The role of claudin-2 on the malignancy of human endometrioid carcinoma

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Introduction and Purpose

- Claudin-1 overexpression characterized type II endometrial carcinoma, while claudin-2 was elevated in type I (endometrioid) carcinoma.
- Claudin-2 is a leaky type tight junction protein and the decrease in claudin-2 enhances cell migration in normal cells.
- Overexpression of claudin-2 increases tumorigenesis of some type cancer cells.
- Histone deacetylase (HDAC) inhibitors which have antitumor effects, downregulate claudin-2 expression and cell proliferation in lung cancer cell line.
- In the present study, we investigated the regulation and the role of claudin-2 in endometriosis and endometrioid carcinoma.

Results

Fig.1

CLDN-2 in endometriosis and endometrial cancer type I (endometrioid)

Fig.2-1

Fig.2-2

Cell cycle

Fig.3-3

Fig.3-1

DNA array	Control vs High-glucose
H200002539	NM_001171095.1
CHsGV10000152	NM_001657.3
	AREG
	2.67

Fig.3-2

Fig.3-4

Cell cycle

Phase contrast Immunocytochemistry

CLDN-2 in type I endometrioid cancer

Fig.4-4

Immunocytochemistry

Fig.4-1

Fig.4-2

Cell invasion assay

Cell migration assay

Fig.4-3

Summary

- 1) In endometrioid carcinoma tissues, marked upregulation of claudin-2 was observed together with malignancy, while in endometriosis tissues, the changes in localization of claudin-2 was observed (Fig. 1).
- 2) Loss of claudin-2 by the siRNA upregulated the epithelial barrier in endometrial cancer cell line Sawano cells. Furthermore, the loss of claudin-2 affected cell cycle and inhibited cell proliferation (Fig. 2).
- 3) In Sawano cells cultured with high glucose medium, claudin-2 expression was downregulated at mRNA and protein levels. The high glucose medium upregulated the epithelial barrier and cell migration and inhibited cell invasion (Fig. 3).
- 4) Histone deacetylase (HDAC) inhibitors tricostatin A and HDAC1 inhibitor downregulated claudin-2 expression, cell proliferation, cell invasion and upregulated the epithelial barrier and cell migration (Fig. 4).

Conclusion

- Taken together, overexpression of claudin-2 closely contributed to the malignancy of endometrioid carcinoma and was regulated via glucose metabolism.
- Downregulation of claudin-2 by HDAC inhibitors may be important in therapy for endometrioid carcinoma.

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Disclosure of Conflict of Interest

Name of first author: Seiro Satohisa

I have no COI with regard to our presentation.