

2019-20

CANCER CARE
ANNUAL REPORT



Focus on Renal Tumors



Children's Mercy
KANSAS CITY

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24 MEET
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WELCOME



“Cancer, we now know, is a disease of the genes. In few other human diseases is it so critical to have the most advanced genomic capabilities readily available.”

This year’s Children’s Mercy Cancer Center Annual Report focuses on tumors that arise in the kidney and illustrates three important areas of focus that a childhood cancer center must possess in this new age of medicine.

First, four of the five tumors that make up the vast majority of childhood kidney cancer rarely, if ever, occur in adults. These are uniquely childhood cancers. The fifth type of cancer that occasionally is seen in older children is the primary kidney tumor in adults, yet itself is a unique subtype less frequently seen in adults. Few circumstances of tumors arising from an organ in our bodies illustrate better the dramatic difference between childhood and adult cancers.

Second, this difference emphasizes the need to have the expertise in childhood cancer readily present as closely coordinated multispecialty care between the pediatric oncologists and the many associated pediatric subspecialists, including surgeons, radiologists, radiation therapists, pathologists and nephrologists, just to name a few, who are experienced in treating childhood cancer.

It is so critical that these disciplines be present in a child’s multidisciplinary team. This team approach provides these patients with the best opportunity for a successful outcome, defined as not only a cure for the child’s cancer, but a treatment approach that maximizes the child’s quality of life after cancer, life intended to last at least another 80-90 years.

Approaching the child with this belief in mind has such great ramifications for the child and family. Ensuring that in the years that follow, specific to the cancer and its therapy, are monitored closely by experts in the long-term surveillance of childhood cancers ensures the child’s ability to not only survive their cancer, but to thrive, living life to the fullest.

Third, and finally, our brief dive into the world of childhood kidney tumors further illustrates the rapid incorporation of cancer genomics and host genomics for diagnostic improvements, prognostic and therapeutic improvements, and family predisposition determination and monitoring. Cancer, we now know, is a disease of the genes. In few other human diseases is it so critical to have the most advanced genomic capabilities readily available. Incorporating these three critical elements – pediatric focus and expertise, acute and long-term vision, and advanced genomic expertise – children with cancer of the kidneys have seen tremendous advances in their cure and their ability to live full and happy lives for years to come.

We are excited to show you in the pages that follow that these critical elements of care and discovery are here at Children’s Mercy, and are provided daily to our children and their families who place their faith in us.

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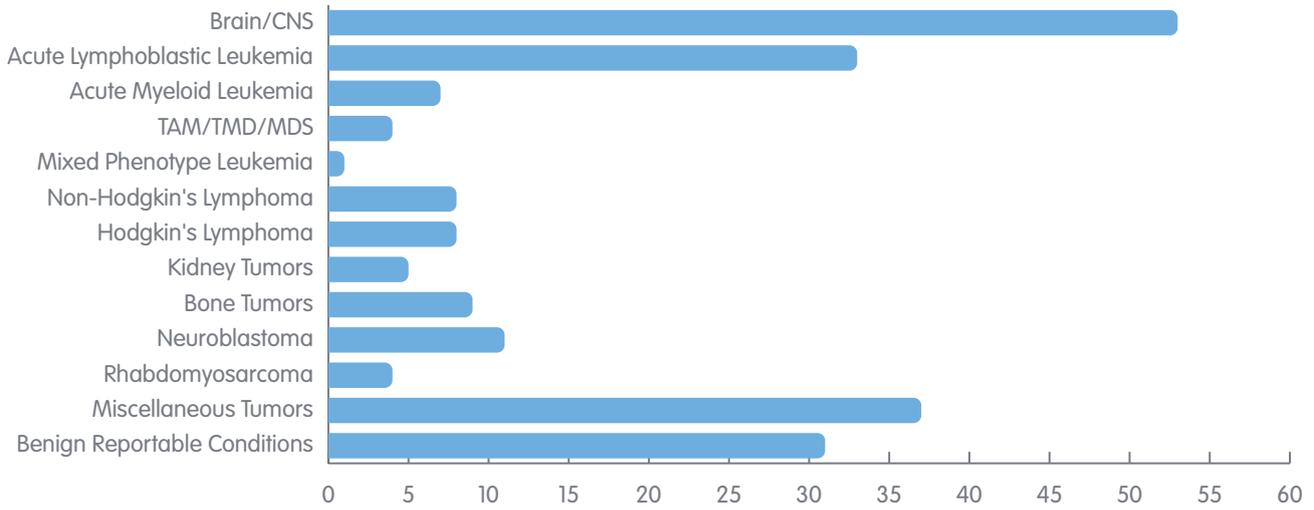
CANCER REGISTRY REVIEW 2019

The Cancer Registry at Children's Mercy Kansas City plays a vital part in the surveillance of cancer in our pediatric population. The Cancer Registry is a HIPAA-compliant confidential database comprised of malignant cancers, benign brain tumors and other specified benign tumors. The database is operated under the guidance of the Cancer Care Committee. Data collected, which includes diagnosis, treatment, recurrence and survival, is standardized for state and national comparisons.

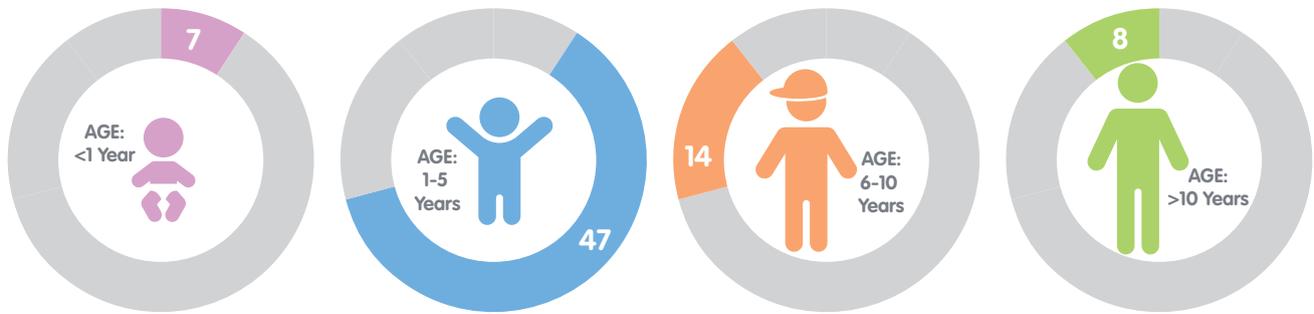
Following each patient's cancer status is a very important part of Cancer Registry data collection. Knowing outcomes of each cancer patient can assist care providers with determining best treatment methods and long-term effects of cancer treatment. Therefore, follow-up letters inquiring about a patient's cancer status are sent out yearly to patients not seen in our facility. Parents and older patients are encouraged to contact the registry by secure email at cancerregistry@cmh.edu to discuss follow-up.

During 2019, the Cancer Registry added 211 patients to the database. Of these patients, there were 180 patients who were diagnosed with malignancies and benign central nervous system tumors. There were 31 patients added to the registry as having benign reportable conditions. These conditions are collected at the request of the Cancer Care Committee for surveillance purposes and are not required to be reported outside our facility. Please see the frequency by diagnosis chart for a breakdown of cancers.

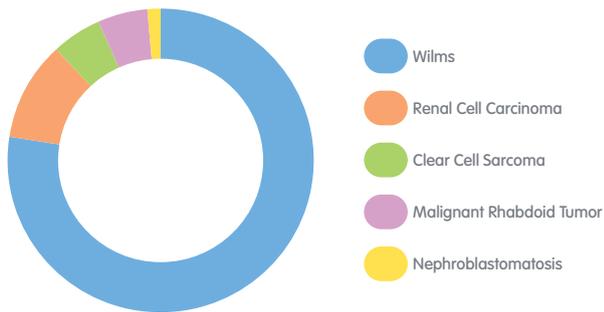
FREQUENCY OF DIAGNOSIS BY DISEASE TYPE - 2019 PATIENTS



RENAL TUMOR PATIENTS BY DIAGNOSIS 2010-2020



RENAL TUMORS DIAGNOSED 2010-2020*

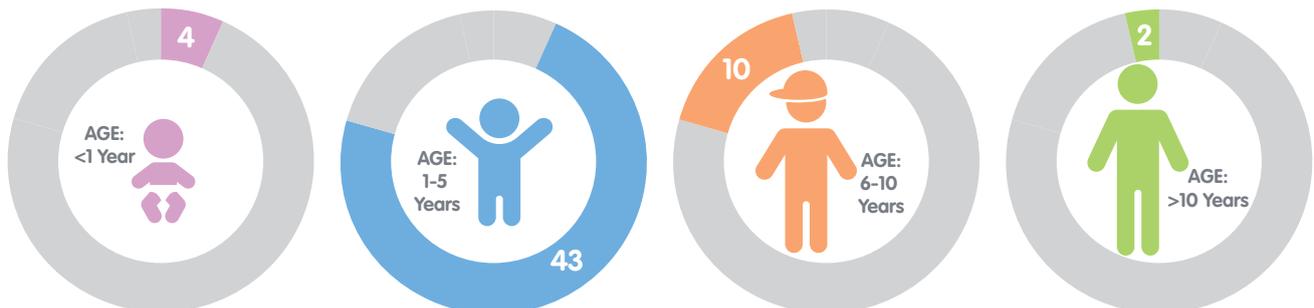


WILMS PATIENTS BY STAGE DIAGNOSED 2010-2020



*Mesoblastic nephroma is considered a benign diagnosis for the purpose of tumor registries; thus it is not included in these diagnoses for our annual report. It should still be considered as a possible diagnosis in children less than 1 year of age with a renal mass.

WILMS PATIENTS BY AGE DIAGNOSED 2010-2020



RENAL TUMORS

The overarching story of the fight against pediatric cancer over the last 60 years has been one of frequent triumphs against common cancers, combined with significant though not uniform progress against other malignancies, while still other diseases have remained stubbornly resistant to conventional therapeutic options. Along the way, much has also been learned about the important burdens borne by survivors of childhood cancer and the need to mitigate those burdens by reducing treatment intensity where possible. Perhaps in no group of childhood cancers is this story better illustrated than in the significant progress and remaining challenges in treating childhood and adolescent renal tumors.

