

Galectins' Involvement in Cancer

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Abstract

One of the malignant tumours that affects women most frequently and fatally in underdeveloped nations is cervical cancer. The late recurrence, metastasis, and the efficient adjuvant therapy, such as radiation, chemotherapy, or combination therapy, are the key factors influencing the prognosis of cervical cancer. The occurrence and growth of tumours are tightly related to galectins, a class of proteins that bind to carbohydrates. They play a role in immune evasion, tumour cell transformation, angiogenesis, metastasis, and susceptibility to radiation and chemotherapy. As a consequence, galectins are considered to be the focus of multimodal cancer treatment. In this study, we largely concentrate on the function of galectins, particularly galectin-1, galectin-3, galectin-7, and galectin-9 in cervical cancer, and we provide theoretical support for prospective targeted cervical cancer treatment.

Keywords: Galectins; Angiogenesis; Metastasis; Cancer

Introduction

Cervical cancer, the second-most frequent female malignant tumour in the globe, ranks second in gynaecological oncology for fatalities in developing nations. The current research revealed a strong correlation between cervical cancer and high risk human papillomavirus (HPV) infection [1]. However, a significant proportion of cervical cancer patients do not have HPV infection, raising the possibility that additional factors, like genetic changes in the cells, may also contribute to the development of the disease. Radiation therapy, chemotherapy, and surgery are the main forms of treatment for cervical cancer, including pelvic lymphadenectomy and radical hysterectomy. While concomitant radiochemotherapy continues to be a cornerstone treatment for advanced cancer, total hysterectomy and radiation therapy are both regarded as curative for localised disease [2-5]. A family of proteins called galectins that bind to β -galactosides are found in a wide variety of organisms, including bacteria, fungi, and animals at various levels. 130 amino acids and a carbohydrate recognition domain make up its highly conserved core sequence. A significant similarity in a conserved amino acid sequence and a strong affinity for β -galactoside sugars are two features common to the galectin protein family. Galectins in mammals have been found to have 15 different subtypes, which have been given names. They can be categorised into three groups based on their molecular makeup: Galectin prototypes: Prototype galectins are proteins with a single carbohydrate recognition domain that frequently form homodimers. Examples of prototype galectins are galectin-1, galectin-2, galectin-5, galectin-7, galectin-10, galectin-11, galectin-13, galectin-14, and galectin-15. Chimeric galectins are proteins with two domains. Numerous intracellular receptors, including cytochromes, cyclins, transcription factors, Bcl-2, and h-ras, as well as the cell membrane, cytoplasm, extracellular matrix, and galectins, are reported to play a variety of roles in the cell [6]. Galectins can be secreted into the extracellular matrix. Galectins cannot be produced outside of the cell by the endoplasmic reticulum, the Golgi apparatus, or the cytoplasm because they lack the signal peptide. The unique method of secretion can stop galectins from sticking to a new generation of glycoprotein oligosaccharide too early. Galectin secretion is influenced by a number of variables, including inflammatory agents and extracellular matrix elements. Numerous earlier experimental studies demonstrated that galectins are crucial for angiogenesis, cell adhesion, invasion, and migration, which are all factors in the initiation and progression of cancer. However, the function and mechanism of the same galectin vary in various tumour

types. In colon cancer, for instance, downregulating the K-Ras-Raf-Erk1/2 pathway led to upregulated Gal-3's contribution to increased cancer cell motility and migration [7]. Gal-3 may aid metastasis in gastric cancer by increasing MMP-1 and protease-activated receptor-1 expression. Studies both in vivo and in vitro have shown that galectin-7 has a tumor-suppressing effect on colon cancer.

Oncogenic Galectins

Numerous intricate processes involving numerous variables are required for the activation of protooncogenes to lead to the occurrence and progression of cancer. The function and control of the body's immune system, genetic alterations, external cellular stresses, and the tissue's microenvironment all influence these parameters. According to studies, the majority of galectins play a role in the growth of different cancers. The processes they are involved in primarily entail the transformation of tumour cells as a outcome of their interactions with oncogenes like HRAS and KRAS [8,9]. Galectins have been identified to play a role in tumour growth via tumour immune evasion, tumour metastasis, and tumour angiogenesis in addition to their roles in cell cycle and cell death.

Galectin Effect in Cancer Cell Proliferation

Malignant tumour cell growth and metastasis are crucial elements that affect how a tumour is treated. For the purpose of early detection and therapeutic tumour treatment, it is crucial to comprehend the elements and mechanisms that affect and control the proliferation and spread of malignant tumour cells. Human glioma and thyroid cancer cells will proliferate more quickly when Gal-1 is overexpressed in tumour cell experiments. Ras/Raf/ERK2 signalling is primarily used by Gal-1 to control the cell cycle. Additionally, Gal-3 aids in the growth of cancer cells and promotes tumors. Hepatocellular carcinoma, glioma,

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and pancreatic cancer cells can all grow more quickly thanks to gal-3. Gal-3 can translocate into the nucleus by binding with Impotin, Sufu, and Nup98. Once there, it can control the cell cycle by interacting with cyclin A, cyclin D, cyclin E, p21 (WAF1), and p27 (KIP1), which promotes the growth of cancerous cells [10]. Cell proliferation and death are abnormal in cancer. Necrosis or apoptosis are the two primary cell death processes in solid tumors. When chemotherapy, radiotherapy, and biological therapies are used to treat cancer, cell apoptosis plays a role in both the tumorigenesis and development of the disease. Stopping the unchecked spread of cancer cells is one method of treating the disease. Stopping the unchecked spread of cancer cells is one method of treating the disease. Targeted apoptosis may end up being the most effective nonsurgical treatment because cancer is known for its ability to avoid apoptosis.

