



INSIDER

THE DESMOID TUMOR RESEARCH FOUNDATION — FUNDING RESEARCH ~ PROVIDING SUPPORT

The DTRF Supports Research to Find a Cure

NEWLY FUNDED PROJECTS

Benjamin Alman, MD

The Hospital for Sick Children, Toronto
"Identifying novel drug therapies for desmoid tumors"

Andrew Beck, MD – Stanford University, gift in support of Dr. Andrew Beck's research evaluating large intergenic non-coding RNA's in desmoid-type fibromatosis.

Dina Lev, MD – MD Anderson Cancer Center
"A rational search for novel anti-desmoid therapies"

Stephen X. Skapek, MD – The University of Chicago
"Deregulated mTOR in desmoid-type fibromatosis: identification and validation of a new therapeutic agent"

ONGOING RESEARCH PROJECTS

Matthew van de Rijn, MD, PhD – Stanford University
"ROR2, a potential novel therapeutic target in desmoids"

Richard Lackman, MD – University of Pennsylvania
"The role of hydroxyurea as first line treatment for primary and recurrent/refractory desmoid tumors"

COMPLETED 3-YEAR PROJECTS

Benjamin Alman, MD

The Hospital for Sick Children, Toronto
"Identifying the desmoid tumor initiating cell"

Dina Lev, MD – MD Anderson
"Molecular determinants of desmoid tumor development and progression"

NEW RESEARCH TECHNIQUE DEVELOPED WITH DTRF DOLLARS



One of the problems plaguing researchers and impeding the search for a cure for desmoid tumors is the lack of tissue available for research. This is a difficulty faced by advocacy groups of all rare tumors. In the past, investigators had to rely mainly on fresh frozen samples on which to conduct their experiments. To obtain a fresh frozen sample, a patient has to know his or her diagnosis pre-operatively and arrange to have the tissue handled appropriately to ensure its delivery to the waiting investigator in a timely fashion.

With the support of DTRF dollars, Dr. Matt van de Rijn and his lab at Stanford University have developed a novel technique that will make more tissues available for study, including tissues collected from decades earlier. Employing this technique on desmoid tumors, Dr. van de Rijn and future researchers will be able to perform advanced gene analyses using next generation sequencing on both old and new paraffin embedded tissues. Dr. van de Rijn presented this groundbreaking technique, called 3SEQ as keynote speaker at the 2009 CTOS meetings.

TED KENNEDY, JR supports the DTRF at the October 2009 gala. See inside for pictures and more information!



For up-to-date information visit our site, www.dtrf.org

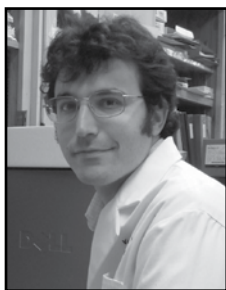
NEWLY-FUNDED RESEARCH



BENJAMIN ALMAN, MD
**The Hospital for Sick Children,
Toronto**
**Identifying novel drug therapies for
desmoid tumors.**

One way to identify new drug therapies is to test existing drugs on tumor cell cultures to see which drugs will kill desmoid tumor cells. In the past, Alman et al had tested 1,000

drugs on desmoid tumor cells and identified one such agent. Unfortunately, this agent is not readily available for use in North America. In this 2010 DTRF-funded study Dr. Alman plans to undertake a comprehensive screen of agents to identify drugs that specifically target cell viability in desmoid tumors. Building on previous work, Dr. Alman will focus on drugs that inhibit desmoid tumor cell growth presumably by blocking beta catenin signaling in mesenchymal cells. The agents identified will be tested for their ability to alter desmoid tumor cell proliferation, beta catenin protein level and differential effects on stem cells. Such drugs will be tested using desmoid cell cultures from patients and also transgenic mice that develop desmoid tumors. Identified agents can then be investigated in clinical trials. The exciting part is that the agents found to have clinical benefit will already have been FDA-approved for use in patients and can therefore be rapidly brought to patient care.



