

Genetic mechanism for the loss of PRAME in B cell lymphomas. Reply.

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Letter to the Editor **Hematology** **Immunology**

The authors reply: We thank Dr. Mraz for insightful comments that provide additional context to the findings in our study, in particular bringing to the forefront studies in other B cell malignancies including chronic lymphocytic leukemia (CLL) (1). As pointed out in the Letter by Dr. Mraz and discussed in our manuscript, PRAME deletions were significantly associated with Ig-λ rearrangements, and this finding is consistent with a mechanism in which PRAME deletions can occur in the context of rearrangement of variable (V) gene loci on chromosome 22 in a subset of patients (2). For this reason, we studied frequencies and treatment outcomes for PRAME deletions in the context of Ig-λ expression, as shown in Figure 1 (2). In particular, we demonstrate that PRAME deletions are independently associated with outcomes in multivariable analysis, making it unlikely that PRAME deletions are a pure surrogate for the prognostic effects of Ig-λ usage. As described by Mraz and Pospisilova, the association of PRAME deletion and Ig-λ rearrangement and expression is not absolute, and PRAME deletion is likely dependent on the exact V segment usage (3). Consistently, we did not observe PRAME deletions in the majority of patients expressing Ig-λ, and, interestingly, a minority of patients with PRAME deletions expressed Ig-κ. Indeed, it remains an open question whether heterozygous or homozygous PRAME deletions can occur [...]

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and EZH2 mutations converge on reduced PRAME expression and downstream phenotypes underscores the pathogenic relevance of the PRAME gene in B cell lymphoma.

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Conflict of interest: CS has performed consultancy for Seattle Genetics, Curis Inc., Roche, AbbVie, Juno Therapeutics, and Bayer and has received research support from Epizyme, Bristol-Myers Squibb, and Trillium Therapeutics Inc.

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