Galectins' Acts in the Oncogenesis of Cancer

As each tumor's rapid growth necessitates the constant formation of new blood vessels, which is crucial for the growth and spread of tumour cells, angiogenesis plays a significant role in the development and evolution of a tumour. Exogenous Gal-1 enhances endothelial cells' potential to form capillary-like tubes in basal membrane Matrigel preparations. By strengthening and sustaining linkages between extracellular matrix contacts and vascular endothelial cell connections inside the tumour microenvironments, extracellular Gal-1 physically enhances tumour angiogenesis. According to studies, Gal-1 can cause angiogenesis, and thiodigalactoside can counteract this effect by protecting against oxidative stress and reducing angiogenesis. Gal-3 is essential for tumour angiogenesis because it acts as a chemoattractant to encourage the transfer of epithelial cells to vascular endothelial cells in vitro and in vivo. Gal-1 and Gal-3 working together can increase the effect on angiogenesis by activating VEGFR1 and reducing receptor endocytosis. Gal-9 is the only galectin that seems to have an inhibitory effect on angiogenesis. Which mechanisms are responsible for this inhibitory action are still being determined. Galectins' angiostimulatory activity has so far been connected to a number of signalling pathways, such as the Ras signalling pathway, the integrin signalling pathway, and the VEGF/VEGFR2 signalling axis. Galectin-1, galectin-3, and galectin-8 have been shown to activate these signalling pathways due to the cross-linking of several receptors, including VEGFR2, neuropilin-1, beta-integrins, and CD166.

The Galectins' Play a Role in Immune Responses

For a number of mechanisms from the host immune onslaught, immune cells play a significant part in the traditional meaning of monitoring the development of tumours. T lymphocytes are the body's primary tumour immunotherapy workers, working in conjunction with natural killer (NK) cells, cytokines-induced killer (CIK) cells, dendritic cells (DC), DC-CIK cells, and other antitumor agents. The primary way that galectins influence immunological responses is by controlling the proportion of effector NK cells and T cells that are activated. Gal-1 increases the activity of regulatory T cells (Tregs) while selectively eliminating TH1 and TH17 cells and encouraging the growth of CD4+CD25+Foxp3+ T cells. T-cell receptor (TCR) and CD8 molecule separation is maintained by gal-3. An important molecular pathway that increases the translation and exocytosis of the immune receptor Tim-3 and its ligand galectin-9 involves ligand-dependent activation of ectopically expressed latrophilin 1 and possibly other G protein coupled receptors. This happens as a outcome of protein kinase C and mTOR (mammalian target of rapamycin). Galectin-9 secretion involves Tim-3, which is also secreted in a free soluble form. Cytotoxic lymphoid cells, such as natural killer (NK) cells, are

impaired by galectin-9 in their ability to fight cancer. Interleukin-2 (IL-2) is necessary for the activation of cytotoxic lymphoid cells, but its secretion is inhibited by soluble Tim-3. Using primary samples from individuals with acute myeloid leukaemia (AML), these findings were confirmed in ex vivo studies. For both a highly precise AML diagnosis and immunological treatment, this route offers dependable targets.

Galectins in Cervical Cancer

Gal-1 has been shown to control cell adhesion and migration, which has been linked to its involvement in several stages of cancer cell invasion and metastasis. Gal-1 increases tumour cells' adherence to the extracellular matrix in ovarian and prostate cancer cell lines. A total of 80 cervical tissues, including 20 benign cervical specimens, 20 invasive squamous cell carcinomas, 20 high-grade squamous intraepithelial lesions, and 20 low-grade squamous intraepithelial lesions, were tested for the expression of galectin-1 (ISCC). According to the pathologic grade—benign cervical tissue, LGSIL, HGSIL, and ISCC—they discovered that the intensity of galectin-1 expression on stromal cells close to the converted cells increased. Most peritumoral stroma samples (72/73; 98.6%) exhibited galectin 1 expression. On a univariate level, the expression of galectin 1 was substantially linked with the extent of cervix invasion and lymph node metastases. Galectin 1 expression was not linked with progression-free survival when the progression-free survival of all the patients evaluated was examined based on galectin 1 expression. Strong Gal-1 expression, as an independent predictor, was closely related to invasion and metastasis in cervical cancer and an independent predictor for poor survival and a likelihood of receiving postoperative radiotherapy, according to Punt et al analysis 's of immunohistochemistry combined with clinical data from 155 patients (including 41 relapses and 30 deaths). Gal-1 functions by encouraging cell invasion and proliferation in cervical cancer cells, which is mostly how it is recognised. HeLa and SiHa cells' ability to grow and proliferate was suppressed as a outcome of the downregulation of galectin 1 by short interfering RNA. Galectin-1 small interfering RNA also markedly decreased the capacity of cells to invade. Because galectin 1 was overexpressed in both cell lines they picked HeLa and SiHa cells to do the galectin 1 small interfering RNA experiment. Radiotherapy and chemotherapy for cervical cancer are also impacted by Gal-1. Gal-1 is a standalone prognostic factor linked to local recurrence in cervical cancer patients receiving curative radiation therapy. In radiation therapy, Gal-1 also has a significant impact.

Conclusion

Galectins are crucial for the development of new blood vessels, tumour metastasis, tumour survival, and tumorigenicity. Additionally, it plays a role in controlling inflammatory and immunological responses as well as helping tumours avoid immune surveillance. Galectin-1, galectin-3, galectin-7, and galectin-9 may one day serve as useful prognostic indicators, a foundation for target gene therapy, and a predictor of cervical lesion progression.

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