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ABSTRACT OF DISSERTATION

Title	Cancer cell-derived novel periostin isoform promotes invasion in head and neck squamous cell carcinoma （癌細胞由来の新規ペリオスチンアイソフォームは頭頸部扁平上皮癌の浸潤を促進する）
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Abstract

Head and neck squamous cell carcinoma (HNSCC) is one of the most common types of human cancer. It recently has been reported that cells expressing the partial-epithelial-mesenchymal transition (p-EMT) program associated with metastasis in HNSCC. We previously identified *POSTN* (which encodes periostin) as an invasion promoting factor in HNSCC. Interestingly, *POSTN* expression was frequently observed in cancer cells with high p-EMT score by using previous single-cell transcriptomic data of HNSCC cases. Although it is known that *POSTN* has 11 splicing variants, the role of them has not been determined in HNSCC. Here, we found that HNSCC cells with EMT features expressed *POSTN* isoforms, Iso3 (lacking exon17 and 21) and Iso5 (lacking exon 17), whereas fibroblast expressed Iso3 and Iso4 (lacking exon 17, 18 and 21). *POSTN* Iso3 and Iso4 are known to be widely expressed in various types of the cells including stromal cells. Therefore, we focused on the role of novel cancer cell-derived *POSTN* isoform, Iso5, in HNSCC. Single overexpression of *POSTN* Iso5 as well as Iso3 promoted invasion. Surprisingly, Iso5 synergistically promoted invasion together with Iso3. Notably, Iso5 as well as Iso3 upregulated p-EMT-related genes. We suggest that a novel cancer-specific *POSTN* isoform lacking exon 17 (Iso5) can be a useful marker for detecting cancer cells undergoing p-EMT. Moreover, a *POSTN* Iso5 can be a novel therapeutic target for HNSCC.