University of Kentucky

# Making Inroads Against Childhood Cancer Through Team Science

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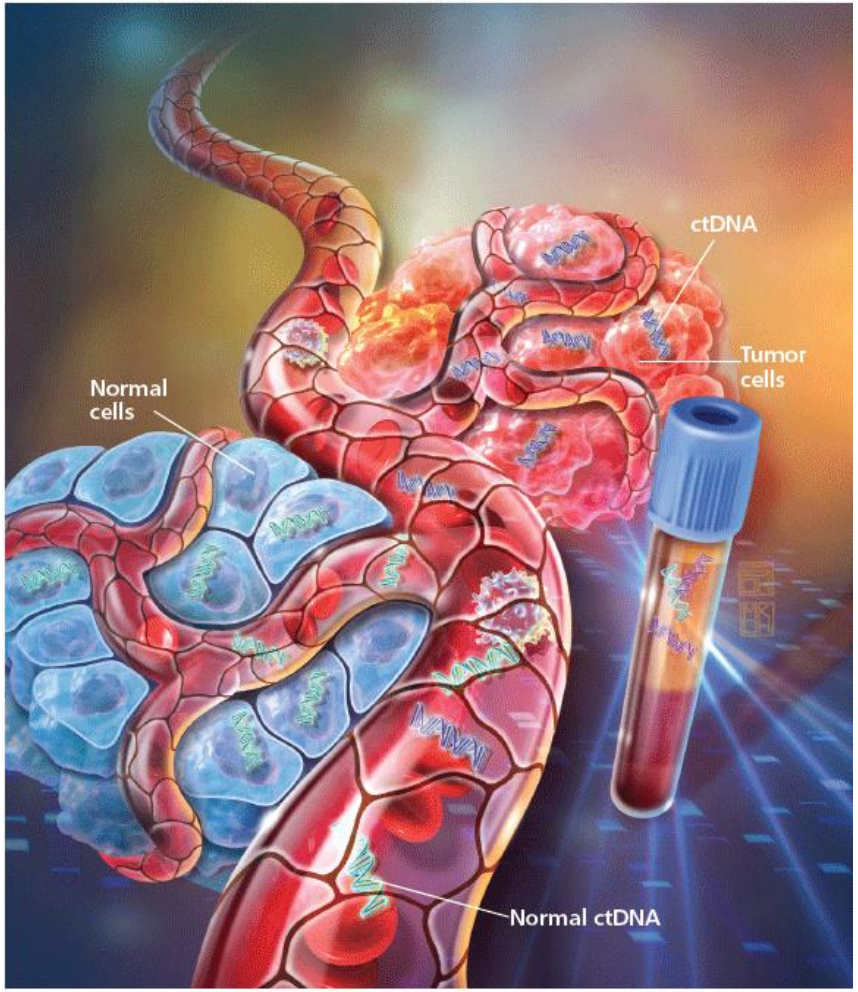
# 1 Develop circulating tumor DNA as a prognostic biomarker in acute lymphoblastic leukemia (ALL).




Circulating tumor DNA is an ultra-sensitive test to detect the presence of cancer cells.

*Can it be used to monitor leukemia response?*

**Jessica Blackburn, PhD**

**Thomas Badgett, MD,PhD**

*https://www.cancernetwork.com*

# Circulating tumor DNA as an ALL biomarker

## Results

- Collected bone marrow samples from 6 ALL patients and have started a biobank
- Isolated cell-free tumor DNA on multiple samples from spinal fluid and blood over time
- Children with leukemia in their spinal fluids have more circulating DNA – need to verify it is tumor specific.

## Funds

- Personnel costs, experimental reagents and testing.

## Return on Investment

- Future grant funding, possible intellectual property and the importance of identifying leukemia relapses as early as possible.

## Impact

- Detecting leukemia spread to CNS and relapses at earlier stages should improve clinical outcome.

