New class of anti-cancer treatment targets stem cell family

Research over the past decade has revealed why cancer has proven so hard to conquer.

The answer lies in a population of cells within each tumour known as cancer stem cells. Cancer stem cells are where the cancer starts, how it spreads, why it continues to grow – and why it returns with a vengeance after apparently successful treatment.

Novogen CEO, Dr Graham Kelly, explained: "Cancer stem cells represent a small proportion of the cells in a tumor and they are completely impervious to therapies such as radiotherapy and chemotherapy.

"Their daughter cancer cells that make up the bulk of a cancer can respond to treatment, but the parent cancer stem cells survive all that we can throw at them and live to produce a whole new generation of daughter cancer cells that now resist all forms of therapy. That is recurrent cancer and recurrent cancer is what patients die from."

Australia biotechnology company Novogen has discovered a new class of anti-cancer compounds called super-benzoypyrans (SBPs) that kill cancer stem cells and their daughter cancer cells.

Dr Kelly said: "Novogen is one of about eight companies worldwide that is developing drugs against cancer stem cells. The other companies are taking approaches that we believe are unlikely to be effective. Our approach is unique and to date has delivered remarkable effects in the laboratory."

Novogen is developing three lead candidate drugs based on its SBP technology: Cantrixil will target abdominal cancer; Trilexium will target cancers of nerve tissues; and Trx-7 will target prostate cancer.

Novogen Ltd

CEO: Dr Graham Kelly

Ticker Codes: (ASX.NRT) and (NASDAQ.NVGN)

Market Cap: ~$25 million (ASX)

Description: Novogen has two main drug technology platforms: super-benzopyrans (SBPs) and anti-tropomyosins (ATMs). SBP compounds have been created to kill the full range of cells within a tumour, but particular the cancer stem cells. The ATM compounds target the microfilament component of the cancer cell and when used in conjunction with standard anti-microtubular drugs, result in comprehensive and fatal destruction of the cancer cell's cytoskeleton.

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Cantrixil has been developed as an intra-cavity drug to be injected into the peritoneal (abdominal) cavity and the pleural (chest) cavity. The intention is to treat patients with late-stage cancer of the ovary, stomach, large bowel, pancreas, breast, lung, and mesothelioma and lymphoma, which has spread to either of these cavities. In such cases, there is no standard of care and life expectancy is rarely more than six months.

Cantrixil has been designed to kill the full hierarchy of tumor cells within the two cavities, but particularly the cancer stem cells that keep replenishing the cancers.

Dr Kelly said: "There is no standard of care for this very common end-of-life condition, so Cantrixil represents a significant potential step-forward in the world of chemotherapy."

The second SBP drug, Trilexium, is being developed as a treatment of brain cancers of both adults and children, and neuroblastoma of children. Trilexium has been selected for its potent ability to kill glioblastoma multiform (GBM) stem cells from adults and neuroblastoma, medulloblastoma and diffuse interstitial pontine glioma (DIPG) cells from children.

Dr Kelly said: "Trilexium is highly effective against a broad range of cancers that arise in nervous tissue. I understand that to be a world-first."

Novogen also has an exciting second drug technology platform known as anti-tropomysins (ATMs) that target the skeleton of the cancer cell.

Dr Kelly explained: "All cells have a skeleton that gives the cell its shape, allows it to move and to adhere to neighbouring cells, and form the spindles that allow it to divide. The skeleton also is the means by which a cell communicates internally and externally. In other words, it is vital to the function and to the survival of the cell."

The cytoskeleton has two components – microtubules and microfilaments. Drugs that target the microtubules (taxanes such as Taxol and Docetaxel and vinca alkaloids such as Vincristine and Vinblastine) after 40 years are still among the most widely used chemotherapies in cancer therapy.

Dr Kelly explained: "Destroying the microtubules is a validated anti-cancer approach, but the problem is that we are only destroying one-half of the cancer cell's skeleton. The other half, the microfilaments, remain intact and so the anti-cancer effect is muted.

"We have developed a drug that targets the other half, the microfilaments. It is a potent anti-cancer drug on its own, but when used in combination with taxanes or vinca alkaloids to produce comprehensive destruction of the cancer cell's cytoskeleton, the anti-cancer effect is profound.

"We are now moving to bring this drug into the clinic for the treatment of melanoma and prostate cancer."

Novogen is working to have Cantrixil and Trilexium in the clinic in 2015, and Trx-7 and its ATM drug in the clinic in 2016.