ANDREW BECK, MD
**Post Doc Fellow at Stanford
University, gift in support of
Dr. Andrew Beck's research
evaluating large intergenic
non-coding RNA's in
desmoid-type fibromatosis.**

DTRF-funded investigators at Stanford have developed a novel technique to analyze RNA from paraffin embedded tissue. This is important as many more

paraffin embedded samples are available for study than frozen. Currently this technology is being used to study "usual" coding mRNA in desmoid tumors in the Stanford lab. In this 2010 study, they will include a new class of "non-coding RNA" and examine the role of these molecules in the clinical behavior of these tumors. Conventional standard microarray expression profiling has been limited in that it only measures known genes that contain probes on the array platform. The new method being used allows for identification of novel transcripts. The new class of RNA (large intergenic non-coding RNA (lincRNA)) is thought to be a major regulator of gene expression. In the past year it has been shown that over one thousand evolutionarily conserved lincRNA's are expressed in mammalian cells and that expression of these lincRNA's correlates significantly with genes important in carcinogenesis. The long term goal is that the characterization of lincRNA's in desmoid tumors will lead to new diagnostic markers and treatment strategies.



DINA LEV, MD
MD Anderson Cancer Center
**A rational search for novel anti-drug
therapies.**

The goal of this study is to investigate the molecular driving forces behind the development and progression of desmoid tumors

Lev et al are trying to identify potential targets that modify beta-catenin tran

scriptional activity using an siRNA screen. Identifying genes and their cognate proteins whose alteration would inhibit beta-catenin activity might provide future targets for novel molecular therapies relevant to desmoid tumor patients.

Aim 1: To validate previous findings of the prognostic power of beta-catenin 45F mutation in predicting the outcome of patients with primary desmoid tumors.

Aim 2: To identify the molecular deregulations contributing to the sensitivity or resistance to the commonly used anti-desmoid therapies, mainly Tamoxifen, NSAIDs and Gleevec.

Aim 3: To identify potential novel anti-desmoid therapeutic targets using a rational siRNA screen. Potentially these targets harbor the capacity to modify the transcriptional effect of beta-catenin.

Note: Dr. Lev has previously identified significant associations between the presence of 45F mutations and an increased rate of desmoid recurrence as well as shorter time intervals to recurrence. Analysis of a large primary desmoid subset showed that desmoids having a 45 F mutation had an estimated five year recurrence - free survival rate of only 47% and a median time to recurrence of 3.16 years. In sharp contrast, the estimated five year recurrence free survival rate for all other desmoid primary tumors was 83%; median time to recurrence not yet being reached.



STEPHEN X. SKAPEK, MD
The University of Chicago
**Deregulated mTOR in desmoid-type
fibromatosis: identification and
validation of a new therapeutic
agent.**

This is a pilot study examining the role of Rapamycin in the treatment of children and young adults with desmoid tumors deemed likely to recur

following resection. Rapamycin directly targets and inhibits mTOR, a growth promoting pathway that may be critical in the development and growth of desmoid tumors. The mTOR cell proliferation/survival pathway was shown to be activated and essential for tumorigenesis when the APC gene is mutated (affecting the Beta catenin signaling pathway). It is an oral drug being evaluated as an anti-neoplastic agent in a variety of cancer types. Skapek et al plan to determine how effectively rapamycin blocks mTOR activation in desmoid tumors and whether mTOR inhibition blocks desmoid tumor blood vessel growth. If Rapamycin is found to be active, they will extend this pilot study to a national collaborative study run through the Children's Oncology Group (COG). The initial pilot study will involve The University of Chicago, UMDNJ and several other COG institutions, including St. Judes Children's Research Hospital.

THE 2009 PATIENT SUPPORT MEETING AND DINNER GALA WERE A SUCCESS!

On October 15th DTRF held its third annual patient support meeting and fourth annual dinner gala. Approximately 60 patients from around the country heard from an exciting roster of speakers who discussed various topics relating to desmoid tumors at the patient meeting.

