

PORTSMOUTH



POLYTECHNIC

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IN VIVO GENOTOXIC ACTIVITY OF COMPLEX MIXTURES

Further details of a research project available for a postdoctoral scientist in the School of Biological Sciences, for a maximum of 3 years.

Despite the postulated association between cigarette smoking and lung cancer in man it is still unclear by which mechanisms, at the cellular level, tumorigenesis is induced by the complex mixture of chemicals present in whole smoke. In contrast there is much evidence to show that whole smoke and many of its constituents exhibit activity in a wide spectrum of genotoxicity assays *in vitro*. It is clear that, in order to develop safer tobacco products and to study their mode of toxicity further, a need exists for the development of *in vivo* short term methods capable of more accurately predicting the putative carcinogenic potencies of different tobacco formulations. This is the primary objective of the project.

Exposures to whole smoke, derived from representative tobaccos with varying *in vitro* genotoxicities, will be undertaken under strictly controlled conditions. Quantitation and characterisation of covalent binding and adduct formation with DNA from lungs, liver and lymphocytes will be achieved after development and adaptation of a sensitive ³²P-post-labelling technique in conjunction with TLC and autoradiography. The genotoxic importance of the adducts will be investigated using a kinetic approach by assessing their relative persistence in the DNA isolated from the various tissues at different times following initial exposures. In addition, the induction of cytogenetic changes present in isolated and cultured lung cells will be studied by detection of micronuclei after adaptation of existing methods for this assay. Acute and chronic effects of dosing by inhalation using whole smoke and after administration of tobacco condensates will also be studied.

Applicants should possess a PhD in some aspect of genotoxicity or a closely related discipline. Experience of DNA binding/adduct analysis and tissue culturing would be an advantage. The project is funded by the tobacco industry and the scientist will join an active research group working on aspects of genetic toxicology under the supervision of Dr RD Combes.

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