Archives of Science

Campbell, Arch Sci 2023, 7:3

Short Communication Open Access

Identification and Treatment of Juvenile Acute Myeloid Leukaemia Stem Cell Splicing Dysregulation

Joseph Campbell*

Department of Oncology, College of Medicine, Haiti

Abstract

Acute myeloid leukaemia in children (pAML) is characterised by frequent relapses and a dearth of somatic DNA alterations. Splicing dysregulation has not been thoroughly researched in pAML, despite seminal findings showing that splicing factor mutations and mis-splicing fuel therapy-resistant leukaemia stem cell (LSC) production in adults. Here, we discuss transcriptome-wide analyses of FACS-purified hematopoietic stem and progenitor cells followed by differential splicing analyses, dual-fluorescence lentiviral splicing reporter assays, single-cell proteogenomics analyses, and the potential of the selective splicing modulator Rebecsinib in pAML.

Keywords: Myeloid leukaemia, stem cells, myeloid

Introduction

Alternative pre-mRNA splicing, which is essential for turning pre-mRNAs into mRNAs that are then translated into functional proteins, requires strictly regulated intron removal and exon joining Different splice isoforms' expression can have a variety of impacts on stem cells' functional traits, including as differentiation, self-renewal, dormancy, and homing. In human adult myeloid malignancies like acute myeloid leukaemia, deregulated alternative splicing has been associated with somatic mutations in splicing regulatory genes like SRSF2, U2AF1, and SF3B1. It also confers a bad prognosis (AML). In some instances, inflammatory cytokine-induced RNA editing by ADAR1—which adds novel splice acceptor sites through adenosine-to-inosine (A-to-I) RNA editing—can also result in mis-splicing in stem cell regulatory transcripts [1,2].

Identification of somatic mutations in pAML by whole-exome sequencing

Given the relative scarcity of somatic mutational drivers in pAML samples, it is possible that other molecular mechanisms, such as changes in pre-mRNA splicing, are what drive the development of LSC and treatment resistance.

4 Malignant pre-mRNA splicing dysregulation has not been documented in pAML, despite being a crucial driver of therapy-resistant LSC formation in adults. We obtained bone marrow or peripheral blood from children with AML (pAML; 1 to 14 years of age) and age-matched non-leukemic people (pNL), and then we performed differential gene expression and splice isoform RNA-seq analysis to learn more about the function of malignant pre-mRNA splicing in pAML. Also, we examined patients with adult secondary AML (sAML; 59 to 82 years) and dnAML (34 to 83 years of age) [3, 4, and 5].

LSCs can be distinguished from normal blood cells based on gene expression and splicing signatures as well as the ability to self-renew in immunocompromised mouse models, according to several adult dnAML and sAML studies. LSCs can be enriched in the CD34+CD38Lineage- HSC or the CD34+CD38+Lineage HPC compartment Similar to adults with AML, children with AML who are more prone to develop resistance to treatment plans intended to kill dividing cells can be identified by the frequency of LSCs [6]. As a result, the identification and eradication of LSCs seem essential. We used RNA-seq on FACS-purified CD34+CD38+Lineage- cells (HSCs) and CD34+CD38+Lineage- cells to examine the cell type and context-specific roles of malignant pre-mRNA splicing in pAML pathogenesis (HPCs) [7,8].

Conclusion

Data were analysed using Microsoft Excel and plotted for graph generation and statistical analyses in Prism GraphPad for splicing reporter assays, qRT-PCR analysis, and flow cytometry (San Diego, CA). Unpaired or paired tests were used to evaluate differences. According to the figure legends, Student's t-tests are considered statistically significant when the p value is less than 0.05. Data (means) were computed and graphed for several group comparisons and stromal co-culture tests. The SD or SEM is represented by error bars, as stated in the legends of each individual figure. Using Prism GraphPad, statistical analyses including the Student's t test and one-way ANOVA were conducted, with comparisons detailed in each figure legend [9, 10].

Acknowledgement

None.

Conflict of Interest

None.

References

1. Derraik JGB (2002) the pollution of the marine environment by plastic debris: a review. Mar Poll Bull 44: 842-852.
2. Barnes DKA, Galgani F, Thompson RC, Barlaz M (2009) Accumulation and fragmentation of plastic debris in global environments. Phil Trans R Soc B 364: 1985-1998.
3. Thompson RC, Swan SH, Moore CJ, vom Saal FS (2009) our plastic age. Phil Trans R Soc B 364: 1973-1976.
4. Avio CG, Gorbi S, Regoli F (2017) Plastics and microplastics in the oceans: from emerging pollutants to emerged threat. Mar Environ Res 128: 2-11.

***Corresponding author:** Joseph Campbell, Department of Oncology, College of Medicine, Haiti, E-mail: Joseph33@hotmail.com

Received: 01-May-2023, Manuscript No: science-23-91435; **Editor assigned:** 03-May-2023, Pre-QC No: science-23-91435 (PQ); **Reviewed:** 17-May-2023, QC No: science-23-91435; **Revised:** 23-May-2023, Manuscript No: science-23-91435 (R); **Published:** 29-May-2023, DOI: 10.4172/science.1000153

Citation: Campbell J (2023) Identification and Treatment of Juvenile Acute Myeloid Leukaemia Stem Cell Splicing Dysregulation. Arch Sci 7: 153.

5. Jambeck JR, Geyer R, Wilcox C, Siegler TR, Perryman M, et al. (2015) Plastic waste inputs from land into the ocean. Science 347: 768-771.

6. Law KL (2017) Plastics in the marine environment. Annu Rev MarSci 9: 205-229.

7. Andrady AL (2011) Microplastics in the marine environment. Mar Poll Bull 62: 1596-1605.

8. Cole M, Lindeque P, Halsband C, Galloway TS (2011) Microplastics as contaminants in the marine environment: a review. Mar Poll Bull 62:2588-2597.

9. Van Cauwenberghe L, Vanreusel A, Mees J, Janssen CR (2013) Microplastic pollution in deep-sea sediments. Environ Poll 182: 495-499.

10. Obbard RW, Sadri S, Wong YQ, Khitun AA, Baker I (2014) Global warming releases microplastic legacy frozen in Arctic Sea ice. Earth's Future 2:315-320.