CHAPTER 3

RESULTS

The pattern of p53 protein expression in cervical cancer

The positive cases showed exclusively granular or diffuse nuclear staining in a varying fraction of expression. The surrounding non-neoplasmic mucosa, lymphocytes, and stromal cells were negative. There was p53 expression in 40% cases and 46.67% controls of cervical carcinomas, demonstrated by granular nuclear positivity (Figure 15-17). In squamous cell carcinoma, there was no evidence of cytoplasmic positivity in any of the tumors, while for adenocarcinoma, positive tumor cells were seen in lymph vessels but lymphocytes were negative (Figure 20). Moreover evidence of cytoplasmic staining was observed in case of adenocarcinoma (Figure 19). Some sections showed background staining but this did not interfere with their interpretation. The analyses are based on the result of nuclear staining only.

The proportion of positive p53 protein expression

The p53 expression was positive in 12 (40%) node negative cervical cancer patients with tumor recurrence and 28 (46.67%) in those without tumor recurrence. The results of the comparison of p53 protein expression in cervical cancer was presented in Figure 7. Positivity of p53 protein was observed in tumor nuclei and a cut-off value of 5% was taken to score a cases as positive for p53 expression. Among the thirty cases with tumor recurrence, 18 (60.0%) failed to show the positivity of p53 expression where as 28 (46.67%) controls demonstrated as positive. A maximum of score +3 was detected in 5 (8.33%). Most of all cases have a maximum score +2. The results of the comparison of proportion of p53 expression in cervical cancer was shown in Table 3. In patient without tumor recurrence, the mean value of proportion of p53 expression was slightly higher than those with tumor recurrence (8.83 vs 7.71% respectively). There was no significant difference of the proportion of p53 expression between two groups($p=0.339$).
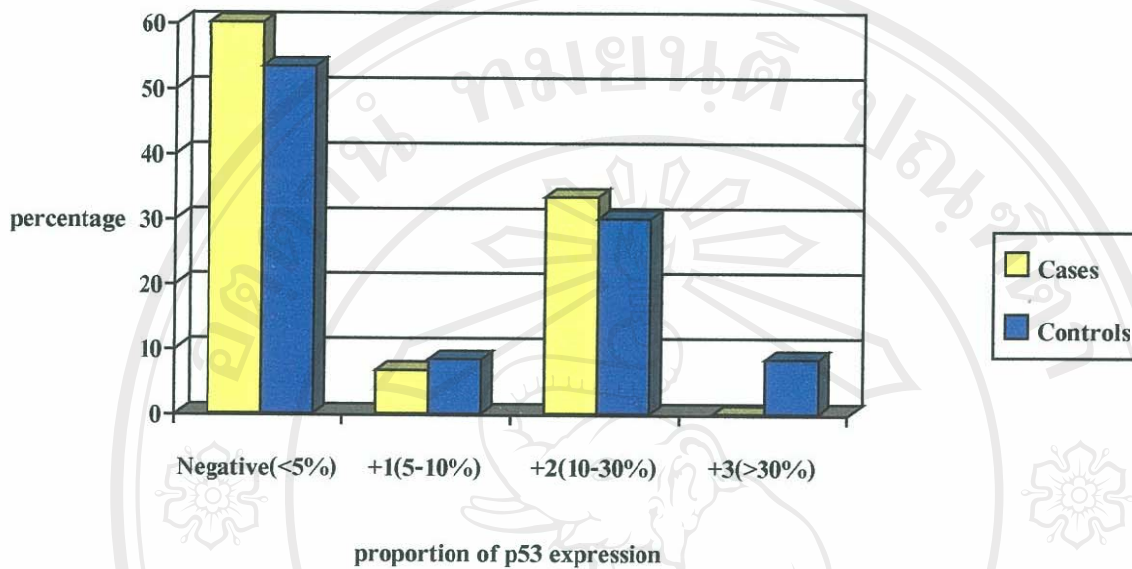
Figure 7 Diagram showing the comparison of p53 expression

in patients with cervical carcinoma

Table 3 The comparison of the proportion of p53 protein expression in patient with cervical

carcinoma analyzed by independent sample t-test

Group of patients	Mean value of the proportion of p53 expresssion (Mean±SD)	*p-value*
Non-recurrence (n= 60)	8.83±12.57	
Recurrence (n= 30)	7.71±10.67	0.339

The p53 protein expression in correlation with tumor recurrence

Using immunohistochemistry technique, the expression of p53 protein and association with tumor recurrence was analyzed by Mantel-Haenzel test. The result of this analysis is presented in Table 4. Thirty patients with tumor recurrence after RDH were matched with two controls each. Forty cases were p53 positive. There were no significant association between expression of the p53 protein and tumor recurrence $(p = 0.549)$.

