

# Ensuring no one has to face GIST alone

In Loving Memory: Barbara Erhart Bruce, Debra Binkley, Paul S. Norton, Joyce Tucker, Timothy Duffey

## Jim Mills shares his journey with GIST

By Kris Hunte

Marketing and Communications Associate

In 2006, GIST patient Jim Mills was generous enough to share his GIST journey to the Life Raft Group. As an avid hiker from the state of Michigan, the then 46-year-old would often spend his free time on the lengthy trails enveloping Lake Superior to stay in shape and make a catalog of adventures. During one morning in May of 2004, halfway down the 46-mile hike of the Pictured Rocks Lakeshore trail, Mills began to feel a gradually increasing discomfort in his abdomen.

"It felt as if I had taken a blow to my stom-

ach, so I decided that I must have injured myself over a tree trunk," claimed Mills. Determined to finish the elongated trail, Mills continued his hike and finished the trail in less than 56 hours. The pain grew more severe with each mile he trekked. Unfortunately, this pain was more than mere physical injury.

"The final seven miles were a miserable, uncomfortable experience and by the time I walked out of the woods, my feet were well blistered and I was holding my right hand over my abdomen."

**See Mills, Page 9**

## Tamara Taggart: Cancer cover girl

By Pamela Fayerman

Vancouver Sun

Tamara Taggart is the cover girl for a British Columbia (BC) magazine that debuted last month.

The CTV news anchor wishes the BC Cancer Foundation hadn't had a reason to request her story for the first issue of Forward, its patient empowerment publication. But as a cancer survivor who's just passed the second anniversary of a brush with death, she couldn't say no.

**See Taggart, Page 6**

## GIST Research Campaign Q&A with Norman Scherzer

By Marisa Bolognese

Development Consultant

In December, the Life Raft Group launched its "We Are the Cure" campaign to fund GIST research. I sat down with Norman to find out more about The LRG GIST research team and the campaign's progress to date.

**Marisa: The Life Raft Group has been funding GIST research for the last seven years. Tell me a little about how this came to be.**

**Norman:** We knew early on that if we, the GIST patient community wanted to save the lives of our loved ones that we'd have to become directly involved in research. So we

put together a team of the world's foremost GIST researchers and asked them to collaborate and cooperate. These scientists have been able to challenge the traditional cancer research norms and they've set new standards for how research can and should be done. We—as a patient community—got a seat at the table so that we could be part of the process and help maintain a sense of urgency that we as patients and caregivers live with every day.

**Marisa: What has come out of the collaboration?**

**Norman:** We've seen something remarkable take place with this team. Not only have scientists at different institutions been willing to

share rare tissue but as importantly, they are sharing data. What this means is that their fellow researchers can know what works and what doesn't work way in advance of published data. So instead of waiting a year to read about an experiment in a journal, these researchers consult with each other, thereby speeding up the research process. The Life Raft Group has aided in this by establishing a tissue bank and a registry of associated data which links patients' clinical histories to that tissue. This has become an important resource to the scientific team and it's another example of how GIST patients are having an impact on research.

**See Research, Page 9**

# LRG Launches Global Medical Team

**By Pete Knox**

Director of Strategic Planning

The Life Raft Group is pleased to formally announce the creation of its first ever Global Medical Team. This team, which consists of leading physicians throughout the world, will provide the LRG the opportunity to consult with experts on a number of medical topics of interest to the GIST community.

Here are the Global Medical Team founding members and their institutions:



Dr. Jonathan Trent  
Sylvester Cancer Center  
University of Miami  
Miami, FL USA



Dr. Matías Chacón  
Instituto Alexander Fleming  
Buenos Aires, Argentina



Dr. Peter Reichardt  
Helios Klinikum  
Bad Saarow, Germany



Dr. Yoon-Koo Kang  
Asan Medical Center  
Seoul, South Korea

The LRG looks forward to working with these experts on a number of upcoming projects designed to help improve the lives of those in the GIST community. Among these are the GIST Cancer Journal, the first scholarly journal devoted exclusively to GIST; an initiative designed to help patients better manage their GIST-related side effects; and a program designed to establish more formal criteria for GIST Centers of Excellence.

Be sure to follow the Life Raft Group on Twitter, Facebook and Google+ to get the latest news about the Global Medical Team.