Approximately 7% of childhood and adolescent malignancies arise from the kidney and include Wilms tumor (also known as nephroblastoma), renal cell carcinoma, clear-cell sarcoma of the kidney, malignant rhabdoid tumor, and congenital mesoblastic nephroma. The vast majority of pediatric renal tumors are Wilms tumor, though congenital mesoblastic nephroma is more common in the first month of life and renal cell carcinoma becomes more common in older adolescents. Clear-cell sarcoma of the kidney and malignant rhabdoid tumor remain rare entities, but continue to pose important challenges, especially when advanced or metastatic at diagnosis.



Joel Thompson, MD

Wilms Tumor

First definitively described by Dr. Max Wilms in 1899, Wilms tumor overall stands as one of the great success stories in pediatric oncology. Improvements in surgical techniques, utilization of radiation therapy, and the use of risk-adapted chemotherapy has led to survival rates above 90% for the majority of Wilms tumor patients. About 650 new cases are diagnosed in the United States each year, with the most common presentation being an abdominal mass which may or may not be painful. Microscopic or gross hematuria can often be seen, and hypertension occurs in over 25% of patients. Occasionally, the tumor can spread through the renal vein, into the inferior vena cava, and even into the right atrium. Spread can also occur to lymph nodes, lungs, liver, or (rarely) bone, bone marrow, or the brain.

An ultrasound is often the first imaging study obtained (often by a referring provider), and definitive work-up consists of a CT of the abdomen to further define the mass and to examine whether vascular invasion has occurred. A CT of the chest is also necessary to evaluate for pulmonary metastatic disease. Evaluation of blood pressure is imperative, and aggressive management (if needed) is indicated. Initial laboratory work includes a complete blood count (as microscopic hematuria can lead to iron deficiency anemia), serum chemistries (including renal function tests), liver function tests, and coagulation assays.

In the United States and Canada, initial therapy consists of radical nephrectomy with adequate lymph node sampling (not sampling or under-sampling the regional lymph nodes has been associated with worse survival, likely due to under-staging of the patient).

Although contraindications to upfront nephrectomy exist (including tumor thrombus in the IVC or bulky pulmonary metastatic disease making anesthesia unsafe), the majority of renal tumors can be safely resected prior to any systemic therapy, allowing for complete and accurate diagnosis, staging and pathologic evaluation. Treatment, including chemotherapy and possibly radiation therapy, then proceeds according to the patient's stage, histology type, and several genetic and molecular factors. Combinations of vincristine and dactinomycin form the backbone of Wilms tumor chemotherapy, with the addition of other agents (including doxorubicin, cyclophosphamide, etoposide, and carboplatin) for more advanced or metastatic disease, for those with anaplastic histology, or for those with loss of genetic material (loss of heterozygosity) at specific locations on chromosomes 1p and 16q. Radiation therapy is necessary to the local tumor bed for those with stage III disease, as well as to any sites of metastatic disease. Fortunately, if patients with metastases only to the lungs have a complete radiographic response in the lungs after six weeks of chemotherapy, lung radiation can safely be avoided in most cases.

An important consideration in the work-up and management of children with Wilms tumor is determining whether an underlying genetic syndrome is present. Up to 10% of Wilms tumor patients have an underlying syndrome such as WAGR, Beckwith-Wiedemann, or Denys-Drash syndromes which predispose them not just to unilateral Wilms tumor, but also to bilateral disease (which can be present at diagnosis in 5-10% of all Wilms tumor patients). For these patients, the therapeutic paradigm shifts somewhat based on recently published data from the Children's Oncology Group (or COG, the largest pediatric oncology

consortium in the United States and Canada), with pre-operative chemotherapy utilized to facilitate removal of the tumors while sparing as much healthy renal tissue as possible.

Despite the general success in curing Wilms tumor, important questions still remain. Many patients with low-stage disease and a lack of poor biologic risk factors can likely be spared exposure to either anthracycline chemotherapy (with the associated long-term risk for cardiac dysfunction) and/or radiation therapy while maintaining excellent cure rates. Identifying how to safely decrease therapy intensity is important for minimizing the long-term health burdens for Wilms tumor survivors. Additionally, in the last decade, gain of genetic material at a specific location on chromosome 1q has been found to be present in up to 30% of Wilms tumors and is strongly associated with poorer outcomes overall. Questions remain about how best to use this information to augment therapy in patients with 1q gain. Unacceptably low outcomes persist for patients with anaplastic histology Wilms tumor and advanced or metastatic disease, despite aggressive chemotherapy and radiation therapy. How best to increase the cure rates in these patients continues to be debated. Similarly, outcomes for patients with relapsed Wilms tumor remain poor. Over the next two to three years, open clinical trials from the Children's Oncology Group (COG) will attempt to answer these questions by improving risk stratification techniques to allow safe decreases in therapy for some and vital therapy augmentation for others, while seeking to improve the outcomes of anaplastic and relapsed Wilms tumor by incorporating novel chemotherapy agents into historically successful therapy backbones. The next decade of Wilms tumor therapy developments will be exciting!



Renal Cell Carcinoma

Renal cell carcinoma, though uncommon in children less than 15 years old, still accounts for over 5% of pediatric and adolescent renal malignancies and is therefore the second most common renal cancer in pediatrics. Work-up, staging, and treatment of pediatric renal cell carcinoma has historically relied on the application of adult renal cell carcinoma recommendations to children and adolescents. It is only the last 15 years that the uniqueness of pediatric renal cell carcinoma has become more apparent.

It is now clear that there are significant histologic and biologic differences between pediatric and adult renal cell carcinoma. In particular, the most common type in pediatrics (“translocation-associated renal cell carcinoma”) is characterized by a genetic fusion involving the TFE3 gene on chromosome Xp11.2 with one of many possible partners. Additionally, about 25% of pediatric renal cell carcinomas do not clearly fit into the clear cell or papillary subtypes that comprise the majority of adult renal cell carcinoma.

These and other biological insights are leading to questions about the applicability of adult renal cell carcinoma treatment recommendations to pediatric patients. Historically, treatment has consisted of partial or radical nephrectomy with lymph node dissection, followed by close observation for those with low-stage disease. Higher stage or metastatic disease has been treated by targeting vascular endothelial growth factor receptor, or VEGF-R (for example, with bevacizumab or sunitinib) or mammalian target of rapamycin, or mTOR (for example, with sirolimus or temsirolimus). Unfortunately, only retrospective reports have been published to demonstrate how effective this approach has been.

Recently, however, collaboration with adult oncology cooperatives has led to the opening of the first prospective, randomized trial for pediatric and adult renal cell carcinoma, with the goal of establishing optimal up-front therapy for advanced stage, metastatic, or recurrent translocation-associated renal cell carcinoma (as noted, the most common subtype in pediatrics). While pediatric renal cell carcinoma has been challenging in the past, the future definitely looks promising.

Clear-Cell Sarcoma of the Kidney

Clear cell sarcoma of the kidney (CCSK) accounts for about 5% of pediatric renal cancers, or about 20 new cases per year in the United States. Historically, it has had a significantly higher rate of relapse than favorable histology Wilms tumor and has required more intensive therapy. CCSK also has a higher rate of metastatic spread to the brain and to the bones than does Wilms tumor, so brain MRI and bone scan or PET/CT are important additional parts of the work-up.

The staging and surgical approach are the same as for Wilms tumor, but diagnosis can be much more challenging, as a number of histologic variants have been reported. Once the diagnosis is made, though, chemotherapy and radiation therapy are both required for a cure. Chemotherapy agents used include vincristine, dactinomycin, doxorubicin, cyclophosphamide and etoposide in varying combinations.

Although cure rates are good for stage I and II CCSK, stage III patients have somewhat lower expected outcomes (73% 5-year event-free survival), and stage IV patients have a dismal prognosis (29% 5-year event-free survival on the most recently published clinical trial). Small numbers make studying this disease challenging, but clearly more work needs to occur to improve outcomes for stage III and stage IV CCSK patients.

Malignant Rhabdoid Tumor

Malignant rhabdoid tumor can occur in many places in the body, but the kidney (rhabdoid tumor of the kidney) and the brain (where it is known as atypical teratoid/rhabdoid tumor) are the most common locations. Malignant rhabdoid tumors in all locations share a common genetic aberration—loss of function of the SMARCB1 gene (though a small percentage instead show loss of the related gene SMARCA4).

This highly malignant tumor is thankfully rare, but unfortunately, about two-thirds of patients present with advanced or metastatic disease. Metastasis can be present in the lungs, lymph nodes, soft tissues, bone and brain, requiring a brain MRI and bone scan or PET/CT to be obtained as part of staging.

Complete surgical resection and radiation are both necessary for treatment of the primary tumor. The addition of extremely aggressive chemotherapy has yielded good cure rates in the small percentage of patients who present with stage I or II disease. Unfortunately, cure rates for stage III or IV disease are dismal (stage IV patients had a four-year event-free survival rate of only about 11% on the most recent clinical trial). A novel medication targeting the molecular pathway, which is activated by loss of SMARCB1, has shown some promise at perhaps improving these cure rates, but clearly this is a cancer that has proven quite resistant to traditional therapies. Further prospective clinical trials are needed to identify better treatment strategies.

Congenital Mesoblastic Nephroma

Congenital mesoblastic nephroma accounts for about 5% of pediatric renal cancers, and more than 90% of cases are diagnosed within the first year of life (and often prenatally). It only rarely occurs beyond 2 years of age. It can be divided into three histologic groups—classic, cellular and mixed. Cellular congenital mesoblastic nephroma frequently harbors a genetic fusion between the ETV6 and NTRK3 genes which appears to confer more aggressive behavior.

