Toward a more informative multimodal data analysis of the pediatric AML transcriptome

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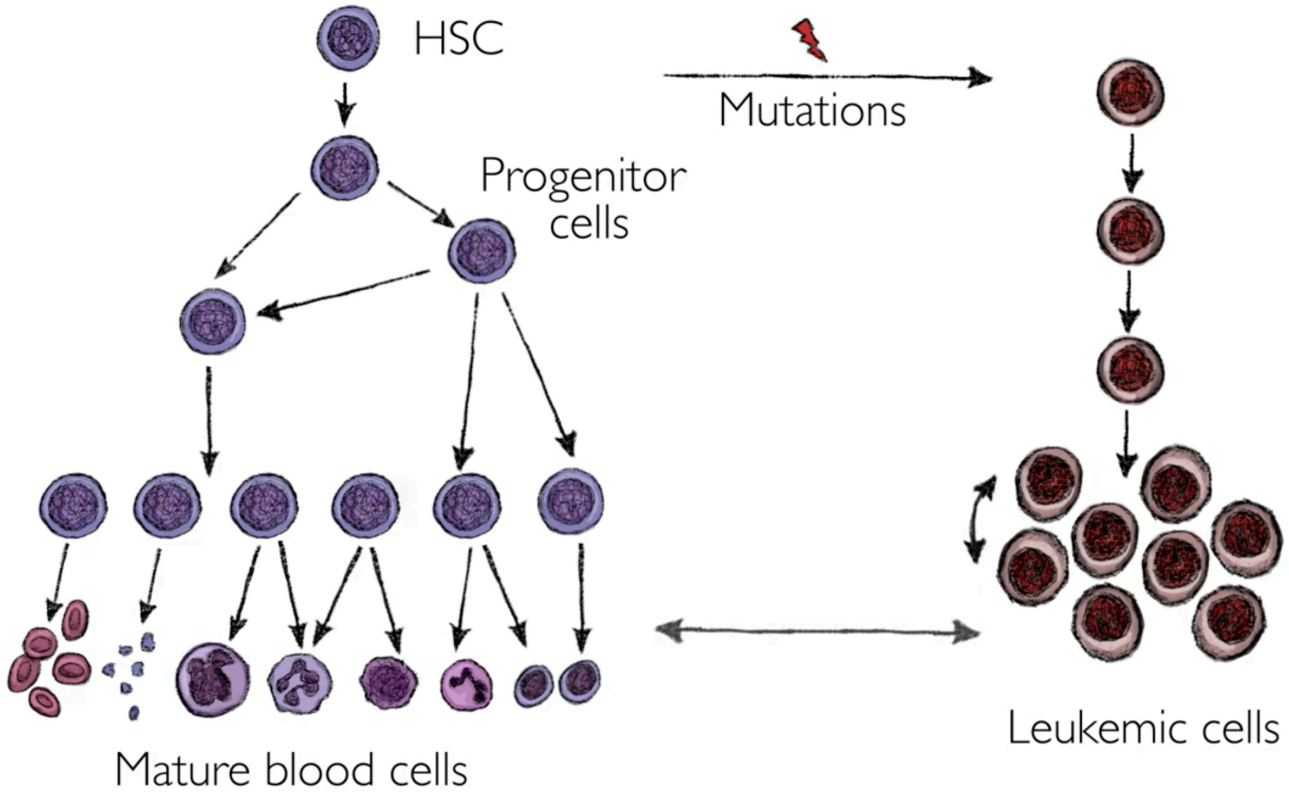
Acute myeloid leukemia (AML) is the most fatal of childhood cancers with no good treatments

- Caused by accumulation of immature myeloid cells in bone marrow
- Affects 25% of children with leukemia
- Chemotherapy for acute lymphoblastic leukemia (ALL) is generally successful
  - Kills healthy and aberrant B-cells → stable prognosis