Table 4 The results of Mantel-Haenzel test of 30 cases with tumor recurrence matched with 60 control without tumor recurrence

Clinical variable	Cases (n=30) No.(%)	Controls (n=60) No.(%)	p-value
Result of p53 staining			
Positive	12 (40)	28 (46.67)	
Negative	18 (60)	32 (53.33)	0.549
Total	30 (100)	60(100)	

The p53 protein expression in correlation with clinicopathological variables for cervical cancer

This study is retrospective analysis of 90 patients of histologically diagnosed invasive cervical carcinoma underwent radical hysterectomy and pelvic lymphadenectomy. There were 84 patients in FIGO stage IB and 6 in stage IIA. The correlations of the p53 protein expression and the clinicopathological variables were analyzed by multiple logistic regression. The results of this analysis of 30 cases with tumor recurrence after radical hysterectomy matched with 60 controls without tumor recurrence is shown in Table 5. The p53 expression was significantly associated with histologic type (p=0.036); (83.33%) of 11 cases and (89.29%) of 25 controls with squamous cell carcinoma, 1(8.33%) case and 3 (10.17%) controls with adenocarcinoma and 1 (3.57%) control with adenosquamous carcinoma were scored positive for p53 expression. Patients with squamous cell carcinoma have an RR of 0.09 (0.01-0.086) compared to patients with adenocarcinoma or adenosquamous carcinoma. No correlation was present with the other clinicopathological parameters, including FIGO staging, tumor characteristics, LVSI, depth of invasion and tumor grade.

Table 5 The correlation of p53 protein expression and clinicopathological variables by multiple logistic regression analysis of 30 cases with tumor recurrence matched with 60 controls without tumor recurrence

