

Late-Breaking: microRNA circolanti nei gliomi pediatrici di basso grado verso una nuova era di medicina di precisione

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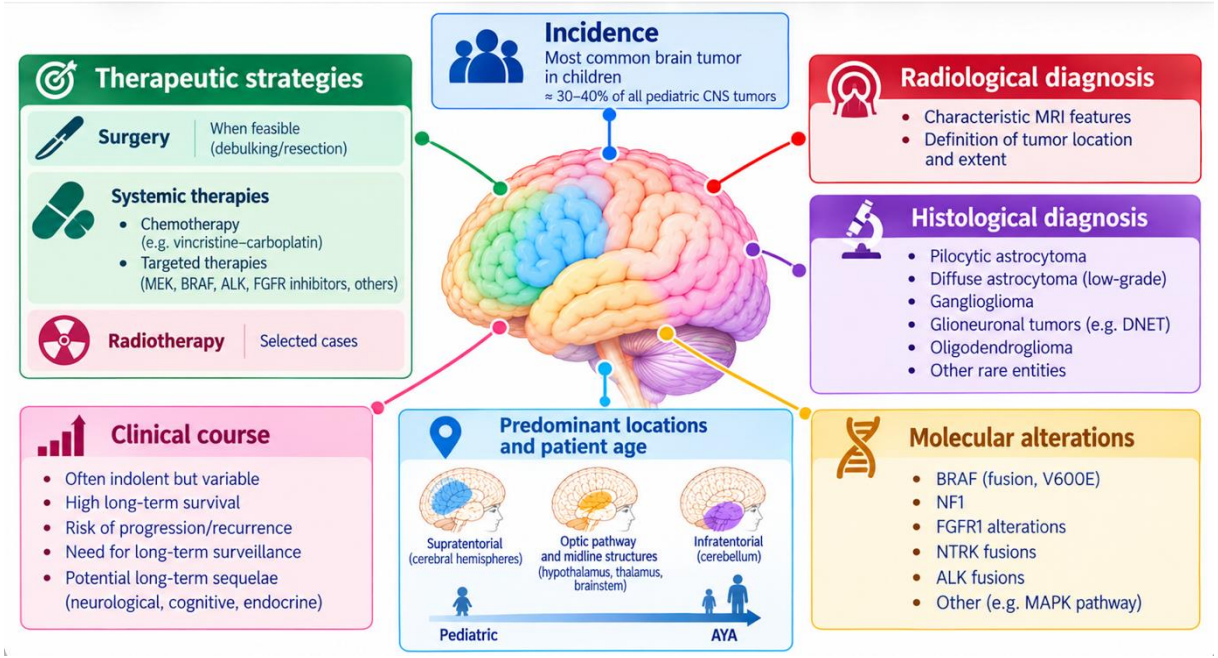
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Disclosures

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NO							

Pediatric low-grade gliomas (pLGG): a favorable prognosis, but a long clinical journey



KEY UNMET NEED

Reliable, minimally invasive biomarkers

- Support diagnosis and differential diagnosis
- Improve biological and risk stratification
- Enable longitudinal disease monitoring
- Assess treatment response
- Detect progression earlier

Louis et al., Acta Neuropathol, 2021; Ryall et al., Cancer Cell, 2020; Packer et al., Neuro Oncology 2016

Liquid biopsy: *a window into tumour biology over time*


www.nature.com/collections/cancer-milestones December 2020

nature milestones Cancer

MILESTONE 3

Tracking cancer in liquid biopsies

The diverse clinical applications that derived from analysis of circulating tumour material eventually led to the coining of the term 'liquid biopsy' by Pantel and Alix-Panabières in 2010. In subsequent investigations,

Nature Milestones – Cacer (2020)

WHY LIQUID BIOPSY?