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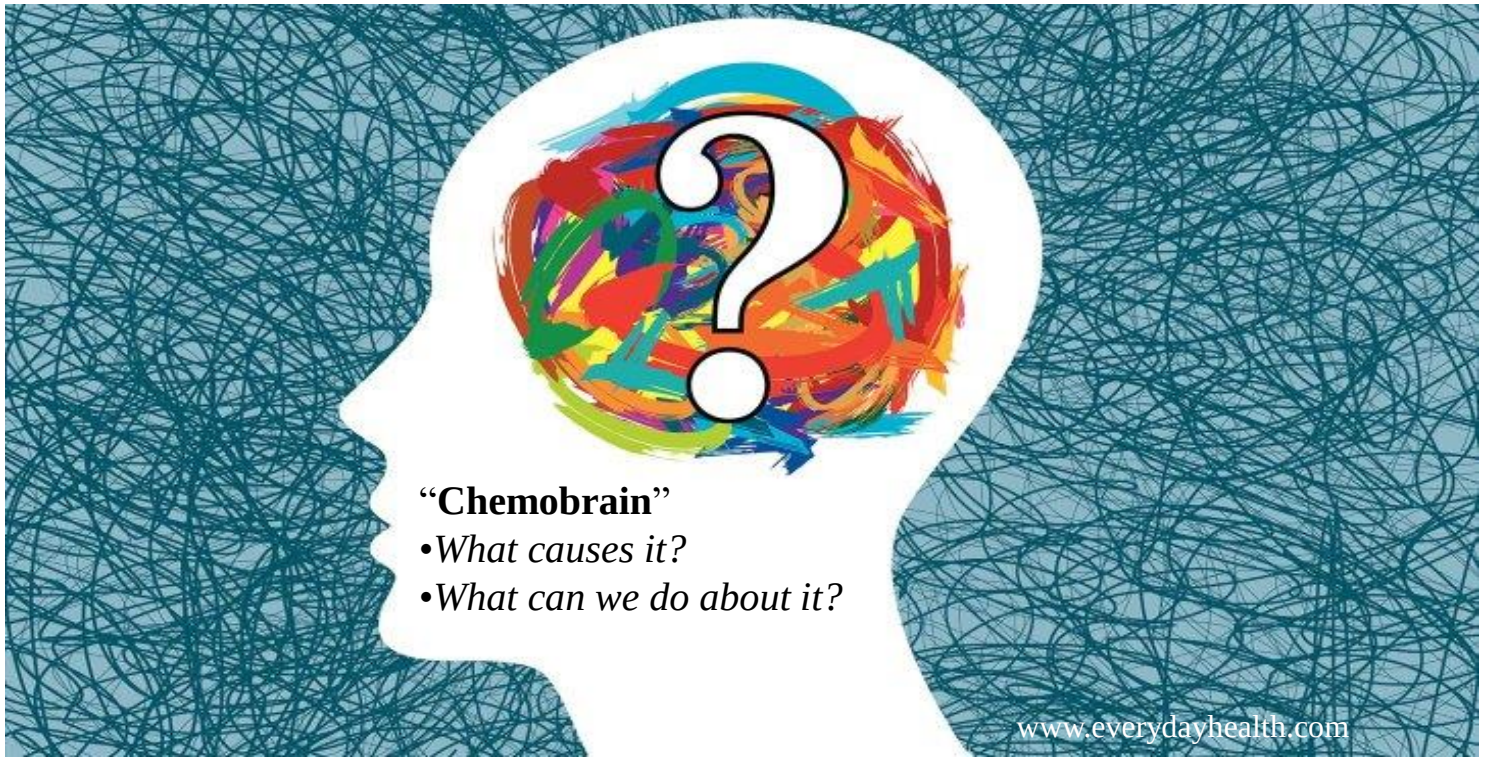
# Acute lymphoblastic leukemia (ALL) therapy and cognitive impairment: mechanisms and prevention








**Daret St. Clair, PhD** **Caryn Sorge, MD** **Heidi Weiss, PhD**

**Subbarao Bondada, PhD** **Allan Butterfield, PhD**

# Chemotherapy-induced cognition impairment: Mechanisms and Prevention

## Results

- Higher levels of a marker of oxidative injury were found in EVs from children treated with doxorubicin and they were lowered by MESNA, an anti-oxidant – need more samples to be sure.
- Higher levels of inflammatory proteins made by immune cells treated with EVs that contained oxidative markers. These cytokines might contribute to brain damage – need to test.
- To date, eight children have been recruited and samples are being collected for analysis.
- Vitamin E reduced markers of oxidative injury in chemotherapy exposed EVs.

## Funds

- Personnel costs, experimental reagents and testing.

## Return on Investment

- Future grant funding, possible intellectual property and the benefit for our patients.

## Impact

- Many pediatric cancer survivors suffer from neurocognitive deficits due to chemotherapy. Identifying strategies to prevent this will greatly improve their quality of life.

