

# Shorter survival rate in cervical cancer association with high expression of Notch-1



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## INTRODUCTION

- Cervical cancer was once of the most common causes of cancer death for American women.
- Recent studies have implicated aberrant Notch signaling in cervical cancers.
- The inappropriate activation of Notch signaling results in increased proliferation, restricted differentiation, prevention of apoptosis in cancer cells and participates in development of the cell by maintaining the self-renewal potential of some tissues.
- There is multiple reports show elevated Notch expression in cervical carcinoma cells and suggests that Notch1 is down-regulated in late-stage HPV-infected tumors.

## HYPOTHESES

High expression of Notch-1 associated with decreased survival rate in cervical cancer.

## PURPOSE

To determine the role of Notch-1 in the clinicopathology of cervical cancer

## METHODS

- Human tissue samples retrieved from the archive of the department of pathology.
- The series was composed of 79 cases of cervical cancer, and all ranged in age from 42 - 92 years.
- Follow-up of patients ranged from up to 32 months. Patients' data, including age, follow up.
- Immunohistochemistry was performed using standard techniques.
- By light microscopy, representative tissue sections were scored semi-quantitatively for cytoplasmic staining.
- The sample tissues lysed in buffer for Western Blotting.
- The association between the expression of Notch1 in cervical cancer patients and survival rate was done according to the Kaplan-Meier method and survival characteristics were compared using the log rank test.
- The statistical software package SPSS® 11.0 was used for all statistical analyses with  $p < 0.05$  considered statistically significant.

## RESULTS

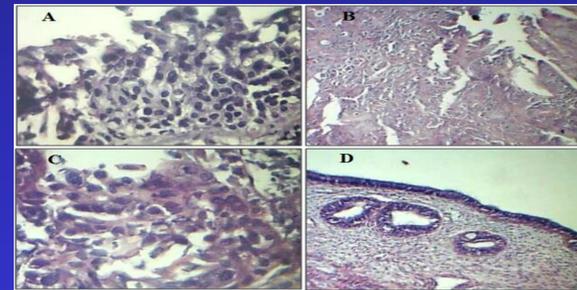


Figure 1. Representative immunohistochemical staining of Notch1 expression, [A] Notch1 was intensively stained, high power view (40x10). [B] Weak stained Notch1 with pleomorphic hyperchromatic nuclei (10x10). [C] Negative staining Notch1 in poorly differentiated invasive squamous cells carcinoma, (40x10). [D] Normal cervical tissue for control (40x10).

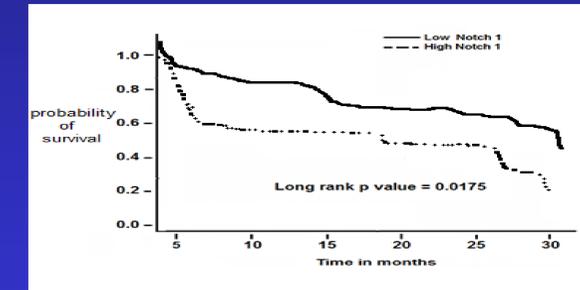


Figure 3. Kaplan-Meier curve show relationship between overall survival in patients with cervical cancer and high level expression of Notch1. Cervical cancer expressing high levels of Notch1 have a significantly shorter survival compared to those expressing low levels of Notch1, Data are expressed as mean  $\pm$  SEM.  $P < 0.0175$  (N=75 per group).

## SUMMARY AND CONCLUSIONS

• Tissue sample of tumors were divided into three groups based on their tumor expression of *Notch1* were analyzed by immunohistochemical staining. The total positive rate of *Notch1* staining was 34(43%), and 22(28%) indicates strong staining intensity; 12(15%) weak staining and 45(57%) negative staining compare with normal cervical tissue. To further confirmation the immunohistochemical result a set of tissue samples (negative, weak, strong) are subjected to western blotting analysis showed stronger immunoreactive bands of the *Notch1* expression in strong immunohistochemical staining.

• Survival time in patient with high expression of *Notch1* was significantly shorter than that in patient with low expression pattern in cervical tumors as show in the Kaplan-Meier curve.

• There is no correlation of expression level of *Notch1* protein with tumor clinicopathological parameters to stage of tumor, nodal involvement, and recurrence of disease but significant related with older age, also the Kaplan-Meier curve showing that the survival rate in cervical cancer patients with high expression *Notch1* were statistically significant with age of patients but not with others clinicopathological parameters.

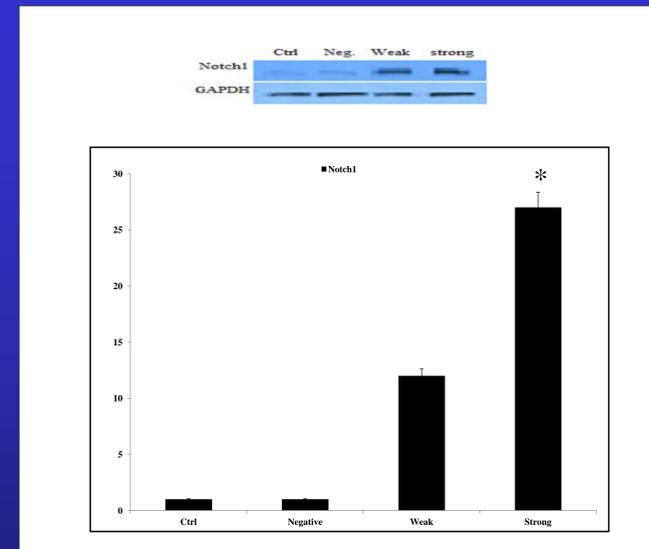


Figure 2 Expression of the Notch1 was quantified in cervical cancer by Western blotting. Results are expressed as highly levels found in cervical cancer tissue with strong immunohistochemical intensity staining compared with negative staining and normal cervical tissue as control. Data are expressed as mean  $\pm$  SEM. N=75 per group; \* $P < 0.05$  vs. normal cervical tissue.

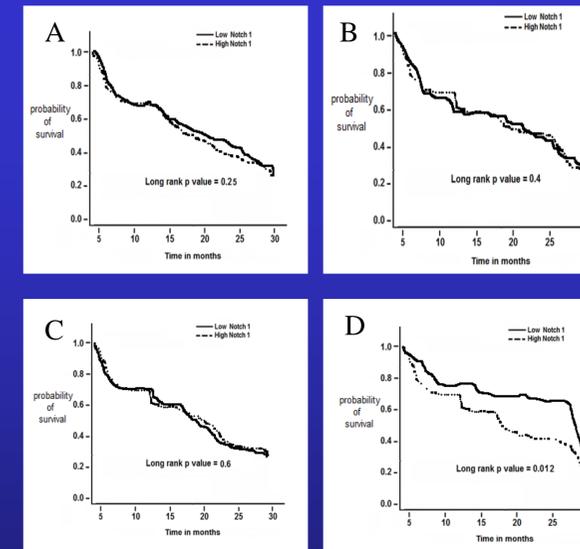


Figure 4. The survival rate related to the expression of Notch1 is not significant relationship with [A] cervical cancer recurrence, [B] advance stages and [C] nodal involvement. Data are expressed as mean  $\pm$  SEM. (long rank  $P = 0.25$ ,  $P = 0.4$ ,  $P = 0.6$  respectively). [D] While older patients with cervical cancer show shorter survival related with high level expression of Notch1. Data are expressed as mean  $\pm$  SEM.  $P < 0.012$ .