



NICO-GENE \ \ MODELING HUMAN POLYMORPHISMS FOR NICOTINE ADDICTION IN MICE

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SUCCESSFUL PROJECTS

Every year, more than five million people worldwide die from the consequences of smoking. These deaths, principally from lung cancer, are avoidable. A formidable obstacle to the prevention of these deaths is that tobacco contains nicotine — the major, if not sole, compound responsible for driving the strong addiction to smoking. The actions of nicotine are mediated by nicotinic acetylcholine (ACh) receptors (nAChRs). Human genetic studies have recently identified alterations in the sequence of some of the genes coding for subunits of nAChRs. These mutations are correlated with a higher incidence of lung cancer and smoking. To increase our understanding of the contribution of different nAChR oligomers to nicotine addiction, new strategies will be developed. These include the detailed study of deletions in mice of nAChR subunit genes, the re-expression of a deleted gene by stereotaxic injection of a lentiviral vector carrying the missing gene, and the quantitative analysis of the behaviours elicited by nicotine in these mice. We aim to bridge the gap from genes to cognition in the understanding of nicotine addiction, on the basis of our recent advances in the molecular biology of nAChRs, and of animal models with modified nAChR gene expression.



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