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WES Leukemia Research Foundation Research Summary

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Project Title: MLL-rearranged Leukemias

I am deeply grateful to the When Everyone Survives Leukemia (WES) Research Foundation for its generous support given to my laboratory team to advance the understanding and development of novel therapies for MLL-rearranged acute myeloid leukemia (AML).

In the early 1980s, a very aggressive subtype of infant leukemia presenting within the first year of life was characterized by MLL-rearrangements that involve chromosomal lesions. Today we know that up to 80% of infant Acute Lymphoid Leukemia (ALL) and about 35-50% of pediatric AML harbor these abnormalities. This chromosomal lesion has also been recorded in patients that suffer from therapy-induced AML after treatment with certain genotoxic agents. Finally, these translocations also occur in sporadic cases of adult ALL and AML, accounting for 5% of adult ALL and 5-10% of AML. The common clinical denominator of all these cases is their *dismal prognosis*. Efforts to identify new therapies to treat AML patients are urgently needed.

Our laboratory generated data indicating that the protein SND1 (short for Staphylococcal Nuclease and Tudor Domain- containing 1) is important for cancer development in MLL-fusion AML. Therefore, inhibition of SND1 activity has the potential to be a therapeutic application in MLL-rearranged AML. In this study, utilizing MLL-fusion AML cells, we started to investigate the molecular mechanisms and targets of SND1 oncogenic activities as well as identify a potential targeting strategy for SND1 in these devastating cancers.

The support from WES was crucial to obtain preliminary results that will now allow us to obtain NIH fundings to move forward our study on how SND1 enforces oncogenic programs in leukemia cells; and on the development of small molecule inhibition of SND1 activities for therapeutical applications in AML (as single agent or in combination with other already approved drugs).