SESSION 7

Prevention and Early Detection of Lung Cancer

S19. Molecular Markers in Early Detection of Lung Cancer

J.K. Field[1], J. Heighway[1], S. Smith[1], T. Liloglou[1], T. Payne[1], S. Duffy[2], D.C. Betticher[3], S. Maier[4]

[1]*Roy Castle International Centre for Lung Cancer Research, Liverpool, United Kingdom;*
[2]*Cancer Research UK, Epidemiology, Mathematics & Statistics, London, United Kingdom;*
[3]*Institute of Medical Oncology, Inselspital, Bern, Switzerland;* [4]*Epigenomics, Berlin, Germany*

In Europe, lung cancer kills more people than breast, colon and prostate cancers together. Five-year survival in the UK is only 5%. Merseyside has amongst the highest incidence of lung cancer in the country. Using genomics, cancer genetics and epidemiological approaches, we are working towards the development of systems to improve the detection of early disease as well as the identification of potential new anti-cancer drug targets. As a core resource for these programmes, we have initiated a population-based study called 'The Liverpool Lung Project' (LLP). This integrated molecular-epidemiological research programme will not only generate a lung cancer risk assessment model but it will provide clinical samples for the early detection and target identification and validation programmes. It is well established that genomic instability (GI) is a characteristic of all human tumours making this abnormality a good candidate for use in molecular diagnostic systems. We have previously demonstrated that GI can be detected in bronchial washings of both lung cancer patients and individuals with non-malignant disease. We have subsequently proposed that the analysis of specific changes that occur predominantly in tumour cells: cancer-specific genomic instability (CSGI) may be exploited in diagnostic approaches. Aberrant DNA methylation is a frequent phenomenon in non-small cell lung cancers of smokers and it appears that many of these alterations are already present in normal bronchial epithelium. We have used a microarray approach to assess the methylation status of 245 CpGs in 59 genes in NSCLC patients as well as normal adjacent lung tissues from smokers. Our results provide compelling evidence that different histological types of lung cancer maybe distinguished from normal tissue based on 'grouped methylation status' (GMS) within the promoters of specific genes. We have show that microarray-based methylation profiling constitutes an excellent tool to identify new markers for population based lung cancer screening Another approach to early detection centres on the exploitation of differences in gene expression between tumour and normal cells. Such expression differences are also highly relevant in the context of the identification of early diagnostics and novel intervention strategies. Supported by the Roy Castle Lung Cancer Foundation UK