Nephrectomy is generally all that is required for treatment of classic, mixed, or stage I or II cellular congenital mesoblastic nephroma. Patients with stage III cellular congenital mesoblastic nephroma may benefit from adjuvant chemotherapy, but exciting new agents targeting NTRK fusions (including NTRK3-ETV6) are increasingly being studied, with one drug now commercially available. These agents hold the promise of extremely effective treatment with significantly reduced side effects for this rare group of patients.

Summary

The battle against pediatric cancer generally, and pediatric renal cancer in particular, is slowly being won, step-by-step, study-by-study, patient-by-patient. Though much work still lies ahead of us, this story is worth being told, which is why we have dedicated this issue of Children’s Mercy Cancer Center Annual Report to the fight against pediatric renal tumors and the inspiring patients, families and professionals on the front lines.

CHASE

the CHAMP

How a Little Boy Defied Big Odds

"Hey mom! You know what $3 + 5$ is?" asks inquisitive 6-year-old Chase Jackman.

"No Chase. What is it?" responds his mom, La Daya Gordon.

"It's 8!" Chase answers.

"Chase loves to count!" La Daya says, smiling. "And he loves to play games. Connect 4. Jenga. PlayStation. He's a goofy, fun-loving kid who gives me like 1,000 hugs a day."

But at just 7 months old, La Daya wasn't sure her baby would live long enough to give her those hugs, or learn to count, or play any games. He was gravely ill, but no one knew it until La Daya noticed his belly looked like it was growing larger and larger.



"I didn't know what was going on, so I took Chase to the Emergency Department at the Children's Mercy Adele Hall Campus. He had been constipated, so I thought that might have something to do with it," she said.



Chase and Mom, La Daya

Doctors weren't sure what was going on either.

"Initially, Chase was seen in the emergency room and was found to have signs of respiratory distress and lymphangioma, a benign lymphatic growth," explained Lindsey Fricke, RN, MSN, FNP-BC, Nurse Practitioner.

Several days later, La Daya brought Chase back to the emergency room. His belly was even larger, and he was sicker.

"Chase wasn't a very big baby, but he looked like he had a basketball in his belly," La Daya said.

Additional imaging confirmed findings consistent with lymphangioma, and Chase was admitted to the pediatric intensive care unit (PICU) to begin treatment with sclerotherapy and medications.

While there, Chase developed a serious condition called abdominal compartment syndrome, and doctors operated, opening his

abdomen to release the pressure building up inside, and leaving his abdomen open to heal.

"That day, doctors gave Chase 72 hours to live," La Daya said. "We probably had 100 family members come to the hospital to support Chase through surgery. We took over the entire waiting room."

Though Chase survived the surgery, he was intubated and in the PICU on a ventilator. In the coming days, doctors continued therapy to shrink the softball-sized tumor they'd

found, but they still weren't sure of the source of the problem.

Troubling Diagnosis

Three weeks later when Shawn St. Peter, MD, pediatric surgeon and Children's Mercy Surgeon-in-Chief, was closing Chase's abdomen, he noticed some suspicious tissue that he collected and sent to the lab.

The lab diagnosed the tissue as a cancerous tumor, and Chase started chemotherapy treatment. But the origin of the cancer remained a mystery.

About one month into treatment, an MRI showed the mass was getting smaller, and it looked like it had originated in the kidney.

"Because his pathology wasn't definitive, the tumor was sent for additional analysis," Lindsey explained. Results determined Chase's cancer was an aggressive tumor called cellular congenital mesoblastic nephroma, which accounts for about 5% of pediatric kidney cancers. More than 90% of cases are diagnosed within the first year of life.

"Our oncologist said Chase was probably born with the cancer, but it often goes undetected because it's so rare," La Daya said.

Aggressive Tumor = Aggressive Treatment

By now, Chase was nearly 1 ½ years old, and had spent months on the hospital's pediatric oncology unit receiving additional cycles of chemotherapy. He also had his left kidney removed during his stay.



Lindsey Fricke, RN, MSN, FNP-BC

After completing treatment, the cancer seemed to be gone.

But just a few weeks after returning home, Chase's stomach looked like

it was getting bigger again. La Daya feared the worst, and she was right, the cancer was back. It was bigger than before—about the size of a football—and it now involved his abdominal cavity and spleen.

After surgery to remove the tumor and his spleen, Chase's oncologist added several weeks of radiation therapy to his treatment regimen, along with the original chemotherapy medications. Fortunately, Chase responded well to the combination therapy, but no one was quite sure what to expect next.

While Chase was sick, La Daya said she considered Children's Mercy their home. "If Chase was in the hospital, I was in the hospital," La Daya said. "I didn't want to leave his side."

Chase even celebrated his first birthday in Children's Mercy. "We had a huge party for him with the doctors, nurses, family and friends," La Daya said.

Lindsey remembers the party well. "Honestly, we weren't sure there would be a second birthday. He was a very sick little boy."

But Chase defied the odds. Today, he's been cancer-free for four years. To be certain he stays healthy, he sees Lindsey and Joel Thompson, MD, pediatric oncologist, in the hospital's Outpatient Cancer Clinic, plus an endocrinologist and a nephrologist.

At his last appointment, he graduated to annual check-ups, and now he is transitioning to the Survive and Thrive Clinic—and that's just what this young cancer survivor is doing!

Follow Me!

During the months and months Chase spent in Children's Mercy, he earned the nickname Chase the Champ, winning the hearts of his doctors, nurses and social media followers.



"When Chase was in the hospital, he would sit at the nurses' station. Everyone just loved him. He was so resilient. He never complained," Lindsey said. "Even now, he doesn't complain, and his smile is just infectious."

While hospitalized, Chase became a bit of a celebrity himself when he got to meet several of the stars involved in the Big Slick Celebrity Weekend, an event that's raised millions of dollars to support the Children's Mercy Cancer Center.

When he was 3 years old, the Make-a-Wish Foundation granted Chase and his family his wish to visit Disneyland. "We've kept that tradition up, traveling about the same time each year to a new location," La Daya said.



And, Chase has become a regular at the annual Walk4Life event, which also supports cancer patients. "Our family and friends all wear their Chase the Champ shirts and walk every year," La Daya said.

Yep! Chase is a popular guy. He's had more than 1,000 shares on Facebook!

Lessons Learned

Throughout Chase's journey, La Daya said she's come to appreciate how fortunate they are that Chase is now a healthy first-grader.

"At one point, doctors told me he might not live 72 hours, and lots of people have reached out to me whose children haven't survived. It's a relief to see how strong Chase is. I've learned about strength and faith along the way.

"And Chase thanks God he has no more cancer," La Daya said. "He has scars on his belly, but to look at him, you would never know all he's been through.

"The doctors and nurses at Children's Mercy were wonderful. We loved everyone here, and still keep in touch with some of the nurses from 4 Henson on social media," she said.

La Daya, Chase and Chase's father, John Jackman, also would like to thank the Hem/Onc team and Lindsey. "We will never forget any of you."

PARTNERS IN THE DIAGNOSIS AND CARE OF PATIENTS WITH RENAL TUMORS

Urology

14

The Pediatric Urology team is dedicated to managing issues related to the urinary tract and genitalia. This includes the management of both benign and malignant renal tumors. Our team works closely with other subspecialties, such as anesthesia, nephrology, oncology, pathology, pediatric surgery and radiology, to determine the ideal timing and surgical approach for renal tumors. Following the latest cancer treatment protocols, we employ traditional open surgeries or minimally invasive approaches, such as cryoablation and laparoscopic procedures.

In children with conditions predisposing them to recurrent benign or malignant renal tumor development, our team offers nephron-sparing surgery. By only removing the tumor and leaving the normal kidney tissue, we can preserve normal kidney function without compromising the child's oncologic outcome. In children who may be exposed to gonadotoxic chemotherapy or radiation as part of their treatment, our team offers fertility preservation counseling for males to help preserve future fertility. We facilitate sperm banking for post pubertal children, or testicular tissue cryopreservation for prepubertal children under a research protocol. Our team has many years of experience dealing with renal tumors. Through collaboration and a multidisciplinary approach, we can successfully treat complex renal tumors with excellent outcomes.

Molecular Genetics

The Molecular Genetics Laboratory is a specialty testing area of the Department of Pathology and Laboratory Medicine. Together with the Genomic Medicine Center, it helps provide comprehensive molecular genetic assessment for patients with renal tumors. The Molecular Genetics Lab can perform testing on a range of sample types such as blood specimens, buccal swabs, fresh tissue and tissue that has been fixed in formalin, allowing testing to be done on a wide variety of cases and for nearly all patients. It also offers a wide variety of methodologies to look for genetic changes, including DNA fragment analysis, multiplex ligation-dependent probe amplification, methylation testing and Sanger sequencing. In doing so, it complements the Genomic Medicine Center, which performs whole genome sequencing on paired tumor and normal samples to look for genetic alterations. When present in the tumor (somatic), such alterations can be important for diagnosis, prognosis and therapy. When present in normal cells (germline), such genetic changes can point to cancer predisposition and a heritable cancer syndrome, which has wider implications for the patient and their family.

For patients with renal tumors, looking for both somatic and germline alterations is critically important. Somatic changes in genes such as BCOR, TP53 and VHL can confirm or rule out a diagnosis, give information about prognosis, or point to a targeted therapy. Germline assessment is also needed as a whole host of genetic syndromes are associated with increased risk of developing renal tumors, such as Beckwith-Wiedemann syndrome, WAGR syndrome, DICER1 syndrome, Von Hippel-Lindau syndrome, and Rhabdoid tumor predisposition syndrome. Testing for all of these conditions can be performed through the Molecular Genetics Laboratory and Genomic Medicine Center and, together with the Cytogenetics Laboratory, it is done comprehensively for all patients with renal tumors at Children's Mercy.

