

# THE TWO FACES OF GALECTIN-3: ROLES IN VARIOUS PATHOLOGICAL CONDITIONS

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## DVA LICA GALEKTINA-3: ULOGE U RAZLIČITIM PATOLOŠKIM STANJIMA

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### ABSTRACT

*Galectin-3, a unique chimaera-type member of the lectin family, displays a wide range of activities. This versatile molecule is involved in fundamental biological processes, including cell proliferation, cell-cell adhesion, apoptosis and immune responses.*

*This review is aimed at providing a general overview of the biological actions and diverse effects of Galectin-3 in many pathological conditions, with a specific focus on autoimmunity, inflammation and tumour progression. We report here-in that Galectin-3 exerts deleterious functions determined by promotion of tumour progression and liver inflammation or aggravation of T cell-mediated autoimmune diseases. On the other hand, Galectin-3 exhibits a protective role in metabolic abnormalities and primary biliary cirrhosis.*

*The paradoxical "yin and yang" functions of Galectin-3 depend not only on its tissue and cellular localization but also on its availability, glycosylation status and the expression level of its ligands.*

**Keywords:** galectin-3, tumour, inflammation, autoimmune disease

### SAŽETAK

*Galektin-3 je jedinstveni himerični član porodice lektina i ostvaruje širok spektar aktivnosti. Ovaj svestrani molekul je uključen u fundamentalne biološke procese kao što su ćelijska proliferacija, međućelijska adhezija, apoptoza i imunski odgovor.*

*Pregledni članak ima za cilj opšti pregled bioloških efekata Galektina-3, kao i njegovih različitih uticaja na mnoga patološka stanja sa specifičnim fokusom na autoimunost, inflamaciju i progresiju tumora. U ovom radu razmatrani su štetni efekti Galektina-3 koje ostvaruje u određenim patološkim stanjima: promoviše progresiju tumora i inflamaciju u jetri ili pogoršava neka autoimunska oboljenja izazvana T limfocitima. Suprotno, Galektin-3 igra protektivnu ulogu u patogenezi metaboličkih poremećaja i primarne bilijarne ciroze.*

*Paradokсне "Jin-Jang" funkcije Galektina-3 zavise od tkivne i ćelijske lokalizacije ovog molekula, a takođe i od dostupnosti, glikozilacionog statusa i nivoa ekspresije njegovih liganada.*

**Cljučne reči:** galektin-3, tumour, inflamacija, autoimunske bolesti



### INTRODUCTION

Galectin-3 is one of the best-studied galectins. Like all members of the lectin family, Galectin-3 has a high affinity for binding  $\beta$ -galactoside and shares a conserved carbohydrate recognition domain (CRD) (1). As a chimeric protein with unique structure, Galectin-3 contains three distinct structural regions: 1) an  $\text{NH}_2$  terminus containing a serine phosphorylation site that is important for regulation of intracellular signalling; 2) a repetitive, proline-rich, collagen- $\alpha$ -like sequence cleavable by matrix metalloproteases (e.g., MMP-2 and MMP-9); and 3) a globular COOH-terminus containing a carbohydrate recognition domain and the anti-death motif NWGR. Upon binding

to multivalent carbohydrates, Galectin-3 can oligomerize through its  $\text{NH}_2$ -terminus or form a pentameric lattice structure on the cell surface (Figure 1A) (1). Thus, it is involved in modulation of intracellular signalling pathways.

As a small molecular weight protein (approximately 30 kDa), Galectin-3 has multiple cellular localizations in many types of cells, in particular, epithelial and immune cells. In general, Galectin-3 serves as a regulator of fundamental biological processes, such as cell proliferation and differentiation, adhesion, migration, survival, apoptosis and immune responses (2). Intracellularly, Galectin-3 occurs mainly in the cytosol, but is also found in the nucleus























