# Epigenetic biomarkers at the origins of childhood cancers since the time of birth

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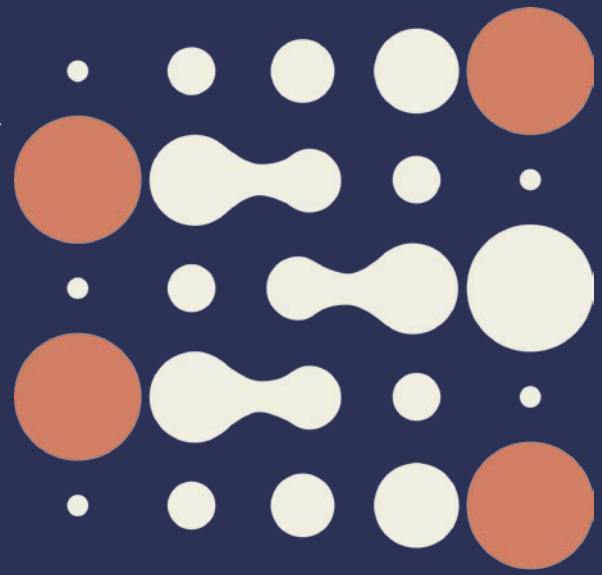

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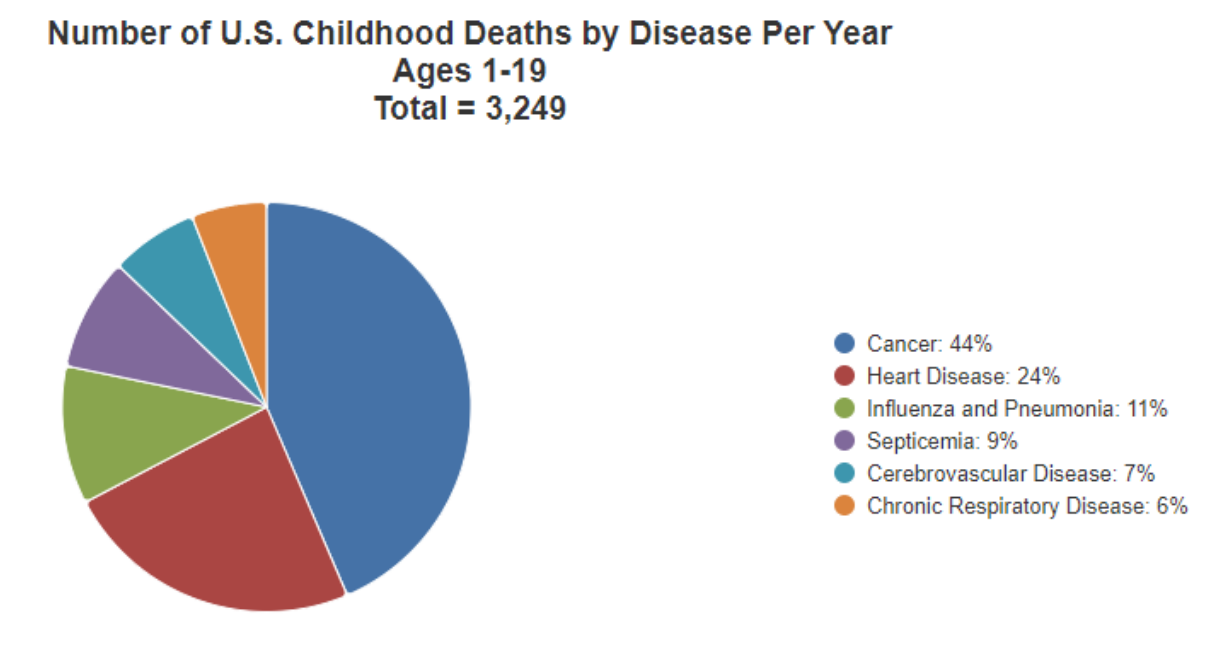
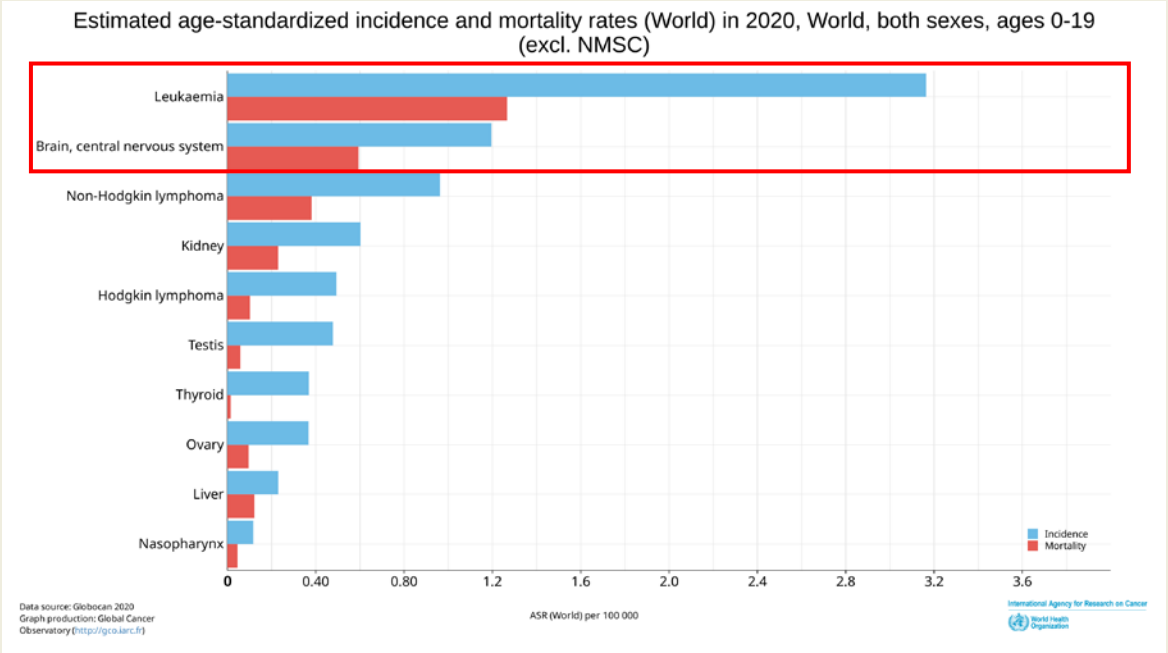
# Introduction

