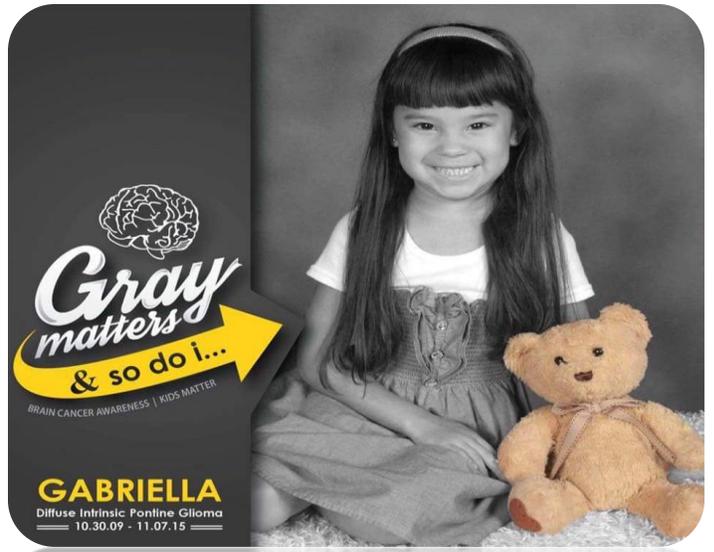
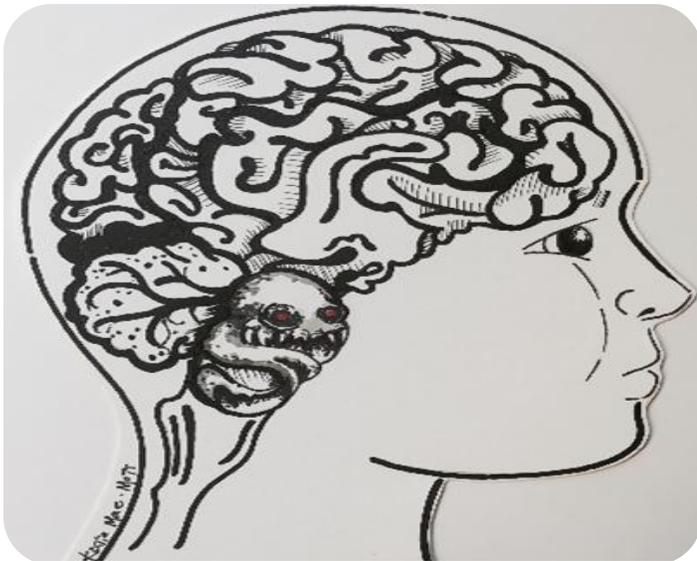


