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Review

The Potential Equivalents of *TET2* Mutations

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Simple Summary: In acute myeloid leukemia (AML) *TET2* mutations have been observed to be mutually exclusive with *IDH1*, *IDH2*, and *WT1* mutations, all of them showing a similar impact on the transcription profile. Because of this, it is possible that *TET2*/*IDH1*/*2*/*WT1* mutated AML could be considered as having similar characteristics between each other. Nonetheless, other genes also interact with TET2 and influence its activity. Because of this, it is possible that other signatures exist that would mimic the effect of *TET2* mutations. Thus, in this review, we searched the literature for the genes that were observed to interact with TET2 and classified them in the following manner: transcription alteration, miRs, direct interaction, posttranslational changes, and substrate reduction.

Abstract: TET2 is a dioxygenase dependent on Fe^{2+} and α-ketoglutarate which oxidizes 5-methylcytosine (5meC) to 5-hydroxymethylcytosine (5hmeC). TET proteins successively oxidize 5mC to yield 5-hydroxymethylcytosine (5hmC), 5-formylcytosine (5fC), and 5-carboxylcytosine (5caC). Among these oxidized methylcytosines, 5fC and 5caC are directly excised by thymine DNA glycosylase (TDG) and ultimately replaced with unmethylated cytosine. Mutations in *TET2* have been shown to lead to a hypermethylated state of the genome and to be responsible for the initiation of the oncogenetic process, especially in myeloid and lymphoid malignancies. Nonetheless, this was also shown to be the case in other cancers. In AML, *TET2* mutations have been observed to be mutually exclusive with *IDH1*, *IDH2*, and *WT1* mutations, all of them showing a similar impact on the transcription profile of the affected cell. Because of this, it is possible that *TET2*/*IDH1*/*2*/*WT1* mutated AML could be considered as having similar characteristics between each other. Nonetheless, other genes also interact with TET2 and influence its effect, thus making it possible that other signatures exist that would mimic the effect of *TET2* mutations. Thus, in this review, we searched the literature for the genes that were observed to interact with TET2 and classified them in the following manner: transcription alteration, miRs, direct interaction, posttranslational changes, and substrate reduction. What we propose in the present review is the potential extension of the *TET2*/*IDH1*/*2*/*WT1* entity with the addition of certain expression signatures that would be able to induce a similar phenotype with that induced by TET2 mutations. Nonetheless, we recommend that this approach be taken on a disease by disease basis.

Keywords: TET2; mutations; equivalent; expression

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1. Introduction

TET2 is a dioxygenase dependent on Fe^{2+} and α-ketoglutarate which oxidizes 5-methylcytosine (5meC) to 5-hydroxymethylcytosine (5hmeC). TET proteins successively