

the early synthesized DNA, or at least a part of it, is associated with nucleolus and acts as template for ribosomal RNA. Predominantly lethal action of 5-azacytidine in the S phase⁵⁻⁷, inhibition⁹ of maturation of 45 S rRNA, the effect of the drug on nucleolus⁸, and the localization of 5-azacytidine in the nuclear and in the chromosomal heterochromatin indicate that this analogue may be of value for the investigation of the function of nucleolus and its relation to heterochromatin.

Zusammenfassung. Die Inkorporation des ¹⁴C-markierten 5-Azacytidins in die embryonalen Mäusefibroblasten, die in Zellkulturen gehalten worden waren, wurde

autoradiographisch untersucht. Die Radioaktivität in Kern und Chromosomen ist häufig mit dem Heterochromatin assoziiert. Die Nukleolen werden vergrößert, und die Chromosomen, die sich in der Metaphase befinden, weisen sternförmige Gebilde auf.

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Tubuloreticular Structures in a Case of Bronchialadenom (Carcinoid Type)

Tubuloreticular structures, reported often in collagen diseases¹, have also been seen in several other diseases, including neoplastic diseases^{2,3}. To our knowledge they have not been previously reported in carcinoid tumours.

One bronchialadenoma (carcinoid type), resected from the left main bronchi of a 39-years-old woman admitted to the Department of Pathological Surgery of Sta. Maria's Hospital in Lisbon, was studied by electron microscopy. Fragments of less than 1 mm³ wide were fixed sequentially in 3% glutaraldehyde in cacodilate buffer, pH 7.3, 2%

osmium tetroxide in veronal acetate buffer, pH 7.3 and in 0.5% uranyl acetate in bi-distilled water. Following dehydration in ethanol, they were embedded in Epon 812 (Luft). The patient showed no evidence of other diseases, namely collagen diseases.

¹ F. GYÖRKEY, J. G. SINKOVICS, K. W. MIN and P. GYÖRKEY, *New Engl. J. Med.* 280, 333 (1969).

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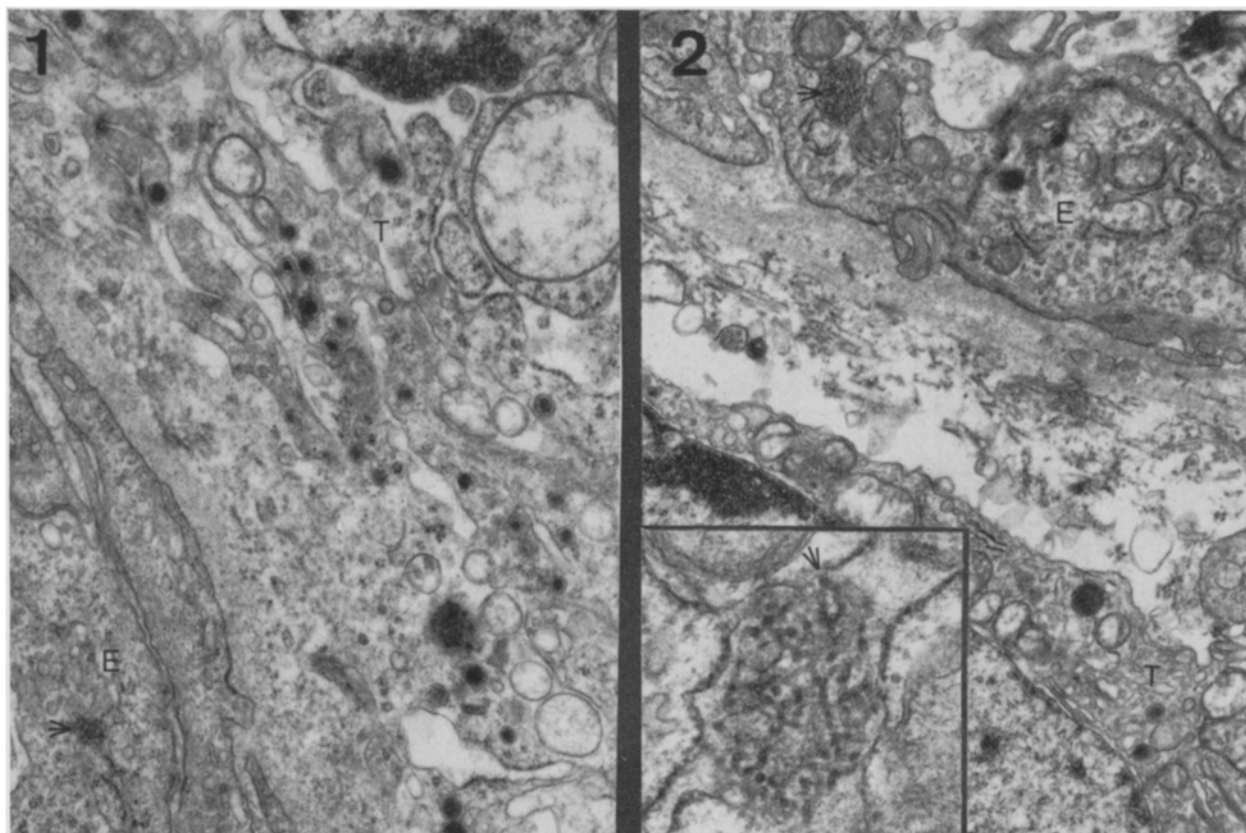