DIPG

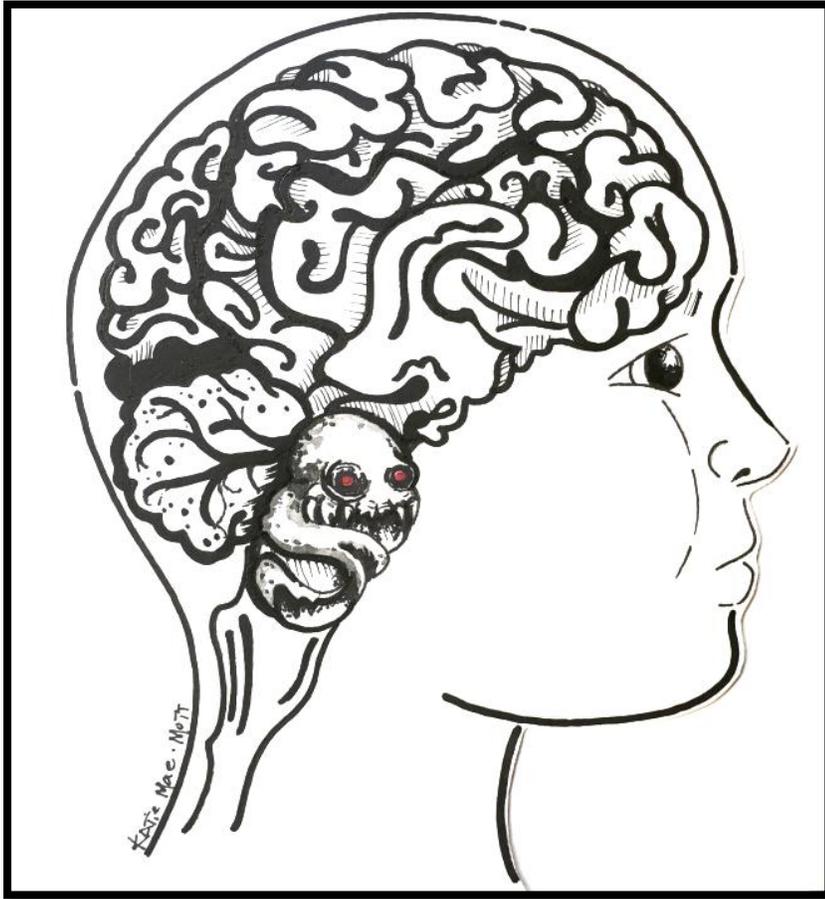


  
**Gray**  
*matters*  
& so do i...  
BRAIN CANCER AWARENESS | KIDS MATTER  
**GABRIELLA**  
Diffuse Intrinsic Pontine Glioma  
10.30.09 - 11.07.15

## Diffuse Intrinsic Pontine Glioma (DIPG) Awareness Project

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## The Monster



This is a story about a monster. A monster that's been allowed to wreak havoc and strike terror in the hearts of even the mightiest of the mighty. It preys on children... upwards of 300 per year in the United States. This monster has a name: Diffuse Intrinsic Pontine Glioma (DIPG)... a malignant, inoperable brain tumor, terminal upon diagnosis. When it attacks, it kills swiftly and brutally. It takes no prisoners. This monster has been known for decades. But what's been done to slay this monster? Virtually nothing in 50 years. "Why," you ask? Because it's a "rare" disease, they say. "No incentive," they say. But "rare" is a relative term and the facts stand for themselves:

- Cancer is the #1 disease killer of children in the United States (Chow, 2014)
- Brain tumors are the leading cause of death from childhood cancers (The Lyla Nsouli Foundation, 2016)
- DIPG is the 2<sup>nd</sup> most common malignant brain tumor diagnosed in children (Johung & Monje, 2012)
- DIPG is the leading cause of death from malignant brain tumors in children (Johung & Monje, 2012)

DIPG has been defined as the worst cancer, located in the worst place. Children die an excruciating death while those with the power to effect change remain virtually unresponsive. They allow these children to deteriorate and regress into beings that become almost unrecognizable. Their rationale hinges upon numbers. Not enough children are unlucky enough to develop DIPG to warrant investment of research dollars. Little consideration is taken into account regarding the severity of this disease, the age of its population, or the years of potential life lost (YPLL) when determining research funding. They are content with relegating fundraising activities to grieving families who, unlike them, will do whatever is necessary to fund crucial

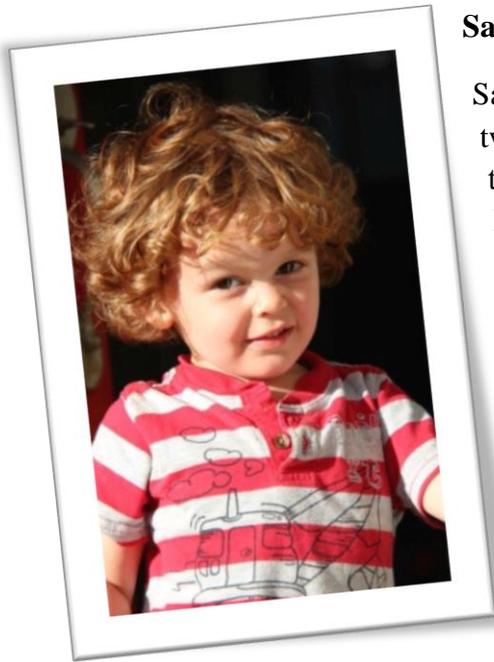
research for our most vulnerable population. *It's a sad state of affairs when the National Cancer Institute and the American Cancer Society direct 4% or less of their research dollars to childhood cancers. And that's not just for DIPG, that's for ALL childhood cancers combined. Children with DIPG fare no better with the pharmaceutical companies. They focus their oncology efforts on the more profitable adult population and are not adequately incentivized to develop less toxic pediatric-specific drugs.* It's time to change the paradigm and commit to developing effective treatment options for DIPG...the worst cancer, located in the worst place.