Minimally invasive
Serial plasma/serum sampling

Molecular information
Detection and monitoring of driver alterations

Clinical relevance
Potential prognostic, predictive and monitoring value

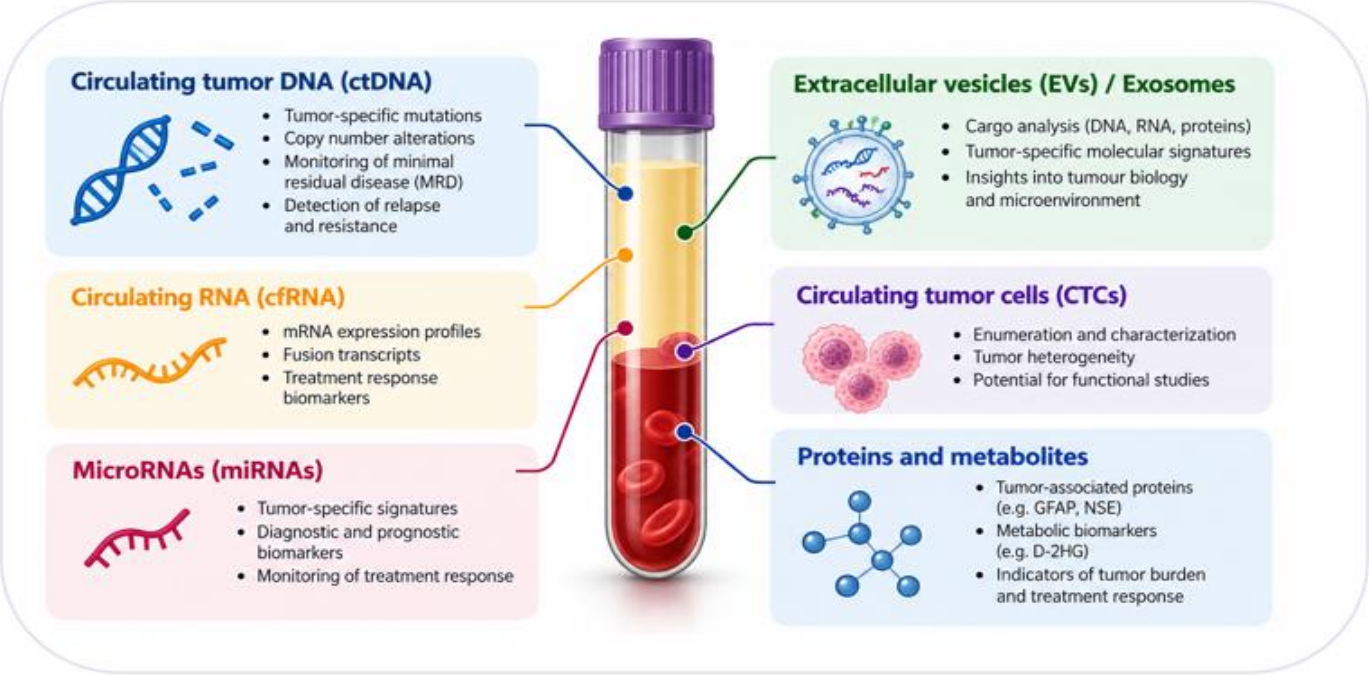
One blood sample = a snapshot → serial blood samples = a trajectory of tumor evolution

Romero D. *Nat Milestones Cancer*. 2020; D'Antonio F, Spinello Z, et al. *Crit Rev Oncol Hematol*. 2025.

Liquid biopsy in brain tumors: what can we analyze?

