

## **Cutting Off the Fuel Supply**

### **A New Approach to the Treatment of Pancreatic Cancer**

#### **Dream Team Leaders:**

Craig B. Thompson, M.D., director, Abramson Cancer Center at the University of Pennsylvania  
Daniel Von Hoff, M.D., Senior Investigator and Physician in Chief at Translational Research Genomics Institute (TGen)

#### **The Project**

As the fourth leading cause of cancer death in the United States, pancreatic cancer remains one of the most deadly forms of cancer. Over 90 percent of patients die within the first year of diagnosis. Recent advancements have had little impact, and a new approach is desperately needed.

Scientists have suggested the possibility of “starving” cancer cells to death by depriving them of a specific nutrient that they require for survival. Recent studies have demonstrated that most cells acquire mutations causing them to become addicted to a continual supply of nutrients to produce the energy needed for survival and proliferation. In most cancers, this nutrient is glucose.

Using modern tumor imaging, it is possible to monitor a tumor’s glucose utilization and such tests are now routinely used in clinical practice. In most cases, the more glucose a tumor is using, the more advanced the tumor and the greater likelihood of spread. Similarly, if a tumor is using less glucose as a response to chemotherapy, then it is a good indication that the tumor is responding to treatment.

Pancreatic cancer presents a unique challenge because it is addicted to another molecule, glutamine, rather than glucose. Glutamine is an amino acid that helps build muscle mass and is used by some cells for energy. When cancer feeds or metabolizes excess amounts of glutamine, it can lead to extreme weight loss by robbing other cells of this important nutrient, a condition from which many pancreatic cancer patients suffer. In addition, the waste that is a by-product of this process generates an intense reaction from surrounding normal cells, which then secrete growth factors that help tumor cells grow. Cancers that use excess glutamine are often resistant to standard forms of chemotherapy, another characteristic of pancreatic cancer.

#### **The Goals**

The goal of this Dream Team is to develop tests using advanced imaging techniques to determine what nutrients pancreatic cancer cells require to fuel their growth and survival. Understanding the cell’s fuel supply will help scientists to develop more individualized treatments with fewer side effects.

This Dream Team will immediately begin a series of clinical trials designed to deprive pancreatic tumors of crucial nutrients. The team will test the drugs in combination with existing standard chemotherapy, with the hope to increase the percentage of pancreatic cancer patients surviving beyond one year while improving quality of life.

## The Quote

“To lose a person with pancreatic cancer can be bad because there is a lot of pain and other negative effects associated with this disease. It’s a bad disease. We all see it takes our friends, our families. Most of all, many of us see patients with it every single day and we get tired of not being able to do something dramatic for these people. We can do a little, help with pain, lengthen survival some, but we want to do something dramatic. It is going to take a tremendous amount of real thinking power to make that difference, so it is a dream come true to be able to put this team together to work towards this goal.”  
Daniel von Hoff

“In the future, you can imagine that we can pull a new therapy off the shelf and if the patient has a particular profile match them up with that treatment, so that we cure their cancer. If they don’t match that profile, then we try something else. This is the challenge of cancer research. Not every cancer that comes along, not even every pancreatic cancer, is going to be identical. We need to be smart enough to know the personality of the cancers and go after the uniqueness, the personality of that cancer.” Chi Dang

“Maybe most of our successes in cancer have been limited because we’ve only been reading the first chapter of the story. We haven’t really gotten to the end. Now we’ve got the Rosetta Stone. We understand the language, and we can read each chapter with more facility. We can treat the cells that grow abnormally, that we typically think of as the cancer, and we can treat the other cells that support that cancerous growth. We have to treat both. That’s what I’m so excited about because we now we’re reading the full story, not just the cover of the book.” Geoff Wahl