| Variables	No. of patients (%) with p53 expression		RR(95%CI)	*p*-value
	cases	controls		
FIGO staging				
IB	10 (83.33)	25 (89.29)	7.00 (0.78-62.57)	0.082
IIA	2 (16.67)	3 (10.17)	1.00	
Histologic type				
Squamous	11 (91.67)	25 (89.29)	0.09 (0.01-.086)	0.036
Adenocarcinoma	1 (8.33)	3 (10.17)	1.28 (0.11-14.59)	0.844
Adenosquamous	-	1 (3.57)	1.00	
Tumor characteristics				
Exophytic	5 (41.67)	13 (54.17)	2.96 (0.63-13.87)	0.168
Infiltrative	6 (50.0)	11 (39.29)	1.37 (0.28-6.78)	0.697
No definite lesion	3 (6.0)	4 (14.29)	1.00	
LVSI				
Presence	10 (83.33)	14 (50.0)	1.50 (0.65-3.48)	0.345
Absence	2 (16.67)	14 (50.0)	1.00	
Depth of invasion				
Inner half(<1/2)	3 (75.0)	10 (35.71)	1.39 (0.58-3.31)	0.464
Outer half(>1/2)	9 (75.0)	18 (64.29)	1.00	
Tumor grade				
Grade I	3 (25.0)	10 (35.17)	0.28 (0.03-2.61)	0.265
Grade II	9 (75.0)	17 (60.17)	0.14 (0.02-1.26)	0.080
Grade III	-	1 (3.57)	1.00	
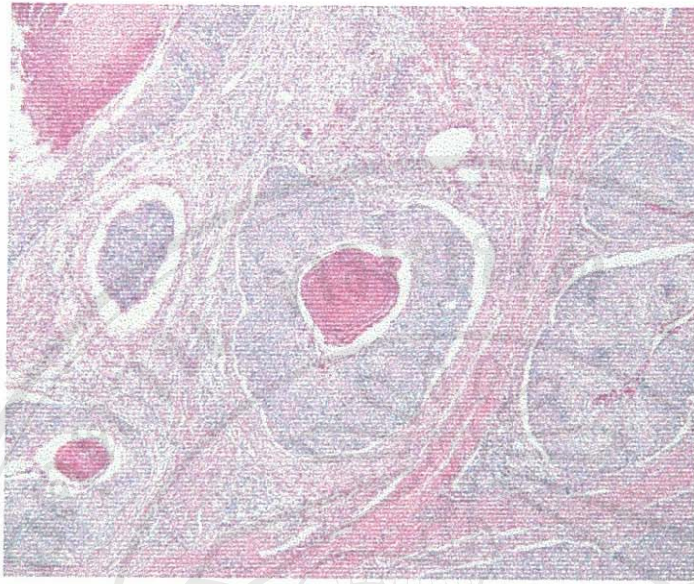
Figure 8 Squamous cell carcinoma (H&E, 10x)
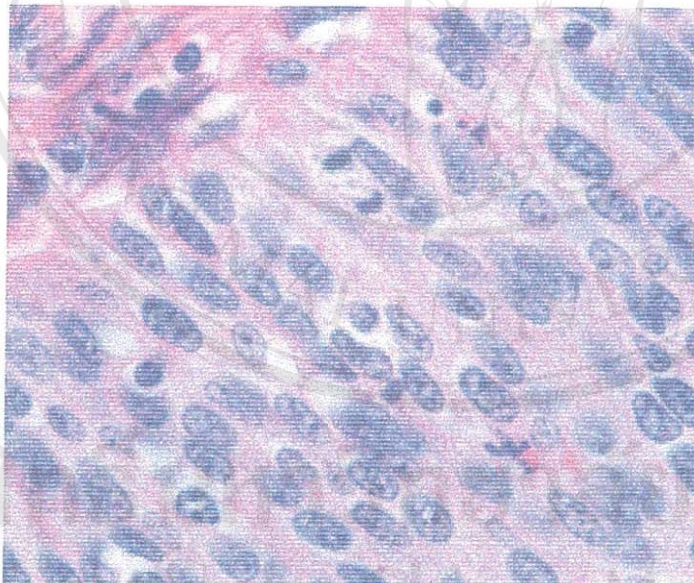

Figure 9 Invasive squamous cell carcinoma (H&E, 100x)
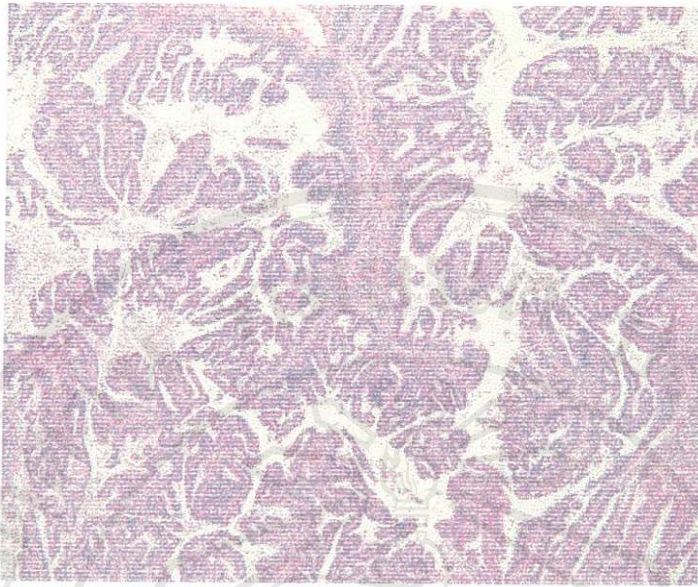
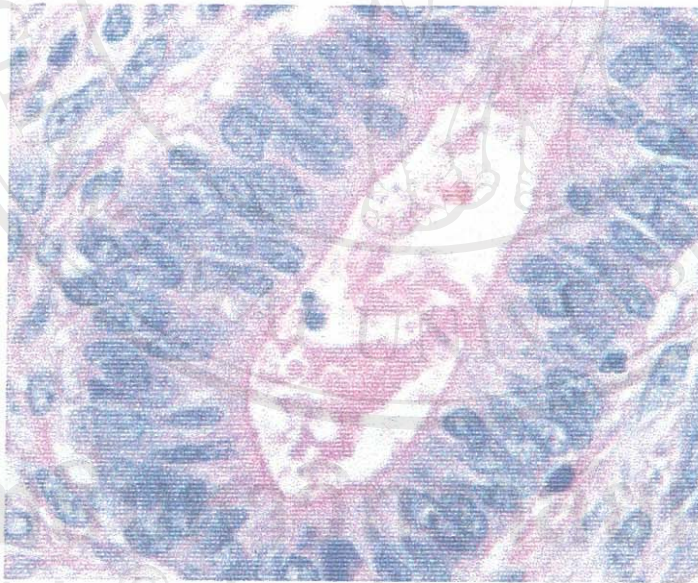**Figure 10** Adenocarcinoma (H&E, 10x)