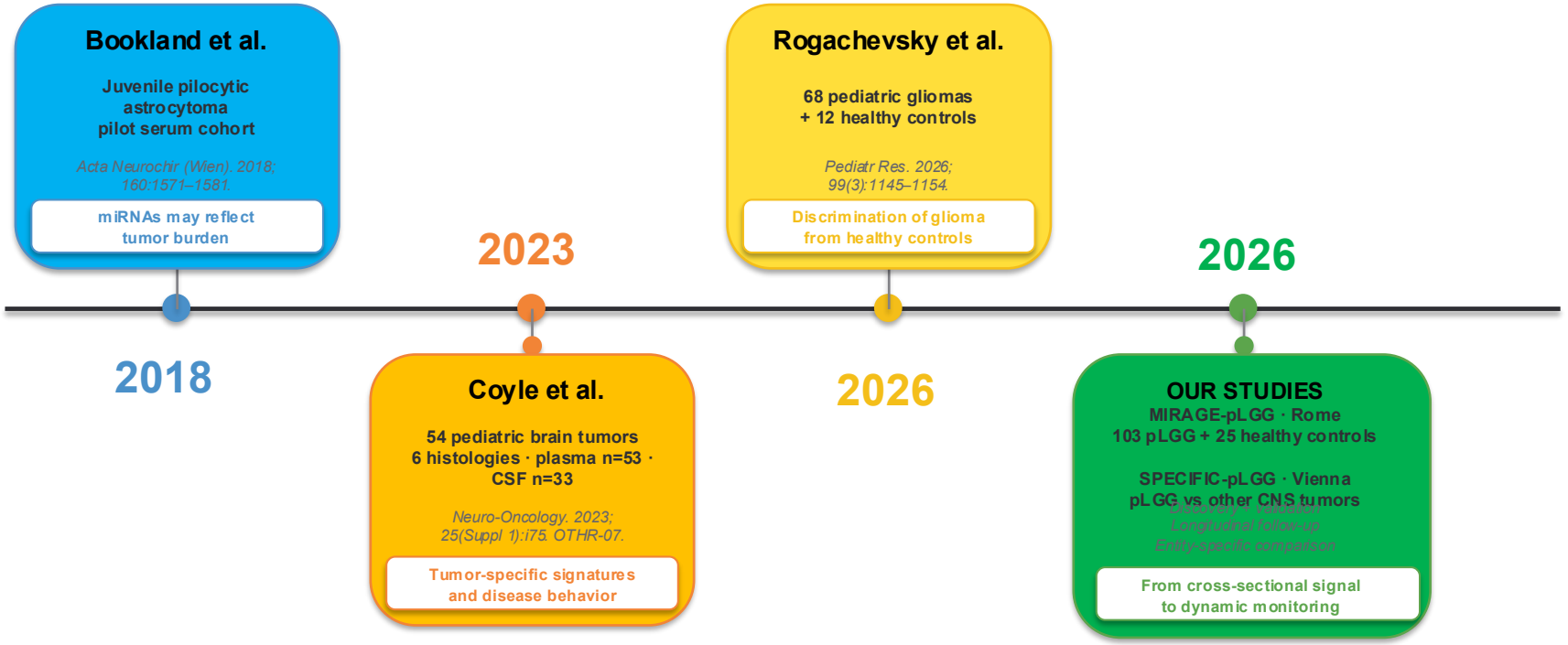
Cerebrospinal fluid (CSF)
ctDNA/cfDNA • mutations • CNVs
methylation • RNA • vesicles

Plasma
ctDNA • miRNA
extracellular vesicles • proteins



Romero D. *Nat Milestones Cancer*. 2020

Circulating miRNAs in pediatric glioma: building the evidence



Proof of concept exists - but evidence remains limited and largely cross-sectional.

Two complementary studies, three biological questions

STUDY 1 · MIRAGE-pLGG

MIcroRNA for Recognition And longitudinal monitoring in pediatric LGG

ROME · OPBG

pLGG ↔ HEALTHY CONTROLS

1 · DETECTION

Can circulating miRNAs discriminate pLGG from healthy controls?

2 · DYNAMICS

Do longitudinal changes reflect disease burden and evolution?

