

The Genetics of Tobacco Use

Why study genetics?

Although there are a number of treatments available to help people stop smoking (the most common being nicotine replacement therapies, such as patch and gum, and varenicline in the UK), these are only moderately effective. While they can double the chances of long-term abstinence from smoking in those attempting to quit, this is against a very low basic success rate. Therefore, most smokers (even those taking medications to help them stop and receiving good behavioural support) who attempt to stop eventually relapse to smoking.

One reason for this is that different individuals respond very differently to the same medications. Pharmacogenetics investigates the role of genetic factors in predicting how individuals will respond to drugs. These factors may influence differences in drug metabolism (pharmacokinetics) or in drug targets (pharmacodynamics), and may in turn influence treatment outcomes. We can also use this approach to investigate why some people start smoking and others don't, and why some but not all people who use tobacco become dependent.

What do we know?

Although genetics will only ever be part of the explanation for why people smoke (environmental influences such as peer pressure, and growing up with smoking parents, are also important), we have begun to identify factors which appear to predict who is likely to become a heavy or dependent smoker, or respond better to particular treatments.

Nicotine is broken down to an inactive by-product, cotinine, at which point it stops having the psychoactive effects which are a large part of its addiction potential. This metabolic process is largely governed by a single enzyme, CYP2A6. The gene which encodes this enzyme can exist in various forms, including variants which result in very low levels of enzyme activity.

In people carrying one or more of these variants of the *CYP2A6* gene, nicotine is broken down much more slowly. As a result, among smokers, these people smoke less frequently, because they don't need to top up their nicotine levels as often. There is also evidence that these people respond differently to nicotine replacement therapies (again, because they metabolise the nicotine delivered from patch or gum more slowly).

Where might this lead?

Increasing what we know about the role of inherited variation in response to drug treatments for tobacco dependence may allow practitioners to individualise treatment type, dose and/or duration based on genetic information, which could be obtained from a simple blood or saliva sample. This could serve to reduce the likelihood of adverse reactions, increase treatment compliance, and maximise the effectiveness of the treatment. Even relatively small improvements in response, when scaled up to the whole population of smokers attempting to quit, may substantially benefit public health.

Professor Marcus Munafò has been researching the genetics of tobacco use for several years now and more information about this can be found in the following article:

Caryn E. Lerman, PhD, Robert A. Schnoll, PhD, Marcus R. Munafò, PhD (2007) Genetics and Smoking Cessation. Improving Outcomes in Smokers at Risk. *Am J Prev Med* 2007;33(6S):S398–S405

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