### **SOME OF THE HEROES...**



**Isaac Jude Palone**

Isaac Jude Palone lived and breathed the hoops. During his “honeymoon” phase after radiation, Isaac went back to playing the game he loved. One afternoon, Mike Gobin, Isaac’s former coach and teacher noticed Isaac playing basketball with other neighborhood kids on the school blacktop and joined in. He marveled at what a role model Isaac had become to the younger players on the court. This encounter fostered the development of a student group at Isaac’s former elementary school whose focus was to promote positive leadership. One of the leaders in this newly formed group was a child who played on the court that day with Isaac. Isaac’s former coach, along with this child and four other children were instrumental in garnering community support for Isaac and his family during their time of need.



### Samuel Lee

Samuel Lee, Curious George devotee and best big brother to twin sisters Ada and Mae, was diagnosed with not one, but two rare diseases. Sam was diagnosed with not only Ollier's Disease, a skeletal disorder requiring multiple corrective surgeries, but also with DIPG, a terminal upon diagnosis brain cancer. Near the end, when Sam's health was failing, his mom leaned in close and asked him what the family could do to make him happy. Sam looked at his mom with surprise and said, "I am happy, Mom." This little boy also had a rare gift...that of comforting others, even at the tender age of 5.



### Gabriella Torres

Five-year-old Gabriella was determined to attend kindergarten...no matter what. Despite being paralyzed and wheelchair bound, this little girl got to start school. Gabriella thoroughly enjoyed attending kindergarten because she got to experience what it was like to be a regular kid.

Gabriella was a girl who knew how to smile. DIPG tried to rob her of her smile, but failed!



## Joey Fabus



**Christmas 2014.** This letter was written to Santa by eight-year-old Joey Fabus. It looks like a typical letter written by a child asking for the usual toys, but if you look closely, you will see a special request: “I want to be able to walk again.” Joey simply wished to get better, but DIPG is first a thief and then a murderer. These children remain cognitively intact (i.e., fully aware) while this disease robs them of their ability to walk, talk, see, hear, chew, swallow, and eventually... even breathe.

### Joey Fabus: Honorary Police Officer



Joey had a wish to become a police officer one day. When the local police department learned of Joey’s wish, they rallied around him and his family and made it happen. Joey met with the Chief of Police and was issued a custom-made uniform. He was sworn in and after the taking the police officer’s oath, he went out on patrol. Joey cherished every moment that day. Thank you to the Bethel Park Police Department for making this little boy’s wish come true.



### Chad Carr

Chad Carr was born into a Michigan dynasty. His dad, Jason was a UM quarterback, his grandfather, Lloyd Carr, a former UM coach, and his other grandfather, Tom Curtis, a former UM safety. Those who live in the Midwest know that as college rivalries go, it doesn't get more intense than the one between University of Michigan and Ohio State. When Chad entered hospice care in November 2015, the rivalry between the two opposing basketball teams was put aside and they came together to organize a spectacular holiday light display at the Carr home for an early

Christmas. Chad's story has been an inspiration and according to his maternal grandfather, "although Chad did not get his miracle, he will be part of the cure." Chad's mom, Tammi, took to social media and chronicled his journey. His story galvanized thousands of ChadTough Champions who are in it to win it when it comes to defeating this monster (aka, DIPG).