STUDY 2 · CROSS-ENTITY

Comprehensive characterization of circulating miRNAs across pediatric CNS tumors

VIENNA · MUW

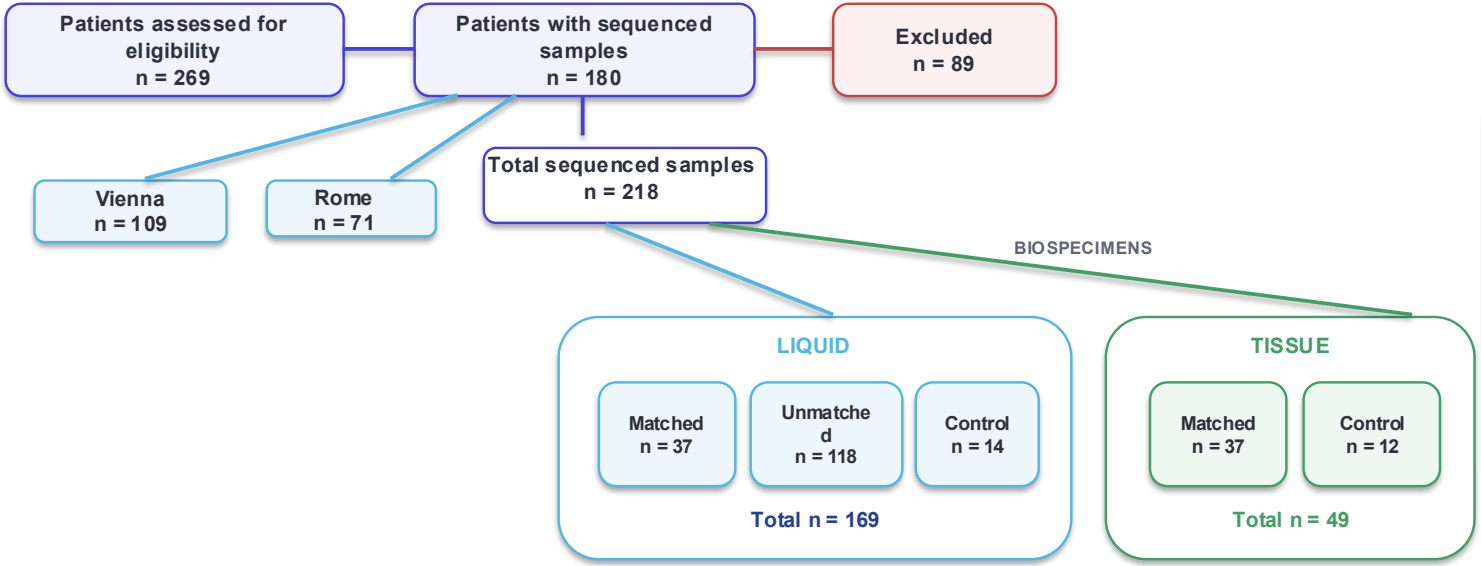
PEDIATRIC CNS TUMORS · CROSS-ENTITY COMPARISON

3 · SPECIFICITY

pLGG · Medulloblastoma · pHGG · Ependymoma · Other CNS tumors

Disease-associated signal → longitudinal behavior → tumor-entity–specific signatures

Study cohort



KEY NUMBERS

180
patients

218
samples

103
pediatric low-grade gliomas

TUMOR ENTITIES

- Embryonal tumors n = 18
- Pediatric high-grade gliomas n = 12
- Pediatric low-grade gliomas n = 103
- Other pediatric CNS tumors n = 18

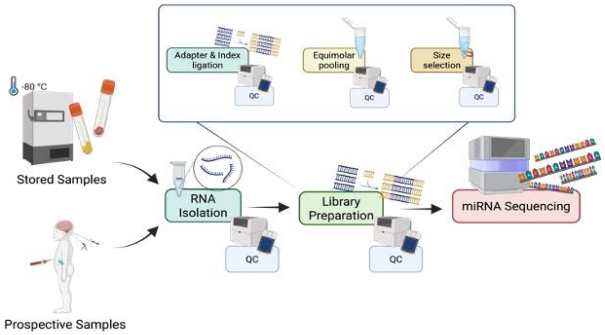
STUDY 1 circulating miRNA cohort

Can circulating miRNAs distinguish pLGG from healthy children?

