer cases, serum galectin-3 levels and immunohistochemical studies at tissue level have both supported the proposed pathogenesis [11,12]. Experimental animal models have similarly shown increased LGALS3 m-RNA levels in colorectal tissue [14]. However, studies examining mutations and genetic variants have been limited in number so far. This creates an uncertainty surrounding the question as to whether the upregulation of protein level occurs somatically or as a result of germline gene mutations and/or gain-of-function mutations. Our findings showed that in the patient group with the rs4644 variant of the LGALS3 gene, the number of patients with a CC genotype carrying a mucinous component was significantly greater than those with a CC genotype carrying a non-mucinous component (p=0.026).

As for the rs4652 variant of the LGALS3 gene, no significant differences were observed between the clinical parameters of the patient and the control groups. Mucinous adenocarcinoma (MUC) represents a histological subtype of CRC, containing a large amount of extracellular mucin in its structure. A large body of literature suggests that colorectal cases with a mucinous component carry a worse prognosis compared to those without such a component [31-33]. The mucinous component is more common in colorectal cancer cases that arise from inflammatory processes. The findings reported by Akkiripik et al. suggest that mucinous secretion of Kras mutations in the colo-rectum may represent a distinct genetic pattern [34]. Kawasaki et al. demonstrated the effect of methylations in the WRN promoter region on mucinous component development [35]. Its relationship with a mucinous component has been demonstrated in SIRT1 histone deacetylase overexpression in colorectal cancer tissues [36].

The level of the interaction between epithelial cells without galectin-3 expression and the extracellular matrix is particularly low. Galectin-3 displays both pro- and anti-adhesive properties and functions as a matricellular protein in various types of the processes. Reduced cell-to-cell interaction and adhesion may contribute to the development of a mucinous component by supporting an inflammatory process. Genetic studies investigating the mucinous component are quite limited and the LGALS3 rs4644 variant CC genotype was correlated to a mucinous component in our study. Cell culture-based studies are needed to explore the effect of galectin-3 (LGALS3) on the development of a mucinous component in colorectal cancers. AXIN1 has traditionally been regarded as a tumor-suppressor protein. A majority of gastrointestinal cancer types carry AXIN1 mutations [19]. Khan et al. [22] detected a mutation that caused no amino acid alteration, while Jin et al. [23] found 3 silent and 6 missense mutations in colorectal cancers. Despite a limited number of functional studies, Sue et al. reported an active role of AXIN1 in the Wnt and c-Jun NH(2)-terminal kinase pathway [24]. Although there exist some data suggesting a role for engaging a cell into apoptosis, C allele frequency of the rs214250 variant of the AXIN1 gene was significantly correlated to tumor size in the advanced tumor stage (T3+T4) (p=0.022). These findings may suggest that AXIN1 plays a role, not only in apoptosis, but also in cancer cell growth and survival. The function of AXIN1 in tumorgenesis should be studied in detail in animal model studies with AXIN1 knock-out colorectal cancer and cell culture studies.

According to combined haplotyping results, the AACC haplotype was quite common in the healthy control group (p=0.004). CCAACT haplotype, on the other hand, was three times more common in colorectal cancer patients compared to the control group (p=0.022). These haplotypes can be used after cohort studies as a protective and prognostic biomarker in colorectal cancers. Despite the available data, the limitation of this study is the limited sample size. Future studies with a larger sample size may provide detailed information related to other pathological parameters.

ACKNOWLEDGEMENTS

The present work was supported by the Research Fund of Istanbul University - Project No: 28753.

DECLARATION OF INTERESTS

The authors have declared that there is no conflict of interest.

REFERENCES

[1] Boyle P, Elena M. Epidemiology of colorectal cancer. British Med Bull. 2002;64:1–25. http://dx.doi.org/10.1093/bmbld/64.1.1.
Altshuler DM, Haralow F, The genetics of CRC. Ann Intern Med. 2002 Oct 1;137(7):603-12.

Rasool S, Ganai BA, Sameer AS, Masood A. Esophageal cancer: a review. J Cancer. 2013 Dec;4(12):856-66.

Shimura T, Takeda Y, Tsuchum S, Hogan V, Iacovazzi PA, Notarnicola M, Caruso MG, Guerra V, Colussi D, Brandi G, Bazzoli F, Ricciardiello L. Molecular pathology of colorectal cancer: implications for disease behavior and prevention. Int J Mol Sci. 2013 Aug 7;14(8):16956-85. http://dx.doi.org/10.3390/ijms140816956.