### Michael Mosier with his sister, Lila

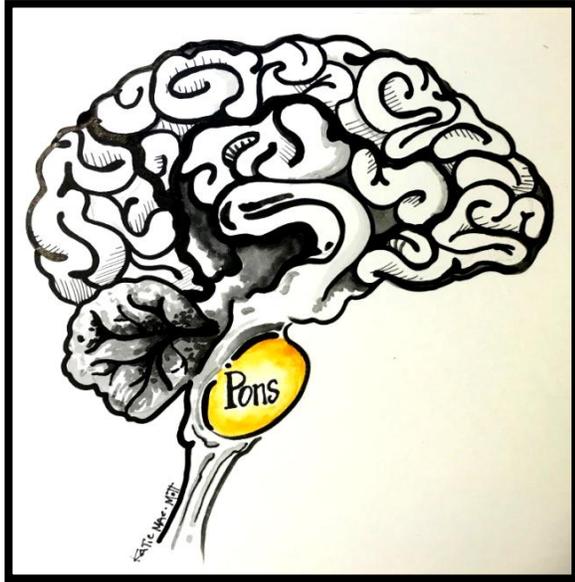


Michael Mosier was diagnosed with DIPG at the beginning of kindergarten. During his illness, Michael created a daily "to do list". This list ran the gamut, from going to school to snapping Legos together. As his disease progressed, rather than complaining, Michael would adapt to his ever-changing status by looking for new activities he could enjoy. During his heroic battle, Michael became

actively involved in fundraising and was able to generate well over \$100,000 in donations for pediatric brain tumor research. Michael was so determined that even in his final days when he could no longer eat, move, or speak he still wanted his teacher to come to his home to go over his classroom lessons. The Michael Mosier Defeat DIPG Foundation is working diligently to check off the final item on Michael's "to do list": **DEFEAT DIPG**. Let's help Michael realize his goal so that no other child has to fight a disease as merciless as DIPG.

## Diffuse Intrinsic Pontine Glioma (DIPG): Definition

DIPG is a highly aggressive, inoperable, malignant brain tumor that forms from the glial (supportive) cells of the brain (Dana-Farber/Boston Children's, 2016). The tumor grows in the area of the brainstem, called the pons, a critical area of the brain which performs the following functions:



Regulates vital body processes, such as respiration and consciousness;  
Houses cranial nerves that facilitate essential functions (e.g., eye movements, chewing, swallowing, facial expressions, hearing, and balance);  
Assists in the transmission of messages between various structures of the brain and the spinal cord.  
(Healthline Medical Team, 2015)

*In plain language...if you see, hear, chew, swallow, walk, talk, sleep or breathe, you are, in one way or another, using the pons area of your brain.*

## Incidence

Each year in the United States, upwards of 300 children are diagnosed with DIPG. This disease strikes in the heart of childhood, typically affecting children between the ages of 5 to 9 (Dana-Farber/Boston Children's, 2016). Diffuse Intrinsic Pontine Gliomas account for approximately 10-15% of brain tumors in the pediatric population, but constitutes 80% of brain tumor-related death (Johung & Monje, 2012; The Lyla Nsouli Foundation, 2016).

## Diagnosis

DIPG is typically diagnosed based on clinical presentation (i.e., signs and symptoms) and radiologic findings on magnetic resonance imaging (MRI) studies. Although stereotactic tumor biopsies are not routinely obtained as the standard of care in the United States, they are becoming more commonplace due to the advances in the surgical ability to safely biopsy brainstem tissue. Access to tumor tissue (i.e., biopsy and/or postmortem tumor specimens) is providing important information about what makes these tumors "tick". The availability of tumor tissue allows researchers to now define the tumor in biologic terms rather than just by radiologic findings and symptomatology, and could conceivably guide individualized treatment regimens in the future (Johung & Monje, 2012; Kieran, 2015; Warren, 2012).

