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β 4 integrin signaling through glycosylation promotes tumor progression

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Malignant transformation is accompanied with aberrant glycosylation of proteins. Such changes in glycan structure also occur in the integrins, which are a large family of cell surface receptors for the extracellular matrix, but the role of glycosylation of integrins in tumor progression remains poorly defined. However, there is now increasing evidence that glycosylation of integrins affects cellular signaling and interaction with the extracellular matrix, receptor tyrosine kinases, and galectins, thereby regulating cell adhesion, motility, growth, and survival. α 6 β 4 integrin is a receptor for laminin-332 and an essential component of the hemidesmosome that provides stable adhesion of basal cells to the underlying basement membrane. On the other hand, the increased expression level of β 4 integrin subunit is correlated with malignant progression and poor survival in various types of cancers. In fact, many studies have revealed that α 6 β 4 integrin plays central roles in tumorigenesis and the metastatic process. Our previous study showed that a defect of N-glycosylation in β 4 integrin decreases its function such as cell spreading, adhesion, and migration. More recently, we have found that N-glycosylation of β 4 integrin contributes to promote α 6 β 4 integrin-dependent tumor development and progression through PI3K signaling. In this seminar, I will discuss our current understanding of the molecular mechanisms of tumor progression driven by the N-glycosylation on β 4 integrin to address the important roles of glycan in integrin-mediated tumor progression.

Biography

Yoshinobu Kariya is Associate Professor of the Department of Biochemistry at Fukushima Medical University, Japan. He has studied Chemistry and Molecular Biology at Sophia University, Japan. In 1999, he moved to Yokohama City University, where he received his PhD in 2003. He has worked at Stanford University in CA (2005-2006) and Tohoku Pharmaceutical University, Japan (2007-2010) as a Postdoc fellow. In 2010, he has joined the Fukushima Medical University. His research interests are in the understanding molecular mechanism of cancer cell invasion and metastasis through the association of extracellular matrix with integrins.

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