103 pLGG

VS

14 healthy controls



01 Blood sampling

02 Plasma / serum

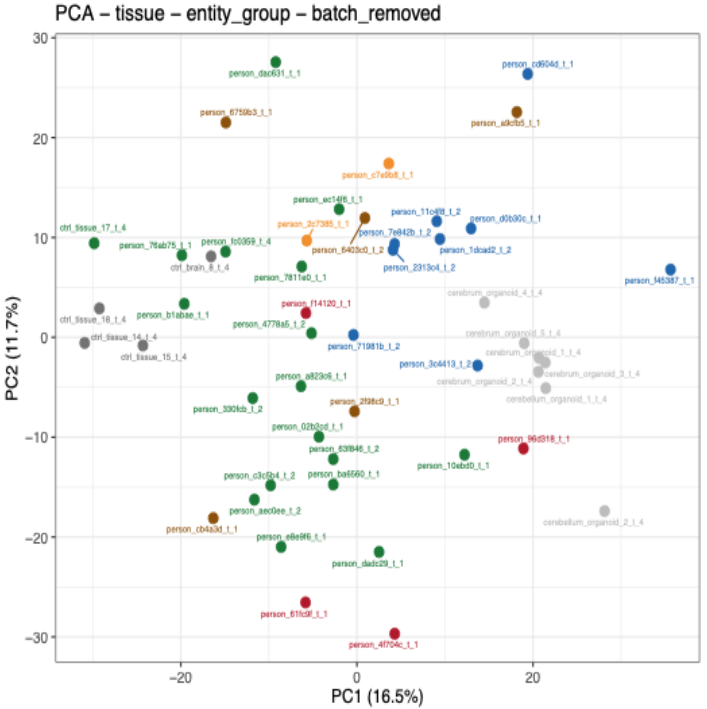
03 miRNA extraction

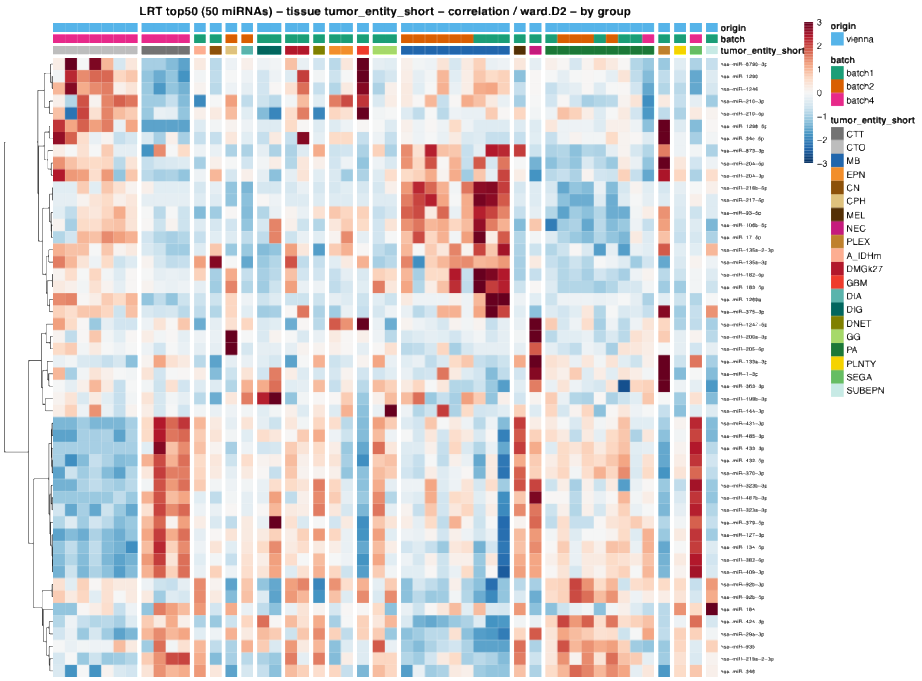
04 Global profiling

05 Bioinformatic analysis

Clinical data: age · location · histology · MAPK alteration · NF1 · extent of resection · disease status

