

Novel approach to cancer drug given major boost

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Scientists at the ProXara Biotechnology Limited have identified a way of switching off one of the key mechanisms that leads to the development and growth of a tumour. Under the Wellcome Trust's Seeding Drug Discovery initiative, the researchers hope to use their findings to develop a drug which could be used to fight cancer. The funding will be used to develop the drug to a point at which it is close to entering a clinical trial.

All cells in the body contain protein kinase B (PKB), a naturally-occurring enzyme that if active prevents cells from committing suicide. Programmed cell death, or apoptosis, is an important process in the body's development, but when this process goes wrong, unregulated cell growth occurs, leading to the development of tumour cells.

Recent research has shown that certain types of genetic damage, common to many cancer cells, lead to the movement of PKB from the interior of the cell to its surface membrane. When PKB attaches to the surface membrane, it becomes active, triggering a signal that tells the cell not to commit suicide. Professor Jeremy Tavaré at ProXara Biotechnology Ltd, a spin-out company at the University of Bristol, believes that by preventing PKB binding to the cell's surface membrane, he can ensure that apoptosis occurs, thus killing the cancer cells.

"There has been a lot of interest in targeting PKB as a way of preventing tumour growth," says Professor Tavaré. "Most of the interest so far has been in developing drugs that block the enzyme's signal. However, such

drugs are very non-specific and can have many adverse side effects. We are working on a novel approach to prevent PKB actually binding to the cell membrane."

Professor Tavaré and his team have discovered a drug-like compound, which prevents PKB binding to the cell membrane and makes the tumour cells commit suicide. They now wish to develop this compound to a point at which it could be used in clinical trials.

"Professor Tavaré's research offers a novel approach to cancer drug research," says Dr Ted Bianco, Director of Technology Transfer at the Wellcome Trust, which is funding the research under its Seeding Drug Discover initiative. "Cancer affects very large numbers of people which is why it receives so much attention from those engaged in medical research. But it is a complex disease to tackle and as a result many of the current anti-cancer drugs have unpleasant side -effects. This work has the potential to provide a more targeted approach to drug therapy with fewer adverse effects."

Professor Tavaré says that the drug would be used initially to target lung cancer, the most common cancer in the UK. Almost 38,000 people are diagnosed with this particular cancer each year. If the approach works it could be adapted to treat other types of cancer or even inflammatory diseases such as arthritis or asthma.

"We anticipate that a drug based on this approach may benefit a significant proportion of people with lung cancer," explains Professor Tavaré. "As well as developing the drug itself, we are also working on a way of identifying which individuals are most likely to respond to the drug."

This targeted therapy is based on five years of research by Professor Tavaré and Dr Paul England. The research has now been given a major

boost by way of a £2.8 million award to the University of Bristol under the Wellcome Trust's Seeding Drug Discovery initiative. The initiative aims to bridge the funding gap in early-stage drug discovery, assisting researchers to take forward projects in small molecule therapeutics that will be the springboard for further R&D by the biotech and pharmaceutical industry.

Source: Wellcome Trust

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