TWO FIRST IN CLASS DRUG TECHNOLOGY PLATFORMS

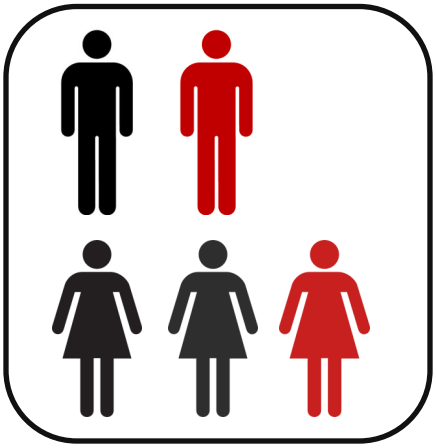
Super-Benzopyrans (SBPs) and Anti-Tropomyosins (ATMs)

Chemotherapy and radiotherapy appear to have reached the limit of their abilities, driving development into new areas such as cancer vaccines, immune checkpoint inhibitors and gene silencing. While each comes with early promise, that promise nevertheless remains completely speculative as to whether it will translate into anything more than the incremental survival benefit that has come with the 'targeted therapeutics' approach of the last two decades.

Novogen is going 'back to the future'. Novogen believes that it has found a way to make chemotherapy finally do for the most common cancers what it has for a handful of cancers – provide meaningful, durable remission.

That way lies in two first-in-class drug technology platforms:

super-benzopyrans (SBPs) and **anti-tropomyosins (ATMs)**.



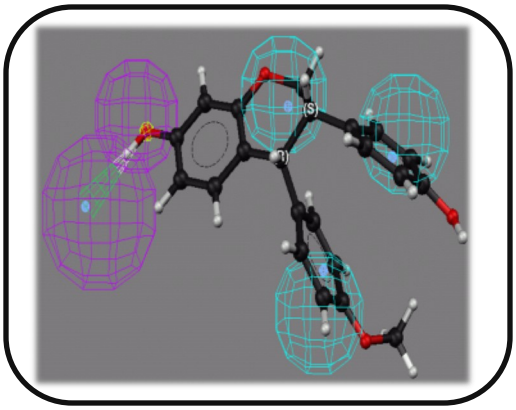
For many of the most common cancers, survival rates have changed little over the past 30 years. 1 in 2 men and 1 in 3 women will develop a malignant cancer in their lifetime. 40% of these will die from their cancer within five years

SBPs are small molecule drugs that target abnormal functions within a cell

ATMs are a family of drugs designed to disrupt the cytoskeleton of the cancer cell by targeting one of its key components, the protein tropomyosin

Novogen believes it has found the means of achieving the long-held goal of turning most forms of cancer into manageable, non-lethal chronic diseases.

Super-benzopyrans (SBPs)



Super-Benzopyrans (SBPs)

Molecular target: the heritage of these compounds is plant auxins (simple benzopyrans). With pleiotropic functions embracing both up- and down-regulation of enzyme phosphorylation activity and gene transduction activity in both plants and animals.

Super-benzopyrans are complex derivatives of the plant auxin, genistein. They retain the central genistein pharmacophore 'privileged scaffold' and therefore the potential for the same multiplicity of functions. The primary anti-cancer function molecular target is believed to be the quinone-binding motif of a splice variant of NADH oxidase known as ENOX2.

The SBPs target a family of oncogenes that are responsible for electron transfer across cellular membranes. These secondary or enabling mutations underpin the cancer cell's ability to behave in a delinquent manner. Inhibiting these mutations, quickly deprives the cancer cell of its ability to function at the most basic levels, quickly leading to its death. The ubiquity of these enabling mutations means that these drugs are effective across most, if not all, forms of cancer; and their oncogenic nature means that the drug action is predominantly limited to cancer cells.

But their outstanding feature is their ability to kill the full hierarchy of cells within a tumor. And that means killing both the cancer stem cell as well as its more common daughter cancer cell. The means is at hand to eliminate the full range of cancer cells, but more particularly the cells believed responsible in most forms of cancer of initiating, perpetuating and spreading the cancer.

The SBPs are the first drug candidates not to distinguish between cancer cells based on their phenotype or surface marker expression. Their molecular target transcends those disparities.

Three lead candidates have been identified, each *pan* cancer-acting, but each with a predilection for a specific tumor type.

* **TRXE-002** tumours of the abdomen (ovarian cancer, colorectal cancer)
* **TRXE-005** tumours of cells derived from the neural crest (primary brain cancer, neuroblastoma, melanoma)
* **TRXE-0025** prostate cancer.

TRXE-002 has been developed as the first intra-cavity product (Cantrixil) intended to be injected into the peritoneal and pleural cavities to treat both early- and late-stage cancers. Cantrixil is owned by CanTx Inc, a joint venture company between Novogen and Yale University. Cantrixil is being brought into a first-in-man study in mid-2015.

