University of Kentucky

Making Inroads Against Childhood Cancer Through Team Science

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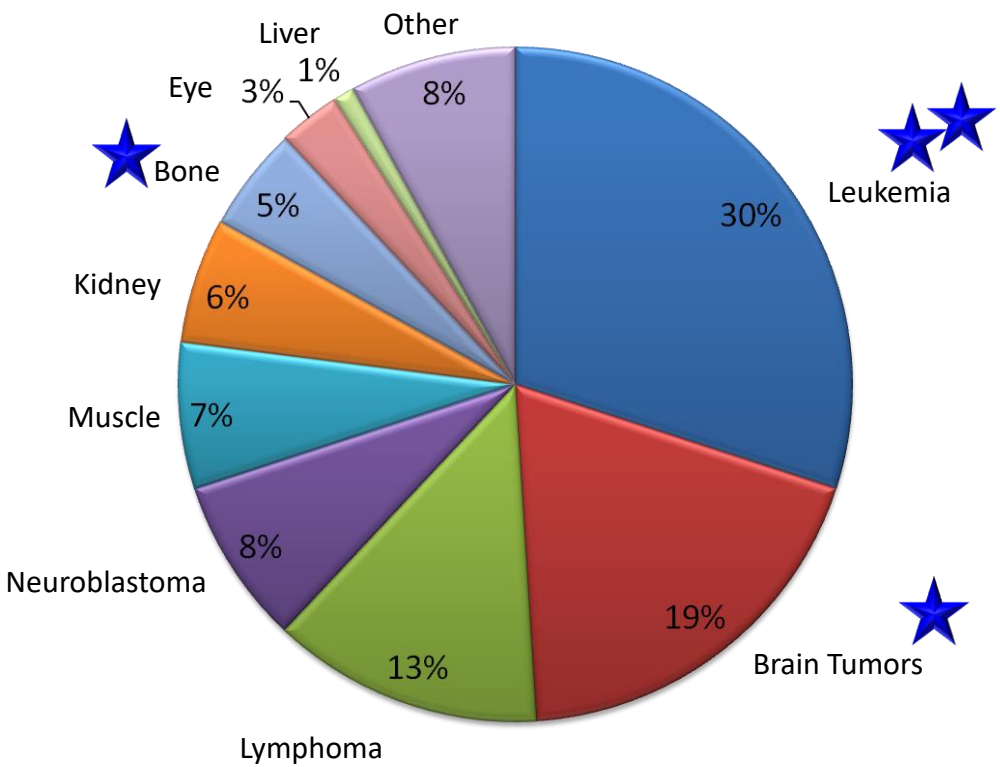
Types of childhood cancers

- Cancer is the major cause of death from disease in young people.
- About 2,500 U.S. children and teenagers die from cancer annually.
- Over 220 KY children a year are diagnosed with cancer each year
- 1,091 KY children were diagnosed with cancer (2011-2015)



Data provided by Dr. Eric Durbin, Director, Kentucky Cancer Registry

UK PCRTF Projects

UK projects:

KY Peds Cancer Research Trust Fund

1. **Develop circulating tumor DNA as a prognostic biomarker in acute lymphoblastic leukemia (ALL).**

2. Elucidate how ALL therapy impacts cognition: mechanisms and prevention.

3. Identify factors associated with high incidence of pediatric brain tumors in Kentucky.

4. Develop mithramycin derivatives as new drugs for the treatment of Ewing sarcoma.

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Jessica Blackburn, PhD

Thomas Badgett, MD,PhD

Aims

1. Create a biobank of primary leukemia samples from Kentucky pediatric ALL patients.
    - UK, UL
    - Goal: 45 patients at diagnosis
2. Determine the extent to which ctDNA correlates with clinical diagnosis of minimal residual disease and relapse.
    - On therapy collection: droplet digital PCR (ddPCR)
    - Compare ctDNA analysis to standard clinical monitoring procedures.
3. Develop a universal ddPCR assay to detect ctDNA in ALL patients.
    - Design universal ALL primer sets based on common methylation patterns.
    - Create an ”off-the shelf” assay for ctDNA in ALL.

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Daret St. Clair, PhD
Caryn Sorge, MD
Heidi Weiss, PhD
Subbarao Bondada, PhD
Allan Butterfield, PhD

Aims

1. Collect blood and spinal fluid from children with ALL before and after chemotherapy.
   - Purify extracellular vesicles from blood and CSF.
   - Correlate with markers of brain injury.
2. Test the ability of extracellular vesicles to activate immune cells to produce cytokines.
   - Test if the FDA-approved drug Mesna prevents immune cell activation from extracellular vesicles.
3. Correlate extracellular vesicle findings with neurocognitive test results in patients.

