

*DSRCT Research*

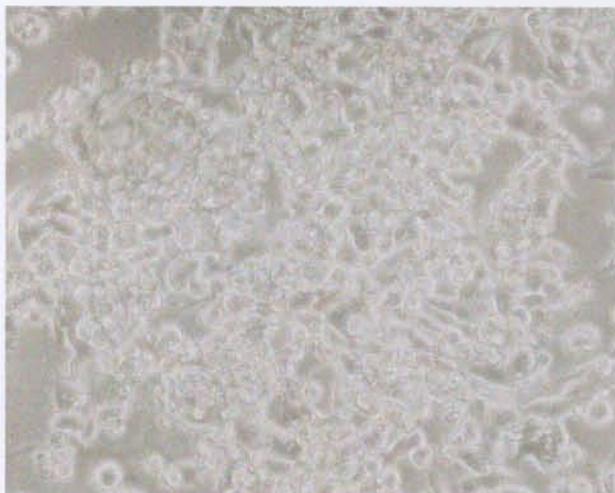


## DSRCT Research

DSRCT (desmoplastic small round cell tumor) is a form of cancer that affects mostly children and young adults. This slow growing but lethal disease is very rare; and very little information and no reliable treatments are available for this disease.

The Stehlin Foundation became aware of DSRCT through contact with Patrick Scranton, who suffered from DSRCT, and his family. Based on the Scranton family's support, the Foundation initiated a program of study publicized on a website produced by Patrick ([www.dsRCT.com](http://www.dsRCT.com)). To date, the Foundation has received biopsies of ten DSRCT tumors from patients receiving information from the website. Two tumors are currently being grown in tissue culture and two have been used as transplants in nude mice in order to test various anticancer agents. After several growth cycles, the tumors will undergo the signature drug screening developed at the Stehlin Foundation, in an attempt to identify more effective conventional and/or experimental treatments for this rare cancer.

**DSRCT cancer cells growing in tissue culture in our laboratory.**



**One of the first steps necessary to research the treatment of DSRCT is to grow the tumor in our nude mice. This has now been accomplished. One of our technicians prepares to transfer one of the established tumor lines from a DSRCT patient.**



# *Drug Development*



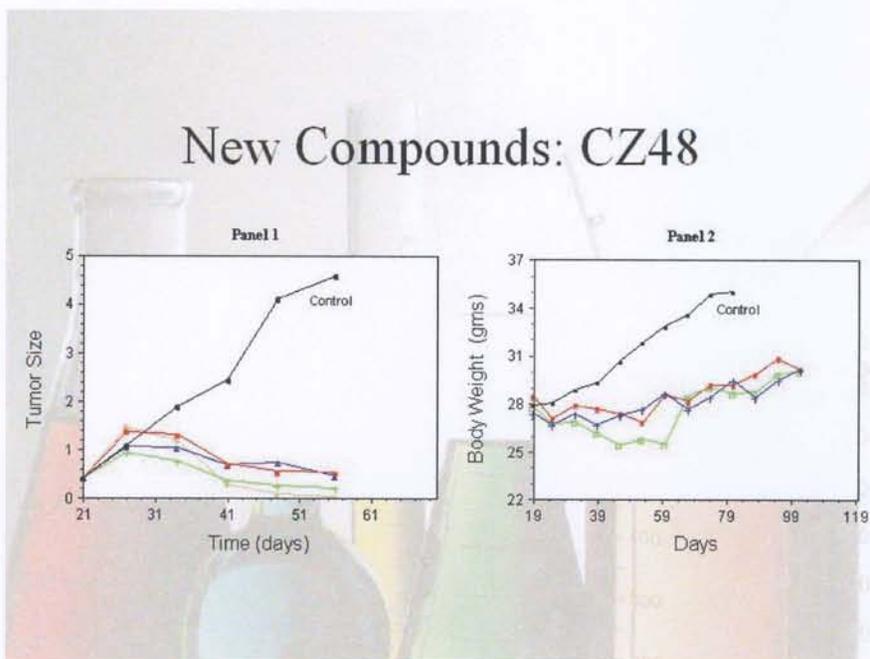
# Drug Development

Cancer has recently become the number one cause of death in the United States. Surgical removal of primary cancers with radiation therapy has made huge strides, but only chemotherapy or immunotherapy can hope to control the metastases, or spread, of cancer. Unfortunately, active drugs are few, not always effective, and frequently very toxic. The need for more effective and less toxic agents is urgent.

A group of such drugs has recently emerged - the camptothecins. The Stehlin Foundation, an early pioneer, has great hopes for the camptothecins, but much work is necessary to bring such hope to fruition. New molecules, in protected and potentially active forms, must be synthesized and tested for activity against human cancer cells cultered *in vitro*. The most active substances must be manufactured in larger amounts to be tested against human tumors transplanted in nude mice to assess toxicity and activity *in vivo*. The most promising drugs must be studied in larger animals, and eventually in man. After clinical trials, the drug must be submitted to the FDA for approval. This time-consuming and expensive process has been the work of the Stehlin Foundation for more than 17 years.

