POSTER 25: SUMOylation Controls AML Cells Migration Through the Regulation of CD36 Gene Expression

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Acute Myeloid Leukemias (AML), is a group of deadly hemopathies, resulting from a deregulation of hematopoiesis in the bone marrow. Despite recent advances in the characterization and prognosis of AML and the hope raised from therapies, the relapse rate is considerable and the overall prognosis remains poor, therefore, therapy improvement is still needed. Our team has previously shown that SUMOylation plays a critical role in the AML response to chemotherapies and differentiation therapies. Thus, targeting SUMOylation constitutes a promising approach in the AML treatment. This hypothesis is being tested by our team, thanks to a collaboration with 'Takeda Pharmaceutical' which developed the TAK-981, a first in class inhibitor of SUMOylation. Our team demonstrated that TAK-981 has a promising anti-leukemic effect both in vitro and in vivo AML models. Our aim isto understand on the transcriptional level, the TAK-981 effect on AML cells, and to determine the function of the TAK981- induced genes in AML. We performed an RNA-seq analysis on a TAK981-treated AML cell line, U937, and we observed limited effect on gene expression. Among the few overexpressed genes, we identified the CD36 gene, expressed in different cell-types, in particular, hematological cells. These results were confirmed by flow cytometry and RT-PCR. We also showed that the transcription factor PPAR8 is involved in the TAK981-induced CD36 overexpression. Moreover, we demonstrated that the TAK981 treatment didn't affect lipid uptake & accumulation, however, it increased AML cells migration. We finally found that the CD36 was highly expressed in migrating cells and that its inhibition by a specific antibody decreases AML cells migration. In conclusion, TAK-981 upregulates CD36 expression, via PP AR8, which increases AML cells migration. Therefore, CD36 could be considered as a target in order to improve AML response to T AK981 which could pave the way to developing clinical-grade antibodies specific to CD36.