# 2013 LRG Research Team Progress Report



## ANETTE DUENSING LAB

### Two major areas of focus:

1. Looking to understand how quiescence (tumor cells escaping death by going to “sleep”) and apoptosis (tumor cells dying) happen in GIST.

Understanding this allows us to kill tumor cells more effectively, and also help understand how resistance develops – leading to drugs that patients are less likely to develop resistance to. This is longer range, helping to improve the understanding of GIST and a critical pitfall in drug treatment and thus develop more effective future treatments and ultimately a cure.

2. Screening of already FDA-approved compounds to see what may work for GIST. This is a more immediate range, trying to help get us better drugs much faster to buy us time until a cure is found.

### Accomplishments:

“Over the past ten years, we have focused on elucidating mechanisms of GIST cell apoptosis and quiescence as well as the establishment for high-throughput strategies. Our work has not only led to the identification of several new compounds for the treatment of GIST, but also the identification of novel concepts in cancer biology.”

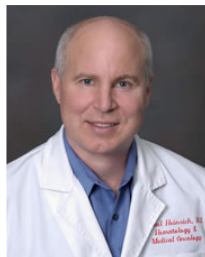
- Has screened nearly 100 compounds for their effectiveness against GIST.
- We now have a much better understanding of quiescence, apoptosis, and how they are related (i.e. DREAM complex) than we would have without Anette’s research.

Better understanding of the biology allows us to increase the precision and effectiveness of our targeted approaches, ultimately leading to more effective treatments. Included in this is a study using an FDA-approved drug in combination with imatinib in order to “wake up” the cell in order to kill it.

## MIKE HEINRICH/CHRIS CORLESS LABS

### Accomplishments:

1. Worked with a pharma company and Jonathan Fletcher to develop a new drug (ponatinib) that is currently in a clinical trial for GIST.



Mike Heinrich (Left), Chris Corless (Right)



2. Working with Brian Rubin, created a new mouse model for GIST—this is important as we need mice that can survive long enough to actually get GIST and help us test the compounds we are developing. In addition, this mouse model may also lead to a SDH-deficient mouse model so we can do more research on drugs for that subtype of GIST.
3. Sequencing has been completed on the D842V tumor – which currently has no approved treatments – this will help us more easily find targets and test compounds against this mutation.
4. Developed a yeast model for SDH-deficient GIST. This allows us to test drugs against that particular mutation, something that has not been done before.
5. Looking at regorafenib (Stivarga) against mutations that are resistant to other GIST drugs.
6. Genetic analysis of GIST to determine the potential for new targets—identifying weak spots in the “fortress”—thus identifying avenues for potential new treatments.

### Summary (of above accomplishments):

- Developed a number of new drug currently or previously in clinical trials for GIST.
- Creating new models (mouse, yeast) to help make it easier to study different drugs vs. GIST, including SDH-deficient, a rare subset of GIST most often affecting young people.
- Doing genetic analysis to help determine if new targets exist that can be exploited by new treatments, including for a mutation – D842V – for which there is currently no approved treatment.

## SEBASTIAN BAUER LAB

### Accomplishments:

1. Focus of research is on development of models that validate and predict the

usefulness of drugs for GIST—translational research.

2. Identified a number of key targets for GIST treatment: HSP90, PI3K, MAPK
3. Identified a number of factors that determine how GISTs develop – p53, DOG1



### Current Focus:

- Looking at “Inhibitors of Apoptosis (IAP)” proteins – which help prevent tumor cells from being killed off – and determining how to remove the protection mechanism.
- Studying a glucose “impersonator” (2-DG) that can’t be metabolized by tumor cells – thus causing them to starve to death.
- Screening novel KIT inhibitors against various KIT mutants to see how they work and better understand the disease and perhaps improve their efficacy.
- Working with Jonathan Fletcher, developed a cell line that is resistant to Gleevec that has been used to better understand how secondary resistance develops, as well as study how outside stressors to cells help drive the resistance process.

## MARIA DEBIEC-RYCHTER LAB



Focus of research is on both molecular analyses and understanding how progression and resistance develop. By better understanding the mechanism, we are more likely to be able to combat it once it happens, or ideally, to prevent it from

happening in the first place.

### Accomplishments:

1. Did molecular screening of patients for a large European study (EORTC) that helped confirm the predictive value and essential role of KIT and PDGFRA mutational testing.
2. First to publish an analysis of how resistance to imatinib develops.