Our work with the camptothecins has led us to synthesize and test over 200 camptothecin derivatives in our laboratory. Some have been inactive, others have been too toxic to consider using, but a precious few have emerged as potential life-saving treatments for patients with cancer. Our pre-clinical investigations have identified compounds like CZ48 as highly efficient cancer killers with extremely low toxicity when tested in our nude mouse model. Studies remain to be conducted before enough information can be gathered to proceed to clinical trials. Our tissue culture testing program has recently identified another two active and very promising new drugs.

Efficacy and toxicity study of CZ48 against a human breast cancer. All concentrations tested (5, 6, 7, and 8 mg/kg) were effective in dramatically reducing the size of the cancer (Panel 1). Toxicity, as measured by body weight loss, was not observed, even at high doses of 100, 200 and 300 mg/kg (Panel 2).



# *Breast Cancer*

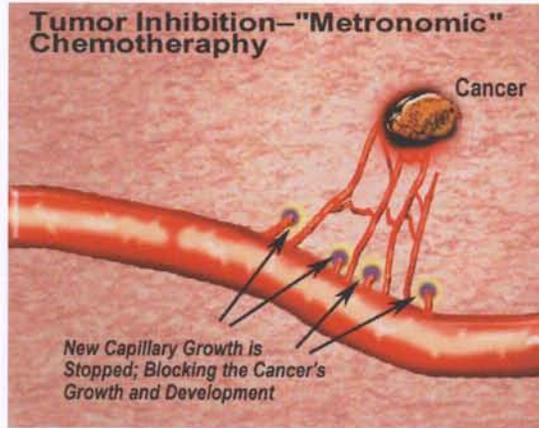


# Breast Cancer

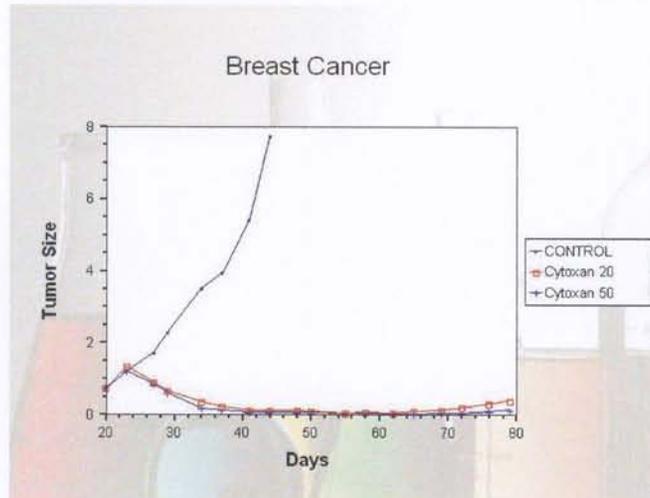
The Stehlin Foundation has always been at the forefront of research and treatment for breast cancer. In 1970, Dr. John Stehlin pioneered the partial mastectomy (lumpectomy) which today is the standard treatment for most breast cancer. Research in the Stehlin Laboratory contributed to the development of Herceptin, now an effective drug against some of the most aggressive forms of breast cancer.

Today, the Foundation is embarking on a research program aimed at reducing the recurrences and metastases of high-risk breast cancer patients. A new method of treating breast cancer, involving low-dose continual administration of chemotherapeutic drugs (metronomic chemotherapy) is being perfected at the Foundation. Such treatment focuses on blocking the formation of new blood vessels critical for the growth and spread of the cancer. Targeting the growth of new blood vessels blocks the supply of nutrients to newly forming cancer cells and prevents the established tumor from growing beyond a certain (small) size. An added bonus of this method is that, due to the very low doses of chemotherapeutic agents used, it is essentially non-toxic.

The initial experiments of this project have been concluded and we are now branching out to include different tumor types and a variety of chemotherapeutic agents, looking for the best treatment modality. We are also investigating a multi-drug metronomic approach with drugs having different mechanisms of action given together at very low doses. The next step is to add a conventional chemotherapy administration in the middle of the metronomic process to attack the stagnant tumor and wipe it out completely.



Treatment of human breast carcinoma with a continuous and prolonged administration of low dosages (metronomic chemotherapy) of Cytosin (a conventional anticancer drug). Drug was administered in the drinking water and given on a daily basis.