## Signs and Symptoms

- Rapid onset: Typically diagnosed within a month of the onset of symptoms. The symptoms progress rapidly and are related to either direct invasion by the tumor of the vital brainstem structures, or by the expanding tumor and/or its resulting edema (i.e., abnormal accumulation of fluid) causing dysfunction or compression of areas in and around the pons (Johung & Monje, 2012).
- Ocular disturbances (including abnormal eye alignment, causing double vision; difficulty controlling eyelid movements, blurred vision) (St. Jude Children's Research Hospital, 2016).
- Hearing issues, including deafness (Zhou, 2014).
- Facial weakness; facial asymmetry (St. Jude Children's Research Hospital, 2016).
- Difficulties with chewing and swallowing (Zhou, 2014).
- Arm and leg weakness; sensory abnormalities; partial paralysis.
- Gait disturbances, loss of coordination, or speech issues (indicating encroachment of the cerebellum by the tumor) (Johung & Monje, 2012).
- Obstructive hydrocephalus (i.e., abnormal accumulation of cerebrospinal fluid [CSF] in the ventricles of the brain) is present in up to 20% of children at diagnosis and indicates obstruction to the flow of CSF by the expanding tumor (DIPG Registry, 2014).
- Nausea and vomiting related to brain edema or hydrocephalus (Zhou, 2014).

*It is important to note that cognitive abilities remain intact, meaning the child is fully aware of the sensory and/or motor losses.*

## Prognosis

DIPG is one of the most devastating pediatric malignancies:

- Median survival rate is 9 months from diagnosis
  - 90% of these children will die within 2 years of diagnosis
  - 5-year survival rate is <1%
  - No cancer has a worse prognosis
- (Johung & Monje, 2012)

## Management Paradigm

- **Surgical Options:** Surgical resection is not a viable option to treat DIPG because the tumor infiltrates the part of the brain (i.e., pons) which controls essential bodily functions (Johung & Monje, 2012). Any attempt to remove the tumor would disrupt vital functions such as breathing and it is therefore too risky of a procedure.
- **Radiotherapy:** The standard of care for children newly diagnosed with DIPG is radiation therapy, typically administered 5 days per week over a 6 week timeframe. Radiation therapy is an aggressive, palliative measure that temporarily controls the tumor growth and improves symptomatology in approximately 75% of patients. Studies have demonstrated that radiation therapy extends the overall survival by an average of 3 months (Johung & Monje, 2012).



**Radiation Therapy Head Mask.** This is a picture of eight-year-old **Joey Fabus** getting ready to undergo radiation therapy. Prior to radiation therapy, children are fitted with a plastic molding that resembles a body cast. To help the child stay in the correct position for therapy, they wear a rigid immobilization mask that attaches to the table (Memorial Sloan Kettering Cancer Center, 2016, National Cancer Institute [NCI], 2010). Children may also require sedation to make sure they do not move during radiation therapy.

- **Steroids:** Steroids are widely prescribed throughout the course of the disease in an effort to reduce the swelling around the brainstem associated with the tumor and/or radiation therapy (radiation treatment frequently produces an inflammatory response, which can temporarily exacerbate signs and symptoms) (Dana-Farber/Boston Children's, 2016). Steroids are associated with a number of side effects including an increased susceptibility to infection, insomnia, mood changes, hunger, weight gain, fluid retention, blood pressure elevations, and glucose instability. Steroid use is typically clinically driven (e.g., symptomatic swelling) and should not be prescribed prophylactically as the side effects are potentially significant and could adversely affect quality of life (Fisher & Monje, 2010).



This picture of eight-year-old **Ryan Mott** demonstrates some the side effects related to steroid use. What Ryan experienced related to DIPG and its management was unacceptable. He gained weight, developed diabetes, and high blood pressure. These children need less toxic, more effective treatment options.