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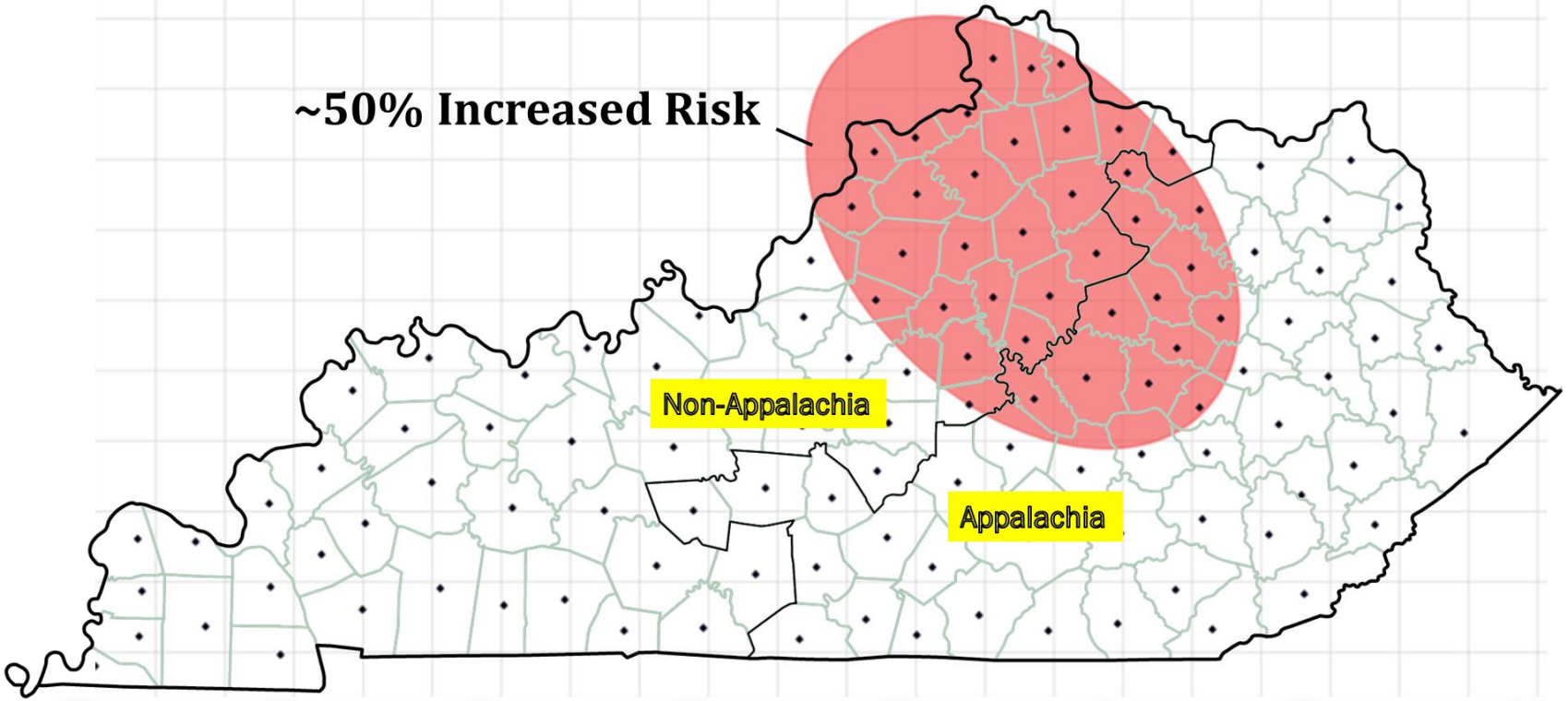
# Identify factors associated with high incidence of pediatric brain tumors in Kentucky

New Study Findings: Pediatric Brain and CNS High Rate Cluster in Kentucky, 2007-2017

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Eric B. Durbin, DrPH

Thomas Badgett, MD,PhD

Bin Huang, DrPH

Thomas Tucker, PhD

# Pediatric Brain Tumor Incidence in Kentucky

## Results

- Initial spatio-temporal scan reveals cluster of 50% increased risk of childhood brain and CNS tumors 2007-2017.
- A cohort of 332 eligible Kentucky brain and CNS tumor specimens have been identified in Kentucky, Tennessee and Ohio pathology laboratories.
- To date: 30 specimens have been obtained from labs, processed and shipped to CHOP for genomic sequencing.
- Study presented at National Cancer Institute's Childhood Cancer Data Initiative (CCDI) Symposium on July 30.

## Funds

- Personnel costs, laboratory processing fees, specimen handling materials and shipping fees