# *Anti-Metastasis Research*

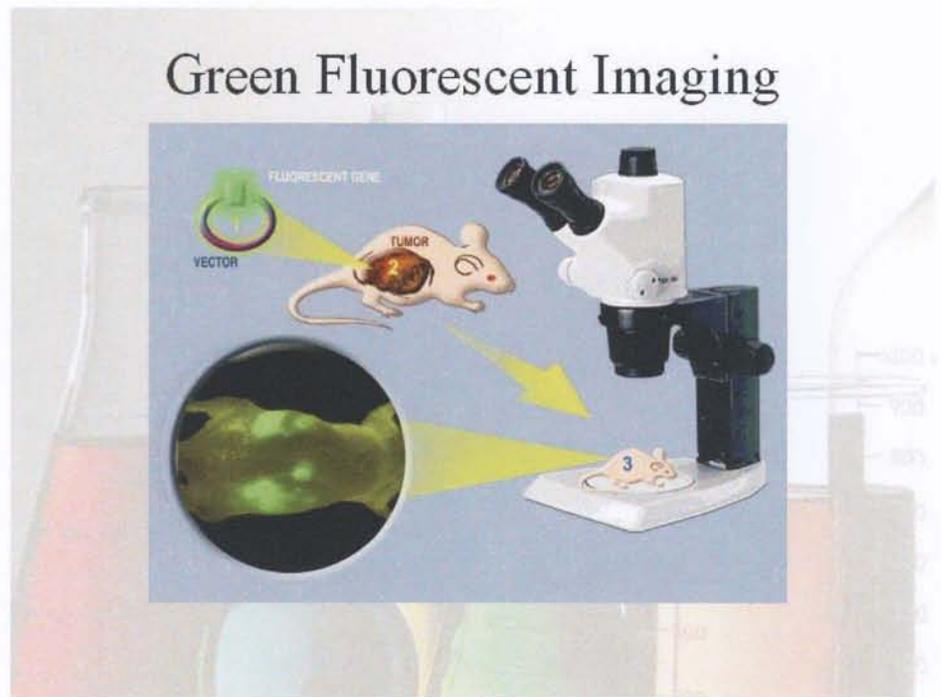


## Anti-Metastasis Research

Cancer's most lethal manifestation is its ability to spread through the body to distant locations, frequently to vital organs. Cancer would not be nearly as deadly or disabling if we could prevent or destroy this spread, called metastasis. One of the major challenges in cancer research is developing a model to be able to identify metastatic tumor growth and follow its development since primary tumors and metastatic ones have somewhat different biological properties. A new method using a green fluorescent protein gene inserted into the tumor cells is being developed here. This will give us the ability to visualize tumor growth in areas distal to the site of the tumor injection due to the emission of green light, while still using **human** tumors in our established nude mouse xenograft model.

Once metastases are identified, they can be quantified based on the intensity of the fluorescent light they emit. This intensity will vary as the animals are treated with new and established chemotherapy drugs. The object is to identify a drug or drug combination as well as a dosing regimen that blocks the metastatic process or acts primarily against the metastatic tumors.

The "glow" of a green fluorescent protein gene, implanted in nude mice, enable our researchers to track human cancer growth and the effects of drug treatment.



# *Education*



# Educational Scholarship Program

This award-winning program was initiated in 1980 for the purpose of giving high school and college students interested in pursuing careers in the basic sciences and medicine an opportunity to work in the Stehlin research laboratory during alternating semesters or during the summer, gaining invaluable hands-on experience on the front lines of cancer research and treatment. Students are paid by the Foundation for their work with the express understanding that these funds be targeted to alleviate expenses associated with their own educational endeavors.

Since the inception of the program, close to 300 students have been awarded scholarships. The students, who are supervised by a professional scientist at the Ph.D. level and/or highly qualified technician, participate in a variety of research and clinical activities. The program has resulted in many gifted students finding a path into the medical and scientific professions, as well as recognizing an important correlation between research, medicine, and the human factor in treating other people.



2005 Educational Scholarship Program recipients.

Students have rotated through the program from the following universities:

- Austin College
- Baylor
- Boston College
- Brown
- Bucknell
- California
- Dartmouth
- De Paul
- Duke
- Georgetown
- Harvard
- Hollins College
- Houston
- Johns Hopkins
- Loyola
- LSU
- Middlebury
- Mississippi
- Northwestern
- Notre Dame
- NYU
- Oklahoma
- Oklahoma State
- Princeton
- Rhodes College
- Rice
- Sam Houston State
- SMU
- St. Thomas
- TCU
- Texas
- Texas A&M
- Texas Tech
- Trinity
- Tulane
- UCLA
- USC
- Vanderbilt
- Washington
- Wisconsin

Students have rotated through the program from the following local high schools:

- Bellaire
- Clear Creek
- Clements
- Cy Fair
- Cypress Falls
- Dulles
- Jersey Village
- Kempner
- Kinkaid
- Kingwood
- Lamar
- Langham Creek
- Lutheran High North
- Memorial
- St. Agnes
- St. Johns
- St. Pius
- South Houston
- Spring Woods
- Strake Jesuit
- Stratford
- Sweeney
- Westbury
- Yates