

Genetic discovery unlocks biosynthesis of medicinal compound in poppy

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Scientists at the University of York and GlaxoSmithKline (GSK) Australia have discovered a complex gene cluster responsible for the synthesis of the medicinal compound noscapine.

The discovery, published in the latest issue of *Science*, reveals that the pathway for synthesis of noscapine is controlled by a complex cluster of ten [genes](#) encoding five different enzyme classes. This is the most complex gene cluster ever found in plants. The discovery has revealed the previously unknown [biochemical pathway](#) for noscapine synthesis. It will also greatly accelerate the breeding of high-noscapine poppy varieties.

The breakthrough came when the scientists discovered that poppy varieties that produce noscapine express a number of genes that are absent in varieties that are noscapine free. They then analysed the inheritance pattern of these genes in hundreds of offspring from crosses between noscapine and no-noscapine varieties. When they saw that all of these genes are inherited together, they realised they could be looking at an incredibly complex gene cluster. The identity and arrangement of genes in the cluster was determined by [cloning](#) and DNA sequencing.

Professor Ian Graham, Director of the Centre for Novel [Agricultural Products](#) at the University of York, said: "We were amazed to find that this gene cluster encodes for almost the entire [biosynthetic pathway](#) for noscapine. With this one discovery we have been able to produce an outline of the pathway and define a number of the steps involved -

something that normally takes years."

Noscapine has been used as a suppressant in cough mixtures for decades. More recently, it has been reported to have anti-cancer activity and is currently in early stage clinical trials. Noscapine was one of the first natural products to be chemically characterised almost 200 years ago. Until now, however, the pathway for production and the genes involved in its synthesis have not been identified.

Tim Bowser, Head of R&D for [GSK](#) Australia's Opiates Division, said: "The fact that the genes are grouped in a cluster means that plant breeding becomes faster and easier. GSK are using this discovery to develop high yielding commercial noscapine poppies in order to establish a reliable route of supply."

Commercial poppy farming traditionally involved lancing the seed capsule to release the latex from which medicinal alkaloids, including noscapine, could be extracted. Since the 1960s commercial industrial techniques have largely switched to large scale poppy harvesting and extraction focussed on other medicinal poppy alkaloids like morphine and thebaine used to manufacture pain medicines. This trend has developed at the expense of noscapine which until now was only available from traditional techniques.

More information: "A *Papaver somniferum* ten gene cluster for synthesis of the anticancer alkaloid noscapine" by Thilo Winzer et al. will be published by *Science* within the *Science Express* web site on Thursday, 31 May 2012.

Provided by University of York

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