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POSTER 14: Role of AhR in Ara-c resistance in Acute myeloid leukemia

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Rational. Acute myeloid leukemia (AML) is a heterogeneous hematological malignancy characterized by cell-differentiation arrest and accumulation of leukemic blasts in bone marrow and blood. It is a childhood rare disease which incidence increases with age. The treatment combines the cytarabine (Ara-c) with an anthracycline. Relapse caused by persistent AML cells still remains a major issue in 30-80 % of cases. AhR, a ligand-dependent transcription factor responding to environmental signals, has been involved in hematopoietic/leukemic stem cells processes (self-renewal and differentiation). However, its involvement in AML drug-resistance requires further investigation.

Methods. Eight pairs of Ara-c-sensitive (S) and Ara-c-resistant (R) AML cell lines have been characterized for AhR expression by western blot and transcriptomics (RNAseq and RT-qPCR) analyses.

Results. Three groups of cells were defined based on the AhR expression: cells that 1) neither expressed AhR in S nor in R, 2) have induced AhR in R, and 3) expressed AhR in S and R. Results also showed that a strong expression of AhR in R cells corresponds to a higher Ara-c resistance. RNAseq discriminated S and R cells and linked AhR in R-cells to enriched AhR targets, suggesting AhR-dependent transcriptional reprogramming in resistance.

Perspectives. The next step will be to validate the role of AhR in Ara-c resistance by modulating its expression and activity, as well as studying the impact of the tumor microenvironment.