Clinical Research

Clinical research is a major piece of the renal tumor success story. Children's Mercy, as a member of the Children's Oncology Group, has been able to add to the research by enrolling patients on both treatment and biology studies. A group of dedicated research professionals within the Division of Hematology/Oncology/BMT ensure that patients get presented opportunities to participate in research that has been reviewed by our institutional ethics board. Studies may be clinical trials offering new treatments, allowing their biological specimens to be submitted for laboratory research, and even studies related to quality of life and survivorship. Over the past four years, we have also been able to build a local repository of renal tumor specimens through our on-site Tumor Bank which includes Wilms tumor, renal cell carcinoma, and rhabdoid cancer of the kidney.

Pathology

Renal tumors are rare and comprise approximately 7% of all malignant pediatric tumors. This is a highly heterogeneous group of tumors, with each type of tumor having its own specific diagnostic modalities, prognosis, treatment, outcomes and association with germline predispositions. Histopathology is the key to establishing the correct diagnosis. Pathologists with expertise in pediatric oncology are essential for the diagnostic evaluation of these rare tumors. Each renal tumor has different histologic features. However, there is considerable overlap in cell type and histologic pattern of different tumors, making the diagnosis difficult to establish, if based on routine histology alone. Therefore, there are multiple ancillary techniques, such as immunohistochemistry, cytogenetic and molecular analysis, that are crucial for the correct diagnosis, prognosis and resulting appropriate treatment. The role of the modern pediatric pathologist is to evaluate all conventional histopathology and all ancillary techniques and synthesize integrated diagnosis.

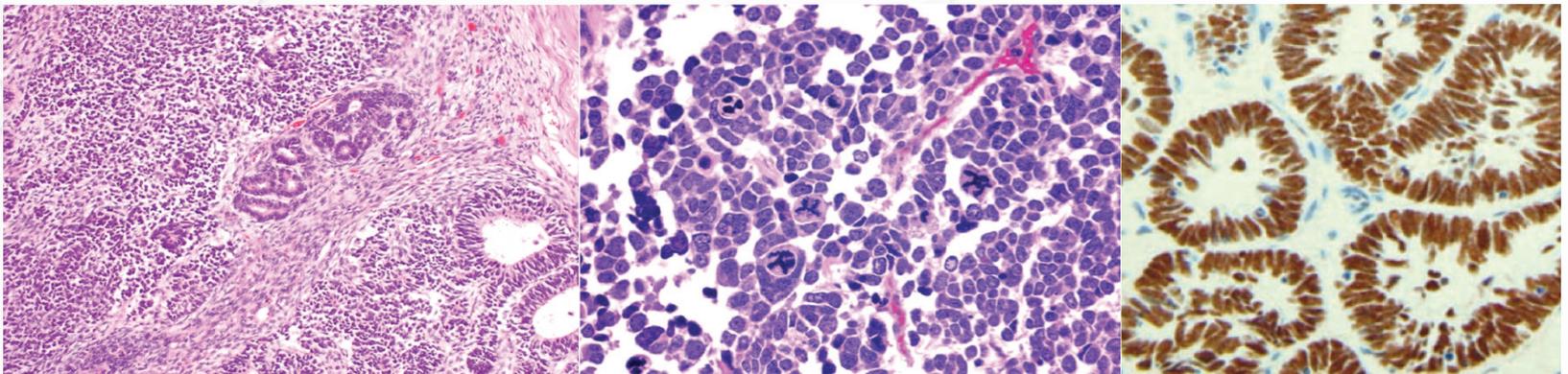
Wilms tumor comprises approximately 90% of pediatric renal tumors, with the remaining types consisting of clear cell sarcoma of the kidney, malignant rhabdoid tumor of the kidney, renal cell carcinoma,

congenital mesoblastic nephroma, and other rare tumors. These tumor spectra include those with low malignant potential (congenital mesoblastic nephroma) to highly aggressive tumors (malignant rhabdoid tumor of the kidney). Thus, showing remarkable intra-tumor histologic and genetic heterogeneity and requiring different treatment. Also, there is an increasing number of pediatric renal tumors demonstrating an association with specific syndromes or diseases, such as Wilms tumor association, with up to 13 different syndromes including Beckwith Wiedemann-syndrome (loss of imprinting at 11p15), Denys-Drash-syndrome (WT1 missense mutations), Li-Fraumeni syndrome (TP53 mutations), and WAGR-syndrome (Wilms tumor, Aniridia, Genitourinary malformations, and mental retardation; microdeletion WT1 and PAX6). The malignant rhabdoid tumor association with Familial Rhabdoid Predisposition syndrome (SMARCB1(INI1) mutation, rarely SMARCA4 mutation), or SDH-renal cell carcinoma association with germline SDH mutations associated with Hereditary Paraganglioma-Pheochromocytoma Syndrome. These highlight the importance of precise pathologic tumor diagnosis, not only for appropriate treatment, but also for genetic counseling.

For histopathologic diagnosis, the pathologist initially utilizes the pattern approach. There are three major histologic patterns that are the basis for the differential diagnoses of any tumor, including pediatric renal tumors: an epithelial, a mesenchymal and an undifferentiated pattern. In Wilms tumors, all three patterns are often present "triphasic pattern," but many Wilms tumors show only one or two patterns or show the other patterns only focally.

Therefore, extensive tumor sampling is required, as well as immunohistochemistry. The most common pediatric renal tumors with an epithelial pattern are Wilms tumor which shows characteristic strong nuclear staining for WT1, as well as lack of staining for CK7, or metanephric adenoma with strong staining for BRAFV600E corresponding to the BRAF mutation. Xp11.2 translocation renal cell carcinomas (rRCCs) typically show large epithelioid cells with copious amounts of eosinophilic cytoplasm and a large eosinophilic nucleolus and positive nuclear TFE3 staining.

Papillary renal cell carcinoma shows strong staining for CK7. The renal tumor with the stromal pattern is clear cell sarcoma of the kidney showing up to nine histologic patterns and specific strong nuclear staining



Triphasic Wilms tumor with primitive blastema, epithelioid component (tubules), and mesenchymal stromal component. The cellular anaplasia (on the left), and positive WT-1 immunohistochemistry (right).

for BCOR as well as CyclinD1. The primitive, undifferentiated pattern of presentation is most common in pediatric renal tumors and may be represented by undifferentiated blastema of Wilms tumor, which shows strong nuclear staining for INI1 as well as for WT1, and malignant rhabdoid tumor with characteristic large nuclei and loss of INI1 staining.

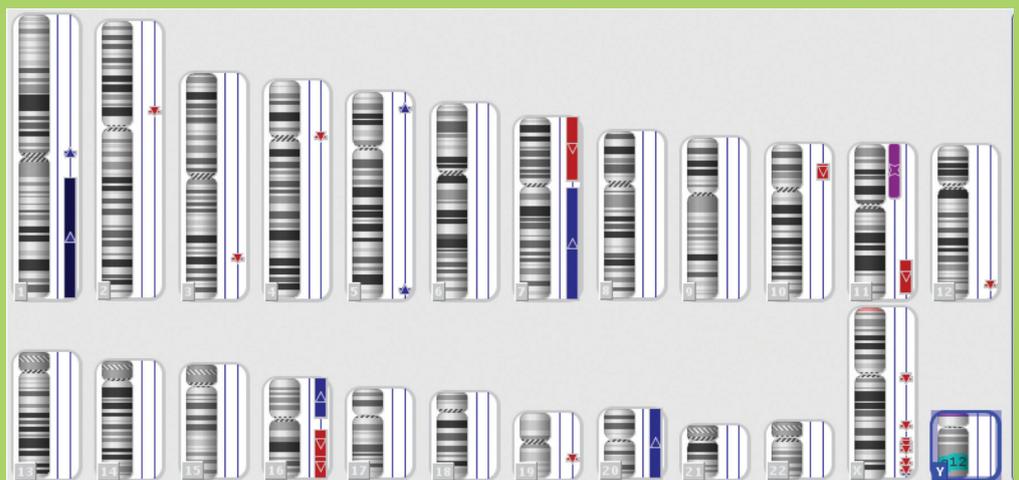
All described types and patterns of pediatric renal tumors are complex in diagnosis and prognosis. There are large consortiums/registries of these tumors in the U.S. and around the world where clinical oncologists, pathologists, cytogeneticists and molecular pathologists study large groups of these tumors to better understand and diagnose these lesions and develop new treatments.

Cytogenetics

Pediatric renal tumors vary by histological diagnosis, pathogenesis, genetics, treatment and outcome. The cytogenetics laboratory processes the fresh renal tumor specimens to gather as much information as possible for diagnostic purposes and to subcategorize tumors by genomics which influence therapeutic measures. The laboratory uses cell culture to grow the tumor cells for chromosome examination, allowing a whole genome view of the tumor and its specific genetic abnormalities (image 1). Samples processed with fixative may be used for detection of diagnosing specific abnormalities using fluorescence in-situ hybridization (FISH). DNA isolated from fresh and fixed tumor may be used for examination by high-resolution SNP microarray of the genome to detect abnormalities of copy number and loss of heterozygosity (image 2), molecular examination using whole genome sequencing, or molecular analysis of specific genes of interest. Appropriate intervention in cancers starts with the correct diagnosis which includes the specific genetic abnormalities that are unique to each individual tumor. As more knowledge is gained regarding the genetics of tumors and correlation with response to treatments, more specific individual therapeutic approaches are used to improve patient outcomes.



Wilms tumor karyotype with an unbalanced translocation between chromosomes 1 and 16 that results in gain of 1q and loss of 16q. This genetic abnormality has prognostic and therapeutic significance.



Microarray analysis of the Wilms tumor shows loss of heterozygosity over 11p (purple), gain of 1q (blue), loss of 16q (red) and other gains and losses over the genome. These abnormalities impact prognosis.

Radiation Oncology

Radiation therapy continues to play an important role in the treatment of pediatric renal tumors, particularly in the multidisciplinary management of Wilms tumor. Successive National Wilms Tumor Study (NWTs) trials helped define the indications for radiation therapy. The NWTs-1 and NWTs-2 studies employed an age-adjusted dose regimen for flank irradiation with an abdominal relapse rate of 3-5% for group II and III tumors with no dose-response relationship observed. The subsequent NWTs-3 trial was pivotal in that it demonstrated that radiation could be omitted for stage II tumors when employing vincristine and dactinomycin chemotherapy. It also showed that the radiation dose for Stage III favorable histology could be reduced from 20 Gy to 10.8 Gy with the addition of doxorubicin to the chemotherapy backbone of vincristine and dactinomycin.

