AACR 2017: Poster 5382/14 – DNMT3A independent hypomethylator phenotype in AML

Cynthia Umukoro | Apr 7, 2017

On Wednesday 5th April, 2017, at the 107th American Association for Cancer Research (AACR) annual meeting in Washington, DC, USA, there was poster session focused on “Epigenetics”.

Kelly et al., from the Lewis Katz School of Medicine at Temple University, Philadelphia, presented results from their study which aimed to identify and characterize the clinical impact of Hypomethylator Phenotypes (HPs) in Acute Myeloid Leukemia (AML).

Using data from The Cancer Genome Atlas (TCGA), the authors carried out a genome-wide CpG methylation analysis on 194 AML samples.

The key results were:

- Two distinct HPs were identified; Good Risk (GR) HP (favorable cytogenetics) and DNMT-HP (enriched in DNMT3A mutations)
- Patients with t(8;21), inv(16), or t(15;17) belonged to the GR-HP+ group
- Median Overall survival (OS) in GR-HP+ and GR-HP- patients; not reached vs 1 year, \( P < 0.001 \)
- Median OS in DNMT-HP+ and DNMT-HP- patients; 0.92 vs 1.34 years, \( P = 0.27 \)
- Hypomethylation within non-CpG islands relative to CpG islands were harbored in DNMT-HP (Odds Ratio [OR] = 0.18) and GR-HP (OR = 0.64)

- Patients with GR-HP+ AML had wild-type IDH, DNMT3A, and NPM1 genes

- Compared to DNMT-HP-, there were significantly more FLT3, NPM1, and DNMT3A mutations in DNMT-HP+ AML patients

In summation, “two HPs exist in AML with unique epigenetic and transcriptomic signatures”. The authors concluded by stating that “association between GR-HP and different favorable cytogenetic changes suggests that a common set of epigenetic features” which may contribute to improved survival in these patients.

References: