



The University of Arizona Cancer Center's **Therapeutic Development Program** works to discover new biological targets and develop agents that will translate into life-changing therapies that efficiently and effectively treat cancer.

The Program oversees all stages of therapeutic discovery and development, from laboratory-based discovery and development to early-stage translational clinical trials. The Therapeutic Development Program relies on a close interaction between basic researchers and clinical investigators, ensuring a seamless translation of laboratory discoveries into clinical settings.

The Therapeutic Development Program is leading cutting-edge studies to identify promising molecular and genetic targets to get us closer to the day when all cancer treatments are tailored to each individual patient. Additionally, the Therapeutic Development Program aims to improve the quality of life of patients undergoing treatment by seeking therapies to reduce the occurrence of common cancer-related conditions, such as bone pain and metastasis.

HIGHLIGHTS

ACTIVITY FOR NEW TARGET

The Lymphoma Team, headed by Drs. Tom Miller and Lisa Rimsza, tested a new agent that works through oxidation in patients with non-Hodgkin's Lymphoma that are not responsive or have relapsed after other therapies. The agent, imexon, was developed in the cancer center's Therapeutic Development Program and is a small molecule which causes tumor cells to become oxidized and die. The clinical trial in 22 patients with different types of advanced lymphoma, producing an overall response rate (tumor shrinkage) in 30% of patients, and in another 35%, tumors stopped growing. Concurrently Dr. Margaret Briehl conducted a laboratory study which showed responses could be accurately predicted using gene expression tests on pre-treatment tissue samples.

NEW DRUG TARGET AND AGENTS

Program members have identified unique new targets for cancer drug development that involve special structures in cancer DNA. The targets, called i-motifs, are "twists" in DNA strands that occur in sections of DNA that activate cancer genes. Importantly, these i-motifs, have been shown to control how cancer genes are both turned on (leading to cancer) and turned off (inhibiting cancer). The team, led by Drs. Laurence Hurley and Danzhou Yang, has used the i-motif to model new drugs, first on the computer, and then by synthesizing compounds in the chemistry lab. The agents that have resulted from this work, have shown activity in pre-clinical models of cancer, but also in humans given the first-generation inhibitor, Quorfloxin.

KILLING TUMOR CELLS

A major problem in many tumors is the majority of cells in the tumor mass have low oxygen levels (hypoxia). which makes these cancer cells highly resistant to both drugs and radiation. Drs. Amanda Baker in the Therapeutic Development Program and Marty Pagel in the Cancer Imaging Program at the cancer center have joined forces to address hypoxic tumor cells. Dr. Pagel is developing imaging techniques such as CEST, which can spot tumors that are acidic (and therefore are also hypoxic)., Dr. Baker is working with agents like the experimental drug TH 302, that are activated only when in hypoxic conditions. Using the CEST imaging technique, tumor hypoxia can be identified in animals and, eventually in humans. That way, patients with hypoxic tumors can be selected for therapy with hypoxia-activate drugs like TH302, which is currently under initial testing in patients in the clinic.