CHAPTER VI

CONCLUSIONS

The role of Notch signaling in cervical cancer remains controversial. Some reports indicated that Notch promotes tumorigenesis, whereas others reported that Notch suppresses cervical cancer. Our data, however, show that Notch1 is expressed in all HPV cervical cancer cell lines tested. Among these, only CaSki expressed detectable cleaved Notch1. During DAPT treatment for 4 days, we found complete abrogation of the cleaved Notch1 and increased cell proliferation in CaSki, but the treatment did not affect cell viability nor cell cycle progression in cervical cancer cell lines. In CaSki, DAPT treatment resulted in significant decrease in *Notch1* expression, whereas *Hes1*, *MAML1* and *TP53* were increased (Figure 6.1). In DAPT-treated SiHa, expressions of *MAML1* were significantly decreased. In all cell lines tested, no changes in *E6/E7* expression were detected with either DAPT treatment or DN-MAML1 overexpression.

Interestingly, DN-MAML1 transduced-CaSki resulted in significantly decreased *Hes1* and *Notch1* expressions. In addition, inhibition of Notch signaling by DN-MAML1 led to increase the percentage of viable cells and promote cell proliferation, but cell cycle arrest could not be detected in CaSki (Figure 6.2). These observations indicated that DN-MAML1 might interfere with transcriptional activation from all four Notch receptors and cause promoting growth and survival of CaSki.

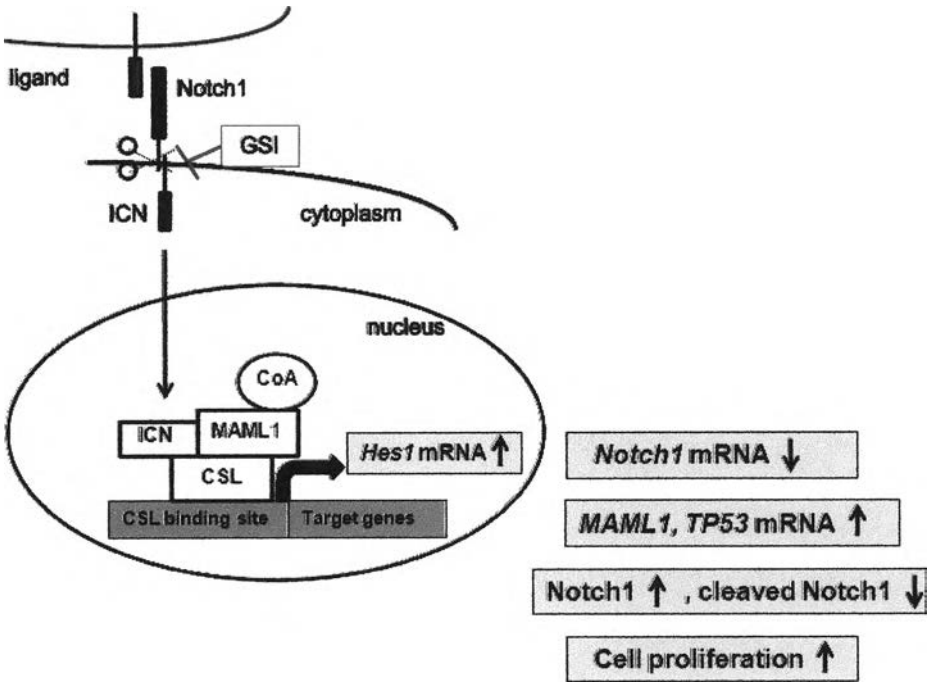

Figure 6.1 Schematic diagram showing the effects of GSI to Notch signaling in CaSki.

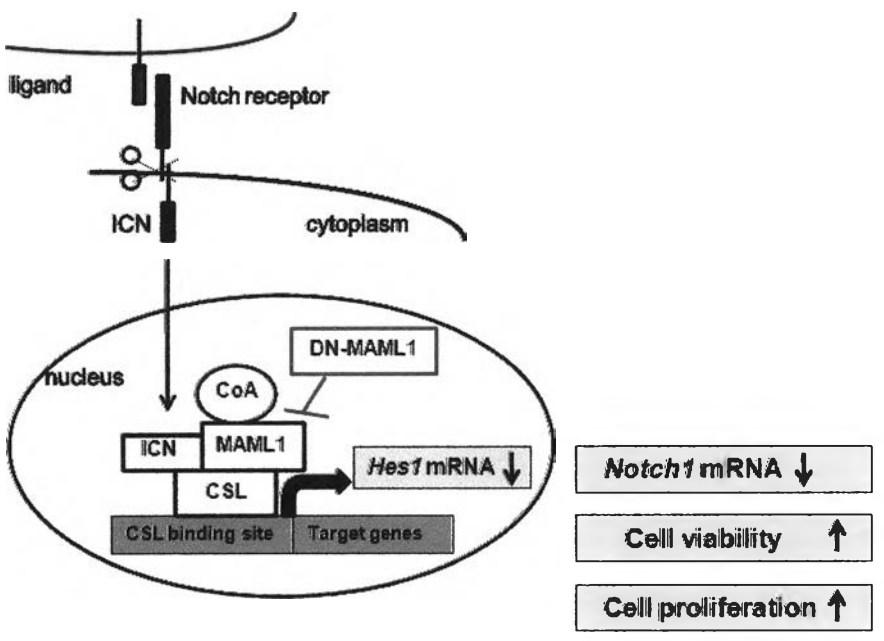

Figure 6.2 Schematic diagram showing the effects of DN-MAML1 to Notch signaling in CaSki.

Suggestions for the future work

On the basis of our data, drugs that inhibit γ-secretase or drugs that inhibit Notch signaling through other mechanisms, alone or in combination with DN-MAML1, may be effective in malignancies where the Notch is pathogenetically important. Further study should be validated the efficacy of DN-MAML1 to Notch signaling in an *in vivo* model, and thus it can serve as a good therapeutic target in cervical cancer.