論　文　内　容　要　旨

Snail-dependent upregulation of Galectin-1 promoted to complete EMT process in Snail-expressing squamous cell carcinoma cells

(Snail 依存的な Galectin-1 発現誘導は Snail による EMT 誘導に関与する)

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The epithelial-mesenchymal transition (EMT) is a process involved in cancer invasiveness. The characteristics of EMT include loss of expression of E-cadherin and increased expression of mesenchymal structural proteins such as vimentin.

Galectin 1 (Gal-1) is a member of the β-galactoside-binding lectin family of proteins that possesses a carbohydrate-recognition domain and exists as a noncovalent homodimer in its secreted form. In this study, Gal-1 was identified as a highly upregulated protein in EMT phenotypic cells. Gal-1 overexpressing squamous cell carcinoma (SCC) cells showed accelerated wound closure in confluent monolayers, a process inhibited by anti-Gal-1 antibody. Recombinant Gal-1 also promoted wound closure in monolayers, indicating that its increased secretion was associated with faster collective cell migration. Gal-1 overexpressing SCC cells formed invasiveness nests in dermis-mimicking collagen gel layers without disturbing the homophilic attachments of tumor cells. Gal-1 also increased the expression of specific integrin subunits (i.e., α2 and β5) in SCC cells. Neutralizing antibody direct against the integrin α2 complex (i.e.,

α2β1) or the integrin β5 complex (i.e., αVβ5) prevented invasion by Gal-1 overexpressing SCC cells. Soluble Gal-1 activated JNK, whereas JNK inhibition clearly suppressed Gal-1-dependent expression of integrins and acceleration of collective cell migration. Moreover, Gal-1 increased EMT incidence of Snail-expressing SCC cells.

In conclusion, Gal-1 accelerated collective cell migration, resulting in nest-forming invasion by SCC cells. The commitment to EMT via Snail was supported by Gal-1. These original findings suggest that the acceleration of collective cell migration via several autocrine factors such as Gal-1 enhances EMT by Snail-expressing SCC cells.