**See Progress, Page 11**





### By Mildred Menos

Assistant Program Director

February 28, 2014 will mark the 7th Annual Rare Disease Day founded internationally by the European Organization of Rare Diseases (EURORDIS) and hosted in the US by the National Organization for Rare Disorders (NORD). This day was created to bring worldwide attention to the rare diseases that affect over 60 million people in Europe and North America alone as well as millions more throughout the world. Increasing awareness among the general public, policy makers, researchers and health professionals is a crucial step in discovering and

advocating towards the path to a cure.

This year's theme, "Join Together for Better Care" is bringing together national Rare Disease Alliances and specialized organizations from over 70 countries around the world with the goal of increasing access to rare disease care. You can show your support by connecting with them on social media, sharing your story on their website and uploading a photo of you and your friends raising and joining your hands, a symbol of the cause. For more information check out: [www.rarediseaseday.org/article/get-involved](http://www.rarediseaseday.org/article/get-involved)

The Life Raft Group joins NORD in their

campaign to raise awareness of rare disease through our own Rare 13 campaign ([www.therare13.com](http://www.therare13.com)) which aims to increase awareness and education of what GIST is, how to diagnose it and to ensure proper programs and services are readily available to GIST patients and their families. We will be promoting Rare Disease Day on Rare 13's Facebook page and encouraging others to do the same in any way they can.

Although GIST is considered a "rare" cancer, when you consider that 13 people are newly diagnosed with GIST every day it becomes clear just how important rare can be.

## Welcome Mildred Menos to the Life Raft Group



Originally from Castleton, NY, Mildred completed her undergraduate degree in Diplomacy and International Relations at Seton Hall University in South Orange, NJ. She then pursued her Master's in International Educational Development from Teachers College

at Columbia University in New York, NY. Previous to joining us she served as assistant to the Chair of the Political Science Department at Columbia University, and most recently as Program Manager at the Initiative for Policy Dialogue, a think tank founded by Nobel Prize winning economist Joseph Stiglitz dedicated to developing world economic policy.

As the Program Department's Assistant Director, Mildred will assist our Program Director with the implementation of the department's initiatives and the expansion of our organization's global presence. She will also be focusing on member outreach, providing support to our local group leaders and building connections with those looking to be more involved in their home states. Please feel free to contact Mildred at [mmenos@liferaftgroup.org](mailto:mmenos@liferaftgroup.org).



## Calendar

Southern California GIST Support Group  
February 22nd, 2014

Rare Disease Day  
February 28th, 2014

LRG Research Team Meeting  
March 14th-16th 2014

Illinois Caregiver Support Group  
March 23rd, 2014

GDOL Chicago  
April 2014

NIH Pediatric and Wildtype GIST Clinic  
May 21st-23rd, 2014

Life Fest 2014 - Teaneck, NJ  
November 7th-9th, 2014

# LIFEFEST 2014

November 7th - 9th

New Jersey

# GISTDAY OF LEARNING *Chicago*

April 2014

**Stay tuned for more info on the location and how to register**

# Taggart from Page 1



"I can definitely say it's not the magazine cover I dreamed I'd be on. I hesitated, initially, because just even saying the word cancer is still hard for me. Not many people know I've even gone through this experience," she said in an interview.

Taggart, 45, had a rare gastrointestinal stromal tumour, commonly called GIST in the medical community.

Since the tumour was removed, she's been taking a drug that has revolutionized the care of patients like her. If she'd developed the cancer more than a decade ago — before the arrival of drugs known as targeted biologic therapies — her doctors told her she'd be dead.

For several months in 2011, before the cancer was diagnosed, Taggart had its common symptoms: fatigue and anemia. But doctors didn't discover the source of her problem until the fist-sized tumour adhered to her small intestines ruptured. She nearly bled to death.

The day it burst, in January 2012, she had the worst headache of her life. She vomited

and passed out in the bathroom at work, on a day she was meant to be celebrating the first anniversary of her start as Mike Killeen's co-anchor on the 6 p.m. news. She went home. Her husband would later call an ambulance.

The tumour had been growing inside Taggart for about two years. It was originally missed by a radiologist after a CT scan that she had for kidney stones.

Despite the delay in a diagnosis and the missed diagnosis by the radiologist — who has apologized — Taggart's not bitter.