Figure 11 Adenocarcinoma (H&E, 100x)

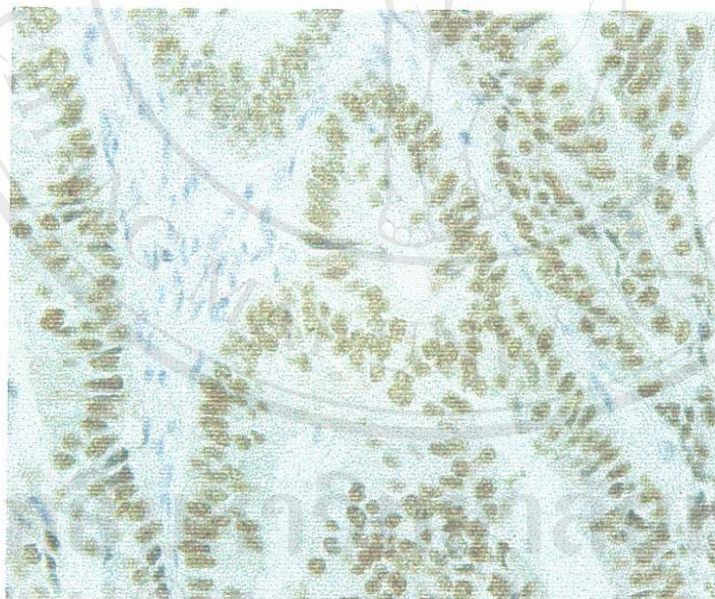**Figure 12** Adenosquamous carcinoma (H&E, 5x)

