ADVANCEMENTS IN THE DIAGNOSIS OF ACUTE MYELOID LEUKEMIA THROUGH THE APPLICATION OF OPTICAL GENOME MAPPING

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INTRODUCTION

- The detection of structural variants (SV) and copy number variations (CNV) of chromosomes plays a pivotal role in the diagnosis of acute myeloid leukemia (AML). Chromosome banding analysis (CBA) and fluorescence in situ hybridization (FISH) are the standard-of-care (SOC) methods, however, there is a growing interest in utilizing advanced diagnostic techniques.
- Optical Genome Mapping (OGM) is a cutting-edge cytogenomic method that enables the simultaneous identification of CNVs and SVs larger than 500 base pairs without the requirement of cell culture, yielding results within a span of 5 days.

AIM

- We aimed to detect chromosomal aberrations in acute leukaemias using OGM, and to test the feasibility of OGM in routine diagnostics in comparison with CBA and FISH analyses.

METHOD

- 9 diagnostic or relapsed AMLsamples were analysed.

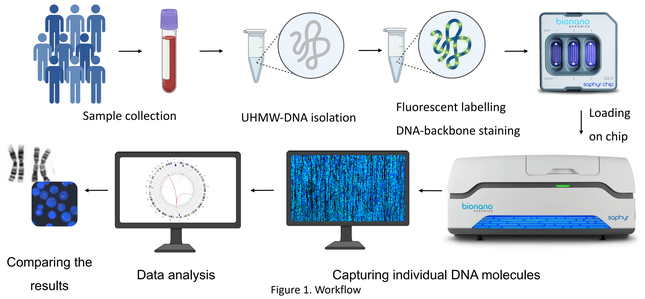


Figure 1. Workflow

- Ultra-high molecular weight DNA was isolated and subsequently fluorescently labeled.
- Data were collected by the optical system of the Saphyr instrument (Bionano, San Diego, USA) and were analysed in Bionano Access software.
- SVs were characterized following the application of both standard and AML-specific filtering, CNVs >5000kb without further filtering.
- The OGM data were compared with the results of karyotyping and FISH.

RESULTS I

- A total of 38 CNVs were detected in the samples using OGM, 184 SVs with standard and 34 SVs with AML-specific filters.
- With the SOC methods, 3 cases with complex karyotype (CK, ≥3 aberrations) were detected, while according to the OGM results, we identified CK in two additional cases.
- Based on the results obtained from 9 samples we categorized them into the WHO 2022 classifications.
- In 2 cases, the application of OGM allowed for refined categorization detecting myelodysplasia-related abnormalities in one case and *MECOM* gene rearrangement in the other.

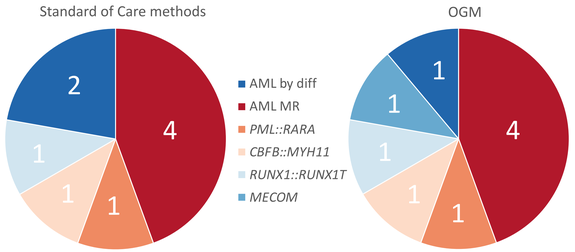


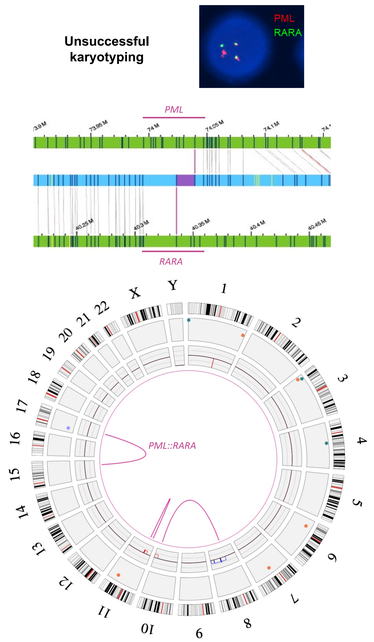
Figure 2. AML - WHO classification 2022

CONCLUSIONS

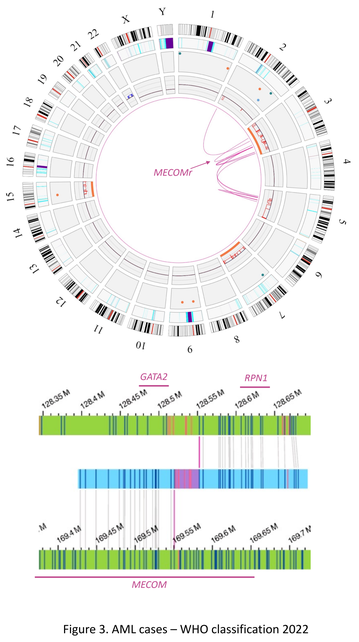
- The use of OGM allows simultaneous identification of copy number variations and >500 kb structural variants.
- The application of OGM represents a significant advancement in the detection of chromosomal aberrations in AML patients, surpassing the capabilities of traditional techniques.
- Identifying additional clinically relevant aberrations, OGM facilitates the prompt and accurate implementation of appropriate treatment strategies.

RESULTS II

AML with *PML::RARA* fusion



AML with CK and *MECOMr*



AML with CK (2 cases)

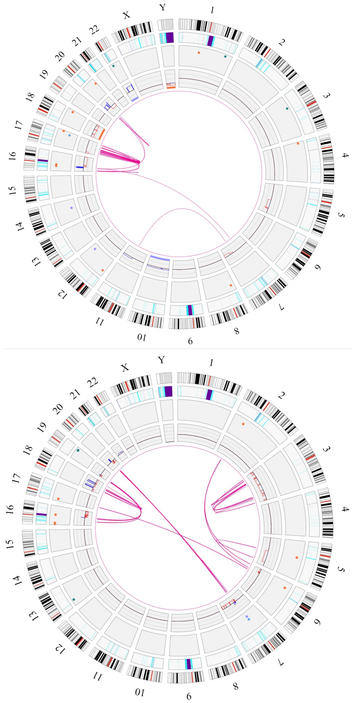


Figure 3. AML cases – WHO classification 2022

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