The timing of radiation seems to be an important consideration with these trials suggesting a compromise in outcome with delays in radiation beyond 10 days, particularly for unfavorable histology. A subsequent analysis of data from NWTs-3 and NWTs-4 did not show inferior outcomes with delays in radiation beyond 10 days. Nevertheless, it is generally recommended to initiate radiation therapy within 14 days of surgery.

Radiation therapy also plays an important role in improving cure rates in the setting of lung metastases, where whole lung irradiation is indicated. The most recent COG trial recommends whole lung irradiation based on response to chemotherapy and LOH of 1p and 16q. The University of Kansas Health System is our primary partner for pediatric radiation therapy services,

with access to the most advanced technology and radiation therapy delivery techniques for the treatment of our patient population. This includes image-guided intensity-modulated radiation therapy (IMRT) for whole lung irradiation, which has been shown to provide superior cardiac protection.

The University of Kansas Health System is also currently constructing a proton therapy facility, bringing the latest state-of-the-art form of radiation therapy to the region. Proton therapy, with its superior radiation dose distribution, promises to significantly reduce radiation dose to normal healthy tissues and decrease the risk of late effects of radiation therapy. We expect to start treating children with proton therapy in Kansas City as of December 2021.

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Genetic Counseling

In some cases, pediatric cancers are associated with inherited mutations in cancer-causing genes. There are several genes that are known to increase the risk of cancer in children. Children with a strong family history of cancer or a cancer type that is associated with a known cancer syndrome can especially benefit from genetic counseling. Genetic counselors are trained to elicit a detailed multi-generation family history and perform a risk assessment, as well as explain the benefits, limitations, and implications of genetic testing to both medical providers and families.

For example, a child with clear cell renal cell carcinoma should be evaluated for the possibility of Von Hippel-Lindau syndrome, which can cause renal tumors along with a wide variety of other tumors both in childhood and adulthood. If a hereditary cancer syndrome is identified, at-risk relatives including parents, siblings and extended family members can be tested for the familial mutation. Individuals with hereditary cancer syndromes frequently need increased lifelong surveillance that is tailored to their particular cancer risks. Genetic testing can identify which individuals in a family need increased surveillance, which may be lifesaving.

The Children's Mercy Division of Clinical Genetics has a genetic counselor who specializes in evaluating for pediatric hereditary cancer syndromes and is regularly involved with families in which hereditary cancer is suspected. We also have a Surveillance for Predisposition to Tumors (SPoT) Clinic that is designed to follow children who have tested positive for a hereditary cancer syndrome and need individualized tumor surveillance. For more information about genetic counseling and genetic testing for pediatric oncology patients, contact genetic counselor Caitlin Schwager, MS, CGC, or the Division of Clinical Genetics.



Caitlin Schwager, MS, CGC

Family Care Team

Multidisciplinary care is integral to the overall outcomes and well-being of our patients. Outside of medically directed care, patients and families have many other needs that are addressed by our Family Care Team (FaCT). Regular FaCT collaboration ensures that all that physical, developmental, emotional, educational and spiritual needs are met for our patients and families. The Family Care Team is available to assist from point of diagnosis through the completion of treatment and beyond for patients with cancer.

18

The **Patient and Family Support** team consists of child life specialists, a school teacher, music therapy, and a patient activity assistant who is also the handler of the facility dog on staff that works on the inpatient unit. Together, the team works collaboratively to support the psychosocial and developmental needs of children and families.

Child life specialists are trained professionals who help children cope with the stress and uncertainty of illness and hospitalization.

explain and teach patients about medical procedures, coping skills and other health care experiences. Coping facilitation promotes effective coping strategies to help reduce anxiety and enhance cooperation with the health care event or diagnosis.

As advocates of family-centered care, child life specialists work in partnership with the medical team to meet the unique emotional, developmental and cultural needs of each child. **Hospital-based**

opportunities for self-expression and development of positive coping skills to promote increased comfort, and to support developmental growth. Music interventions are designed after an assessment of need and generally involve the use of both live vocal and instrumental music as well as technology. Goals may include, but are not limited to the reduction of pain or anxiety; increased self-expression and positive changes in mood; increased physical strength and endurance; greater relaxation; learning positive coping strategies; and the support of developmental skills. Patients are encouraged to take an active role in making music and learning how to use music as a helpful and fun tool. **Patient activity coordinators** provide patient and family activities and volunteer supervision.

Clinical social workers are master's-level licensed professionals working as part of the primary team to provide comprehensive and compassionate family-centered care. Social workers understand that any change in the child's health can alter a family's life in many ways and are trained to provide a thorough assessment and address the ongoing needs of the patients and families. Social workers can help with therapeutic support, including adjustment to illness, crisis intervention, development of coping skills, family concerns, end-of-life and bereavement; care planning including education on advance directives, school concerns, legal issues, transition to adult care, and end-of-life concerns; and community/resource referrals



Sydney Shryock, BS

Child life specialists are child development experts who work to ensure life remains as normal as possible for children in health care settings through preparation, coping and normalization. Preparation is provided by child life specialists to

school teachers establish a positive learning climate of success for students with chronic and serious medical conditions, and coordinate educational plans with home schools. **Music therapists** provide



Lacey Lee, LMSW

to assist with financial concerns, transportation and lodging needs, support and mental health referrals. Every patient has an assigned clinical social worker who follows the patient and family through diagnosis, treatment, relapse, survivorship or bereavement.

The **Parent to Parent Program (PTP)** continues to offer support and comfort to all of the families within our division through the use of specially trained parent volunteers and a clinical social worker dedicated specifically to PTP program management. There are many services offered through the PTP program including parent volunteers available to share, listen and support our current parents/caregivers; two stocked parent rooms that offer weekly dinners, breakfasts, therapeutic and educational activities and a safe place to unwind while a child is an inpatient; “care bags” for families upon unexpected admissions to help ease some burden of a hospital stay; and new parent journals. The Parent to Parent program also offers

an extensive bereavement follow-up program that supports families for approximately 13 months after a child’s death. We have successfully introduced social media into our bereavement follow-up program and have been able to offer additional support in that way. PTP has worked closely with a number

of local organizations, as well as the Children’s Mercy Cancer Center, and has established ongoing philanthropic support of the parent rooms to serve the increasing needs of our inpatient families.

The **Adolescent and Young Adult (AYA)** program is designed to support patients receiving treatment for cancer or blood disorders. The team of providers includes a clinical social worker and child life specialist who work in collaboration with other disciplines toward the goal of improving the quality of care for the AYA population. Recent accomplishments include the development of a teen unit and teen room on our inpatient floor, a formalized peer mentoring program, additional programming and education around fertility preservation, and improvements to the process around transitioning to adult care. Ongoing projects include the Hematology/Oncology Teen Advisory Board, activities to promote peer interaction, and ongoing education and support.

There are two dedicated **psychologists** to assist patients and families with coping with the diagnosis and treatment of cancer. They are available to meet with patients and their families both while hospitalized and when outpatients. In addition to clinical therapeutic services, the psychologists are also able to complete neuropsychological evaluations to assess any impact of medical treatment on brain functioning and to assist with school re-integration and planning.

As a member of the Hem/Onc/BMT team, the **chaplain** regularly provides spiritual and emotional support to patients and families during the course of a child’s illness, as end-of-life discussions are necessary, at the time of death, and beyond. Providing tailor-made rituals for patients and families at the time of significant events like bone marrow transplant is another way a chaplain provides support. At the request of the family, the chaplain can contact a family’s own clergy person/spiritual leader. For families who live outside of the Kansas City area, again at the request of the family, the chaplain contacts a local leader from the family’s faith tradition to provide additional support. The chaplain provides education about the spiritual resources that are available within the hospital, such as the activities in the Lisa Barth Chapel like Sunday worship, concerts and celebrations from various faith traditions. The chaplain participates in team meetings. Providing support to the staff is another important role of the chaplain.

CANCER PROGRAMS

Survive & Thrive

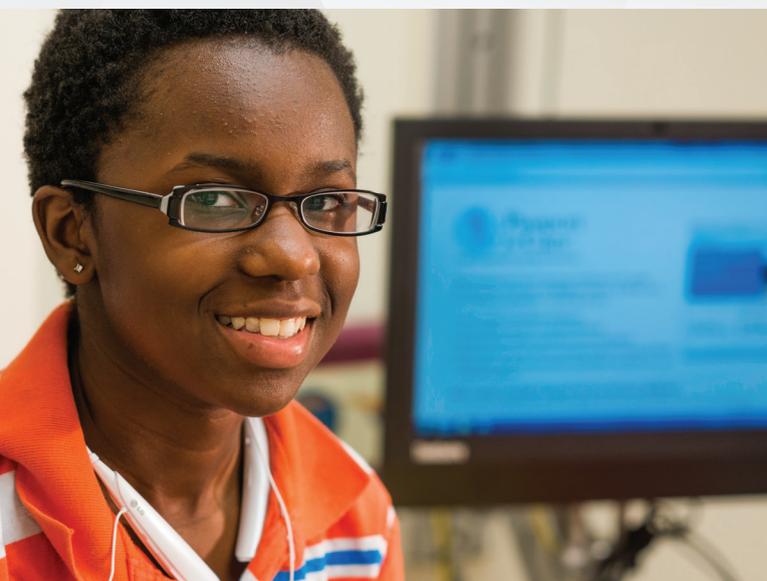
The Survive & Thrive Program offers comprehensive medical and emotional care to childhood cancer survivors who are at least two years off treatment and five years from the date of diagnosis. The program offers five clinics per month with more than 350 survivors receiving care. Childhood cancer survivors are at risk for health problems or late effects from their cancer and treatment. Late effects can be physical or emotional and typically appear in the second decade of life. The development of late effects may be influenced by the type of cancer, the treatment, age at diagnosis, and genetic predisposition. An estimated 95% of childhood cancer survivors will develop at least one late effect at some point during their life. Late effects may be preventable or modifiable, which is why lifelong follow up is important for all survivors.