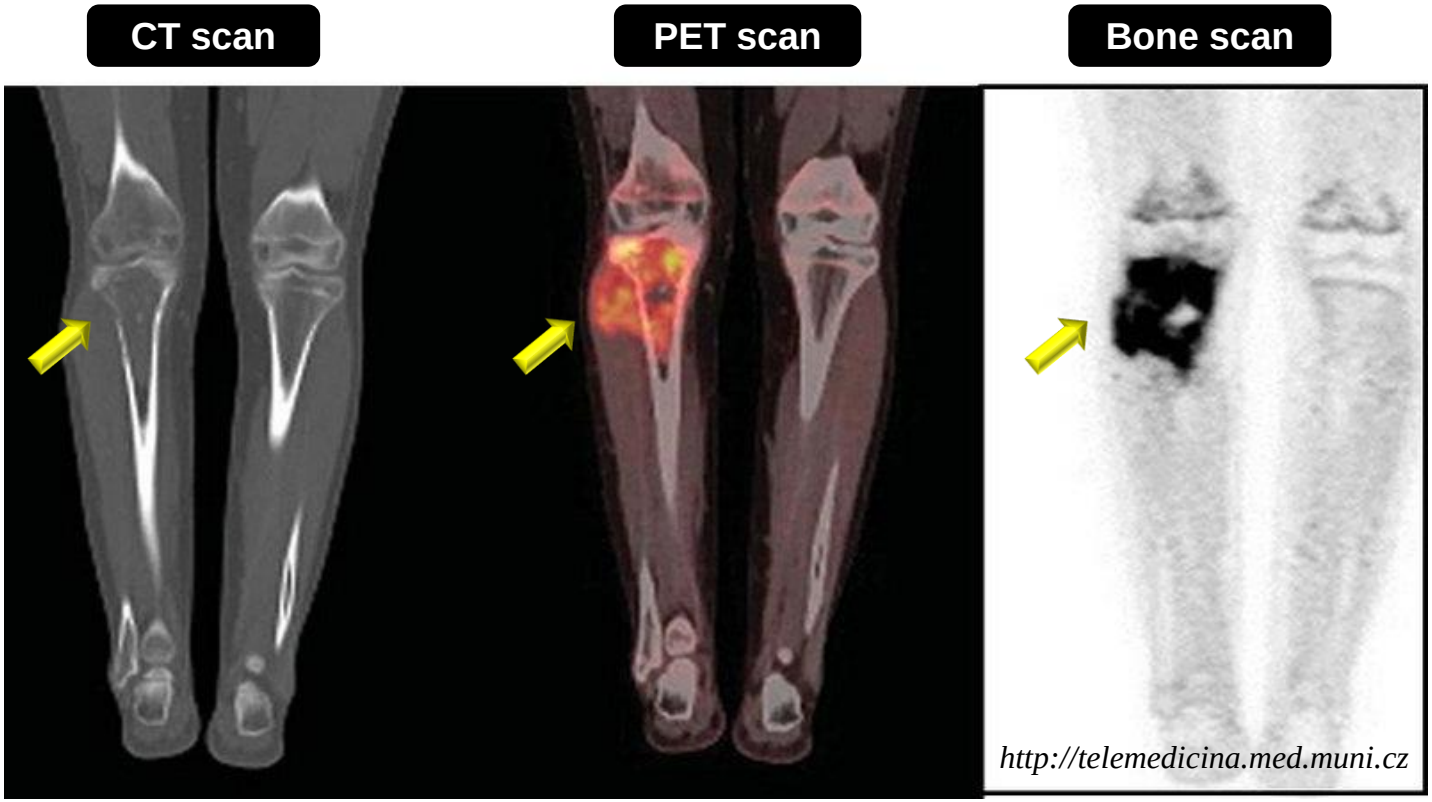
## Return on Investment

- $1.25 million in sequencing from CHOP, future grant funding

## Impact

- Understanding the factors responsible for increased cancer in Kentucky children may lead to early detection and prevention strategies, improved treatment, better long term outcomes and reduced healthcare costs.

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



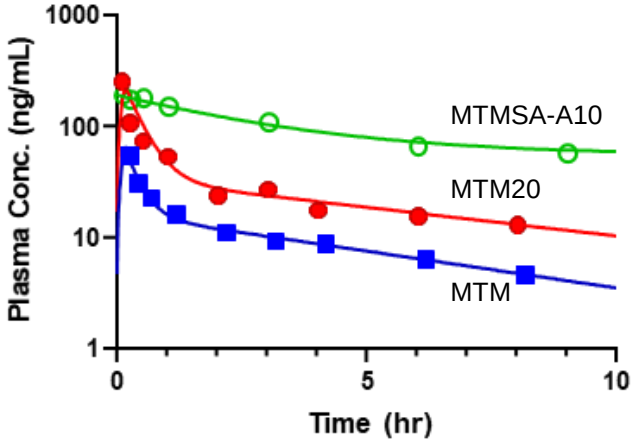

Markos Leggas, PhD

Jurgen Rohr, PhD

# Mithramycin derivatives as new drugs for the treatment of Ewing sarcoma

## Results

- More effective mithramycin derivatives developed at UK
- Small scale synthesis achieved at UK
- Preliminary testing in animal models with promising anti-cancer activity
- Large scale synthesis and pre-clinical safety/toxicity testing in progress




- Plan to submit project to NCI Experimental Therapeutics (NExT) Program for steps leading to clinical trial

## Funds

- Drug manufacturing costs, pre-clinical animal testing, personnel costs, outsourcing

## Return on Investment

- Future grant funding, intellectual property secured, UK is seeking licensing partners

## Impact

- These drugs target Ewing sarcoma in a precise manner and are unlike any other drugs currently being used to treat these patients. This may offer the first successful and unique Ewing sarcoma treatment in more than 40 years.


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