

## CLINICAL STUDY

# Activities of adenosine deaminase and 5'-nucleotidase in cancerous and non-cancerous human gastric tissues

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**Abstract:** *Introduction:* Gastric cancer is still one of the most common fatal types of cancer in the world. The abnormalities in purine metabolism are a characteristic feature of many human tumors. Little is known about the correlation between the activities of key enzymes of purine nucleotide pathway and some clinical indicators of gastric cancer invasiveness and aggressiveness.

*Method:* Seventeen (11 men, 6 women) patients with gastric cancer were admitted to the hospital. The activities of Adenosine deaminase (ADA) and 5'-nucleotidase (5'NT) in their cancerous and non-cancerous tissues were measured.

*Results:* 5'NT activities were significantly higher in cancerous tissues than in non-cancerous tissues.

*Conclusion:* 5'NT activities increased in gastric cancer tissues but had no association with clinicopathologic findings (Tab. 2, Ref. 9). Full Text (Free, PDF) [www.bmj.sk](http://www.bmj.sk).

Key words: gastric cancer, adenosine deaminase, 5'-nucleotidase.

Gastric cancer is still one of the most common fatal types of cancer in the world. The possible mechanisms leading to gastric carcinogenesis have not been clarified yet. The aim of this study was to determine the activities of these enzymes in cancerous and non-cancerous human gastric tissues.

The abnormalities in purine metabolism are a characteristic feature of many human tumors. Little is known about the correlation between the activities of key enzymes of purine nucleotide pathway and some clinical indicators of gastric cancer invasiveness and aggressiveness (1).

Adenosine deaminase is an enzyme catalysing the hydrolytic deamination of either adenosine or deoxyadenosine to inosine or deoxyinosine, respectively. This enzyme reaction seems to be one of the rate-limiting steps in adenosine degradation (2).

5'-Nucleotidase (5'NT) is another enzyme functioning in nucleotide metabolism. It generates nucleosides from various types of nucleotides and adenosine is produced mainly by dephosphorylation of AMP catalyzed by 5'NT (1–3).

In several studies, activities of these enzymes were found to be increased or decreased, depending on cancerous cells studied.

The aim of this study was to determine the activities of these enzymes in cancerous and non-cancerous human gastric tissues.

## Materials and methods

Seventeen (11 men, 6 women) patients with gastric cancer were admitted to the Section of Surgical Oncology, Ankara University Medical School and Ankara Numune Training and Research Hospital between May 2000 and January 2001. Mean age was 58 (range 33–77). All patients underwent diagnostic procedures before surgery using endoscopic examination, chest x-ray, CT scan of abdomen and tumor markers. The diagnosis of gastric cancer was verified histologically. The International Union against Cancer TNM classification and staging system was used for tumor assessment.

Clinical and pathologic features of the studied group are demonstrated in Table 1.

Biopsies were taken from both cancerous and cancer-free adjacent mucosae during surgery. Non-cancer diagnosis of adjacent tissues was made by histopathological investigation.

Tissues were homogenized by using a homogeniser (B. Braun-Melsungen) and then centrifuged at 10 000 X g for 1 h. The upper layer was taken and used for enzymatic analyses. ADA, 5'-NT activities were measured (4, 5).

Data were expressed as mean + SEM unless mentioned otherwise in the text. Statistical significance was estimated using the ANOVA analysis, Mann-Whitney-U test, student-t test, as appropriate. The level of significance was set to  $p < 0.05$ .

Spearman rank correlation test was used to express the association between the different variables.

All the statistical analyses were made using a commercial statistical software package (SPSS for Windows release 6.0. SPSS Inc. Chicago, Ill).

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**Tab. 1. Clinical and pathologic features of the studied group.**

Median age, years (range)	
Gender (M/F)	11/6
Localisation	No of patients
Antrum	10
Corpus	4
Cardia	3
Grade	
I	7
II	9
III	1
T	
T1	-
T2	1
T3	14
T4	2
N	
N0	2
N1	3
N2	7
N3	3
N4	1
M	
M0	13
M1	4
Stage(TNM)	
1	1
2	1
3	9
4	6

**Tab. 2. ADA and 5'-NT activities (mean±SEM) of cancerous and non-cancerous gastric tissues.**

	ADA <sup>a</sup>	5'-NT <sup>a</sup>
Cancerous tissues	36.9±6.1	0.59±0.008
Non-cancerous tissues	52.87±13.8	0.49±0.004

<sup>a</sup>– Activity unit (specific activity), mIU/mg protein.

## Results

### ADA and 5'NT activities in cancerous tissues

The mean 5'NT activity was 0.59 mIU/mg in cancerous tissues, and 0.49 mIU/mg in non-cancerous tissues. The differences were statistically significant ( $p < 0.05$ ). The mean ADA activity was 36.9 mIU/mg in cancerous tissues and 52.87 mIU/mg in

non-cancerous tissues but the differences were not significant ( $p > 0.05$ ) (Tab. 2).

