Peer Review File

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Reviewer A

Comment 1: Line 29: “apparent that KMT2A is promiscuous”
Please rephrase this sentence as it is missleading. Promiscuous is more used for an enzyme or a reaction but not for a fusion breakpoint.

Reply 1: Thank you for pointing out this error in terminology. We have rephrased the sentence as below.

Changes in the text: Line 29-30 was updated to state: “apparent that KMT2A is able to pair with many different genes, with over 100 different fusion partners identified (1).”

Comment 2: Line 36-38: “including t(6;11)(q27;q23), t(10;11)(p12;q23), and t(10;11)(p11.2;q23). Subsequent studies supported these results and further expanded high risk KMT2Ar AML to include t(4;11)(q21;q23) and t(11;19)(q23;p13.3)”
Please include fusion names to identify fusion partner for clarification.

Reply 2: Thank you for this recommendation. The text has been updated to include the fusion partners.

Changes in the text: Lines 36-38 were updated to state: “including t(6;11)(q27;q23), t(10;11)(p12;q23), and t(10;11)(p11.2;q23), in which the *KMT2A* partner genes are *AFDN, MLLT10*, and *ABI1*, respectively. Subsequent studies supported these results and further expanded high risk KMT2Ar AML to include t(4;11)(q21;q23) and t(11;19)(q23;p13.3), with associated fusion partner genes *AFF1* and *MLLT1*, respectively.

Reviewer B

In this editorial commentary, the authors provide a succinct overview of recent studies that have reported on the role of rearrangements of KMT2A in prognosis of pediatric AML. Advances in molecular sequencing have revealed numerous different KMT2A fusions that are prognostically significant. The article is well-written, featuring a logical progression of information that enables the reader to comprehend the intricate nature of KMT2A rearrangements. The authors maintain a balanced perspective by addressing the difficulties linked to altering treatment strategies according to the specific KMT2A rearrangement. They suggest that prospective studies will be essential, utilizing risk stratification criteria to delineate the optimal therapeutic approach for these patients.

Reply: Thank you for your kind review of our manuscript.

Changes in the text: No changes were required to address this comment.