Fig. 1. T, tumor cell; observe the presence of neurosecretory-type granules. E, endothelial cell. Arrow points to tubuloreticular structure. Fig. 2. T, tumor cell. 2 neurosecretory-type granules can be seen. E, endothelial cell with tubuloreticular structure inside endoplasmic reticulum (arrow). Inset-enlargement of tubuloreticular structure. The tubules are associated with intracisternal dense material. Arrow points to apparent continuity of 1 tubule with endoplasmic reticulum membrane.

Tubuloreticular structures were found inside endoplasmic reticulum from endothelial cells of the tumor vessels (Figures 1 and 2). The branched tubules which measured 220–250 Å in cross section, seem at some points to be continuous with the cisternal membrane and are associated with intracisternal dense material (Figure 2). No similar structures were seen inside tumor cells.

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¹² H. L. MOSES, P. R. GLADE, J. A. KASEL, A. S. ROSENTHAL, Y. HIRSHAUT and L. N. CHESIN, *Proc. natn. Acad. Sci., USA* **60**, 489 (1968).
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¹⁴ The author thanks to Prof. Dr. J. M. CORTEZ PIMENTEL and to Dr. L. LEITE NORONHA for help and advise.

These structures were thought to represent the nucleoprotein strands of paramyxovirus¹, polio virus⁴, and to be related with type C oncornavirus⁵. Recent ultrastructural cytochemical evidence does not support their direct viral significance^{2,6}, and together with their detection in normal and sometimes highly differentiated cells^{7–9}, it seems to indicate that they are a cell organelle. However their presence in viral infections^{4,10}, virus-induced tumors¹¹, and virus-infected cell lines^{12,13} raises the question of their aetiological significance to viral diseases and makes them a suggestive finding in human neoplasia¹⁴.

Résumé. Les structures tubuloréticulaires ont été observées dans le reticulum endoplasmique des cellules endothéliales d'un adénome carcinoïde bronchique. Vu leur présence fréquente dans les infections virales, elles peuvent avoir une signification étiologique dans ces maladies-là, ce qui laisse supposer sa présence dans les cas de cancer humain.

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Effect of Irradiation on the Plasminogen Activator Content in Rat Vessels

The fibrinolytic activity of vessels has been found to be confined to the endothelium of vasa vasorum in the adventitia¹. Studies in tissue culture have demonstrated that fibrinolytic activators also are synthesized in the vessel walls². Irradiation damages the vessel endothelium and leads to fibrotic changes of the vessel walls³ and increased frequency of thrombosis⁴. Irradiation has also been shown to decrease enzyme synthesis⁵.

To elucidate the effect of irradiation on the plasminogen activator content of the vessel walls, we compared the fibrinolytic activity histochemically in rat vessels before and after irradiation.

30 Sprague-Dawley rats of uniform age and weighing about 250 g were used. 20 of the animals were irradiated with 1000 rads in a single dose. 10 of them were killed and examined after 1 month and 10 after 2 months. The remaining 10, non-irradiated animals, served as controls. The heart, abdominal aorta and iliac veins were removed. The specimens were immediately frozen in expanding CO₂, packed hermetically in Parafilm® to prevent drying, and stored at –60 °C until examined.

Cryostat sections, 8 µm thick, were cut and collected on cleaned glass slides. Sections of the heart were placed in planes through the coronary sulcus. The fibrinolytic activity was determined histochemically with the method of TODD⁶, as modified and graded in arbitrary units by PANDOLFI et al.⁷. Four slides of every sample were incubated for 15, 30, 45 and 60 min, respectively. The

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Comparison between the fibrinolytic activity in vessel walls of non-irradiated and irradiated rats (Arbitrary units. Median value and range)

Group	Vena iliaca sin.	Vena iliaca dx.	Aorta	Coronary vessels
(A) Non-irradiated	2 (1.5–3)	2 (1–4.5)	3.25 (1–4.5)	2.25 (1.5–5)
(B) Irradiated (1000 rads) and killed after 1 month	1.5 (0–2.5) ^b	0.5 (0–3) ^a	1.5 (0.5–3.5) ^a	1.75 (0.5–2.5)
(C) Irradiated (1000 rads) and killed after 2 months	0.5 (0–1) ^c	0.5 (0–1.5) ^c	0.5 (0–1.5) ^c	1 (0.5–1.5) ^c

^a $p < 0.05$; ^b $p < 0.01$; ^c $p < 0.001$.