EDITORIAL

From surgical to molecular scalpel: *ERJ* lung cancer series for 2009

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Despite progress in tobacco control, at least in industrialised countries, lung cancer will remain the leading killer among cancers for the next decade. However, translation of molecular carcinogenesis discoveries to the clinical setting gives realistic hope of major improvements in early diagnosis and will, furthermore, enable therapy to be tailored thus reducing the mortality rate. Tobacco exposure accounts for 85–90% of lung cancer deaths [1]. This range corresponds to 16,000–24,000 lung cancer deaths in the USA that are not attributable to tobacco carcinogens. Lung cancer in nonsmokers could, therefore, rank among the seven to nine most fatal cancers in the USA [2]. An important study, of more than 630,000 people for incidence and 1.8 million people for mortality, has highlighted the major role of tobacco in lung cancer as its primary result and showed neither a temporal trend in favour of an increased incidence of lung cancer in nonsmokers nor a higher incidence in females, but supported claims that the death rate in males is higher than that in females; it also showed that further studies into the high incidence of lung cancer among females in Pacific Rim countries are necessary [2]. If tobacco exposure remains the main cause, lung cancer in nonsmokers should always be kept in mind, since carcinogenesis and, probably, treatment modalities differ.

Lung cancer results from the association of genetic susceptibility [3] and accumulation of molecular genetic and epigenetic abnormalities under known (tobacco) or unknown carcinogen exposure throughout the cancerisation field, as represented by the respiratory tract [4]. The natural history of the different types of lung cancer, other than a generally fast and fatal progression, is actually unknown. This is particularly obvious for the adenocarcinomas, in which a single TNM stage can characterise a wide range of growth and progression. While a more precise molecular classification is awaited, a subclassification on histological grounds seems necessary [5].

The 2009 series on lung cancer, beginning in the present issue of the *European Respiratory Journal (ERJ)*, will probably raise more questions than allow definitive conclusions, but the advancement of so many studies represents a milestone of evaluated data, generally acquired in multidisciplinary approaches by clinicians and biologists. This series will cover

the many facets of fighting lung cancer, from advances in staging *via* state of the art in positron emission tomography/computed tomography scan practices, as reviewed in this issue [6], to the frontiers of upfront “omics” applied to diagnosis and therapy. The series authors are the experts in this field, as they have already written a large part of the whole story, and now they have kindly agreed to share their experience in a cooperative review, in order to give *ERJ* readers a transcontinental perspective.

The second article in the series will involve two expert thoracic surgeons from Japan and Spain [7] in order to investigate the possibility of performing “less than a lobectomy”, particularly for the patients detected in early diagnosis programmes [8] or in randomised screening protocols [9]. The diagnosis and treatment of early proximal lung cancer will be reviewed by experts from three continents [10] in order to delineate the indications of local treatment, as well as innovative techniques exploring the bronchial wall beyond the ocular level. Since patients are still mainly treated by chemotherapy and, if needed, chemotherapy associated with radiotherapy for locally advanced tumours, European experts from four centers will share the task of describing the state of the art for advanced disease [11, 12] and multimodality treatment for locally advanced cancers [13]. Tailored therapy relying on the definition of molecular targets represents a major hope for the improvement of results in terms of response and overall survival associated with fewer side-effects. The first molecules or antibodies are now being prescribed in clinical settings and dozens of new drugs are at different stages in the pipeline of development; two centers, in France and the USA, will provide their expertise in targeted therapy of nonsmall cell lung cancers [14, 15]. The molecular scalpels we intend to use against this wild killer need to be not only perfectly sharpened but also guided to the chinks in the armour.

International experts from four centers will gather together their knowledge in the field of molecular pathology [16, 17], in which two leaders started the fight many years ago, and bring together innovative concepts in the signalling pathway abnormalities of tumours to allow, by using validated biomarkers, a Trojan horse approach for early detection and targeted therapy. Two young and bright translational researchers [18, 19] will review the high throughput techniques being developed in cohorts of volunteers and that will soon be applied to patient care.

To really eradicate lung cancer it is mandatory to get to the root of the problem and define the characteristics of the stem cells

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that give birth to the disease; for this, the animal model of human lung cancer is the best approach [20]. The discovery and validation of these molecular scalpels needs a prospective reflection to define a coordinated strategy. The person in charge of the TP53 databank [21], which gathers all the published mutations found on this genome, will focus his expertise on the predictive abnormalities related to lung cancer. The principal investigator of the European Early Lung Cancer programme [22] will provide the first results of 5 yrs of coordinated efforts from the 12 programme centers' clinicians and biologists, who have gathered and explored information from 2,500 patients, and controlled and constituted a precious biological resource centre.

The *European Respiratory Journal* 2009 lung cancer series will provide readers with a cutting edge overview of the major advances in clinical management, as well as a comprehensive approach to the translation of innovative genetic and epigenetic techniques to the practice of pulmonologists. The series will demonstrate that all these results come from a tight collaboration between clinicians and researchers. This collaboration must be enforced, and we hope this series will give clinicians the willingness to participate in the bioclinical protocols running throughout Europe and continue to fight against the tobacco epidemics.

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