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INTRODUCTION TO SPECIAL ISSUE

Galectins go with the flow

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Galectins, a family of conserved carbohydrate-binding proteins, have recently emerged as regulators of endothelial cell biology and angiogenesis. This series of reviews dissects the individual roles of galectin-1, -3, -8 and -9 in angiogenesis, highlights their regulation by hypoxia and emphasizes the relevance of these endogenous lectins at different stages of tumor metastasis.

The human vasculature is the body's infrastructure that facilitates the transport of molecules and cells throughout the body. In addition, blood vessels contribute to proper development and homeostasis of immune responses, coagulation and neovascularization. The cells responsible for these activities are the cells lining the luminal side of all blood vessels, i.e. endothelial cells. Although most studies on angiogenesis have focused on ligand binding to canonical receptors via protein–protein interactions, emerging findings have illuminated essential roles for glycans in the proper function of endothelial cells. It has become evident that galectins, a family of glycan-binding proteins, exert multiple roles in endothelial cell biology both in health and disease. In recent years, many different aspects of galectin biology have been uncovered and exciting progress is still being made. The current issue of *Glycobiology* presents a collection of reviews that discuss these current advances and provide insights in the challenges that lie ahead in this "sweet" research field.

The review by Funasaka et al. (2014) reports on the multifunctional roles of galectin-3 during different steps of tumor metastasis. Moreover, the authors link tumor metastatic activity to the angioregulatory function of galectin-3 and the functions of processed galectin-3 variants in tumor angiogenesis. Finally, they discuss the opportunities of galectin-3 as a target for angiostatic therapy.

The involvement of galectin-3 in tumor progression is further exemplified in the papers by D'Haene et al. (2014) and Compagno et al. (2014) who review the role of galectins in central nervous system tumors and prostate cancer, respectively. Both reviews discuss the possible contributions of specific galectins to tumor progression, focusing on the regulation of tumor angiogenesis and metastasis, and both also make several suggestions for future research that could help to understand how alterations in glycan composition and galectin expression might contribute to disease progression.

The reviews by Troncoso et al. (2014) and Thijssen and Griffioen (2014) address two galectins that have more recently emerged as angioregulatory proteins, i.e., galectin-8 and -9, respectively. Both articles indicate that studying these galectins is complicated by the existence of multiple isoforms that might exert different functions in endothelial cell biology. In addition, Troncoso et al. (2014) describe the emerging role of galectin-8 in lymphangiogenesis and discusse the ligands that could explain the angiostimulatory activity of galectin-8. Overall, evidence is accumulating that both galectins contribute to neovessel formation. Consequently, Thijssen and Griffioen (2014) point towards an important future research challenge, i.e., to unravel the cross-talk between all the different angioregulatory galectins, as this will help to understand how galectins fine-tune endothelial cell function under normal and pathological conditions. Thijssen and Griffioen also summarize the well-established function of galectin-1 in angiogenesis. Finally, Kuo and Le (2014) review current literature that links galectin-1 expression to hypoxia and irradiation. These authors suggest that targeting galectin-1 might radiosensitize tumors and increase therapeutic efficacy.

Altogether, the collection of reviews on galectins in vascular biology presented in this issue of *Glycobiology* gives a comprehensive overview of the current standing as well as of the future challenges in this research field. More importantly, this collection of papers gives insight in the opportunities that lie ahead for the treatment of cancer and other diseases in which galectins "go with the flow."

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