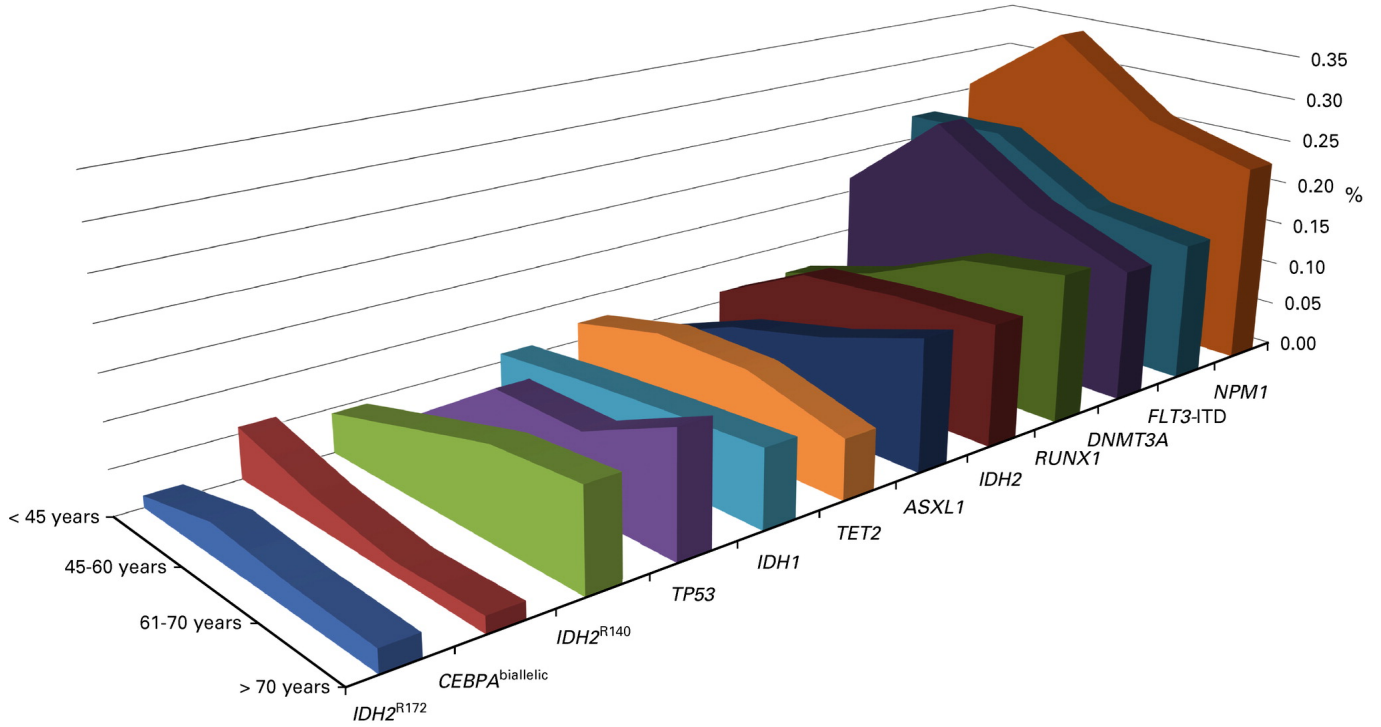


van Galen *et al.*, 2019

Current treatment strategies for pediatric AML are based adult genomes/transcriptomes

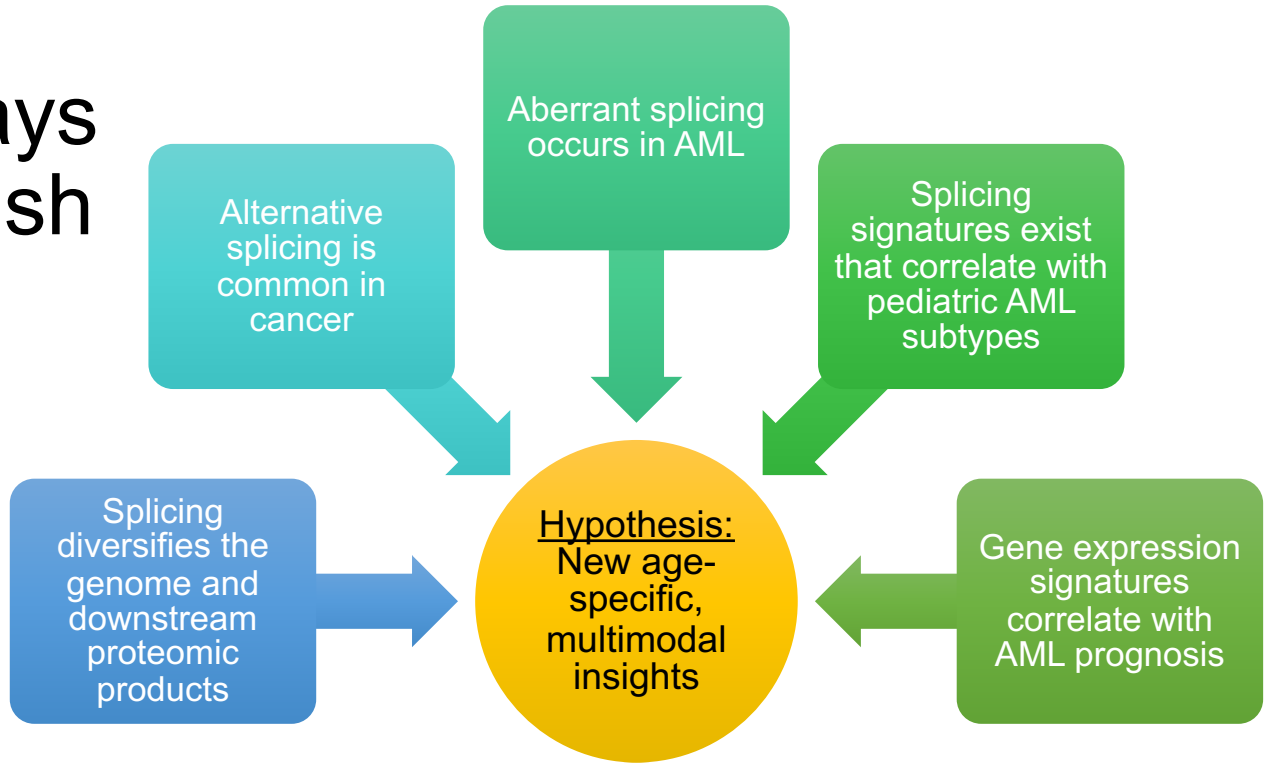
- Mean age of AML onset is 45 years
- ”Pediatric” considered 0 years to ~30 years old
- Age-specific genomic signatures have been linked to prognosis (Bullinger *et al.*, 2017)
- Hematopoietic expansion has age-specific regulation (Bullinger *et al.*, 2017)