**Causes not well understood**

?

Cancer is the **number one** cause of death by disease in children




https://curesearch.org/childhood-cancer-deaths-per-year. Accessed on Jan 15, 2024

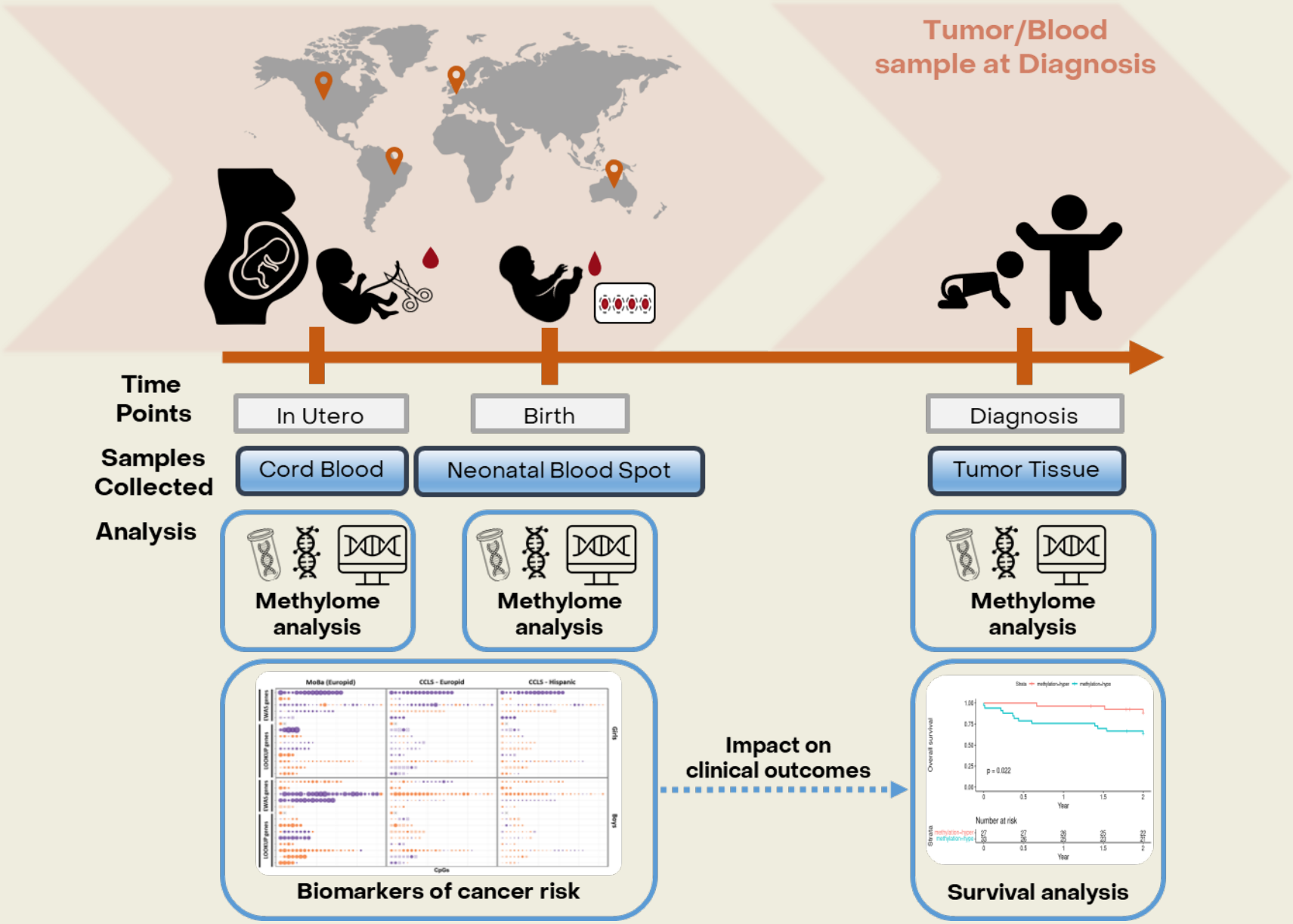
# Introduction

- **Epigenetics** has a **driver role** that dictates what the different cells of the embryo will become and are heritable so can have **long-lasting consequences** if deregulated.