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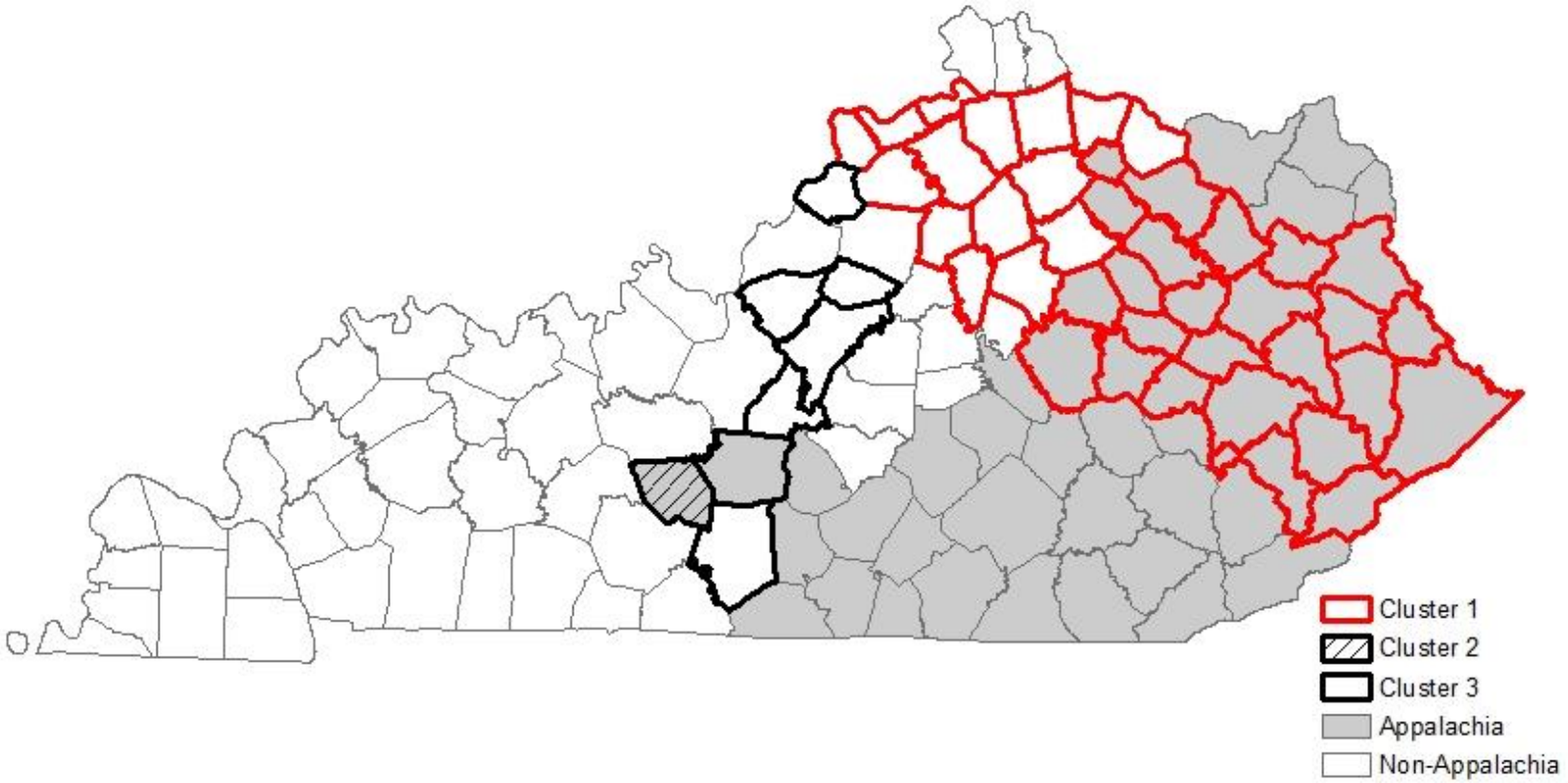
Pediatric Brain and CNS High Rate Clusters
Kentucky, 1995-2017



Data provided by Dr. Eric Durbin, Director, Kentucky Cancer Registry.

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W. Jay Christian, PhD **Chunyan He, ScD** **Jong Cheol Jeong, PhD** **Adam Resnick, PhD *(CHOP)***

Eric Durbin, DrPH **Thomas Badgett, MD,PhD** **Bin Huang, DrPH** **Thomas Tucker, PhD**

Aims

1. Identify potential environmental causes for increased incidence.
    - Geospatial analysis of incidence data from the Kentucky Cancer Registry and EPA environmental data.
2. Discover genetic causes for increased cancer incidence.
    - Obtain tissue from almost 300 pediatric brain tumors in Kentucky 2008-2018.
    - Perform NextGen sequencing: find Kentucky-specific mutations and mutational signatures
3. Develop informatics systems integration.
    - Expand big-data platforms and develop data sharing and open access for authorized investigators in Kentucky and beyond.
    - Children's Brain Tumor Tissue Consortium, CHOP, Pediatric Neuro-Oncology Consortium, NIH Kids First Data Resource.

$1.25Million, CHOP/Kids First

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Markos Leggas, PhD 

 Jurgen Rohr, PhD

Aims

1. Obtain large quantities of mithramycin analogue A10 via industrial scale bacterial fermentation
    1. Non-GLP material will be synthesized at the University of Kentucky (Rohr lab).
    2. GLP (Good Laboratory Practices) material will be synthesized at a CRO.
2. Conduct pharmacology, toxicity and safety studies with mithramycin analogue A10.
    1. Non-GLP studies at the University of Kentucky (Leggas lab).
    2. GLP studies will be conducted at a CRO (Charles River)

Goal

Evaluate promising mithramycin analogues for preclinical safety/toxicity to be able to submit an investigational new drug (IND) to the FDA

Thank you for helping us reduce the burden of disease caused by pediatric cancer in the Commonwealth