What about splicing?

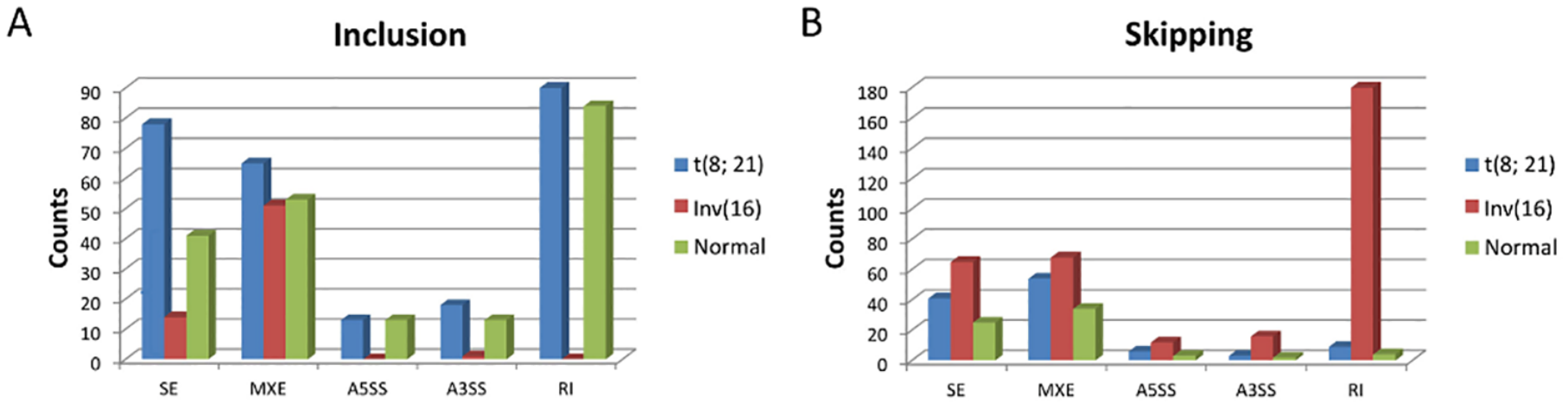


Bullinger *et al.*, 2017

Alternative splicing and correlated molecular pathways could help to better distinguish pediatric vs adult AML



PEGASAS correlates gene ontology and alternative splicing events



Hsu *et al.*, 2016

Hypothesis: Alternative splicing and correlated molecular pathways could play important roles in distinguishing pediatric vs adult AML