- Epigenetic alterations likely play a **pivotal role** in the **development of pediatric cancer**, especially considering the possibility that its origins may trace back to the in utero period.
- Unlike genetic, epigenetics changes are **potentially reversible**, hence, offering interesting targets for prevention.

**Hypothesis**

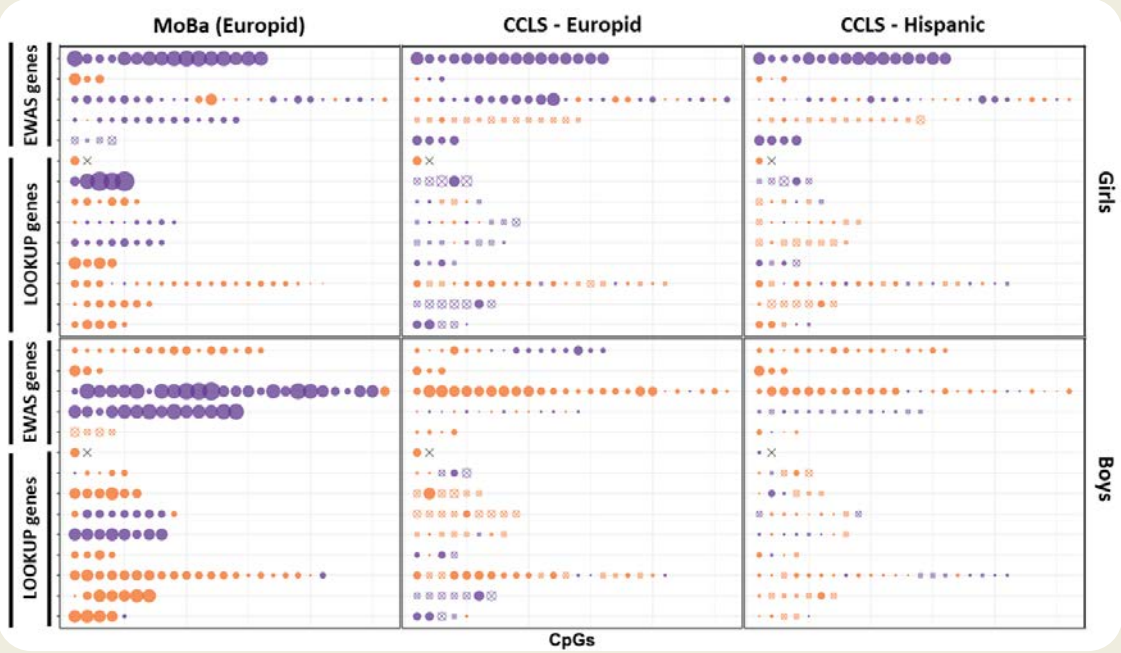
Methylome changes associated with childhood cancer risk can be identified in blood cells at birth, and these changes can serve as sensitive biomarkers for prevention as well as targeted therapy.

