# OPTICAL GENOME MAPPING: THE NEW FRONTIER OF CYTOGENOMIC DIAGNOSIS?

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The primary aim of a cytogenetics laboratory is to define the most appropriate diagnostic strategies in order to provide clinicians with relevant and actionable information for optimal patient management. Together with molecular biology data, these findings represent an essential and indispensable component for the diagnosis, prognosis and treatment of onco-hematological diseases.

Optical genome mapping (OGM) is an emerging genome-wide cytogenomic technology that enhances the detection of structural and copy number variants compared with conventional cytogenetic methods through the analysis of ultra-high molecular weight DNA molecules linearized in nanochannels. OGM improves the identification of cryptic and complex genomic rearrangements and facilitates the discovery of novel cytogenomic biomarkers, with a significant impact on risk stratification and therapeutic targeting. Recent expert recommendations support its integration into the cytogenomic and molecular work-up of hematological malignancies in the context of the updated WHO and ICC classifications.

In hematological malignancies, chromosomal aberrations represent key diagnostic and prognostic biomarkers. Standard cytogenetic approaches, including chromosome banding analysis, fluorescence in situ hybridization and chromosomal microarrays, remain the current diagnostic backbone but are limited by resolution, culture dependency and target-restricted analysis. OGM has demonstrated high concordance with standard methods while providing additional clinically relevant information, particularly in cases with complex karyotypes and cryptic rearrangements, leading to a more accurate prognostic stratification. When integrated with targeted next-generation sequencing, OGM enables a comprehensive genomic characterization within a single workflow.

Despite its clear advantages, OGM does not fully replace conventional techniques and its application must be guided by disease-specific clinical indications. Expert consensus recommends OGM as a first-line or second-line tool depending on the diagnostic setting, particularly in cases with failed karyotypes, normal cytogenetics with suspected cryptic aberrations, and entities requiring genome-wide structural variant assessment

The presentation will briefly outline the technical basis of OGM and, through selected representative clinical cases, will highlight its major advantages in improving diagnostic precision and prognostic stratification, as well as its current limitations and optimal positioning in routine diagnostic practice.

**References**

1. **Kanagal-Shamanna R et al.** — Am J Hematol. 2025;100(6):1029-1048. https://doi.org/10.1002/ajh.27688
2. **Levy B et al.** — Am J Hematol. 2024;99(4):642-661. https://doi.org/10.1002/ajh.27175
3. **Puiggros A et al.** — *Optical genome mapping: a promising new tool to assess genomic complexity in chronic lymphocytic leukemia (CLL).* Cancers. 2022. https://doi.org/10.3390/cancers14143376
4. **Puiggros A et al.** — *Optical genome mapping: technical basis and applications in hematological malignancies.* Sangre. 2023. https://doi.org/10.1016/j.sang.2023.05.001
5. **Ramos-Campoy S et al.** — *TP53 abnormalities are underlying the poor outcome associated with chromothripsis in chronic lymphocytic leukemia patients with complex karyotype.* Cancers. 2022. https://doi.org/10.3390/cancers14133217