Examples of late effects that may occur in survivors include hearing loss, heart dysfunction, infertility, organ dysfunction (i.e., restrictive or obstructive lung disease), endocrine dysfunction and development of a second cancer. In the Survive & Thrive Clinic, survivors are monitored for development of late effects according to the Children's Oncology Group Long-term Follow-up Guidelines. The team ensures diagnostic tests and labs are completed according to the guidelines and referrals are made to other specialists when necessary.

The Survive & Thrive team works closely with health care providers in other specialties to ensure each survivor's unique health needs are met. Specialists the team works closely with include Endocrinology, Cardiology and Developmental & Behavioral Sciences.

In 2016, Children's Mercy launched the Cardio-Oncology Program to better meet the needs of cancer patients at risk for developing cardiotoxicity (damage to the heart and vascular system). The Cardio-Oncology program offers specialized treatment that incorporates screenings by pediatric cardiologists during cancer treatment and after for survivors. Monitoring for and addressing cardiac concerns early can reduce the risk of severe or life-threatening heart problems. We also offer a collaborative clinic with Endocrinology (EaST) clinic on a monthly basis to provide coordinated care and decrease visits.

A visit to the Survive & Thrive Clinic includes a thorough physical exam, recommendations for long-term follow-up care, education on late effects of cancer treatment and how to maintain a healthy lifestyle. Assessments by a dietitian and social worker are included in the survivorship clinic visit to ensure all needs of the survivor are met. In conjunction with the hospital-wide Transition to Adulthood Program, preparation for transition to adult providers is incorporated into each visit once survivors reach 15 years of age. The Survive & Thrive team works with each survivor to teach skills to advocate for their health care needs and develop an individualized transition plan. At the time of transition, the team works with the survivor, family and adult health care providers to ensure the transfer of care is smooth for everyone involved in the process.



Bone and Soft Tissue Sarcoma Program

Sarcoma accounts for approximately 15% of all childhood cancers. Each year, Children's Mercy treats approximately 15-20 children with bone or soft tissue tumors, the most common of which are osteosarcoma, Ewing sarcoma, and rhabdomyosarcoma. The Bone and Soft Tissue Sarcoma Program at Children's Mercy (in collaboration with the Sarcoma Center at the University of Kansas Cancer Center) consists of highly-trained specialists in Pediatric Oncology, Orthopedic Oncology, Radiation Oncology, Rehabilitative Medicine, Radiology, Pathology and Interventional Radiology who focus on providing cutting-edge, family-centered sarcoma care from diagnosis through treatment and post-therapy monitoring. We believe no child should have to leave the Kansas City area in order to receive elite, streamlined sarcoma care, and providing such care is our daily priority. Additionally, with an expanding panel of collaborative research opportunities, we are helping to identify the next generation of sarcoma therapies right here in Kansas City.

The Bone and Soft Tissue Sarcoma Program at Children's Mercy is led by Joy Fulbright, MD, and Joel Thompson, MD. The program consists of - Orthopedic Surgery (Howard Rosenthal, MD, and Kyle Sweeney, MD) Radiation Oncology (Ronny Rotondo, MDCM, FRCPC), Rehabilitative Medicine (Kimberly Hartman, MD), Pediatric Oncology, Pathology, Interventional Radiology and Radiology. Our goal is to provide seamless care coordination from radiation oncology to pathology and orthopaedic surgery, with a multidisciplinary tumor board and enhanced collaborative research across disciplines.

Leukemia and Lymphoma

The Leukemia and Lymphoma Program at Children's Mercy is comprised of experts in the diagnosis and management of hematologic malignancies in children and young adults. Under the direction of Keith August, MD, the Leukemia and Lymphoma Program is a



Keith August, MD

collaborative effort dedicated to delivering state-of-the-art clinical care and to generate innovative and collaborative research efforts. Members are multidisciplinary and include faculty from the section of

oncology, bone marrow transplant, hematopathology, cytogenetics and the cancer genomics program. Comprehensive patient care meetings occur twice monthly where every leukemia and lymphoma patient is discussed among program members. Children's Mercy has a number of clinical trials available to ensure that patients in Missouri and Kansas have access to exciting new treatments that are rapidly transforming the care of children with leukemia and lymphoma. Members of the Leukemia and Lymphoma Program are actively involved in the development of clinical trials for leukemia and lymphoma on a national and international level through the Children's Oncology Group and other clinical research consortiums.

Neuro-Oncology Program

The Children's Mercy Cancer Center Neuro-Oncology Program is a multidisciplinary program led by Kevin Ginn, MD. The primary focus of the program is to provide access to advanced cancer therapy and to improve outcomes for children in the Kansas City region with brain and spinal cord tumors. Central nervous system tumors remain one of the leading causes of cancer-related death and morbidity and these patients benefit from the individualized care plans developed by multiple subspecialists available at Children's Mercy.

At Children's Mercy, we treat approximately 50 new patients a year and each patient is discussed at our twice-monthly multidisciplinary tumor board. These tumor boards allow in-depth discussion of new or established patients ensuring thorough care planning to improve patient care. Our involvement in National Consortiums such as Beat Childhood Cancer and the Children's Oncology Group (COG) as well as pharmaceutical industry relationships allows us to provide access to cutting-edge clinical trials for both new and relapsed patients. Research collaborations through the Midwest Cancer Alliance Partners and the University of Kansas Cancer Center have resulted in research investigating new therapies for glioblastoma and atypical teratoid rhabdoid tumor which are two of the most devastating tumors in pediatrics. The goal of the Neuro-Oncology Program continues to be comprehensive care and cutting-edge therapy provided close to home for every patient with a central nervous system tumor that enters the doors of Children's Mercy.

Experimental Therapeutics

The Experimental Therapeutics in Pediatric Cancer Program at Children's Mercy was founded in 2010 with a goal of providing access to early phase clinical trials after relapse and/or progression has resulted in limited remaining options for therapy. Over the years we have developed strong relationships with consortiums and pharmaceutical companies increasing our ability to have open trials available when they are needed. On average 25 clinical trials are open at any time through our collaborations with Beat Childhood Cancer, Children's Oncology Group, Aflac Cancer Center at Emory Children's Hospital and industry partners. The Experimental Therapeutics team includes three physicians, each with their own specific area of interest including neuro-oncology, solid tumors, blood cancers and cancer genomics (including ethnic diversity and its relation to outcome/response). The team also includes a nurse coordinator and three clinical research coordinators, who are vital to our mission and help to maintain the trials and monitor study patients.

In addition to patients from the Kansas City region, we have received a number of outside referrals from centers in Wichita, St. Louis, Oklahoma, Colorado, Iowa, Arkansas, Illinois and Texas. With the continued development of the Children's Mercy Research Institute and our strong relationship as a consortium partner in the NCI-Designated University of Kansas Cancer Center, we are poised to become a national leader in innovative cancer treatments for children. Access to early phase clinical trials has made a significant difference for children with cancer in Missouri, Kansas and the region.

Children's Mercy Cancer Center was selected to join the Children's Oncology Group Pediatric Early Phase-Clinical Trial Network (PEP-CTN) as a non-core member beginning in 2021. The PEP-CTN is the early phase clinical trial arm of the Children's Oncology Group and previously included only 21 core member institutions. In the Fall of 2020, Children's Oncology Group member institutions were invited to apply as a non-core member and the PEP-CTN would choose up to 20 sites based on infrastructure, experience and patient numbers. Given our experience with consortium and industry-based early phase trials within our Experimental Therapeutics in Oncology Program and the infrastructure in place to run early phase clinical trials safely and effectively, Children's Mercy was invited to join this prestigious group of pediatric oncology centers. Our involvement in the PEP-CTN provides the opportunity for regional children and adolescents battling cancer to access these trials on the forefront of cancer therapy research.

Spanish-Speaking Cancer Clinic

The Spanish-Speaking Cancer Clinic offers pediatric oncology services to Hispanic patients and families who speak limited English. The team is dedicated to providing quality medical care that recognizes Spanish language needs and cultural differences related to health care.

The team is dedicated to better understanding the ethnic and genetic differences in outcomes among Hispanic patients with leukemia. Ongoing research in partnership with the genomics program focuses on the genetic factors in these differences, which will help us provide better treatment to patients. The program also provides trainee education to develop and improve Spanish-language skills and promote cultural awareness in the clinical setting.

Adolescent and Young Adult Program

Children's Mercy provides dedicated services for adolescents and young adults with cancer (age 13 to 22). The AYA program is designed to support patients receiving treatment for cancer or blood disorders and specializes in providing psychosocial support and connecting patients with clinical trials through their early 20s.

The team of providers includes a clinical social worker and Child Life specialist who work in collaboration with other disciplines toward the goal of improving the quality of care for the AYA population. Recent accomplishments include the development of a teen unit and teen room on our inpatient floor; a formalized peer mentoring program; additional programming and education around fertility preservation; and improvements to the process around transitioning to adult care. Ongoing projects include the Hematology/Oncology Teen Advisory Board; Teenapalooza events to promote peer interaction; and ongoing education and support.

Histiocytosis Program

The Histiocytosis Program at Children's Mercy provides a comprehensive setting for care of rare diseases. The experienced team collaborates to treat conditions such as Langerhans Cell Histiocytosis, Hemophagocytic Lymphohistiocytosis, sinus histiocytosis with massive lymphadenopathy, and Erdheim-Chester disease.

The program provides a team approach to care that features collaborations between multiple services when needed, including the expertise of a pediatric hematologist/oncologist, pediatric nurse practitioner, and a pediatric social worker. The Histiocytosis Program also collaborates with pediatric orthopedic surgeons, pediatric endocrinologists, pediatric dermatologists and pediatric pathologists.



