# Innovations in Cancer & Blood Disorders

Rady Children's Hospital San Diego

*Rady Children's - A comprehensive system focused solely on children.*

## PEOPLE

## Dr. Zage: Finding novel treatments for solid tumors

Peter Zage, M.D., Ph.D., an attending hematologist/oncologist at the Peckham Center for Cancer and Blood Disorders at Rady Children's Hospital-San Diego and an associate professor-in-residence in pediatric oncology at UC San Diego Moores Cancer Center, is an expert in the treatment of children with neuroblastoma and retinoblastoma. His research aims to identify novel targets and develop new treatments for children with solid tumors.

The Zage lab's primary focus are studies to better understand the pathways involved in the regulation of growth factor receptor trafficking and degradation in tumor cells, and their role in tumor growth, as well as studies to evaluate the effectiveness of new therapies against pediatric solid tumor cells.

Recently, Dr. Zage and hematology/oncology fellow Megan Paul made a notable discovery in the pathogenesis of medulloblastoma, one that suggests a potential therapeutic target. Their findings ("The Role of G-CSF Receptor Surface Expression in Medulloblastoma Pathogenesis") were presented at the recent American Society of Pediatric Hematology/Oncology (ASPHO) meeting in Pittsburgh. Along with this research, Dr. Zage has recently initiated a national, multicenter clinical trial of a novel therapy combination for treating relapsed or refractory solid tumors ("A National Phase I Study of Cabozantinib in Combination with 13-cis-Retinoic Acid in Children with Relapsed or Refractory Solid Tumors").

Dr. Zage joined the Peckham Center in 2016. Previously, he held a faculty position in the Section of Pediatric Hematology/Oncology at Baylor College of Medicine and Texas Children's Cancer Center, where he was a member of the Solid Tumor, Neuroblastoma, Retinoblastoma, and Developmental Therapeutics teams. After earning his medical and doctoral degrees from Columbia University in New York, he completed his residency in pediatrics at the University of Chicago Children's Hospital and a fellowship in pediatric hematology/oncology at Children's Memorial Hospital (now Lurie Children's Hospital).

**PROGRAMS**

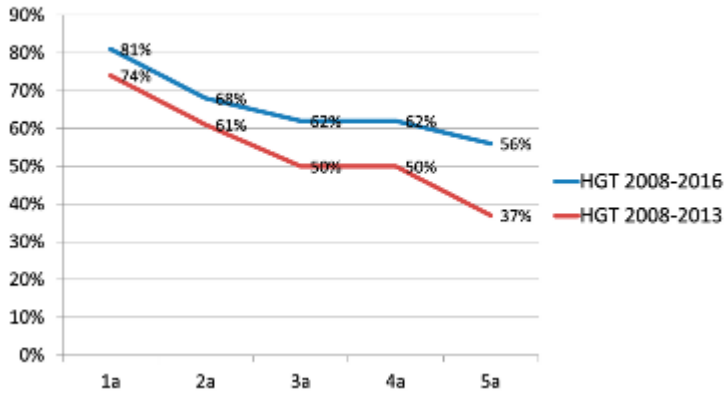
# Improving pediatric care on the U.S.-Mexico border

The Peckham Center for Cancer and Blood Disorders is partnering with the Mexico Ministry of Health to establish a population-based cancer registry in Baja California, the first of its kind in Mexico. The goal of the registry is to collect cancer epidemiology data and assess the cancer burden to inform cancer control policy in the U.S.-Mexico border region.

The registry was officially launched at the Binational Health Commission in Tijuana by Alejandro Mohar, M.D., director of cancer control for Mexico's Ministry of Health. More than 50 officials from hospitals in Tijuana attended the event.

Recently, William Roberts, M.D., director of the Peckham Center, and Paula Aristizabal, M.D., M.A.S., medical director of Rady Children's International Outreach Program, along with representatives from UC San Diego's Moores Cancer Center (Elena Martinez, Ph.D.) the National Cancer Institute (Susan Shurin, M.D.) and the Hospital General de Tijuana (Rebeca Rivera, M.D.), met with Dr. Mohar in San Diego to discuss the registry's implementation.

The Peckham Center, through its International Outreach Program, has been working with the Hospital General de Tijuana (GHT), the largest public hospital in northwestern Mexico, for more than a decade. (See the previous "Innovations" story.) In 2008, Rady Children's Hospital and St. Jude Children's Research Hospital formed a partnership with the GHT, resulting in the creation of a pediatric oncology unit at the GHT. The unit has led to dramatically improved clinical outcomes, particularly a five-year overall survival rate of 56 percent for acute lymphoblastic leukemia at the GHT in 2016. In 2017, the overall survival rate climbed even higher – to 76 percent – compared with 50 percent for the rest of Mexico. Future initiatives by the partnership aim to provide regional programs to improve care at a larger scale.




Five-year event-free survival for pediatric ALL increased from 37 to 56 percent.