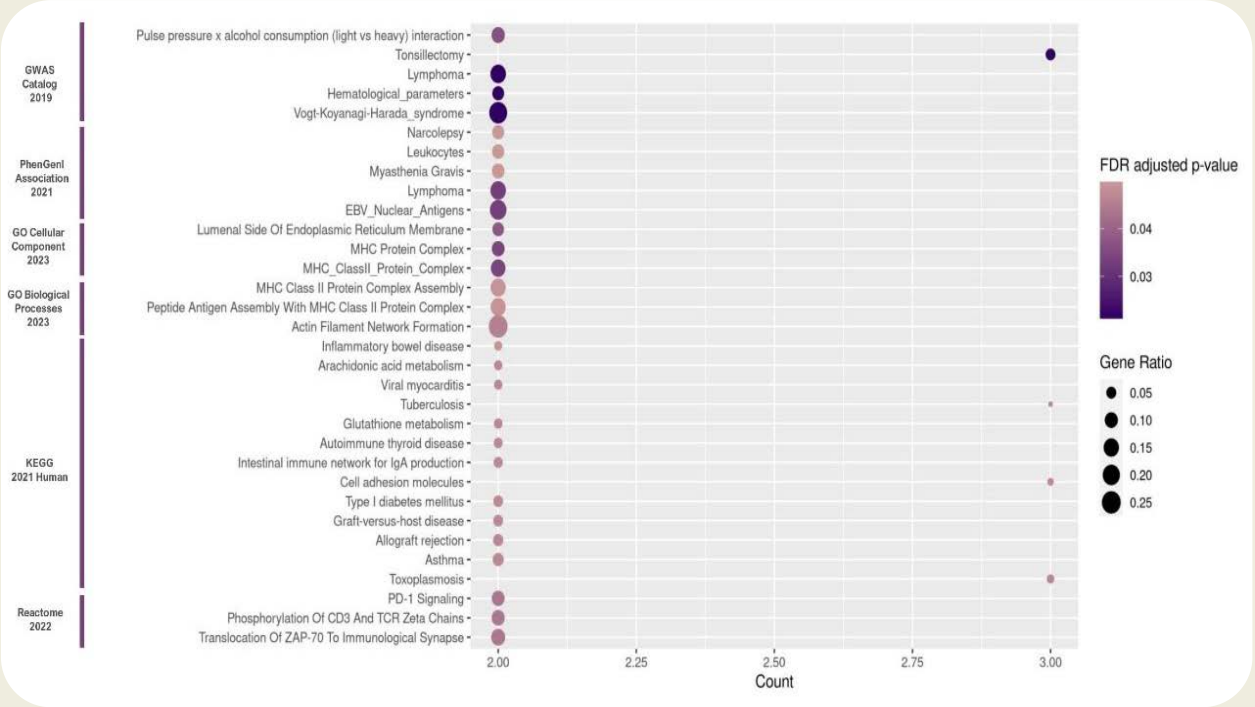
# Design


Tumor/Blood sample at Diagnosis
Time Points
In Utero
Birth
Diagnosis
Samples Collected
Cord Blood
Neonatal Blood Spot
Tumor Tissue
Analysis
Methylome analysis
Methylome analysis
Methylome analysis
Biomarkers of cancer risk
Impact on clinical outcomes
Survival analysis