Figure 13 Immunohistochemical staining of p53 protein in colorectal

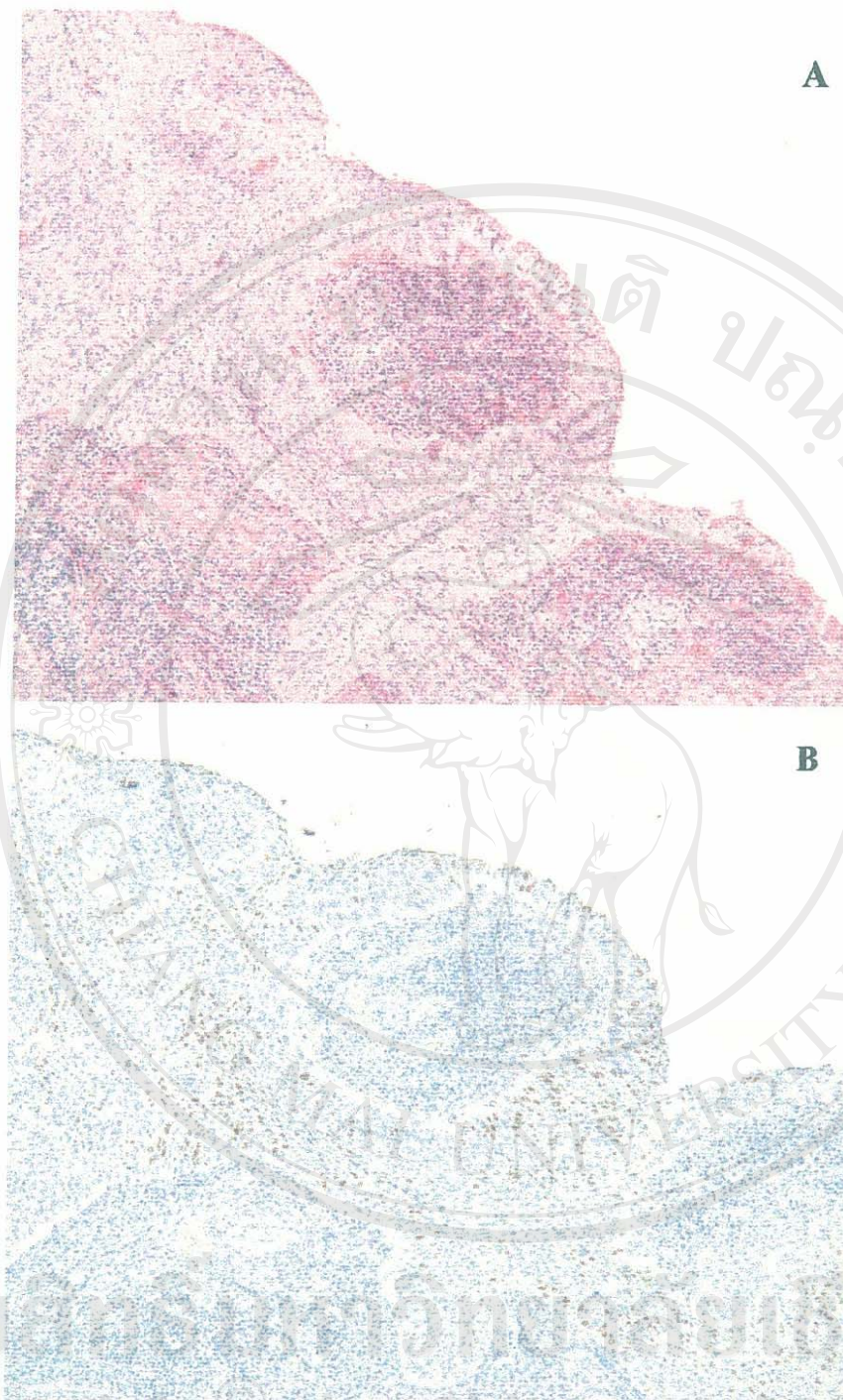cancer, as a positive control. (magnification, 40x)

Figure 14 Invasive squamous cell carcinoma (A) stained with H&E
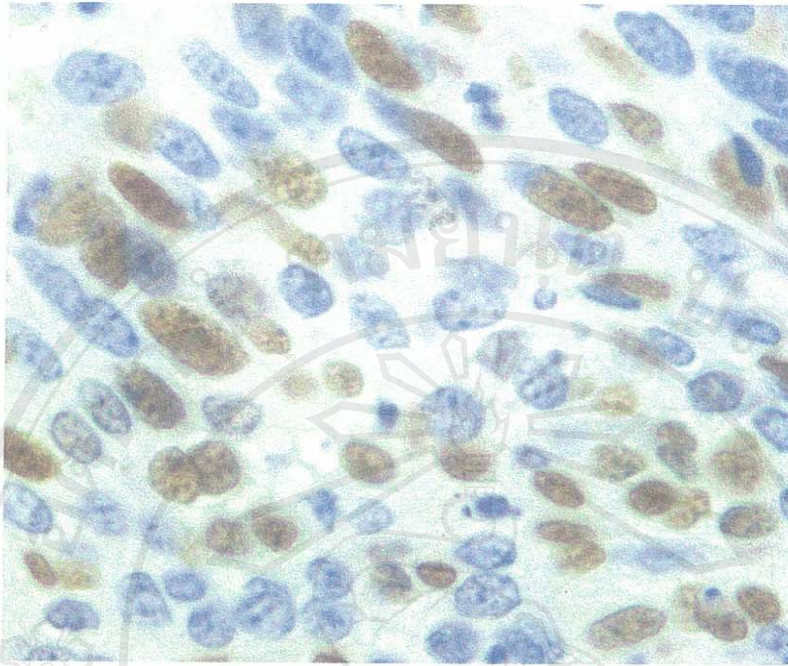and (B) immunostained with antibody to p53 protein
(magnification 10x)

