1. DeLoach JR, Sprandel U, eds. *Red Blood Cells as Carriers for Drugs*. Basel, Karger, 1985.
2. De Flora A, Zocchi E, Guida L, Polvani C, Benatti U. Conversion of encapsulated 5-fluoro 2'deoxyuridine 5'monophosphate to the antineoplastic drug 5-fluoro 2'deoxyuridine in human erythrocytes. *Proc Natl Acad Sci USA* 1988, **85**, 3145–3149.
3. De Flora A, Benatti U, Guida L, Zocchi E. Encapsulation of adriamycin in human erythrocytes. *Proc Natl Acad Sci USA* 1986, **83**, 7029–7033.
4. Zocchi E, Tonetti M, Polvani C, Guida L, Benatti U, De Flora A. *In vivo* liver and lung targeting of adriamycin encapsulated in glutaraldehyde treated murine erythrocytes. *Biotechnol Appl Biochem* 1988, **10**, 555–562.
5. Zocchi E, Tonetti M, Polvani C, Guida L, Benatti U, De Flora A. Encapsulation of adriamycin in liver-targeted erythrocytes increases the therapeutic index of the drug in a murine metastatic model. *Proc Natl Acad Sci USA* 1989, **86**, 2040–2044.
6. Tonetti M, Astroff B, Satterfield W, De Flora A, Benatti U, DeLoach JR. Construction and characterization of adriamycin loaded canine red blood cells as a potential slow delivery system. *Biotechnol Appl Biochem* 1990, **12**, 621–629.
7. Tonetti M, Astroff B, Satterfield W, De Flora A, Benatti U, DeLoach JR. Pharmacokinetic properties of doxorubicin encapsulated in glutaraldehyde treated canine erythrocytes. *Am J Vet Res* (in press).
8. Pavel DG, Zimmer AM, Patterson VN. *In vivo* labeling of red blood cells with ^{99m}Tc: a new approach to blood pool visualization. *J Nucl Med* 1977, **18**, 305–308.

Acknowledgements—This research was supported in part by the Target Project of Italian C.N.R. "Biotechnology and Bioinstrumentation" and by the Associazione Italiana per la Ricerca sul Cancro.

Eur J Cancer, Vol. 27, No. 7, p. 948, 1991.
Printed in Great Britain
0277-5379/91 $3.00 + 0.00

Neuron-specific Enolase (NSE) in Bronchial Washings: a Better Diagnostic Marker for Small Cell Lung Cancer

E. Kosmas, A. Panayotou, S. Parastatides, A. Damianos, M. Komis, S. Michaelides, B. Baroutsou and V. Polychronopoulos

SMALL CELL lung carcinoma (SCLC), which accounts for about 20% of lung cancers, is the most sensitive to chemotherapy and radiation. This has emphasised the importance of an accurate diagnosis of this cell type. Enolases are glycolytic enzymes catalysing the conversion of 2-phosphoglycerate to phosphoenolpyruvate. There are three dimeric isoenzymes, one of which is found in neurones and cells of neural origin; this has been called neuron-specific enolase (NSE) [1, 2].

SCLC shows neuroendocrine properties and a positive correlation between serum NSE and extent of disease has been shown [2–4]. Serum NSE concentration was raised (>12.5 ng/ml) in 60–77.5% of patients with SCLC. The 80–91% of patients with extensive disease and the 37–50% of patients with limited disease were serum NSE positive [2–7].

The diagnostic significance of NSE, in both serum (S-NSE) and bronchial washings (BW-NSE) aspirated during fiberoptic bronchoscopy after addition of 10 ml normal saline was examined in 14 patients with SCLC (6 of them with extensive disease and 8 of them with limited disease), as well in 20 patients with extensive inoperable non-small cell lung cancer (NSCLC). We examined also a group of 9 individuals who underwent fiberoptic bronchoscopy for other reasons (persistent cough, undiagnosed pleural effusion, haemoptysis with normal chest X-ray) in order to obtain the normal concentration of NSE in bronchial washings. The results of the control group showed that the range of BW-NSE values in non-malignant lung disease was 2.2–13.7 ng/ml (mean [S.D.] = 8.3 [6.2] ng/ml) and the S-NSE was within normal values (<12.5 ng/ml) in all of them.

All the patients with extensive SCLC showed a rise in S-NSE (23 [5] ng/ml) and all presented extremely raised levels of BW-NSE (79.3 [26.4] ng/ml).

The 25% of patients with LTD-SCLC had increased levels of S-NSE (19.3 [6.3] ng/ml), while the other 75% showed a significant rise of BS-NSE (49.8 [17] ng/ml).

The 35% of patients with NSCLC presented a moderate rise of S-NSE (16.8 [8.3] ng/ml) and BW-NSE (20.6 [12.2] ng/ml), while the rest showed levels of S-NSE and BW-NSE similar to those of the control group.

These results are preliminary, so we are not yet able to support them by a reliable quantitative statistical analysis. It has become obvious using the initial results that the sensitivity of BW-NSE in SCLC (85.7%), especially in limited disease, was greater then the sensitivity of S-NSE (57%), while the specificity of both was equal (76%).

Correspondence to E. Kosmas, 20 Spetson Str, 16673 Ano Voula, Athens, Greece.
The authors are at the Department of Thoracic Medicine, Amalia Fleming General Hospital of Athens, Greece.
Received 12 Feb. 1991; accepted 22 Feb. 1991.

1. Rider CC, Taylor CB. Evidence for a new form of enolase in rat brain. *Biochem Biophys Res* Comm 1975, **66**, 814–820.
2. Carney DN, Marangos PJ, Ihdde DC. Serum neuron specific enolase: a marker for disease extent and response to therapy of small cell lung cancer. *Lancet* 1982, i, 583–585.
3. Ariyoshi Y, Kato K, Ishiguro Y, Ota K, Sato T, Suchi T. Evaluation of serum neuron specific enolase as a tumour marker for carcinoma of the lung. *Gann* 1983, **74**, 219–225.
4. Esscher T, Steinholtz L, Bergh J, Nou E, Nilsson K, Pahlman S. Neuron specific enolase: a useful diagnostic serum marker for smal cell carcinoma of the lung. *Thorax* 1985, **40**, 85–90.
5. Fischbach W, Jany B, Nelkenstock R. Bedeutung der neuronspezifis chen Enolase in der diagnostik von Bronchialkarzinomen und neuroendokrinen tumoren. *Dtsch Med Wochenschr* 1986, **111**, 1721–1725.
6. Gasser RW, Herold M, Muller-Holzner E, Muller LC, Salzer GM, Huber H. Neuronspezifische Enolase als Tumormarker beim Kleinzelligen Bronchuskarzinom. *Dtsch Med Wochenschr* 1988, **113**, 1708–1713.
7. Akoun GM, Scarna HM, Milleron BJ, Benichou MP, Herman DP. Serum neuron specific enolase: a marker for disease extent and response to therapy for small cell lung cancer. *Chest* 1985, **87**, 39–43.