Di Lella S, Sundblad V, Corliani P, Guardia CM, Estrin DA, Vasta GR, et al. When galectins recognize glycans: from biochemistry to physiology and back again. Biochemistry. 2011 Sep;20:50(37):7842-57. http://dx.doi.org/10.1021/bi102111m.

Newlaczyl A, Yu. G. Galectin-3: a jack of all trades in cancer. Cancer Lett. 2011 Dec;293(1):122-38. http://dx.doi.org/10.1016/j.canlet.2011.09.009.

Yu F, Finley RL, Ir, Raz A, Kim HR. Galectin-3 translocates to the perinuclear membranes and inhibits cytochrome c release from the mitochondria. A role for synxin in galectin-3 translocation. J Biol Chem. 2002 May 327;18(15):5899-27. http://dx.doi.org/10.1074/jbc.M112501200.

Song S, Mazurek N, Liu C, Sun Y, Ding QQ, Liu K, et al. Galectin-3 mediates nuclear beta-catenin accumulation and Wnt signaling in human colon cancer cells by regulation of glycogen synthase kinase-3beta activity. Cancer Res. 2009 Feb 15;69(4):1349-53. http://dx.doi.org/10.1158/0008-5472.CAN-08-3151.

Shimura T, Takenaka Y, Tsuchum S, Hogan V, Iacovazzi PA, Notarnicola M, Caruso MG, Guerra V, Colussi D, Brandi G, Bazzoli F, Ricciardiello L. Novel binding partner of beta-catenin. Cancer Res. 2004 Sep 15;64(18):6363-7. http://dx.doi.org/10.1158/0008-5472.CAN-04-1816.

Kikuchi A, Raz A. Galectin-3, a novel binding part of beta-catenin. Cancer Res. 2004 Sep 15;64(18):6363-7. http://dx.doi.org/10.1158/0008-5472.CAN-04-1816.

Kikuchi A, Raz A. Galectin-3, a novel binding partner of beta-catenin. Cancer Res. 2004 Sep 15;64(18):6363-7. http://dx.doi.org/10.1158/0008-5472.CAN-04-1816.

Colussi D, Brandi G, Bazzoli F, Ricciardiello L. Molecular pathways involved in colorectal cancer: implications for disease behavior and prevention. Int J Mol Sci. 2013 Aug 7;14(8):16956-85. http://dx.doi.org/10.3390/ijms140816956.

Di Lella S, Sundblad V, Corliani P, Guardia CM, Estrin DA, Vasta GR, et al. When galectins recognize glycans: from biochemistry to physiology and back again. Biochemistry. 2011 Sep;20:50(37):7842-57. http://dx.doi.org/10.1021/bi102111m.

Newlaczyl A, Yu. G. Galectin-3: a jack of all trades in cancer. Cancer Lett. 2011 Dec;293(1):122-38. http://dx.doi.org/10.1016/j.canlet.2011.09.009.

Yu F, Finley RL, Ir, Raz A, Kim HR. Galectin-3 translocates to the perinuclear membranes and inhibits cytochrome c release from the mitochondria. A role for synxin in galectin-3 translocation. J Biol Chem. 2002 May 327;18(15):5899-27. http://dx.doi.org/10.1074/jbc.M112501200.

Song S, Mazurek N, Liu C, Sun Y, Ding QQ, Liu K, et al. Galectin-3 mediates nuclear beta-catenin accumulation and Wnt signaling in human colon cancer cells by regulation of glycogen synthase kinase-3beta activity. Cancer Res. 2009 Feb 15;69(4):1349-53. http://dx.doi.org/10.1158/0008-5472.CAN-08-3151.

Shimura T, Takenaka Y, Tsuchum S, Hogan V, Iacovazzi PA, Notarnicola M, Caruso MG, Guerra V, Colussi D, Brandi G, Bazzoli F, Ricciardiello L. Novel binding partner of beta-catenin. Cancer Res. 2004 Sep 15;64(18):6363-7. http://dx.doi.org/10.1158/0008-5472.CAN-04-1816.

Kikuchi A, Raz A. Galectin-3, a novel binding partner of beta-catenin. Cancer Res. 2004 Sep 15;64(18):6363-7. http://dx.doi.org/10.1158/0008-5472.CAN-04-1816.

Kikuchi A, Raz A. Galectin-3, a novel binding partner of beta-catenin. Cancer Res. 2004 Sep 15;64(18):6363-7. http://dx.doi.org/10.1158/0008-5472.CAN-04-1816.