"I was upset for 24 hours when I learned the tumour was visible on a scan I had in 2010. When I met the radiologist again, I told him 'I need you to know that I hated you for 24 hours.' But he was looking at my kidneys for kidney stones. Only when he was asked to go back and look at the scan again did he see a tumour in my small intestines.

"I wished he would have seen it initially, but I also wished none of this had ever happened. But it did, and now I want other patients to be aware that when something doesn't feel

right in their bodies, we have to be our own best advocates."

Fortunately, one of the world's leading experts on gastrointestinal stromal tumours, Dr. Charles Blanke, was at the BC Cancer Agency when Taggart was taken to Vancouver General Hospital. He has since moved to Portland, Oregon, but Taggart still emails him with questions and she's confident in her new oncologist.

Blanke pioneered the research and use of a life-saving drug called Gleevec for gastrointestinal stromal tumour patients. Taggart is on the generic version now, but when she was first prescribed the daily medication, it cost \$6,000 a month. It was paid for by the cancer agency.

"People like to complain about the health care system, and it's not perfect, but boy, when you need it for something so urgent, it's there. And the medical and nursing care is unbelievable," says Taggart.

This article was reprinted with permission from the Vancouver Sun.



# Tanner finds chuckles in cancer treatment

**By Mark Washburn**  
Charlotte Observer

**A**fter turning 50, Rob Tanner went to the doctor in May for that checkup all men are supposed to begin getting at 50.

"That's not supposed to be there," the doctor said during the routine prostrate check.

"That" turned out to be a lemon-sized tumor between Tanner's rectum and prostate, and within days tests showed that it was not only a rare cancer called GIST, for gastrointestinal stromal tumor, but it was in a place where few have ever been found. They usually occur in the stomach.

Tanner, marking his ninth anniversary this month as morning host on WSOC-FM (103.7), was put on the drug Gleevec to shrink the tumor, which had not metastasized. But the tumor didn't shrink much, and now Tanner had a surgery on Feb. 3 at Moffitt Cancer Center in Tampa to have it removed.

Tanner has been sharing his progress with listeners, both on the show and on Facebook, and it has become a bit of a comedy routine. "What are you going to do? Cry about it?" says Tanner. "You have to laugh."

His bosses at CBS Radio put a recliner, donated by Tyndall Furniture, in the studio for Tanner to relax in when he feels like he needs it. And co-workers cut him some slack, at least at the beginning.

"We went and got him his coffee, but just for a week," says producer Chris Allen.

"Whenever someone tells me to do something, I say, 'Hey, I can't do it; I've got cancer,'" says Tanner.

Tanner admits he was depressed by the diagnosis for the first few days. "I freaked out a little bit. Now I know what it feels like when people are told they have cancer."



But his faith, his wife Missy, their two children and others in the family helped him develop a positive outlook. It also helped that he didn't have to go through debilitating chemotherapy, and that his prognosis is good. Tanner came to Charlotte in an unusual way. D.J. Stout had been made program director for WSOC in late 2004, and he was winnowing down a stack of 60 potential morning hosts. Tanner, then working at a small station in Lakeland, Fla., near Tampa, kept making

the cut.

Bill Schoening, CBS Radio's market manager in Charlotte, happened to be visiting Lakeland, and called Stout to say he'd heard a guy on the radio there who might be a good fit for Charlotte. "I just talked to that very guy this morning," Stout told him. "He's coming up for an interview."

Tanner was Stout's first hire at the station. "Tanner in the Morning" started on WSOC in January 2005 and is usually among the top five Charlotte morning shows in ratings. Also on the show are Guenn Schneider and Captain Jim Slade.

"Tanner is the most down-to-earth on-air talent I've ever worked with," says Stout. "There's no big ego, none of that 'I'm a big, bad morning guy.'"

Stout says the station plans what he calls "How's Tanner's Cancer?" segments, interviewing Tanner by phone while he's recuperating.

Tanner expects to be out of work for about three weeks. "I'll be in the hospital for five to seven days if things go well. If they don't go well, I will be out in about three hours."

OK, but seriously. Hasn't this whole thing taught you something?

"Life's short," says Tanner. "Enjoy every day. Spend time with your children. Any day you could walk into your doctor's office and he could say, 'That's not supposed to be there.'"