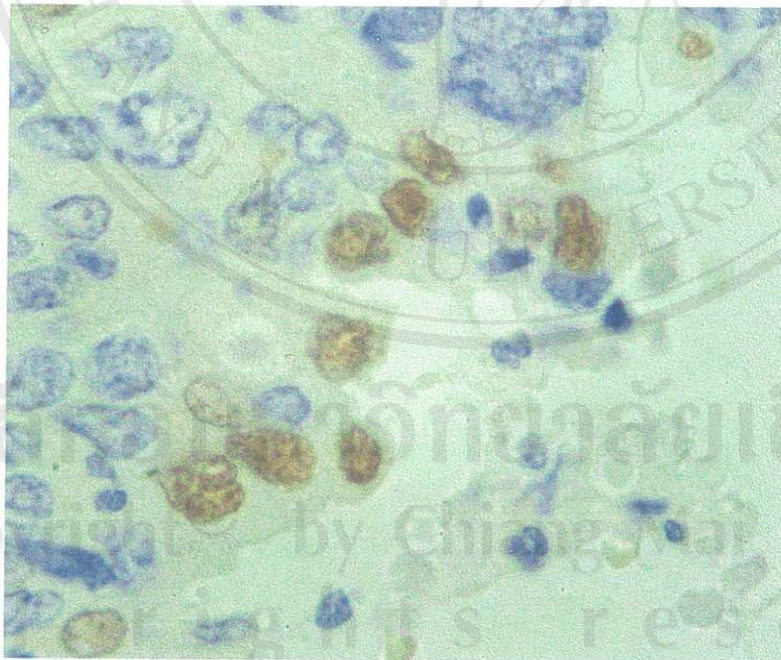**Figure 15** Immunohistochemical staining of p53 protein in
squamous cell carcinoma (magnification 100x)

Figure 16 Immunohistochemical staining of p53 protein in
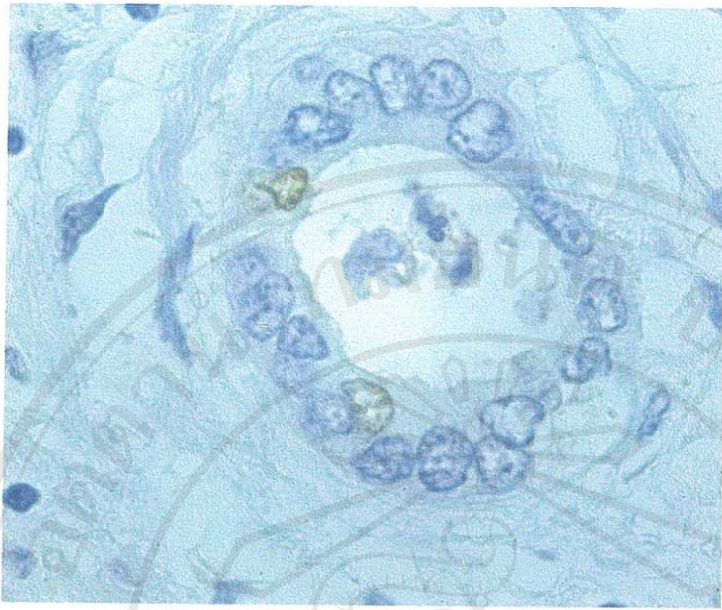adenocarcinoma (magnification 100x)

Figure 17 Immunohistochemical staining of p53 protein in
glandular part of adenosquamous carcinoma
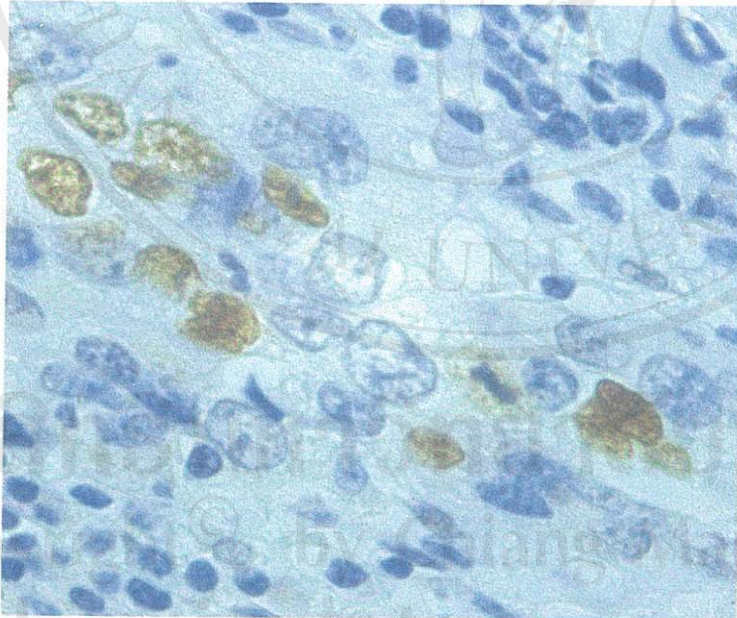(magnification 100x)