Following the patient meeting, the DTRF hosted approximately 260 guests who were entertained by Beatles band Oh-bla-di-blada at the magnificent Ritz Carlton.

Money for desmoid tumor research was raised from our 3 live and over 200 silent auction items ranging from sports memorabilia to vacation homes, from admittance to the Golden Globes after party to a week at a luxurious Lake Tahoe house!

DTRF was also honored to have as our keynote speaker this year, Ted Kennedy, Jr. who gave an inspiring talk on his personal challenge with osteosarcoma and the obstacles we face fighting a rare disease.

We are looking forward to seeing you at our walk/run and patient meeting in Philadelphia, PA on November 13th and 14th.

SAVE THE DATE!



DEFINITION OF DESMOID TUMORS AFFECTS INSURANCE COVERAGE

As attendees of the October, 2009 patient support meeting witnessed, even a room full of scientists who have dedicated their lives to treating desmoid patients cannot agree on the definition of desmoid tumors. As desmoid tumors do not generally metastasize, they do not meet the accepted definition of cancer. However, desmoid tumors can result in severe morbidity and sometimes mortality due to their remarkable propensity to invade adjacent tissues, even bone, as well as their strong tendency to local recurrence.

Because desmoid tumors may not traditionally be labeled as cancer, some chemotherapeutic, surgical and radiation therapy options are not covered by all insurance companies. Further, some patients have been denied help from cancer advocacy groups because of the terminology.

Yet, many experts consider desmoids a form of sarcoma, a connective tissue cancer. Dr. Raphael Pollock, Professor and Head, Division of Surgery, University of Texas MD Anderson Cancer center affirms, "We always consider desmoids to be a form of cancer because of their tendency to invade and recur. All desmoid patients are cared for through the Sarcoma Disease Site Center here for that reason.". Many sarcoma experts recommend that patients enlist their primary physicians in communication with their carrier's medical directors. Dr. George Demetri, Director of the Ludwig Center at Dana-Farber/Harvard Cancer Center and Sarcoma Center, suggests, "Refer these medical directors to a recognized expert if there is any question whatsoever for a successful appeal in the face of such administrative fallacy."

FUNDRAISING EVENTS ACROSS THE COUNTRY helped support the **Desmoid Tumor Research Foundation** and its mission of finding a cure.

There were many fun and exciting events this year that raised money to fund research. Just a few of them...

CIRQUE DE SURVIVOR was an afternoon of circus magic in San Francisco on November 1, 2009. Money and spirits were raised through the magic and wonder of circus! All were dazzled by the high-wire adventure to make magic and weave dreams of a cure into a reality. Dana King, an Emmy Award winning news anchor generously donated her services as emcee. There were jugglers, musicians, aerial artists, trapeze artists and musicians on hand to entertain the many that supported DTRF and the quest to find a cure.

THE ROCK 'N ROLL FUNDRAISER on June 6th in Basking Ridge, New Jersey was a tremendous success. Guest were entertained by two bands and participated in a silent and live auction which included a week at Walt Disney World Resorts and a signed guitar by the members of Bon Jovi.

A BEEF 'N BEER FUNDRAISER (a Philadelphia tradition) was held in Glenside, PA in honor of Claudia Gomez a 26 year old FAP patient. Pat Ciarrocchi, a Philadelphia newscaster and step-mother to a young man with a desmoid tumor, was the guest auctioneer and raised the profile of the event. The night was a huge success, with close to 150 in attendance and a full array of raffle baskets and auction items. One guest commented, "We have wanted to do something to help for so long, and this was a great way to do that."

Sera Snyder ran the **PHILADELPHIA DISTANCE RUN** on September 20th and raised funds just by doing something that she loves.



For up-to-date information visit our site, www.dtrf.org



SUPPORT DTRF

You can help DTRF continue its mission of funding research and providing support.

- >Please send a check to DTRF, P.O. Box 273, Suffern, NY 10901
- >or make a donation online at www.dtrf.org