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EDITORIAL

Highlights in lung cancer

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Lung cancer is a leading cause of death and a major public health problem throughout the world. Although chest physicians supervise the care of most of these patients in many European countries, the number of papers on lung cancer published in the *European Respiratory Journal* (*ERJ*) does not reflect the magnitude or the importance of the disease. Thoracic oncologists, both clinicians and biologists, prefer to send what they consider their best work to more cancer-orientated journals even if the impact factor is no higher. If we consider that the respiratory physician has to divide his time and expertise between infectious, inflammatory, thromboembolic and environmental respiratory diseases, but actually devote most of his time to asthma, chronic obstructive pulmonary disease and lung cancer, it seems pretty obvious that he may not find the information he needs on lung cancer in the *ERJ*. This new series on lung cancer is an opportunity to provide an overview on controversial or "hot" topics in the field, and to raise the respiratory physician's curiosity in an area he should know more of or discover in the coming years before one of his patients picks it up on the "Net". It could also be an incentive for thoracic oncology groups to submit original work to our Journal.

The first paper in this Series is a meta-analysis from Brussels by STEELS *et al.* [1] on a controversial point regarding the prognostic value of p53 expression abnormalities in patients with lung cancer. Immunohistochemisty using anti-p53 antibodies is now a "routine" technique used in many pathology laboratories on standard paraffin-embedded blocks, it can be performed on bronchial biopsies as well as on surgical samples [2]. There is still much to be clarified in this area of immunohistochemistry before this type of technique and other microbiological tools can be used as routine methods [3]. The role of p53 in the activation of cycle arrest, senescence, differentiation and the regulation of programmed cell death is of major importance in physiological and pathological state. After being considered as the "guardian of the genome" [4], it is now called "death star" or "natural born killer" [5]. The complexity of gene regulation means that the pivotal role of p53 in inducing cell death or cycle arrest is only partly understood. More than 2,000 mutations of p53 have been published and even if hot spots are described in lung cancers [6], the corresponding changes of function to a particular genetic modification may not be interpreted as a simple negative/positive result. Even if fast, high output (complementary deoxyribonucleic acid (cDNA) microarray) molecular biology techniques may be available in the near future [7], the pivotal question will remain for the physician: "What will we do with these results?" At present, it may be important to take this into account when comparing two groups of patients included in a prospective study, as well as other independant prognostic factors. The role of p53 in the treatment algorithm remains uncertain.

The second review concerns the controversial topic of screening for lung cancer using spiral computed tomography (CT) [8, 9]. Screening of lung cancer was viewed with optimism in the 1970s, but the results of several randomized trials failed to demonstrate a mortality decrease in the groups screened by chest radiograph or sputum cytology, despite an increased rate of resection in the screened population [10]. The Japanese have persisted with nonrandomized screening studies and have built a huge bank of information [11]. They were the first to use low-dose spiral CT to screen populations, and their preliminary results were shown 4 yrs ago at the meeting of the World Lung Cancer Congress in Dublin, Ireland.

A paper published by HENSCHKE *et al.* [12] added significantly to the debate, and different groups either started to organize further nonrandomized trials or tried to find funding for randomized trials. The place of screening with CT and the clear need to take this topic forward with proper large scale randomized trials is discussed by VAN KLAVEREN *et al.* [13] in the second article. The third paper will present the new World Health Organization International Association for Study of Lung Cancer (IASLC) Lung Cancer Classification [14]. This topic is probably less controversial, as the group of pathologists who wrote it spent a long time finding a common language. Because this now has to be transferred to clinicians, this review will probably be of interest to the majority of readers. The fourth paper will present data from the Liverpool Lung Project, which also aims to detect lung cancers at a very early stage, working in an area where the incidence is dreadfully high and the prognosis particularly poor [15]. The fifth paper will attempt to illustrate the question: "Will molecular biology be helpful in understanding the process of cancerization in its earliest stages?" [16, 17].

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Finally, there will be two reviews looking at biological agents as a novel therapy for lung cancer. These approaches, derived from the huge amount of data and knowledge gathered by researchers during the last 10 yrs, really attempt to consolidate responses gained with conventional therapy, particularly chemotherapy. The authors will discuss the rationale for the application of growth modifiers, such as tyrosine kinase inhibitors, including the thinking behind anti-angiogenesis and the application of cyclo-oxygenase inhibitors.

References

1. Steels E, Paesmans M, Berghmans T, *et al.* Role of p53 as a prognostic factor for survival in lung cancer: a systematic review of the literature with a meta-analysis. *Eur Respir J* 2001; 18: 705–719.
2. Tenaud C, Negoescu A, Labat Molleur S, Legros Y, Soussi P, Brambilla E. Methods in pathology: p53 immunolabeling in archival paraffin-embedded tissues: optimal protocol based on microwave heating for eight antibodies on lung carcinomas. *Mod Pathol* 1994; 7: 853–859.
3. Nishio M, Koshikawa T, Kuroidi T, *et al.* Prognostic significance of abnormal p53 accumulation in primary, resected non-small cell lung cancers. *J Clin Oncol* 1996; 14: 497–502.
4. Lane D. Cancer: p53, guardian of the genome. *Nature* 1992; 358: 15–16.
5. Vousden KH. p53: death star. *Cell* 2000; 103: 691–694.
6. Hainaut P, Hollstein M. p53 and human cancer: the first ten thousand mutations. *Adv Cancer Res* 2000; 77: 82–137.
7. Wang DG, Fan JB, Siao CJ, *et al.* Large scale identification mapping and genotyping of simple nucleotide polymorphisms in the human genome. *Science* 1998; 280: 1077–1082.
8. Jett JR. Spiral computed tomography screening for lung cancer is ready for prime time. *Am J Respir Crit Care Med* 2001; 163: 812–813.
9. Patz EF Jr, Goodman PC. Low dose spiral computed tomography screening for lung cancer: not ready for prime time. *Am J Respir Crit Care Med* 2001; 163: 813–815.
10. Fontana RS, Sanderson DR, Woolner LB, Taylor WF, Miller WE, Muhm JR. Lung cancer screening: the Mayo program. *J Occup Med* 1986; 28: 746–750.
11. Sone S, Li F, Yang ZC, *et al.* Characteristics of small lung cancers invisible on conventional chest radiography and detected by population based screening using spiral CT. *Br J Radiol* 2000; 73: 137–145.
12. Henschke CI, McCauley DI, Yankelevitz DF, *et al.* Early Lung Cancer Action Project: overall design and findings from baseline screening. *Lancet* 1999; 359: 99–105.
13. van Klaveren RJ, Habbema JDF, Pedersen JH, de Koning HJ, Oudkerk M, Hoogsteden HC. Lung cancer screening by low-dose spiral CT. *Eur Respir J* 2001 (in press).
14. Travis WD, Colby TV, Corrin B, Shimosato Y, Brambilla E. Histological typing of tumours of lung and pleura. *In*: Sobin LH, ed. World Health Organization International Classification of Tumors. 3rd Edn. New York, Springer Verlag, 1999.
15. Field JK, Liloglou T, Xinarianos G, *et al.* Genetic alterations in bronchial lavage as a potential marker for individuals with a high risk of developing lung cancer. *Cancer Res* 1999; 59: 2690–2695.
16. Hirsch FR, Brambilla E, Gray N, *et al.* Prevention and early detection of lung cancer - clinical aspects. *Lung Cancer* 1997; 17: 163–174.
17. Gazdar AF, Minna JF. Molecular detection of early lung cancer. *J Natl Cancer Inst* 1999; 91: 222–225.