TRXE-005 is believed to be the first drug candidate with specific activity against cancer cells of neural origin, including stem-like neural cancer cells. Formulated as Trilexium, this product is being brought into the clinic for the treatment of glioblastoma multiforme and melanoma.

TRXE-0025 is highly active against prostate cancer cells that are refractory to docetaxel. It is being developed as a treatment for late-stage, post- docetaxel prostate cancer.

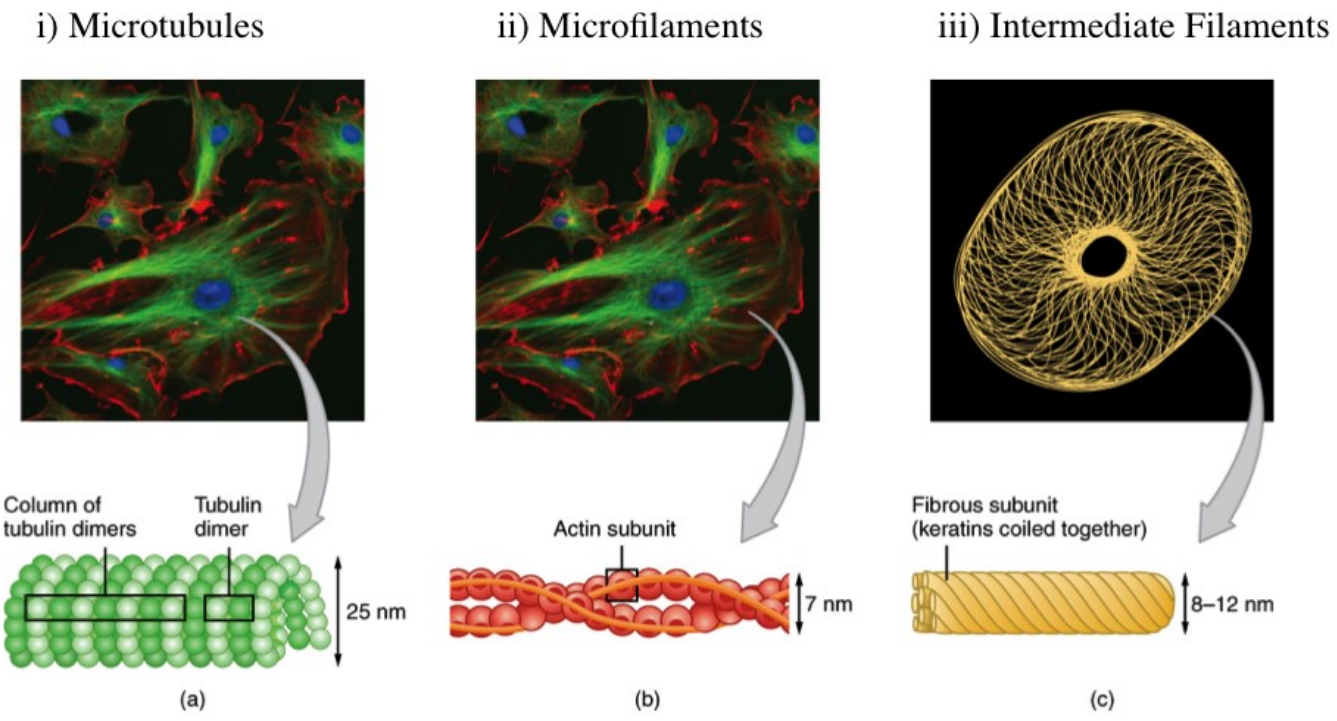
Anti-tropomyosins (ATMs)

The lead ATM drug candidate is ATM-3507 (Anisina).

Anisina targets the architecture of the cancer cell, or the cytoskeleton. It shares this function with the taxanes (paclitaxel, docetaxel) and the vinca alkaloids (vincristine, vinblastine).

The cytoskeleton has two main components – the micro-tubules and the micro-filaments:

* The taxanes and vinca alkaloids destroy the micro-tubules.
* The ATMs destroy the micro-filaments by inhibiting the ability of the structural protein, tropomyosin, to dimerize.



Adapted from: cnx.org/content/m46023/1.5/

The anti-microtubular drugs continue after 30 years to be among the most widely prescribed drugs in chemotherapy despite have important functional limitations.

Using an ATM drug in conjunction with an anti-microtubular drugs results in comprehensive destruction of the cancer cell's cytoskeleton, producing a profound anti-cancer effect.

Anisina is being developed as a drug to be used in combination with taxanes or vinca alkaloids in the treatment of prostate cancer and melanoma.