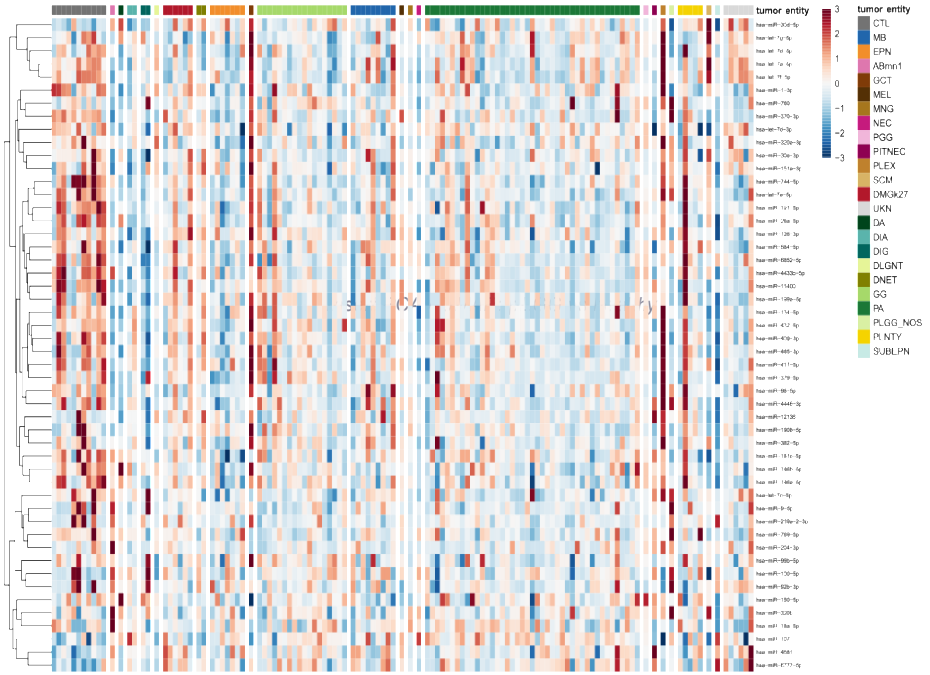
CNS tumors -associated tissue miRNA profile