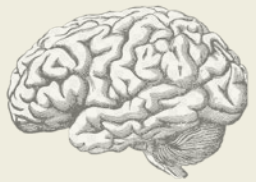
# Epigenetic alterations at birth predisposing to childhood pre-B leukemia

## Molecular imprint at birth

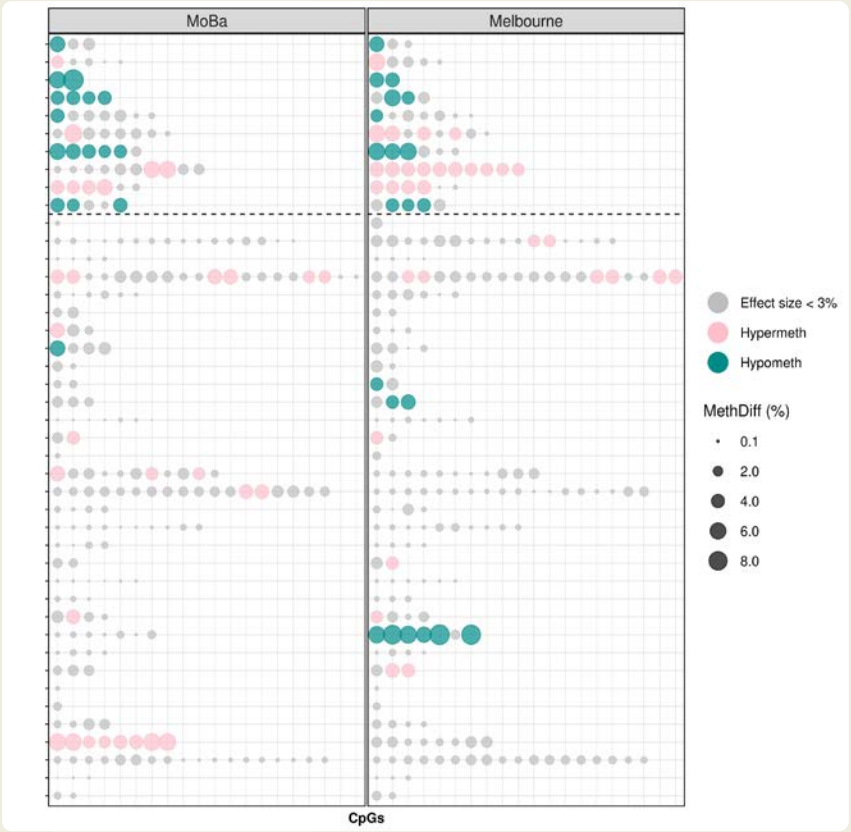


# Epigenetic alterations at birth associated to childhood CNS tumors

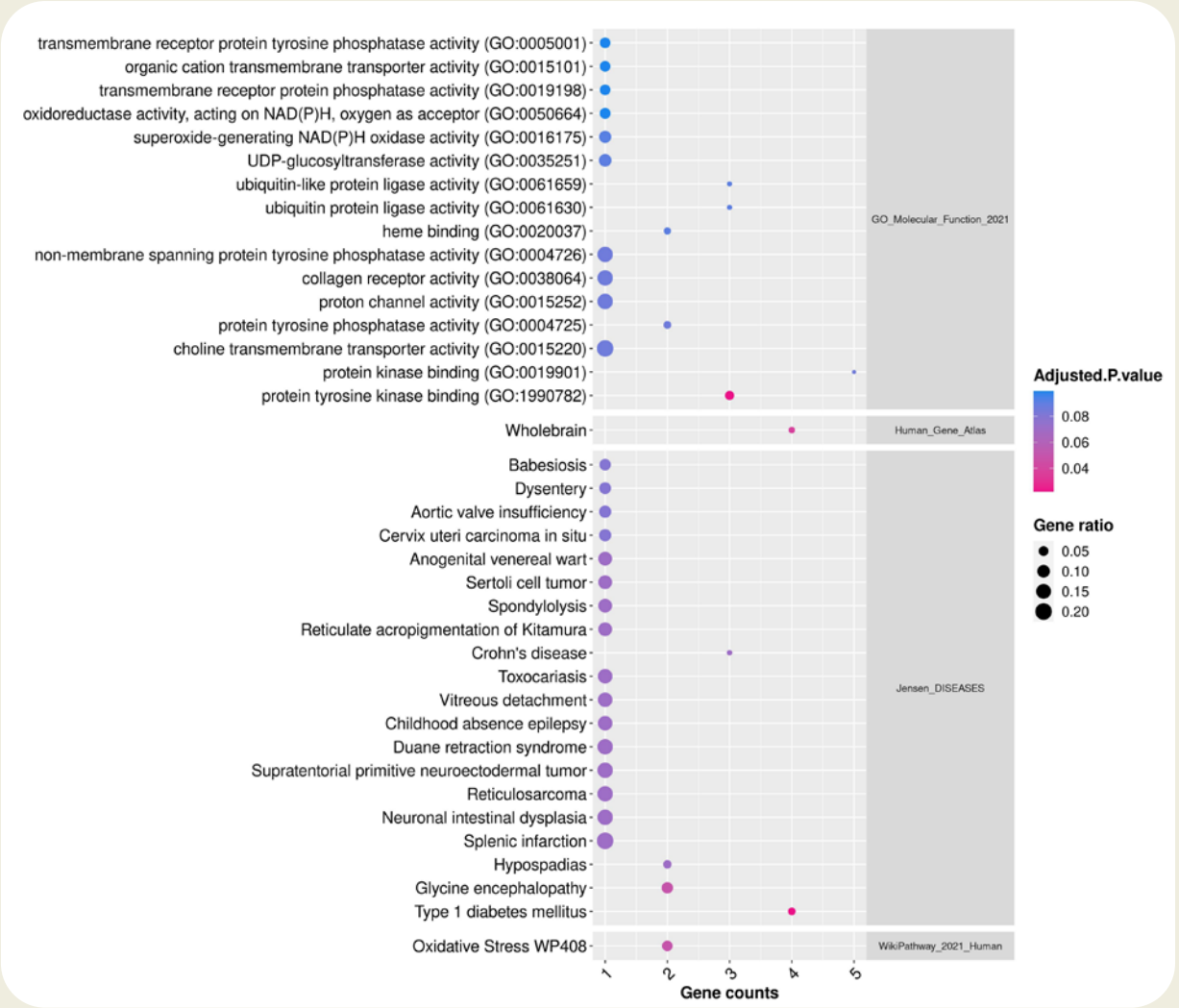


## Molecular imprint at birth



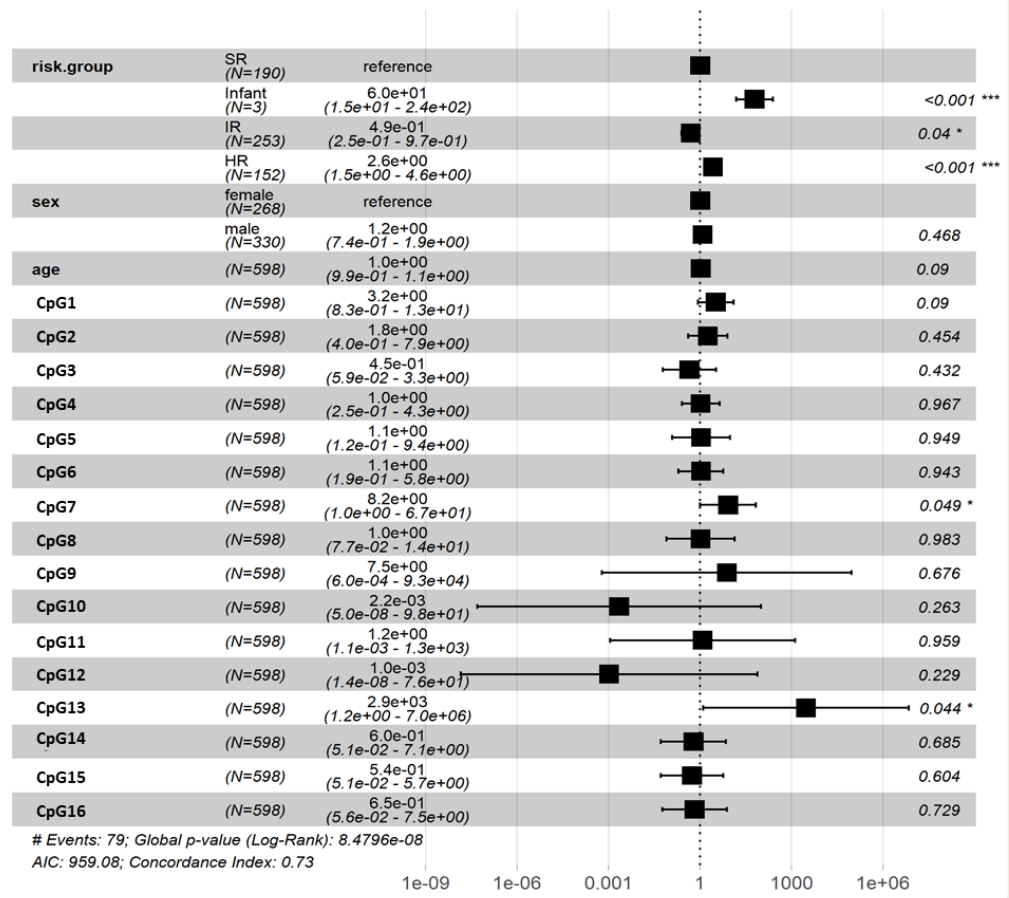

We checked for CpGs considered as informative of the brain methylation* to assist in interpreting the