This article was reprinted with permission from the Charlotte Observer.



Rob Tanner and his radio show crew

# Save the Date

**1ST ANNUAL GIST AWARENESS DAY**  
SUNDAY, JULY 13, 2014

- 
- Afternoon of fun activities for families
    - GIST experts and advocates
    - To make a difference!
    - Music and more!

**PLUS: Help break a Guinness World Record**

**Interested in hosting an event in your city?  
Want to help us plan the event?**

Contact The Life Raft Group  
liferaft@liferaftgroup.org  
(973) 837-9092



## Research from Page 1

**Marisa: In this new “We Are the Cure” campaign you mention that GIST research is in danger? Has something changed?**

**Norman:** Unfortunately the pool of money for research has been shrinking. As a rare disease we are affected more than other more common cancers like breast and colon. Institutions like the National Cancer Institute are funding just four to five percent of all research proposals which means that a rare cancer like GIST is lost amongst the roughly 200 cancers competing for funding. The fact that the Life Raft Group is the single largest supporter of GIST research in the world tells you a lot about how important the GIST community is to the state of GIST

research and what would happen if we cannot sustain our current level of funding.

**Marisa: What kind of projects does**

**the funding support?**

**Norman:** So many. I'll just give you a few examples. Dr. Matt van de Rijn's lab at Stanford is using immunotherapy to fight GIST cells using antibodies to trick cloaked tumor cells into revealing themselves. Dr. Anette Duensing's lab in Pittsburgh is doing amazing work to overcome the DREAM complex, which helps GIST cells fall asleep, thus evading death from drug treatment. By combining Gleevec with another drug, they hope to essentially wake the cells up for Gleevec to find and kill. Dr. Brian Rubin's lab at the Cleveland Clinic not only has created new, stronger mouse models to support many research labs, but is currently working on intense combination therapy of up to three drugs that if effective, could delay

resistance for many years. And these are just a few highlights from this highly collaborative and forward-thinking team.

**Marisa: How much do you hope to raise through your “We are the Cure” campaign and how is it going so far?**

**Norman:** The LRG is committed to raising several million over the next two years to keep the research going at the same, if not higher, level. So far we've raised over \$150,000 and we have several fundraising events planned for this year with all funds going towards research.

**Marisa: How can people help and do you have any final thoughts to share?**

**Norman:** Anyone can make a contribution through our website, send a check or ask their families and friends to join with us to find this cure. The GIST community may be small but we are determined. We have the tools in place to find a way to put an end to this disease. We can't stop now.

## Mills from Page 1

It wasn't until late September when Mills decided to visit his family doctor to diagnose his condition. Through numerous specialized doctors and various tests, it was discovered that he had a “tumor of unknown origin.”

It was later identified as a 17x18cm GIST located in the back side of his stomach.

In October of the same year, Mills received surgery to have the GIST removed along with his gall bladder and appendix. Despite the successful surgery, Mills displayed a small amount of shock of the tumor given his otherwise healthy condition due to his affinity for exercise.

“It was amazing that I never noticed anything except a slight bulge in my upper abdomen that I unsuccessfully fighting for years with sit-ups and abdominal crunches.”

One year later, Mills was adamant to head back to Pictured Rocks as sort of a commemoration to the time he overcame the rare cancer. The hike helped regain the con-

fidence in his physical well-being that he had lost since his surgery. As a result, Mills made plans to return to his hiking adventures full-time and find new trails to conquer.

Let us fast forward to 2014.

Now in his 50s, Mills is still GIST free and enjoying the flora and fauna of hiking, leaving his memories of Pictured Rocks behind to create new experiences elsewhere.

“I hiked the more scenic mid-section of [Pictured Rocks] several more times,” said Mills. “It got so that I was recognizing rocks and roots that I'd tripped over previously. I needed another place to hike.”

One of those newer trails was Fox River Pathway, a 30-mile trail renowned as the location where famous author Ernest Hemingway fished for trout, inspiring him to write the 1925 short story, “Big Two-Hearted River.” Mills labeled the hike as very satisfying and the quietest and least used trails he had ever been on.

“I didn't see a single person from the moment I was dropped off at the head of the trail next to Lake Superior until two days later,” said Mills.