Figure 18 Immunohistochemical staining of p53 protein in
squamous cell carcinoma with the intensity of staining
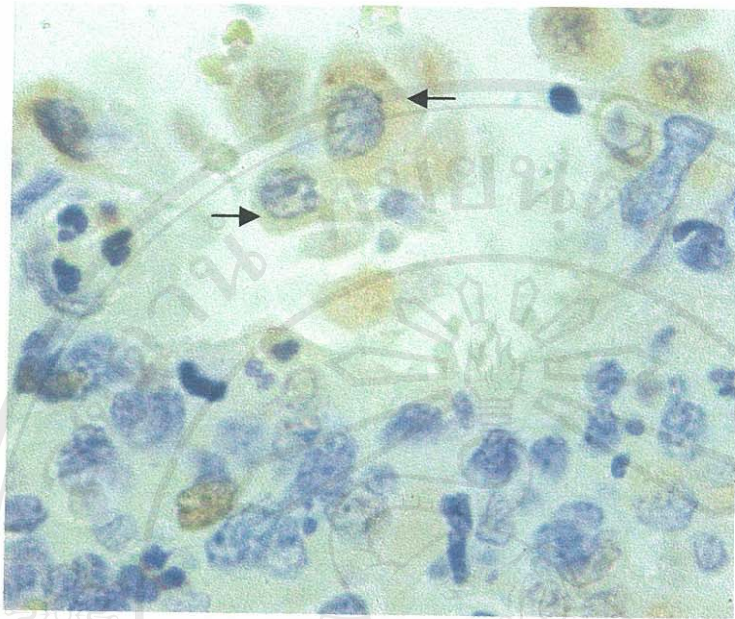varied from cell to cell (magnification 100x)

Figure 19 Evidence of cytoplasmic staining of p53 protein in adenocarcinoma of uterine cervix.(arrow) (magnification, 100x)
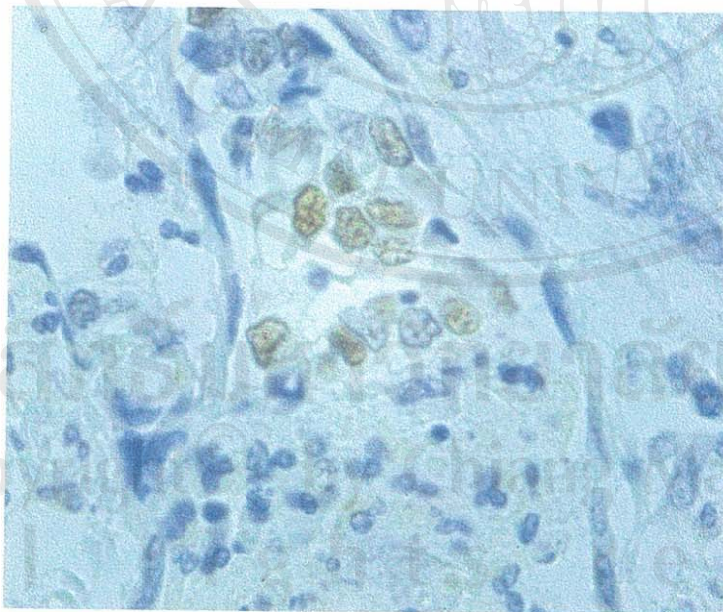

Figure 20 Immunostaining of p53 protein within lymph vessel of adenocarcinoma. (magnification, 100x)