Aim 1

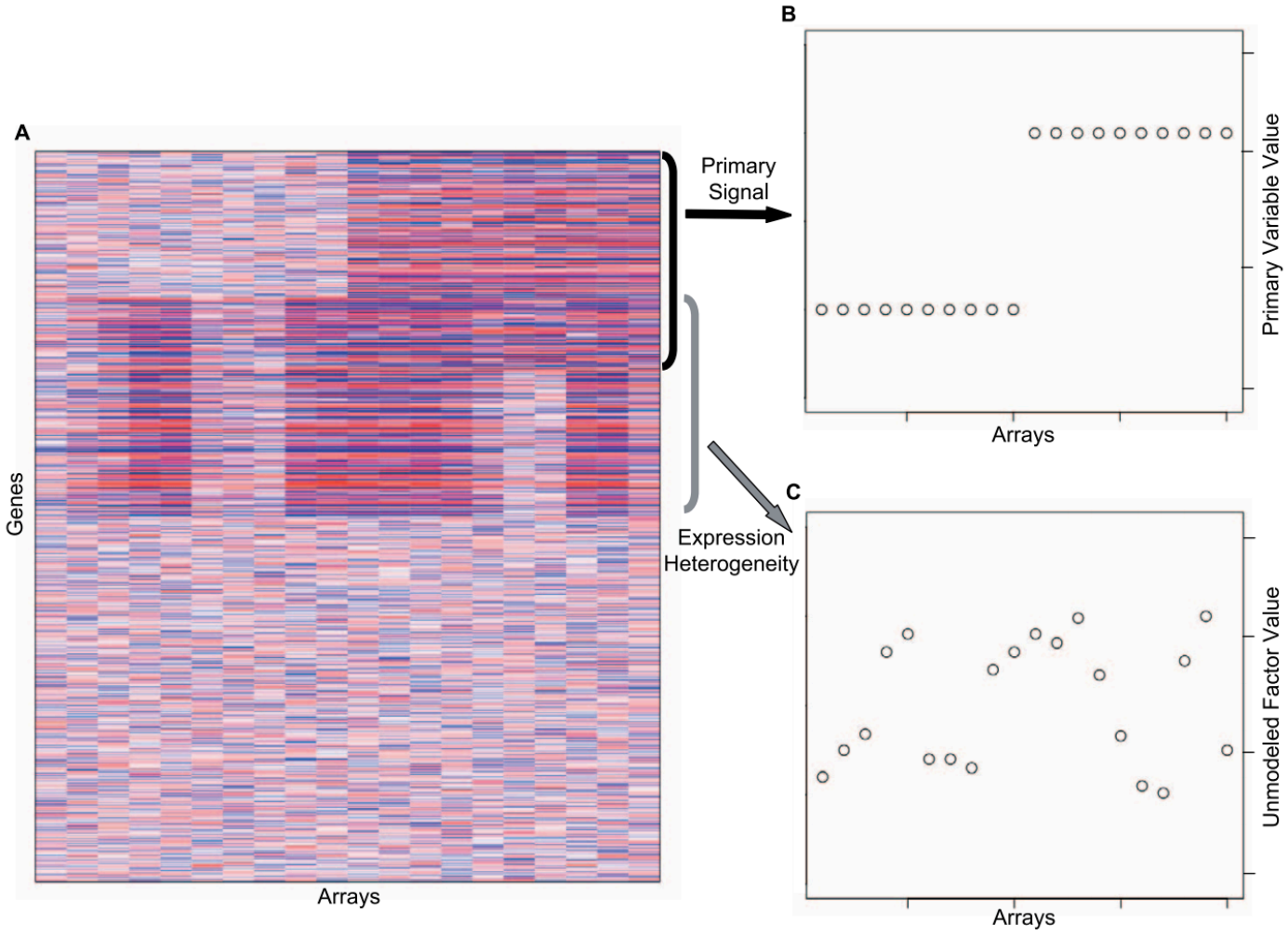
Improve analysis of splicing in large heterogeneous RNA-seq datasets

Aim 2

Discover age-specific, pathway-dependent alternative splicing patterns in pediatric AML RNA-seq data