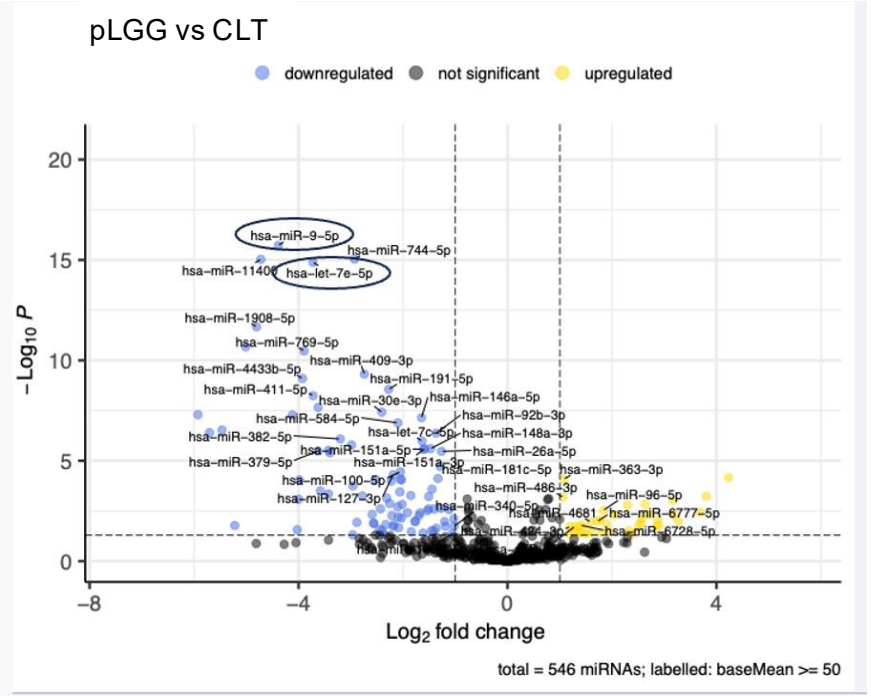




Global profiling reveals a disease-associated tissue miRNA pattern

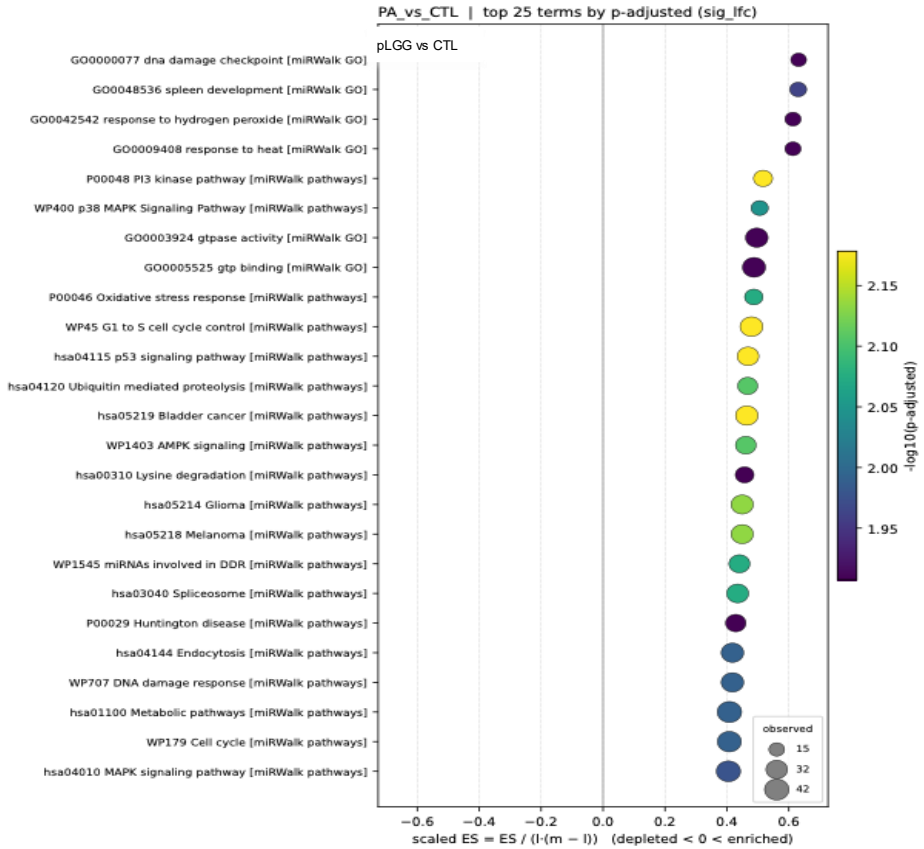
A pLGG-associated circulating miRNA profile vs healthy controls





Global profiling reveals a disease-associated circulating miRNA pattern

Which miRNAs drive the pLGG-associated signal?



The enrichment analysis shows that the identified miRNAs converge on biologically relevant pathways, including **MAPK/PI3K signaling, DNA damage response, p53 signaling, and cell-cycle regulation**, supporting the **biological relevance of the signature**, although its **specificity for pLGG remains to be established**

ONGOING STEP: Longitudinal validation of the circulating miRNA signature

SELECTED miRNA SIGNATURE

Targeted validation by ddPCR

PRESURGICAL BASELINE

Before tumor resection (when available)

Can the signature be detected before surgery?

AFTER GROSS TOTAL RESECTION

No measurable residual disease

Does the miRNA signal decrease or become undetectable?

RESIDUAL DISEASE

Persistent measurable disease

Does the signature remain detectable with stable disease burden?

