

B cell lymphomas and the role of TET enzymes



A recent study published in *Nature Immunology*, highlighted how the loss of TET enzymes can lead to B cell lymphoma. The study by Shukla, et al., may provide us with opportunities for designing novel drug treatment strategies to target cancerous cells.

Previous study highlighted mutations that cause TET enzymes to lose function within individuals suffering from blood and tissue cancer. In this present study, Shukla, et al., investigated TET deficiency and how this may be connected to genomic instability, a cause for cancerous cells.

Using murine models, the researchers found that through deletion of TET2 and TET3 enzymes in mature B cells, resulted in severe consequences for B-cell homeostasis, in addition to an increase in markers for genomic instability. They reported unusual DNA structures called G-quadruplexes and R-loops.

They found that TET enzymes may play a role in regulating the formation of these structures, which further highlight the role of TET enzymes in regulating genomic instability with regard to B cell malignancies.

Further observations lead to them reporting that DNMT1 was upregulated in TET-deficient B cells. DNMT1 is a key enzyme responsible for maintaining DNA methylation. They reported that the deletion of the *Dnmt1* gene in TET-deficient B cells in mice could alter the levels of G quadruplexes and R-loops,

reducing their levels. In addition, deletion of this gene was associated with a delay in the development of aggressive B-cell lymphomas.

This study highlights that regulating G-quadruplexes and R-loops may be just one way TET enzymes control genomic stability, although there is much more work to be done.

Journal article: Shukla, V., et al., 2021. [TET deficiency perturbs mature B cell homeostasis and promotes oncogenesis associated with accumulation of G-quadruplex and R-loop structures](#). *Nature Immunology*.

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