Cancer Genomics

The Children's Mercy Cancer Genomics Program brings together pediatric oncologists, molecular pathologists, genomics research faculty, bioinformaticians, genetics counselors, and many more, with the primary goal to improve survival through genomics sequencing. We are proud to offer comprehensive somatic (cancer cell) and germline (non-cancer cell, potentially heritable) molecular testing to every child treated for cancer at Children's Mercy. This allows our team to better classify the molecular subtype and the risk of recurrence, and to tailor treatments for each individual patient. In some cases, we may identify a genetic variant that predisposes to cancer and we can then offer genetic counseling, testing to immediate family members and surveillance for children and adolescents identified to be at risk of cancer. Surveillance identifies cancers at earlier stages and saves lives. In addition to clinical sequencing, our team is actively leading genomics research projects in leukemia, lymphoma, solid tumors and brain tumors. We are exploring the underlying biology driving childhood cancers and, through collaborative partnerships with the University of Kansas Cancer Center, the National Cancer Institute, and other pediatric hospitals, we are committed to sharing our knowledge and accelerating the pace of genomics discoveries, which benefits the scientific community, our patients and their families.

Liver Tumor Program

The liver cancer treatment team at Children's Mercy combines the medical and surgical expertise of the Division of Hematology and Oncology with the Liver Care Center. This program provides specialized services and research for treating pediatric patients with malignant liver tumors.

The program provides specialized treatment for pediatric hepatoblastoma, the most common malignant liver tumor in the United States. Once patients complete treatment, the team continues to follow their progress through a quarterly liver tumor clinic.

Stem Cell Transplant and Cellular Therapies

The process of caring for a child who needs a transplant is complex and requires the skills and expertise of a team of specialists. Each year, the BMT Program performs approximately 40 transplants for children and adolescents up to age 21. Transplants are done to treat varying forms and stages of cancers, immune disorders, blood (hematologic) disorders, and metabolic disorders. Our immunotherapy program offers new therapies to a growing number of patients.



He's a **TRIPP!**

**How Cancer Treatment
Saved This Fun-loving
5-year-old's Life**

At 5 years old, Tripp Chase loves to play with his toy cars, dinosaurs and Legos. He's a typical boy, except for one thing. He was diagnosed with an aggressive form of Wilms tumor in 2019—a kidney tumor that required the state-of-the-art cancer care available at Children's Mercy Kansas City.

Tripp's cancer story began when he was just 3 years old. Jolynda Chase, Tripp's mom, said he had been a healthy child until one night when he started crying and grabbing his stomach in pain.





“He hadn’t had a bowel movement in three days, so we thought he might just be constipated,” Jolynda said. But when Tripp’s doctor in Colby, Kan., X-rayed his abdomen, it looked like he had an enlarged liver.

The next week at a follow-up appointment, Tripp had an abdominal ultrasound that confirmed he had a large mass either on his right kidney or liver. “Our doctor wanted Tripp to have a CT scan, and referred us to Children’s Mercy for the test,” Jolynda said.

On Wednesday, July 17, 2019, Jolynda and Tripp made the six-hour drive from their Winona, Kan., home to Kansas City. Later that day, Tripp’s family learned the source of the problem—he had a large tumor on his right kidney, a tumor that needed to be removed immediately.

Two days later, on Friday, July 19, Tripp had surgery to take out his right kidney and the tumor. A biopsy confirmed Tripp had a common type

of childhood kidney cancer called Wilms tumor. What wasn’t common was that it had already spread to Tripp’s lymph nodes.

“About 650 cases of Wilms tumor are diagnosed in the United States each year,” explained Joel Thompson, MD, pediatric oncologist with Children’s Mercy and Tripp’s physician. “In most cases, surgery is the initial treatment.”

Unfortunately, analysis of Tripp’s tumor revealed more widespread, aggressive anaplastic disease. “Based on the pathology, from the outset, we knew Tripp’s treatment would be more challenging. He would need both radiation and intense chemotherapy for the best chance of survival,” Dr. Thompson said.

Family Sacrifices

For Tripp’s family, there was no question that he was in the right place to get the care he needed, but it came at a steep price.

“I had just given birth to Tripp’s baby sister two months earlier,” Jolynda said. Plus, Tripp has two older brothers, ages 6 and 11. Jolynda stayed in Kansas City to be at her son’s side during treatment, while Tripp’s father took care of the other three children in Winona with the help of family and friends.

“Tripp’s parents are the calmest people ever,” said Lindsey Fricke, RN, MSN, FNP-BC, Nurse Practitioner. “You never would have known that anything crazy was happening in their lives. I know this had to be difficult for them, but they took everything in stride. I never heard Jolynda complain.”

Dr. Thompson agreed and said Tripp’s family support was remarkable.

“If they were stressed, they never let us see it, and I don’t think Tripp sensed it either,” he said. “That allowed us to focus on his treatment, and help Tripp get better.”

Tough Therapy for a Tough Tumor

Tripp’s treatment began just two weeks after his right kidney was removed. Dr. Thompson prescribed radiation therapy and chemotherapy, a powerful one-two punch reserved for the most aggressive Wilms tumor cases.

While chemotherapy was performed at Children’s Mercy, Tripp’s radiation therapy was delivered at the University of Kansas Medical Center, the hospital’s partner in radiation oncology. In all, Tripp received 11 radiation treatments, and eight months of chemotherapy.

“Tripp did well with the radiation therapy, but the chemotherapy was hard on him,” Jolynda said. Though technically he was able to return home between treatment cycles, he often ended up back in the hospital when he would spike a fever.

“This is an intense regimen of chemotherapy, and there are side effects,” Dr. Thompson said. “As



Joel Thompson, MD

it wipes out the patient's immune system, they're at higher risk for infection, and that's what happened to Tripp.

"Toward the second half of his chemotherapy treatments, Tripp would get a fever about day eight of every cycle. It was almost like clockwork," Dr. Thompson added.

Jolynda knew if her son's fever rose above 100.5 degrees, it was an emergency. "We tried to return home,

Thompson said. "I knew if he could tough this out, there was about a 75 to 80% chance that he would be cured."

Thriving After Treatment

Though the cancer scare isn't completely behind Tripp, it's now been nine months since he finished treatment, and he's thriving!

"Tripp is back in school and loves being with family and friends, playing with his brothers and his baby sister," Jolynda said. "We are all glad to be back home."

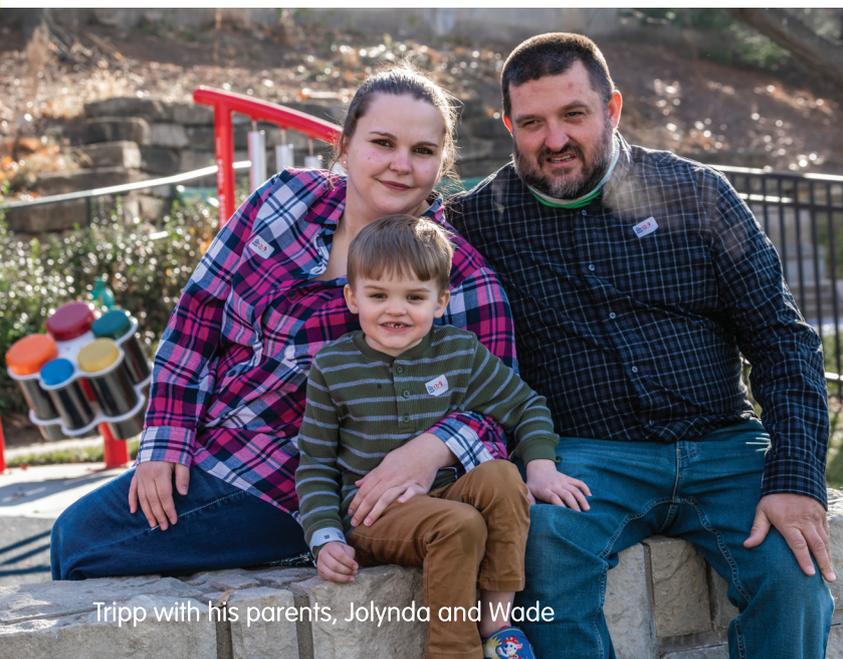
"Tripp is a fun-loving kid," Lindsey added. "He's always playing with his cars or attacking me with his dinosaurs at his check-ups."

"Tripp's diagnosis was a big shock for us. I never thought something like this would happen to our family and it was really hard to take. There were a lot of stressful, sleepless nights," Jolynda admitted. "But we couldn't have asked for better doctors or nurses than we had at Children's Mercy."

For Dr. Thompson and Lindsey, Tripp epitomizes the reason they care for kids with cancer.

"It was heartbreaking to see Tripp undergo the short-term pain and suffering of his treatment, but I knew there was a good chance that in the long term, he could beat cancer," Dr. Thompson said.

"After Tripp's last visit, as I was walking out of the exam room, I thought to myself, 'This is why I do what I do, because of how good Tripp feels and looks.' He's now a normal 5-year-old and on the other side of this."



Tripp with his parents, Jolynda and Wade

but over the months, Tripp had to be flown back to Kansas City 10 times. The flight crew called him their little frequent flyer," Jolynda said.

Chemotherapy also took a toll on Tripp's appetite and digestive system. Eventually he needed a feeding tube to be sure he received adequate nutrition. And, chemotherapy affected the nerves in his legs, causing some neuropathy and pain. But overall, Tripp fought through the treatment and its side effects.

"For his stage of diffuse anaplastic Wilms tumor, this was pretty standard treatment, but it is extremely intense, and there can be a lot of side effects, which Tripp experienced," Dr.

Dr. Thompson said even when Tripp was hospitalized and not feeling well, he'd curl up in the chair beside his bed, snuggling with his warm fleece blanket, and playing peek-a-boo.

"Now that he's healthy and on the other side of treatment, wow, his personality is out!" Dr. Thompson said. "That's so great to see."

