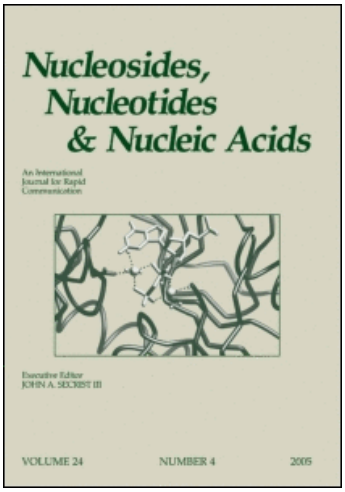

Nucleosides, Nucleotides and Nucleic Acids

Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597286

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Online publication date: 27 October 2004

To cite this Article Vannoni, D. , Pietro, M. C. Di , Rosi, F. , Bernini, A. , Leoncini, R. , Tabucchi, A. , Carlucci, F. , Floccari, F. , Santoro, A. , Tanzini, G. and Marinello, E.(2004) 'Metabolism of Adenosine in Human Colorectal Tumour', Nucleosides, Nucleotides and Nucleic Acids, 23: 8, 1455 — 1457

To link to this Article: DOI: 10.1081/NCN-200027676

URL: http://dx.doi.org/10.1081/NCN-200027676

NUCLEOSIDES, NUCLEOTIDES & NUCLEIC ACIDS
Vol. 23, Nos. 8 & 9, pp. 1455–1457, 2004

Metabolism of Adenosine in Human Colorectal Tumour

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ABSTRACT

The aim of this work is to analyse the activities of the enzymes metabolising adenosine in fragments of neoplastic and normal-appearing mucosa, surrounding the tumour in 20 patients affected by colorectal cancer. The results show that the activities of the enzymes are markedly higher in tumour in comparison to normal mucosa to coope with the accelerated purine metabolism in cancerous tissues.

Key Words: Adenosine; Purine metabolism; Colorectal cancer; Tumors; Neoplasia.

INTRODUCTION

It is known that adenosine plays an important role in the life of the cells and changes in its concentration regulate a number of important physiological process; its production enhance during particular conditions as anoxia or ischemia. The steady-state concentration of adenosine is maintained by the activities of cytosolic 5′nucleotidase

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DOI: 10.1081/NCN-200027676
1525-7770 (Print); 1532-2335 (Online)

(e-Ns), linked to membrane 5′ nucleotidase (ecto 5′NT), adenosine kinase (AK) and adenosine deaminase (ADA). Solid tumours routinely show severe hypoxia and necrosis, due to their rapid growth, so that some functions necessary for cellular homeostasis cannot be executed, with the consequence of adenine nucleotide degradation and adenosine release.

The aim of this work is to analyse the activities of the enzymes involved in adenosine metabolism in an uncontrolled cell proliferating tissue such as colon–rectal tumour.

MATERIALS AND METHODS

We analysed 20 patients, 11 males and 9 females aged between 46 and 80 years. 7 of them were affected by rectal cancer, 4 by right colon cancer and 9 by left colon cancer. 14 of them were T3, the others T4; 6 presented lymphonoid metastasis and 2 also pulmonary metastasis. The grade was so distributed:8 patients were G1, 11 G2 and 2 patient G3.

The enzymes were assayed, according to the literature,[1,2] in fragments of neoplastic and normal-appearing mucosa, surrounding the tumour in a region close (less than 3 cm) and distant (at least 10 cm) to the tumour.

RESULTS

The results are reported in Table 1.

ADA and AK activities significantly increase in cancer ($p < 0.01$) with respect to the close or distant normal tissue; ecto 5′NT activity increases in tumor ($p < 0.05$) comparing to the normal distant tissue while not significant differences were found in the activities of e-Ns, in the three analysed fragments. No significant correlations were found between the enzymes levels and some clinico-pathological factors or clinical course of the disease such as the tumor's depth of invasion (T), lymph node status (N), distant metastasis (M) and tumor grade (G).

Table 1. Enzyme activities (mean ± SD) in non cancer (close and distant from the tumoe) and cancer human colorectal tissues.

Enzyme	Non-cancer distant	Non-cancer close	Cancer
AK	8.20 ± 2.85	8.44 ± 2.45	17.59 ± 7.80**
ADA	399.39 ± 97.19	428.00 ± 122.62**	614.06 ± 253.98**
e-Ns	686.40 ± 162.36	683.38 ± 248.17	667.17 ± 496.18
Ecto-5′NT	33.10 ± 19.17	37.29 ± 17.00	61.61 ± 52.18*

Values are expressed as nmoles/h/mg proteins in the case of AK, ADA and endo 5′-NT and as nmoles/h/g tissue in the case of ecto-5′NT.

*$P < 0.05$.

**$P < 0.01$.

DISCUSSION

Results suggest that the enzyme activities increase to cope with the accelerated purine metabolism in cancerous tissues. The contemporary increase of ADA and AK activities might be an attempt of the cancer cells to provide more substrates needed to accelerate the salvage pathway activity. The rise of ecto 5′NT activity, increases available adenosine to interact with the adenosine receptors coupled to G-protein with the consequent rising of the cAMP levels and stimulation of the cellular growth, which is very active in neoplastic tissue.

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