The regulation of claudin-2 in endometriosis and endometrioid carcinoma cells

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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.

**Fig. 1**

EM1 EM2 G1 G3
H.E.
CLDN-2
CL-2
actin
cont CL-2A CL-2B
siRNA
cont siRNA-CL-2A siRNA-CL-2B

**Fig. 2**

Cell cycle
cont G0/G1 S G2/M
siRNA-CL-2B

**Fig. 3-1**

Barrier function
control High-glucose
CL-2 CL-4 CL-7 LSR TRIC actin

**Fig. 3-2**

Western blotting
cont High-glucose

**Fig. 3-3**

Cell invasion assay
control High-glucose
Cell migration assay
control High-glucose

**Fig. 4-1**

Barrier function
TEER (ohm cm²)

**Fig. 4-2**

Cell invasion assay
cont 0.1µM TSA 1µM TSA
Cell migration assay
cont 0.1µM TSA 1µM TSA

**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 endometriod 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 trichostatin 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*

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*I have no CCOI with regard to our presentation.*