

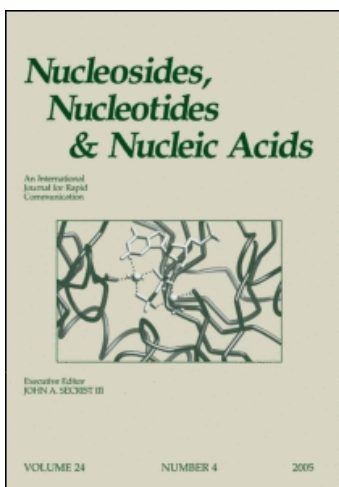
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G. B. Chheda^a; J. G. Antkowiak^b; H. Takitat^b; A. K. Bhargava^c; H. A. Tworek^a

^a Departments of Biophysics, Roswell Park Memorial Institute Buffalo, New York ^b Thoracic Surgeryt Roswell Park Memorial Institute Buffalo, New York ^c Laboratory Medicine Roswell Park Memorial Institute Buffalo, New York

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EVALUATION OF 5-CARBAMOYLMETHYLURIDINE AS AN INDICATOR OF TUMOR BURDEN IN LUNG CANCER PATIENTS

G.B. Chheda*, J.G. Antkowiak†, H. Takita† A.K. Bhargava§ and H.A. Tworek*
Departments of Biophysics*, Thoracic Surgery† and Laboratory Medicine§
Roswell Park Memorial Institute
Buffalo, New York 14263

Abstract

Elevation of 5-carbamoylmethyluridine in the urines of non-small lung carcinoma patients suggests that this nucleoside may be used as an indicator of tumor burden for these patients.

* * * * *

In our laboratory¹, investigation of nucleosides and related substances from twenty-four hour urine collections has led to the characterization of several novel compounds, including 5-carbamoylmethyluridine (ncm^5U). Since modified nucleosides have previously been shown to be elevated in the urine and blood of a variety of cancer patients, comparison of urinary and serum ncm^5U levels in non-small cell lung cancer patients and normal subjects was investigated. After initial desalting and clean up of 5 ml urine and serum samples, nucleosides were isolated by affinity phenylboronate gel chromatography^{2,3}. The nucleosidic material was fractionated by reversed phase high performance liquid chromatography and ncm^5U was quantitated using UV detector; uracil- β -D-arabinofuranoside was used as an internal standard. Injection amounts were maintained at 0.1 A_{260} units of nucleoside fraction per 10 μl of injection volume. Assay elution was conducted with 0.01 M $\text{NH}_4\text{H}_2\text{PO}_4$, pH 3.0 at 0.7 ml/min.

Levels of ncm^5U were found to be elevated in the urine and serum of non-small cell lung cancer patients when compared to the levels found in normal subjects ($p < 0.001$). The mean urinary ncm^5U level of the patient group (0.916 ± 0.259 nmoles $\text{ncm}^5\text{U}/\mu\text{moles}$ creatinine) was elevated approximately 2X over that found in the control group (0.448 ± 0.103). The mean patient serum ncm^5U level (1.370 ± 0.333) was elevated approximately 1.5X over that of controls (0.911 ± 0.174). Significant elevation of ncm^5U occurred in the urine of 17 out of 18 (98%) patients (Fig. 1) and in the serum of 7 of 12 (58%) patients. Patients with malignancy surpassing stage I who demonstrated significantly elevated serum levels, also exhibited elevated urinary levels.

Because ncm^5U is non-specific and under the present urinary assay, does not discern non-advanced malignancy in all cases, its value as a quantitative tumor indicator may be enhanced when used in conjunction with other markers, especially those possessing greater

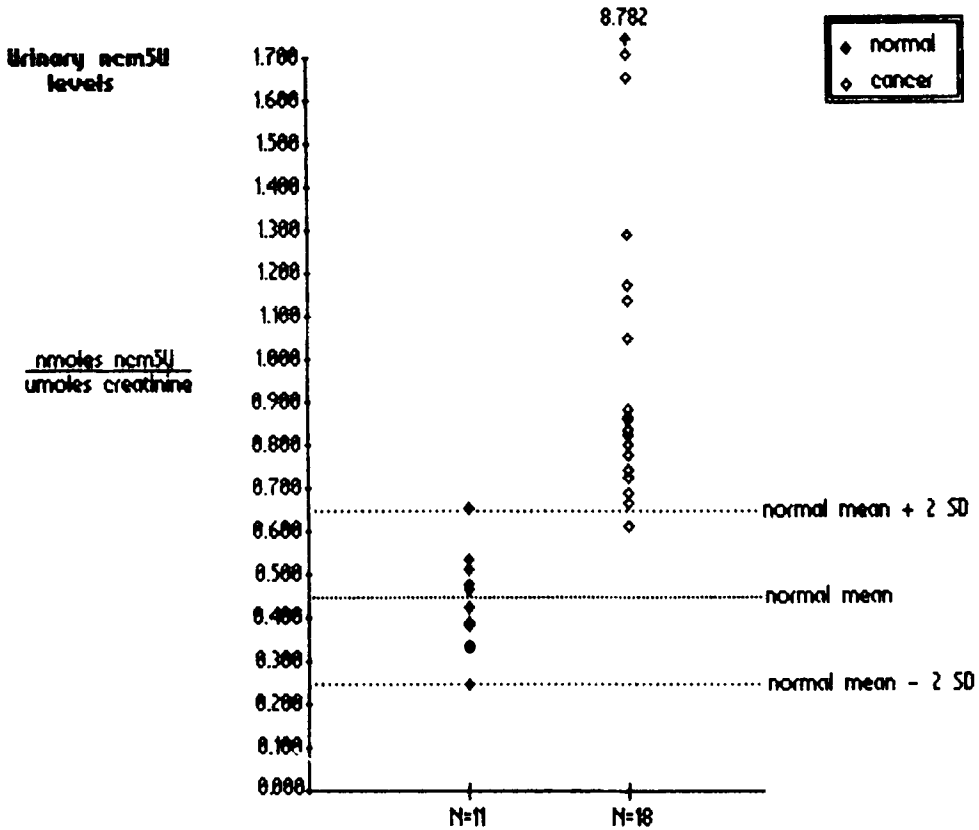


Fig. 1. Comparison of Urinary ncm⁵U Levels in Non-Small Cell Lung Cancer Patients and Normal Subjects.

specificity but poor sensitivity. This investigation suggests potential application of ncm⁵U as a monitor of tumor load since urinary and combined urinary/serum levels seemed generally to reflect advanced malignancy. A greater sample size is however needed to further support these results.

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