An additional location Mills discovered was Isle Royale National Park, a large island in Lake Superior, now considered his favorite place to traverse. In 2010 and 2011, Mills

took an indirect series of paths about 62-70 miles from one end of the island to the other. He has most recently returned to Isle Royale to enjoy the aquatic aspect of the park, taking his boat and spending time paddling, fishing, and portaging from the waters of Michigan's largest Great Lake.

Jim Mills has lived a healthy life following the removal of his GIST in 2004, but as a supportive member of The Life Raft Group community he understands that he is in the minority in that regard. For several years, Mills has attended a number of GIST support group meetings in his local area where people talk about their latest issues with the cancer and how they're dealing with not only its unpleasant ramifications, but also the taxing experiences of GIST-centric medications such as Gleevec and Sutent. For someone who has been GIST free for over nine years without having to take medication, Mills felt slightly overwhelmed.

“Sometimes I hated going because it was depressing,” stated Mills. “Members died, members got new GIST tumors, medication is no longer working, and people are under a lot of physical and mental stress. I'm the one person who is always doing ‘great.’”

Although Mills' reluctance is understandable, if we've learned anything from success it is that it should be used as a guiding light rather than a black hole, regardless of the situation. Jim Mills' successful journey of battling and conquering GIST creates a ray of hope for all GIST patients across the world. We at The Life Raft Group commend Jim Mills on his achievements and look forward to hearing similar stories from other GIST survivors.



# LRG Staffers reunited



LRG Staffers new and old reunited at the wedding of the LRG's Events and Design Coordinator Matthew Mattioli and his partner, Anthony Cashin.



## Fundación GIST Mexico reaches 1,000 medical students



Last October, Fundación GIST Mexico reached the goal of having more than 1,000 students of medicine learning about GIST in the year. In an effort to increase awareness and knowledge about GIST, Fundación GIST México has visited 10 universities and has presented a short video endorsed by the Tec de Monterrey (a recognized university) in which Dr. Eduardo Guzman Huerta, a surgical oncologist, explains everything about the diagnosis and treatment of GIST. The process has not been easy, but with the collaboration of the universities and the support of organizations like Alianza GIST and the Life Raft Group, we have reached 1,105 students. The students are eager to learn and help GIST patients.

## Timothy Duffey, passes away at age 49



Timothy E. Duffey, age 49, of Brick, NJ passed away after a long courageous battle with cancer Saturday, December 14, 2013 at his home. Born in Bangor, Maine, he lived in Ocean Township before moving to Brick 16 years ago. He was employed as a Supervisor for over 30 years for D&D Trenchless Solutions in Tinton Falls. Timothy was a communicant of St. Dominic's RC Church in Brick and was a past officer for Elks Lodge #742 of Long Branch. He greatly loved to Quad.

Surviving is his wife, Lynne (Jasones), his son and daughter, Shane and Olivia; a brother Tom of Maine and his sister Robin Le Gere of Maine. Also surviving are his three nephews, Andrew, Austin and Alec and two nieces Stephanie and Dayna; as well as his sister-in-law Jeannine Schwartz. Timothy will be greatly missed by his mother, Shirley and her husband Bobby Gross of Maine and also by his mother and father-in-law, Carole and Andy Novak of Brick. He leaves behind many loving friends.



## Progress from Page 3

3. Developed tools that help researchers better evaluate how effective drugs are, including test panels and mouse tumor models, making it easier to take these drugs into clinical trials.
4. Along with a team of French researchers, developed a new prognostic indicator (Genomic Index) that can be used to make treatment decisions for intermediate and high-risk GIST patients. By better understanding prognostic factors, you get a more holistic view of the actual disease and can tailor treatment to their specific disease.



### TAMÁS ORDOG LAB

Research focuses on better understanding the biology of Interstitial Cells of Cajal (ICC)—the “pacemaker” cells of the gut. Abnormal growth of ICC’s leads to GIST, so understanding their biology, and the factors

that cause them to grow abnormally, can help us better understand how the disease originates. Armed with this understanding, we are using isolated ICC precursors (stem cells) and animal models from other diseases and biological processes (diabetes, eating disorders, aging, and GIST) to study compounds that could be used to restore normalcy to ICC’s and make abnormal ICC’s more sensitive to treatment.

Dr. Ordog is a leader in the understanding of ICC’s, having studied them since 1998. As opposed to fighting GIST after it develops, he is trying to understand how it does in order to prevent it from ever developing.