The results of the partnership were featured at the 2017 American Society of Hematology Annual Meeting and published in its journal

## Quick Links

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*Blood Advances*. The program was also among the top eight projects at the inaugural ASH Global Capacity-Building Showcase.

Read the journal article.



## RESEARCH

# Dr. Thornburg leads cutting-edge studies on hemophilia

Courtney Thornburg, M.D., M.S., is the co-principal investigator for two national hemophilia studies and a site investigator for a hemophilia clinical trial of a novel subcutaneous therapy. All three studies aim to reduce hemophilia-related complications and improve quality of life in patients with hemophilia and inhibitors. Inhibitors are currently the most serious complication of hemophilia care and result in increased bleeding, as well as higher healthcare utilization and cost.

The first study, ATHN 8 – PUPs Matter, is an ongoing observational study for previously untreated patients (PUPs) with moderate and severe hemophilia (A or B). It is the first national cohort study to collect data on very young children. The primary goal is to determine the percentage of PUPs with confirmed inhibitors within the first 50 days of receiving factor. This will provide the basis for ongoing clinical studies to improve the outcomes in these high-risk children. Conducted in collaboration with the American Thrombosis and Hemostasis Network, Children's Mercy Hospital and the Blood Center of Wisconsin, the study seeks to enroll 250 newly diagnosed children. Learn more.

The second study, INITIATE (Individualized ITI Based on FVIII Protection by VWF) is a randomized, controlled, double study of immune tolerance induction (ITI) therapy for the treatment of hemophilia A FVIII inhibitors. ITI therapy in the study involves daily factor replacement with Wilate [von Willebrand Factor/Coagulation Factor VIII Complex, Octapharma, USA] to tolerize the immune system to FVIII. Participants will be randomized to one of two arms. In the standard arm, participants will be assigned randomly selected batches of Wilate. In the investigational arm, participants will be assigned a batch of Wilate based on a novel laboratory assay. The primary endpoint is the time to inhibitor resolution. The study seeks to enroll up to 120 pediatric and adult patients with hemophilia A and FVIII inhibitor. Learn more.

The last study, "A Study of Fitusiran (ALN-AT3SC) in Severe Hemophilia A and B Patients with Inhibitors," evaluates a synthetic interfering RNA product that reduces antithrombin production to rebalance the coagulation system. Fitusiran is given once monthly as a subcutaneous injection to prevent bleeding. Patients will be randomized to receive the new drug or continue receiving their current factor treatment. They will be followed for nine months to assess bleeding and side effects. Learn more.

## INNOVATIONS

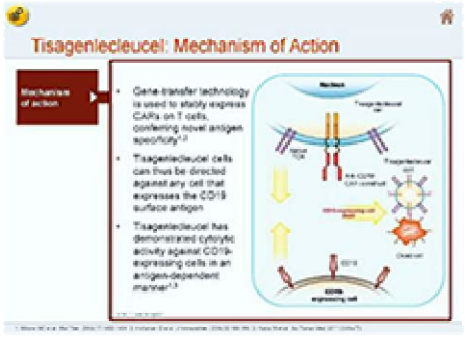
# Rady Children's certified as CAR T-cell treatment center

Rady Children's Hospital has become one of approximately 40 treatment centers certified to provide Kymriah (tisagenlecleucel), the first Food and Drug Administration-approved CAR T-cell treatment.

The gene therapy, made by Novartis, is specifically approved for the treatment of patients up to 25 years of age with B-cell precursor acute lymphoblastic leukemia (ALL) that is refractory or in second or later relapse. The FDA requires special certification for all sites offering the treatment to confirm that the institution is qualified to handle serious adverse reactions, should they occur.

Kymriah employs a combination of cellular therapy, gene therapy and immunotherapy to target and destroy cells expressing the CD19 protein. The protein is expressed on B cells and B-cell precursors but not on bone marrow stem cells or other tissues. In early multicenter clinical trials, 83 percent of patients with refractory or multiply relapsed B-ALL were able to achieve remission within three months of Kymriah infusion.

Patients are treated by collecting their own T-cells using leukapheresis. The cells are genetically modified to target CD19, and the new therapeutic cells are reinfused to the patient. Deborah Schiff, M.D., a member of Rady Children's Blood and Bone Marrow Transplantation Program and a clinical professor of pediatrics at UC San Diego School of Medicine, is overseeing the treatment, and patients will be managed by this BMT team.




Click to enlarge

Due to the high cost of the therapy, Novartis is providing information on financial assistance as well as patient support programs through its KYMRIAH CARES program. Services may include transportation, lodging and healthy meals.

Approximately 3,100 patients age 20 and younger are diagnosed with ALL each year, according to the National Cancer Institute. In an estimated 15-20 percent of patients, the cancer does not respond to standard chemotherapy or returns after initial treatment.

To refer a patient or for more information, please contact Dr. Schiff at dschiff@rchsd.org.