Melanoma find raises hope of better drugs

By Martin Johnston

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Use of energy in the cells of deadly skin cancer offers a vital clue for researchers.

Melanoma researchers have made an important finding in how cancer cells use energy, which they hope will help drug designers to unpick the disease's frequent resistance to a new class of medicines.

There was excitement when the new drugs, such as vemurafenib, started coming out of trials in 2010 and 2011, and predictions that within a few years, late-stage melanoma would, for many, become a survivable disease.

That hasn't happened yet, although the new drugs - which inhibit a protein from the mutated "BRAF" gene found in nearly half of melanomas - are extending the lives of those with advanced melanoma.

Many gain four to six months of life, and some survive for more than a year. The costly drugs are not state-funded in New Zealand, leaving patients to pay themselves, get them through trials, or rely on drug company programmes for free access.

Scientists at Melbourne's Peter MacCallum Cancer Centre observed in scanning images of melanomas during treatment with BRAF inhibitor drugs that the tumour cells stopped processing glucose, but did not necessarily die.

"We previously thought the reduction in glucose uptake by melanoma was a result of cell death caused by cancer treatments," said the centre's director of cancer imaging, Professor Rod Hicks.

"We have now found most cells actually die as a result of being starved of glucose, while a small number manage to find a way to survive."

He credited MacCallum colleague Dr Tiffany Parmenter, who gained her PhD at Otago University, with first explaining the significance, at a molecular level, of the reduced glucose uptake. The findings have been published in the American journal Cancer Discovery.

The head of cancer therapeutics at the centre, Professor Grant McArthur, said research efforts would now focus on the genetic changes that allowed melanomas to survive blocked glucose use.

"This vulnerable stage, when melanoma cells are overcoming their sugar addiction, presents an attractive target for new treatments. We're investigating combination therapies to eradicate cancer cells that are managing to survive, even when their fuel source is cut off."

Professor Michael Eccles, Otago University's director of developmental genetics and a melanoma researcher, said the MacCallum findings were "a highly significant discovery ... [mainly] because it explains how deregulated glucose metabolism in the cancer cells is tightly
"[This] also helps to explain why almost half of melanomas have a BRAF mutation," the professor said.

"Knowing this gives us an insight into the vulnerabilities of melanoma that will eventually guide an improvement in melanoma treatment."

**What is melanoma?**

- The deadliest form of skin cancer.
- Risk factors include repeated, severe sunburn in childhood and adolescence.
- New Zealand has one of the world's highest rates of the disease.
- It is the commonest type of cancer diagnosis for NZ men aged 25-44.
- It is commonly cured by surgery if detected at an early stage.
- Often fatal if detected late.
- 2341 new cases diagnosed in 2010.
- 324 deaths in 2010.