NZ-designed drug shows exciting early promise against lung cancer

New Zealand scientists have discovered a new class of drugs that could become the next big thing in the treatment of lung cancer.

Medicinal chemist Dr Jeffrey Smaill and cancer biologist Dr Adam Patterson, investigators with the Maurice Wilkins Centre for Molecular Biodiscovery, have just arrived back in New Zealand from the world’s premier conference for molecular targets and cancer therapeutics in Boston, US, where they announced the discovery of a new class of anti-cancer drugs.

The drugs are a type of prodrug – an inactive compound that is converted into an active drug by the body’s metabolic processes. They were discovered at the Auckland Cancer Society Research Centre at The University of Auckland, and have shown dramatic results against lung cancer in pre-clinical trials.

Dr Smaill says that the new prodrug “sticks” to the cancer tumour for over 72 hours compared with other drugs that stay in the tumour for only a few hours.

“Our experiments show that this new prodrug is much more active than the current gold-standard drug treatment for advanced or spreading lung and pancreatic cancer,” says Dr Patterson. “It’s very common for tumours to start re-growing after you stop administering this type of cancer drug. But after we stopped doses of this prodrug, the tumours still hadn’t re-grown 30 days later. The prodrug appears to act like a slow-release chemotherapy.”

Dr Patterson says they are not yet sure why the prodrug stays in the tumour for so long or why it is so effective. One theory being investigated is that the released active drug is targeting the tumour’s stem cells, which initiate tumour regrowth.

“The results from our pre-clinical trials also show that this prodrug need only be taken once every four to seven days. Many of the new molecular targeted anti-cancer drugs currently on the market need to be taken once or twice every day,” says Dr Patterson.

Drs Smaill and Patterson, based in the laboratories of Professors Bill Denny and Bill Wilson in the Auckland Cancer Society Research Centre, started working on this new class of prodrugs in 2005 after receiving significant salary support from the Maurice Wilkins Centre for Molecular Biodiscovery, a Centre of Research Excellence hosted by The University of Auckland. In 2007, the project received further funding from the US-based biopharmaceutical company Proacta Inc. and a grant from New Zealand’s Foundation for Research, Science and Technology.

Dr Smaill says the new prodrug targets proteins found in solid tumours called Human Epidermal Growth Factor Receptors (HERs). These proteins are involved in cell growth and have been implicated in the development of a variety of cancers.
“The main problem with previous drugs developed to target HER proteins is that they also block the function of these proteins in normal tissues. This can cause side effects such as severe diarrhoea, skin rash, nausea and vomiting, ultimately limiting the amount of drug that can be given to the patient,” says Dr Smaill. “This new class of prodrugs are designed to release a HER inhibitor in the tumour that can irreversibly attach to the active site on the HER proteins, stick there and stay, permanently shutting off the growth signal from the receptors to the nucleus of the cancer cell.”

Dr Patterson says solid tumours have a chaotic blood supply, and because of this about two-thirds of tumours end up with patches that contain low levels of oxygen, termed hypoxia. “These hypoxic tumour cells are more resistant to cancer treatments and are more likely to spread and become invasive. Potentially these cells may represent a tumour-selective target that we can exploit. These prodrugs are designed to be metabolically activated only in the hypoxic cancer cells found in tumours – not healthy normal cells. If we can target and kill these cells we should be able to dramatically improve the outcome for cancer patients.”

Drs Smaill and Patterson say that their next step is to select the strongest lead compound to put forward to Proacta Inc. in December this year. They will then commence studies for an Investigational New Drug (IND) application to the US Food and Drug Administration (FDA), with Phase 1 clinical trials in humans anticipated in late 2010.

**Contact:**
Suzy Botica, Communications Adviser
The University of Auckland
Ph: +64 9 373 7599 ext. 89589 or +64 21 245 0817
Email: s.botica@auckland.ac.nz

Dr Adam Patterson
The University of Auckland
Ph: +64 9 373 7599 ext. 86941
Email: a.patterson@auckland.ac.nz

Dr Jeffrey Smaill
The University of Auckland
Ph: +64 9 373 7599 ext. 86798
Email: j.smaill@auckland.ac.nz

Notes for editors:

A photo of Dr Jeffrey Smaill and Dr Adam Patterson is attached here. For a higher resolution photo, please contact Suzy Botica (details above).

The Maurice Wilkins Centre for Molecular Biodiscovery is one of eight Centres of Research Excellence (CoREs) in New Zealand. The Maurice Wilkins Centre is associated with more than 200 researchers from a wide range of areas, including biology, chemistry, engineering and medicine. The centre’s main focus is on developing new drugs and vaccines to fight serious human diseases.

www.mauricewilkinscentre.org
The Auckland Cancer Society Research Centre was founded in 1956 and is jointly managed by The University of Auckland and the Auckland Cancer Society. The centre is regarded internationally as one of the world’s leading anti-cancer drug development laboratories.

www.health.auckland.ac.nz/cancer/

Proacta Inc. is a clinical-stage biopharmaceutical company working to develop hypoxia-activated prodrugs for the treatment of cancer. Its headquarters are in San Diego, California. Proacta was founded on intellectual property derived from research carried out at The University of Auckland in New Zealand and Stanford University in the United States.

www.proacta.com