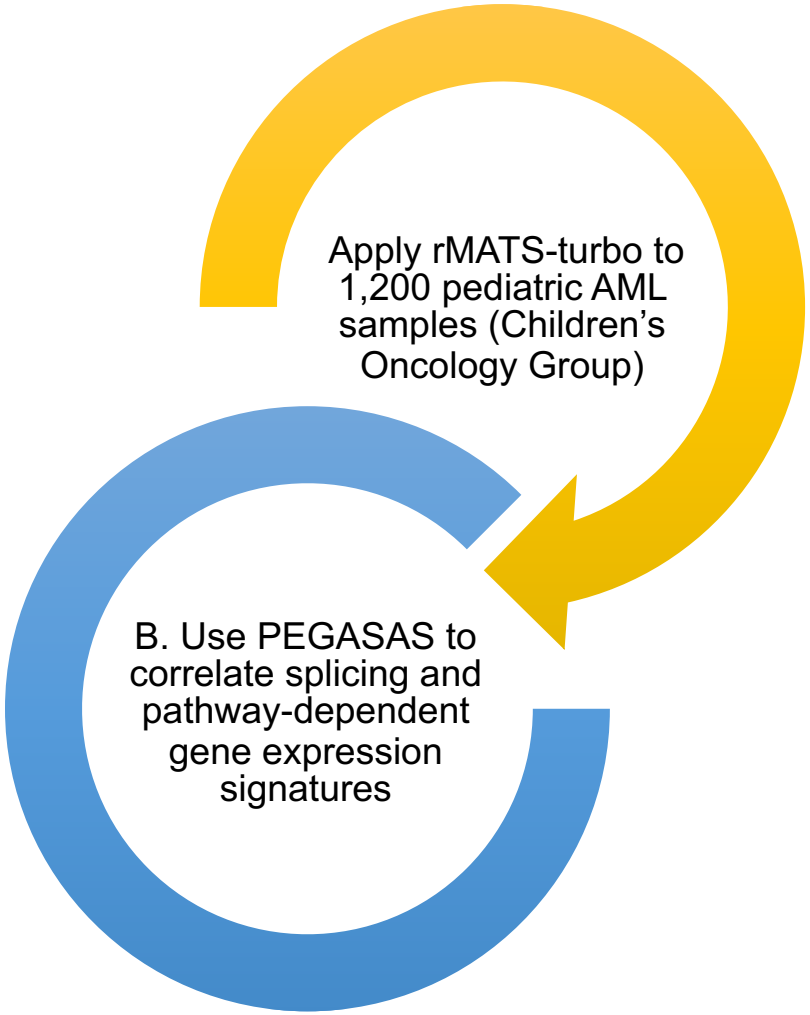
Aim 1: Improve analysis of splicing in large heterogenous RNA-seq datasets

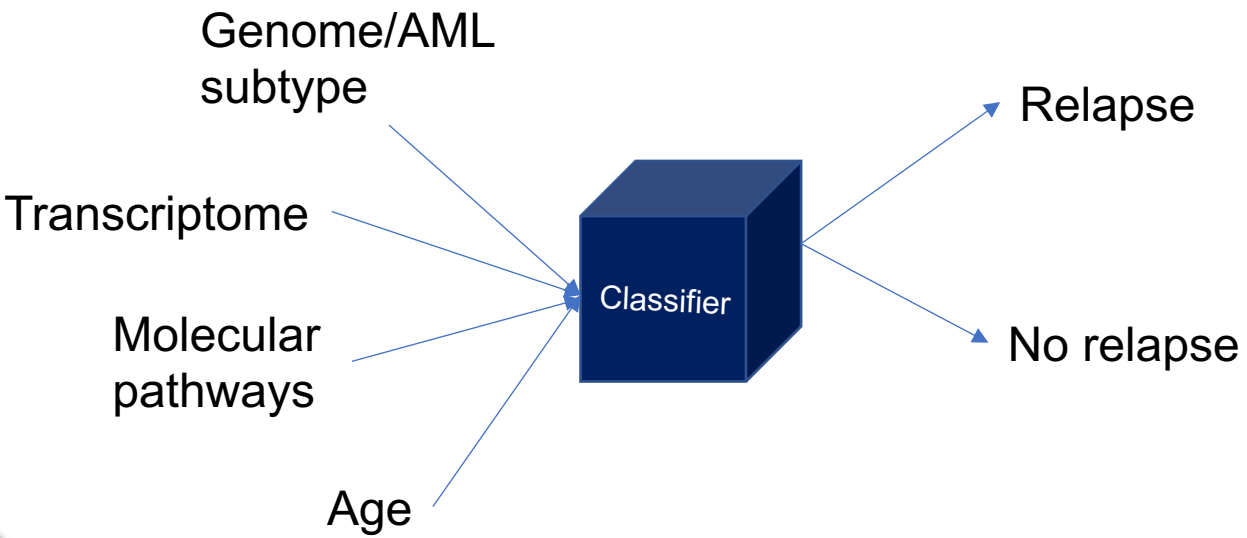
- PEGASAS lacks an approach to make batch effect-informed correlations
- Capture and use expression heterogeneity to mitigate batch effects → Surrogate variable analysis (SVA)
- Using SVA could improve reproducibility and downstream accuracy
- Approach
  - Compare pathway-relevant exons detected with/without SVA



Leek & Storey, 2007

Aim 2: Discover age-specific, pathway-dependent alternative splicing patterns in pediatric AML RNA-seq data





Age and genetics: how do prognostic factors at diagnosis explain disparities in acute myeloid leukemia?

Manali I Patel [1], Yifei Ma, Beverly S Mitchell, Kim F Rhoads

Affiliations + expand

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