#### Some of his accomplishments include:

1. Led the first study describing loss of ICC’s in diabetes
2. Introduced the concept of ICC turnover from stem cells, in collaboration with Dr. Rubin, conducted a study that looked at the role of these ICC stem cells in the development of resistance to targeted GIST therapy.
3. In addition to adding an epigenetic focus that is not found elsewhere in the team, by working on the development of purified ICC models, Dr. Ordog is also providing tools that will enhance the research capabilities of other LRG team members and outside researchers as well.

### BRIAN RUBIN LAB



The GIST researchers in Dr. Rubin’s lab have no other source of funding other than the LRG. Dr. Rubin is most interested in how sarcomas are diagnosed and also prognostic factors. He has developed a number of

cell-based and mouse models that are used not only in his research but that of the other team members. Ultimately the lab is trying to identify the proteins that drive the development of GIST, and develop therapeutic strategies that target these proteins.

#### Accomplishments:

1. Working with Jonathan Fletcher’s lab, documented that 80-90% of GISTs contain KIT mutations – this study laid the groundwork for using imatinib to treat GIST.
2. First to identify the KIT exon 9, 13, and 17 mutations
3. One of the first labs to develop a mouse model for familial GIST
4. Recently identified two pathways (autophagy, FGFR3) that help resistance to targeted therapies develop. By better understanding these, new treatments can be developed that are less likely for patients to develop resistance to.
5. Developed a cell line that harbors a specific imatinib-resistant KIT mutation (T670I) that has been used by members of the LRG research team to better understand the biology of GIST.

#### Current Focus:

- Developing better GIST mouse models
- Exploring combination therapies of up to 3 drugs; looking at how to sequence them to minimize toxicity and delay resistance for years.
- Screening of over 150 compounds either already in development or FDA-approved for a condition other than GIST to see if they are effective against GIST.
- Using current mouse models to understand the interaction of loss of a particular gene and activation of KIT, in order to help better understand how progression develops.

### MATT VAN DE RIJN LAB



The major focus of research is on immunotherapy as an alternate approach to combatting GIST. The immune system is a highly effective protective device that has been abused by tumor cells and conversely may

be useful in breaking these tumor protections down. Immunotherapy as a field of cancer research has struggled in the past, but in the last five years or so there have been impressive successes, particularly in large cancers like breast.

#### Accomplishments—Recent Progress:

1. Using mouse models, successfully attacked GIST with antibodies, essentially telling immune system to eat the cancer cells.
2. Found that GIST cells highly express CD47 protein, part of a process that the body developed to protect normal cells. CD47 tells macrophages (scavengers which eat bad cells) in the body not to “eat” the normal cells. The tumor cells abuse this system to protect themselves.
3. Studying the effects of antibodies on CD47 to fundamentally silence CD47, thus exposing the tumor cells to macrophages.

### JONATHAN FLETCHER LAB (TEAM LEADER)



Focus of research is on imatinib-resistant GIST. In the past year, collaborating with other members of the LRG research team, new immortal cell lines were developed that help understand how to most effectively target imatinib resistance.

#### Accomplishments – Recent Progress:

1. Working along with the entire LRG research team, undertook a major project, the comprehensive evaluation of imatinib-resistant GIST by studying the entire GIST genome to look for mechanisms that lead to drug resistance. The most important finding was that there are few relevant resistance mutations, other than those involving the KIT gene itself, in imatinib and sunitinib-resistant GIST, and highlights the need for more effective ways of targeting KIT and PDGFRA.
2. Along with Dr. Heinrich’s lab, development of ponatinib for treatment of resistant GIST.
3. Study of regorafenib to see which imatinib-resistant KIT mutations it inhibits. Mutations that are not inhibited by sunitinib but are inhibited by regorafenib were identified, providing a rationale for cycled treatment—a new approach in GIST.
4. Clinical trial cycling sunitinib and regorafenib. Lab studies have confirmed potential efficacy of this approach – a phase 1B trial is planned to be opened in 2014.



# THE LIFE RAFT GROUP

## LRG STAFF

Executive Director	Norman Scherzer
Deputy Executive Director	Roger Campbell
Science Director	Jerry Call
Strategic Planning Director	Pete Knox
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Program Associate	Michelle Durborow
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Program Associate	Elizabeth Pierre
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Special Projects Asst.	Eileen Glasser
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