- **Clinical Trials:** There have been more than 250 clinical trials (i.e., research studies) over the last 35 years involving patients with DIPG and none demonstrated an improved survival benefit. Clinical trials involving the administration of chemotherapeutic agents were unsuccessful related to numerous factors. Studies demonstrated that anti-cancer drugs could not effectively penetrate the blood-brain barrier (i.e., a protective, highly impermeable barrier designed to prevent the passage of potentially harmful substances into the central nervous system) to reach the tumor (Zhou, 2014). It is also important to note that clinical trials essentially took place at a time when biopsies of the pons were considered unethical and autopsies to obtain tumor tissue were typically not done. Limited tissue availability for study attributed to the lack of understanding of the biology and pathophysiology of DIPG, therefore, most clinical trials were based on the assumption that pediatric gliomas behaved similarly to adult malignant gliomas found in the upper part of the brain, and not in the pons (Kieran, 2015).
- **The Future:** Presently, there are numerous clinical trials taking place at major medical centers across the United States and in other countries. This is due in part to the advancements in neurosurgical technique; acquisition of tumor tissue (i.e., biopsy and/or postmortem) for research, and through funding that relies almost exclusively on philanthropic resources. Numerous major medical centers, researchers and philanthropic organizations, foundations and individuals, are working in a collaborative effort in order to realize a shared goal: Defeat DIPG. <https://www.defeatdipg.org/current-research/>

## Funding Research



### Jack Demeter

*“If we truly want to cure cancer, we will attend to the very worst ones”*

-Janet Demeter, Jack’s mom.

Pediatric cancer research remains consistently underfunded. According to Williams (2016), there are more than 150 types of childhood cancers, yet pediatric cancer only receives a small part of federal funding (i.e., our tax dollars) from the National Institutes of Health (NIH) and National Cancer Institute (NCI). The NCI directs 96% of its federal funding for research to adult cancers, leaving only 4% for childhood cancers (Chow, 2014; People Against Childhood Cancer [PAC2], 2016). That’s not just for one type of pediatric cancer, that’s for ALL pediatric cancers combined. Even more abysmal, is the funding provided for pediatric cancer research by the American Cancer

Society (ACS). This organization routinely uses children as marketing tools, yet earmarks even less of its donated dollars to childhood cancer research and training than the NCI. Children with cancer are marginalized as evidenced by that fact that funding from the NCI and the ACS is directed toward older populations even though almost 23% of the US population is comprised of children ages 0-17 (Childstats.gov, 2016).

The pharmaceutical industry focuses primarily on developing treatments for older patients because: 1) cancer occurs more frequently in this population, thus increasing their profit margin, and 2) they are not adequately incentivized to develop less toxic pediatric-specific drugs. According to Chow (2014), since January 2000, the Food and Drug Administration has approved 88 new drugs for use in adult cancers, yet only approved 3 drugs for treatment of childhood cancers. It's important to note that as of 2014, the treatments that existed in the 1970's for many childhood cancers have remained essentially unchanged (CURE Childhood Cancer, 2016).

*How many times must it be said that children are not simply small adults before the NCI and ACS listen? Childhood cancers differ from those that affect adults, both in their biology and types (Williams, 2016). Finding solutions for childhood cancers (including DIPG) requires targeted research for targeted cures. It's time to employ a kid-centric approach (Chow, 2014).*

#### **Rationale for increased funding for childhood cancers:**

- Number of years of potential life lost (YPLL) per child that dies of cancer is upwards of 70 and beyond (PAC2, 2016).
- Incidence rates for childhood cancer have increased by 0.6% per year since 1975 (ACS, 2014).
- 1 in 285 children in the US will receive a cancer diagnosis before the age of 20 (ACS, 2014).
- “Etiologic differences and genomic variations within even the same cancer type suggest that the childhood and adult cancers may be discrete diseases. These observations warrant a specific focus on pediatric cancers” (NCI, 2013, p.2).
- Drug development for pediatric cancer patients has lagged behind its adult counterpart for decades (NCI, 2013).
- Late effects of cancer treatment: Survivors of pediatric cancers have increased morbidity and mortality rates related to their “cure,” including chronic illnesses, secondary cancers, and early death (NCI, 2014). It is important to note that about 1 in 530 adults between the ages of 20 and 39 have survived a childhood cancer (ACS, 2014).

**Joey Fabus**



## Legislative Updates

### **H. R. 2019: Gabriella Miller Kids First Research Act**

Sponsor: Rep. Gregg Harper (R-MS3)

Introduced to Committee: May 16, 2013

Dec 11, 2013: Passed House

Mar 11, 2014: Passed Senate

Apr 3, 2014-Enacted-Signed by the President

Act eliminates taxpayer financing of political party conventions and redirects the funding to pediatric medical research (\$126 million over 10 years) (govtrack.us). Full funding for the Gabriella Miller Kids First Act remains intact for its second consecutive year: 2016.