methylation levels of the CpGs identified in blood within the context of the brain.

*Edgar et al. Transl Psychiatry (2017)

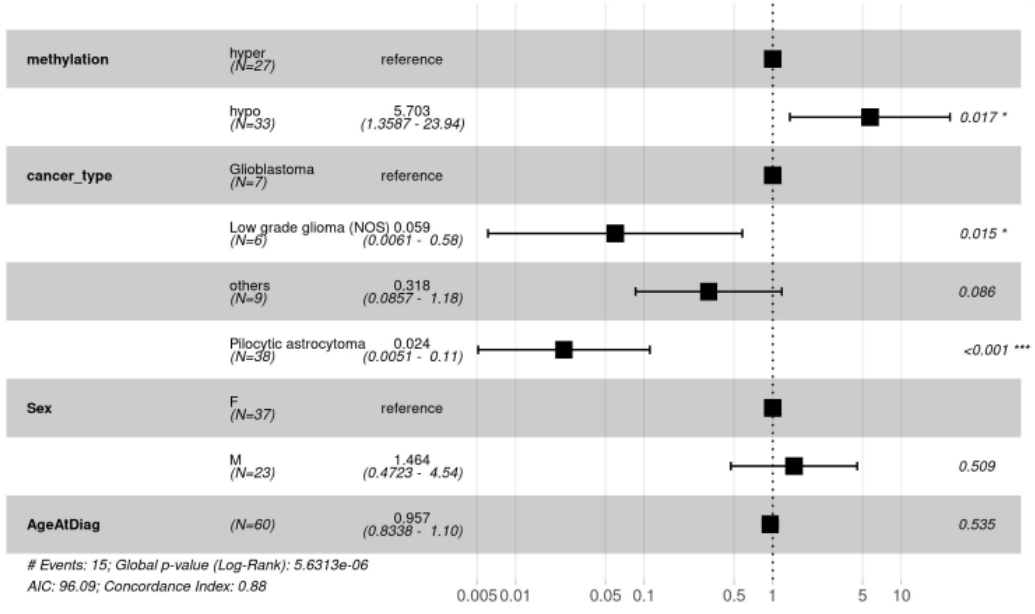


# Association with prognosis

pre-B leukemia




CNS tumors



# Conclusion

- The identification of a methylome signature at birth associated with childhood cancer development may change the paradigm of tumorigenesis by uncovering molecular precursors of childhood cancer and its early origins.
- Epigenome alterations evident before diagnosis could be interesting actionable targets for risk assessment and prognosis.

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- INCa – PEDIAC (PI: Z. Herceg; Co-I: A. Ghantous)
- INCa – PEDIAHR (PI: A. Ghantous; Co-I: Z. Herceg)

# Key take-home messages

Our work presents an innovative approach for the discovery of a new generation of biomarkers for pediatric cancer development that can be applied to future preventive and therapeutic strategies.