Cancerous and non-cancerous 5'NT activities were tightly correlated ( $R = 0.56$ ,  $p < 0.05$ ). In contrast, no significant association was found between cancerous and non-cancerous ADA activities.

### Correlation between ADA and 5'NT activities in cancerous tissues and clinicopathologic features

ADA and 5'NT activities of cancerous tissues had no association with age, gender, localisation and other clinicopathologic findings.

## Discussion

Due to their rapid growth, solid tumors routinely experience severe hypoxia and necrosis leading to adenine nucleotide degradation and adenosine release. The released adenosine constitutes supportive environment for tumor growth by means of protection against ischemia. At the same time it stimulates the growth and angiogenesis as well as suppresses immune responses (2).

Adenosine is produced mainly by dephosphorylation of AMP catalyzed by 5'NT. Adenosine deaminase is an enzyme catalysing the hydrolytic deamination of either adenosine or deoxyadenosine to inosine or deoxyinosine, respectively. This enzyme reaction seems to be one of the rate-limiting steps in adenosine degradation (1, 2).

The activity of 5'NT is variable in malignant cells. 5'NT activities were found to be higher in some types of cancerous tissues such as breast, pancreas and stomach (1, 2). Durak et al demonstrated that ADA and 5'NT activities were higher in gastric juices from gastric cancer patients compared to those with benign lesions of stomach (1).

The level of ADA activity in gastric cancer tissues continues to be a matter of debate. Some researchers found a significantly increased ADA activity in cancerous gastric tissues (1). However, Namiot et al found out that the activity of ADA did not differ significantly between cancerous and non-cancerous gastric tissues and concluded that the determination of ADA activities has no value in diagnostic work (6). Kojima et al analysed ADA activities of peripheral lymphocytes in patients with gastric cancer and found decreased levels of lymphocyte ADA activity.

With respect to adenosine levels, some authors suggest that purine and pyrimidin metabolisms are increased in cancerous tissues and cells, and in high concentrations, the substrates of these metabolic pathways (adenosine and deoxyadenosine) have cytotoxic effects (1). On the other hand, adenosine is also known to be an important factor promoting the tumor growth (2, 9).

In our study, 5'NT activities were found to be increased in cancerous tissues and no significant change was observed in ADA activities of cancerous and non-cancerous tissues. Based on these findings, we think that tumor tissue may be promoting the 5'NT enzyme activity and inhibiting the ADA activity whilst both effects share a common aim of increasing the levels of adenosine that acts as a tumor-supporting factor.

In conclusion, 5'NT activities increased in gastric cancer tissues however the latter increase had no association with clinicopathologic findings.

## References

1. Durak I, Çetin R, Canbolat O, Çetin D, Yurtarslani Z, Unal A. Adenosine deaminase, 5'-nucleotidase, guanase and cystidine deaminase activities in gastric tissues from patients with gastric cancer. *Cancer Lett* 1994; 84: 199–202.
2. Spychala J. Tumor-promoting functions of adenosine. *Pharmacology & Therapeutics* 2000; 87: 161–173.
3. Namiot Z, Kemon A, Stasiewicz M, Marcinkiewicz A, Namiot A, Gorski J. Adenosine deaminase activity in gastric cancer. *Cancer Lett* 1994; 82: 95–98.
4. Guisti G. Enzyme activities. 1087–1091. In: Bergmeyer UH (Ed). *Methods of enzymatic analysis*. Weinheim Bergest: Verlag chemia 1974.
5. Donald WM. Enzymes. 718–720. In: Tietz NW (Ed). *Textbook of clinical chemistry*. Philadelphia: WB Saunders Company 1986.
6. Namiot Z, Stasiewicz M, Namiot A, Kemon A, Kralisz M, Gorski J. Adenosine deaminase activity in patients with the intestinal type gastric carcinoma. *Cancer Lett* 1996; 109: 199–202.
7. Kojima O, Majima T, Uehara Y, Yamane T, Fujita Y, Takahashi T, Majima S. Alteration of adenosine deaminase levels in peripheral blood lymphocytes of patients with gastric cancer. *Jpn J Surg* 1985; 15: 130–133.
8. Camici M, Tozzi MG, Allergini S et al. Purine salvage enzyme activity in normal and neoplastic human tissues. *Cancer Biochem Biophys* 1990; 11: 201–209.
9. Jonathan B, White TD, Hoskin DW. The extracellular fluid of solid sarcomas contains immunosuppressive concentrations of adenosine. *Cancer Res* 1997; 57: 2602–2605.

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