New insights into mushroom-derived drug promising for cancer treatment

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A promising cancer drug, first discovered in a mushroom commonly used in Chinese medicine, could be made more effective thanks to researchers who have discovered how the drug works. The research is funded by the Biotechnology and Biological Sciences Research Council and was carried out at The University of Nottingham.

In research to be published in the *Journal of Biological Chemistry*, Dr Cornelia de Moor of The University of Nottingham and her team have investigated a drug called cordycepin, which was originally extracted from a rare kind of wild mushroom called cordyceps and is now prepared from a cultivated form.

Dr de Moor said: "Our discovery will open up the possibility of investigating the range of different cancers that could be treated with cordycepin. We have also developed a very effective method that can be used to test new, more efficient or more stable versions of the drug in the Petri dish. This is a great advantage as it will allow us to rule out any non-runners before anyone considers testing them in animals."

Cordyceps is a strange parasitic mushroom that grows on caterpillars (see image). Properties attributed to cordyceps mushroom in Chinese medicine made it interesting to investigate and it has been studied for some time. In fact, the first scientific publication on cordycepin was in 1950. The problem was that although cordycepin was a promising drug, it was quickly degraded in the body. It can now be given with another drug to help combat this, but the side effects of the second drug are a

limit to its potential use.

Dr de Moor continued: "Because of technical obstacles and people moving on to other subjects, it's taken a long time to figure out exactly how cordycepin works on cells. With this knowledge, it will be possible to predict what types of cancers might be sensitive and what other cancer drugs it may effectively combine with. It could also lay the groundwork for the design of new cancer drugs that work on the same principle."

The team has observed two effects on the cells: at a low dose cordycepin inhibits the uncontrolled growth and division of the cells and at high doses it stops cells from sticking together, which also inhibits growth. Both of these effects probably have the same underlying mechanism, which is that cordycepin interferes with how cells make proteins. At low doses cordycepin interferes with the production of mRNA, the molecule that gives instructions on how to assemble a protein. And at higher doses it has a direct impact on the making of proteins.

Professor Janet Allen, BBSRC Director of Research said: "Research to understand the underlying bioscience of a problem is always important. This project shows that we can always return to asking questions about the fundamental biology of something in order to refine the solution or resolve unanswered questions. The knowledge generated by this research demonstrates the mechanisms of drug action and could have an impact on one of the most important challenges to health."

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