PROGRESSION

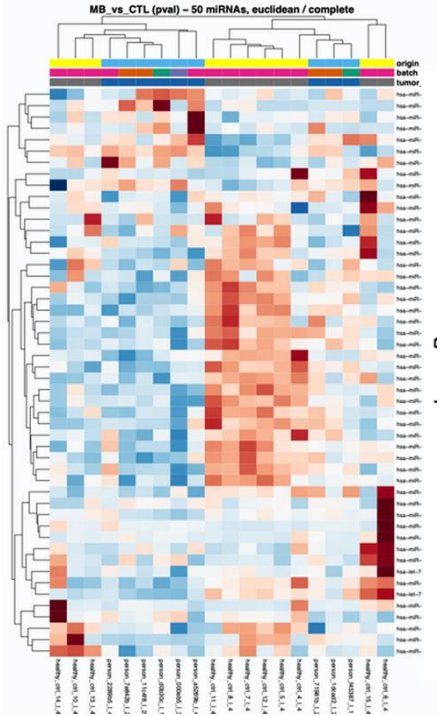
Increasing disease burden

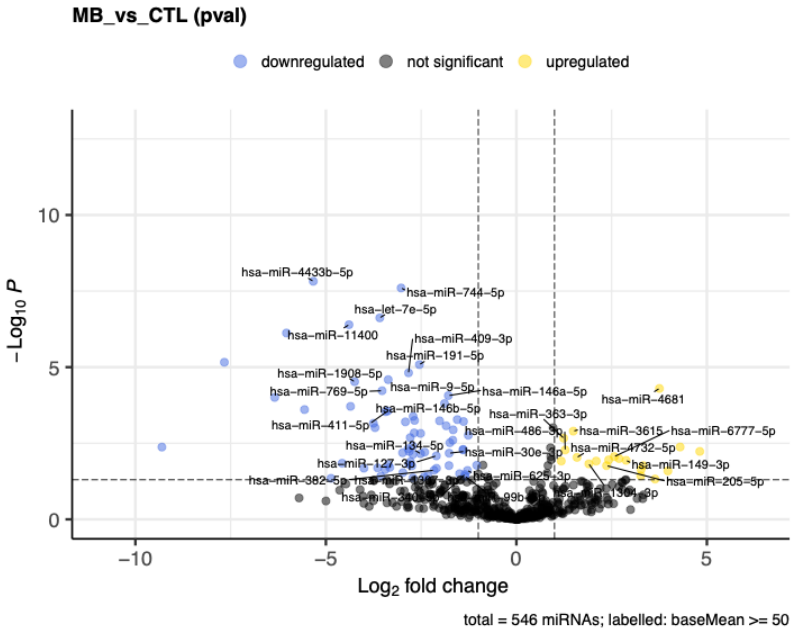
Does the miRNA signal increase or change with progression?

GOAL: Determine whether longitudinal changes in the same miRNA signature mirror disease burden and evolution

Serial samples → each patient becomes their own biological control

Exploring tumor-associated circulating miRNA profiles across pediatric CNS tumor entities





Preliminary data suggest a distinct circulating miRNA profile in medulloblastoma compared with healthy controls.

Study 2: Comprehensive characterization of circulating miRNAs across pediatric CNS tumors

Cross-entity comparison to identify shared and tumor-entity–specific miRNA signatures



CROSS-ENTITY COMPARISON

01 Shared vs unique miRNA signatures

02 Tumor-entity specificity

03 Potential diagnostic classification

Circulating miRNAs in pLGG: from biological signal to clinical relevance

A minimally invasive opportunity to complement imaging during a long clinical journey

01 CLINICAL NEED

pLGG patients require prolonged surveillance, while tumor tissue is not always safely accessible for biopsy.

MRI remains essential but cannot fully capture tumor biology, highlighting the need for minimally invasive biomarkers such as liquid biopsy.

02 OUR SIGNAL

We identified a circulating miRNA profile associated with pLGG versus healthy controls.

Enrichment in MAPK/PI3K, DNA-damage response, p53 and cell-cycle pathways supports its biological relevance.

03 WHAT COMES NEXT

Longitudinal validation will test whether the signature tracks disease evolution over time.

Cross-entity comparison will determine whether the signal is specific to pLGG or shared across pediatric CNS tumors.

From a disease-associated signal → toward a dynamic, clinically informative biomarker for pLGG

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Thank you for your attention!



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