### **H. R. 3381: Childhood Cancer STAR Act**

Sponsor: Rep. Michael McCaul (R-TX10)

Introduced to Committee: Jul 29, 2015

### **S. 1883: Childhood Cancer STAR Act**

Sponsor: Sen. John “Jack” Reed (D-RI)

Introduced: Jul 29, 2015

Referred to Committee: Jul 29, 2015

The “Childhood Cancer Survivorship, Treatment, Access, and Research Act of 2015” (Childhood Cancer STAR Act) advocates the discovery, accelerated expansion and accessibility of promising childhood cancer treatments (also for other purposes). Status: Not enacted (govtrack.us).

### **H. RES. 586: DIPG Awareness Week**

Sponsor: Rep. Steve Knight (R-CA25)

Introduced: Jan 13, 2016

Referred to Committee: Jan 13, 2016

Expresses support for designation of the fourth week in May as “DIPG Awareness Week”. Goal of resolution is to raise awareness and promote research for diffuse intrinsic pontine glioma (DIPG) and pediatric cancers as a whole. Status: Not enacted. (govtrack.us). This resolution calls for the NCI to elevate the consideration of low-survival-rate cancers and years-of-life lost when determining research grants.



### **H. R. 5858: RACE for Children Act**

Representatives: Michel McCaul(R-TX10); G.K. Butterfield (D-NC01); Chris Van Hollen (D-MD08); Sean Duffy (R-WY07)

### **S. 3239: RACE for Children Act**

Senators: Michael Bennet (D-CO); Marco Rubio (R-FL)

Introduced July 14, 2016

Referred to Committee: July 14, 2016

Bill amends the Federal Food, Drug, and Cosmetic Act to support the development of promising drugs to treat pediatric cancers. This bill updates the Pediatric Research Equity Act (PREA) (govtrack.us).

### **A Parent's Perspective by Janet Demeter**



“Jack-Jack”, Jack, aka James-William Gregory Demeter

Jack was born August 30<sup>th</sup>, 2008; my little Saturday night man. His sister Sophie-Marie was just 2-and-a-half at the time, so it was a wonderful time of handfuls! Just some 5 weeks after he was born, we lost everything we had in a wildfire, October 12, 2008—the “Marek” fire, in Lakeview Terrace, Kagel Canyon, and Lopez Canyons in the San Fernando Valley. It was an ominous experience. Jack was diagnosed with DIPG October 28<sup>th</sup>, 2011; he had just turned three. He was the love of my life.

Jack knew his polygons, parallelograms, trapezoids, counted into the hundreds, and was working on his alphabet in phonetic sounds, and in 3 languages. He loved music (he had a tiny violin) and musical instruments. We got him into a

preschool program after radiation treatment; they loved him there, and he was so excited to go to school! He loved everything about it, and would say, “I’m here!” each time he arrived. When he got on the bus, he’d say, “you’re P, for Patti! You’re R, for Rose, and you’re M, for Michael!” He would greet everyone in this way on the bus.

Two weeks before he died, he was visited by “two white ghosts”, that he later said were angels because they had wings. They joked with him and made him laugh. They told him that he would have to go with them soon, because he had something important to do. I was beside myself. After finally struggling with basic body functions, he passed away Sunday, July 30<sup>th</sup>, 2012 at 6:40am, and went with the angels. He showed himself to us in many ways in the days recent to his death. He still lets me know he is there with heart rocks of all sizes, and sometimes we play as daisies on a hill somewhere in the clouds of my mind. I don’t know how to go through the rest of my life without him but to think that some of us are privileged to meet, for a short time, a special

guardian angel in a person. I hold on to my gratitude for this, and remember when I can to take life one moment at time; that each one is filled with God, and Jack—now part of the fabric of the Universe again.

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