With treatment behind him, Tripp will continue to see Dr. Thompson and Lindsey regularly for the next five years for follow-up appointments to be certain the cancer doesn't return, and to monitor his kidney and heart functions, both which could have been impacted by the radiation and chemotherapies.



Lindsey Fricke, RN, MSN, FNP-BC

CHAMPIONS FUELING CANCER CARE AND RESEARCH

Hope Hero honoree, Arden, was all smiles for the 9th Annual Hope Gala led by Braden's Hope for Childhood Cancer. The virtual event, held on September 26, raised more than \$575,000 for pediatric cancer research projects driven by teams from Children's Mercy, KU Cancer Center, and the Stowers Institute for Medical Research.



The Children's Mercy Cancer Center Auxiliary hosted a virtual trivia night to raise \$6,600 in support of the annual Holiday Hero campaign and families battling pediatric cancer and blood disorders at Children's Mercy. The Cancer Center Auxiliary also hosts their annual Holiday Hero campaign, raising more than \$100,000 to support patients and families battling pediatric cancer and blood disorders.

BRADEN'S HOPE



BIG SLICK

Big Slick hosts Rob Riggle, Paul Rudd, Jason Sudeikis, Eric Stonestreet and David Koechner went online, from home, for this year's fundraising event benefiting pediatric cancer research at Children's Mercy.

CANCER CENTER AUXILIARY



In 2020, more than 300 champions invested in cancer care and research at Children’s Mercy through creative events, heartwarming tributes, and more. Our community of champions ensures that kids in Kansas City and across the region have the best care possible, right here at Children’s Mercy.



The Long family enjoyed the outdoors during the 5th Annual Noah’s Crown Town 5K. The virtual event, held on April 19, supported Noah’s Bandage Project, a major supporter of pediatric cancer research at Children’s Mercy.



DREAM BIG DAY

NOAH’S BANDAGE PROJECT

BLACK & VEATCH GOLF TOURNAMENT

Children’s Mercy Dream Big Day was a virtual family-friendly festival, celebration and walk to rally our community around finding answers and hope for kids. More than 900 people and 70 teams came together virtually to raise more than \$227,000 and help kids’ dreams – big or small – become a reality.



Even though Black & Veatch had to cancel their annual charity tournament to benefit Children’s Mercy due to COVID-19, the company still showed their commitment to the hospital with a donation of 5,000 face masks for staff at Children’s Mercy!



30

The Black & Veatch Building, on the Children's Mercy Adele Hall Campus in Kansas City, Mo., houses the Division of Hematology/Oncology/Blood and Marrow Transplant.

PHILANTHROPIC DONORS TO THE CANCER CENTER IN 2019-2020

Thank you to the donors of \$25K+ and donors that established a planned gift:

Alex's Lemonade
Stand Foundation

Ann and Matt Anthony

Austie Strong
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Alyssa and Steve
Barton

Big Slick

Black & Veatch
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Braden's Hope for
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Children's Mercy
Cancer Center
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The Jared Coones
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Curing Kids Cancer

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DeBruce

DeBruce Foundation

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Sarah and Scott
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GROWING FOOTPRINT OF CANCER RESEARCH

With the opening of the Children's Mercy Research Institute (CMRI), the footprint of Children's Mercy research took a giant step forward. For the Cancer Program, collaboration and the building of research infrastructures has been developing over the last several years. Here are some of the researchers building our program.



Doug Myers, MD, Immunotherapy Laboratory located in the CMRI

Lab Members: John Szarejkeo, PhD

Principal Collaborators: John Perry, PhD

Cancer focus: Immunotherapy of solid pediatric tumors with a focus on using chimeric antigen receptor T-cells and tumor antigen-specific T-cells for treatment of neuroblastoma.



John Perry, PhD, Targeted Therapy Laboratory located in the CMRI

Lab Members: Jackie Nemechek, PhD; Fang Tao; Jennifer Pace; Kealan Schroeder, MPH; and John Szarejko, PhD

Principal Collaborators: Doug Myers, MD; Todd Bradley, PhD; Scott Younger, PhD; Scott Weir, PharmD, PhD (KU); Alan Gamis, MD; Erin Guest, MD; Chandni Dargan, MD; Bradley Stockard, PharmD, PhD; and Sara McElroy, MD

Cancer focus: Targeted therapies for relapsed/refractory leukemia.



Cancer Genomics Program led by Erin Guest, MD, Midhat Farooqi, MD, PhD, and Tomi Pastinen, MD, PhD, located in the CMRI

Program Members: Byunggil Yoo, MS; Neil Miller; Maggie Gibson; and Emily Farrow, PhD

Key Collaborators: Sarah McDermott, MD; Linda Cooley, MD; Sultan Habeebu, MD; Mark Hoffman, PhD; Amy Hont (CNMC); Holly Meany (CNMC); Catherine Bollard (CNMC); Jason Wang (Cook Children's); Dinesh Rakheja (Children's Dallas); Keith August, MD; Tristan Flatt, DO; Atif Ahmed, MD; and Elizabeth Gonzalez Dominguez, MD

Cancer focus: Genomics, TransCMRIptomics, and epigenomics of leukemias and solid tumors.

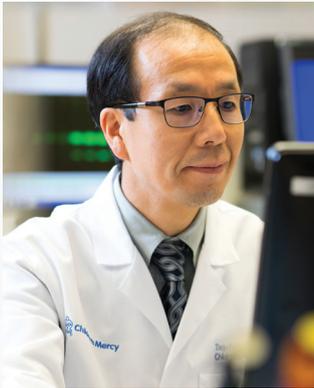


Cancer Research Informatics and Data Science led by Mark Hoffman, PhD

Program members: Sierra Davis; Earl Glynn; and Janelle Noel-MacDonnell, PhD

Key Collaborators: Karen Lewing, MD; Nikki Wood, DO; and Doina Caragea, PhD (Kansas State)

Cancer focus: Acute lymphoblastic leukemia.

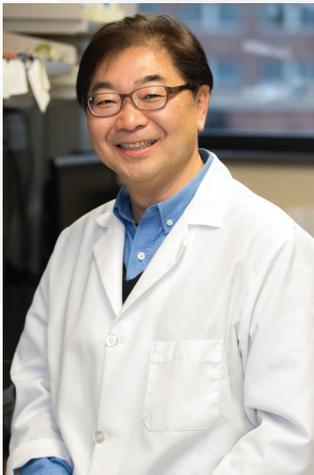


Taeju Park, PhD, Brain Tumor Research Laboratory located in the CMRI

Lab members: Neka Large and Olivia Funk

Principal Collaborators: Tom Curran, PhD, FRS; Anuradha Roy, PhD (KU); Scott Weir, PhD (KU); Frank Schoenen, PhD (KU); Justin Douglas, PhD (KU); David Johnson, PhD (KU); and Kevin Ginn, MD

Cancer focus: Development of novel chemotherapy drugs to treat brain tumors, including glioblastoma and diffuse midline glioma.



Tomoo Iwakuma, MD, PhD, Translational Laboratory Oncology Research (TLOR) located in the CMRI

Lab Members: Alejandro Parrales, PhD; Atul Ranjan, PhD; Shigeto Nishikawa, MD, PhD; Atsushi Kaida, DDS, PhD; Mohamed Alalem, MD, PhD; Elizabeth Thoenen; Hongyi Ren; and Etsuko Iwakuma, NS

Principal Collaborators: Scott Weir (KUMC); Sufi Thomas (KUMC); Francisco Diaz (KUMC); Shrikant Anant (KUMC); Anuradha Roy (KU); Frank Shoenen (KU); and John Karanicolas (Fox Chase)

Cancer focus: p53, osteosarcoma, Ewing sarcoma, liver cancer, head and neck cancer, lung cancer.



Glenison Samuel, MD, Godwin Lab at University of Kansas Cancer Center

Lab Members: Jennifer Crow, PhD, and Soumya Turaga, PhD

Principal Collaborators: Andrew Godwin, PhD (Principal Investigator-KU); Yong Zeng, PhD (University of Florida); Joaquina Baranda, MD (KU); Kyle Jackson, MD, MPH (Indiana University); Michael Merchant, PhD (University of Louisville); Genomic Medicine Center (Children's Mercy); and Mihaela Sardu, PhD (Stowers Institute)

Cancer Focus: Predictive and prognostic biomarkers, liquid biopsies based on extracellular vesicles, and therapeutics in Ewing Sarcoma; pediatric sarcomas.

PUBLICATIONS

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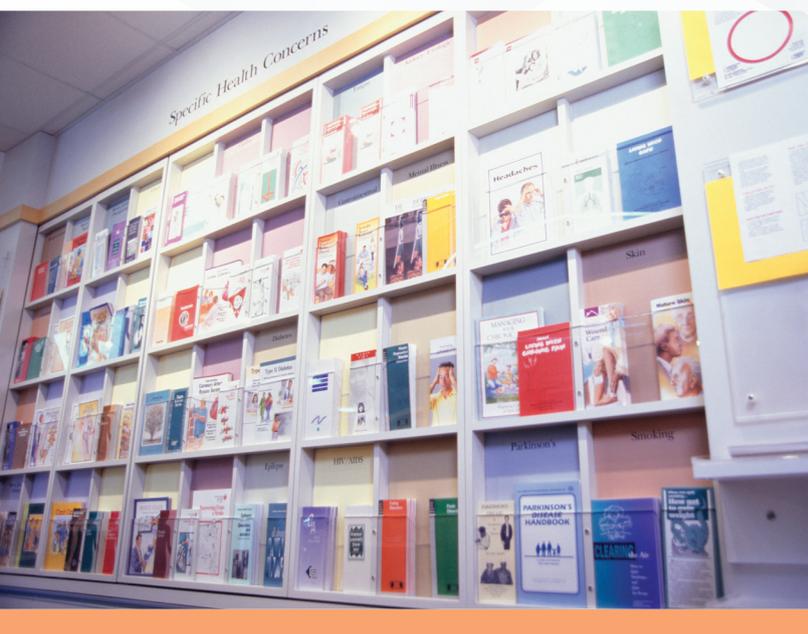
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