UNIVERSITÀ DEGLI STUDI DEL SANNIO Benevento

DST

DIPARTIMENTO DI SCIENZE E TECNOLOGIE

Dottorato di Ricerca in Scienze e Tecnologie per l'Ambiente e la Salute

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Metabolic vulnerabilities in acute myeloid leukemia

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Aula 3, CUBO

Via dei Mulini, BENEVENTO

ABSTRACT

Acute myeloid leukemia (AML) is a heterogeneous malignancy with poor outcome. Despite recent advancements in the therapeutic setting, personalized approaches are limited to the presence of few selected genetic lesions. However, metabolic reprogramming plays a crucial role in the response of leukemic stem-progenitor cells to therapy and can be targeted for innovative combinations. In the past years we have profiled the intracellular and biofluid AML metabolic landscape, which is characterized by dysregulated amino acid, nucleotide, lipid, and bioenergetic metabolism. In particular, we provided a map of alterations in the metabolism of polyamine, purine, keton bodies and polyunsaturated fatty acids and tricarboxylic acid cycle. Preclinical data suggests that polyamine metabolism can be targeted for therapeutic purposes in AML. By integrating the intracellular metabolome with genetics, we distinguished three AML clusters : NPM1-mutated), chromatin/spliceosome-mutated and TP53-mutated/aneuploid AML that were confirmed by biofluid analysis. Interestingly, integrated genomic-metabolic profiles defined two subgroups of NPM1-mut AML with diverse drug sensitivity. These results pave the way for novel therapeutic combinations targeting metabolic vulnerabilities.