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**Low-coverage whole genome sequencing of low- grade dysplasia strongly predicts advanced neoplasia risk in ulcerative colitis**

**Al-Bakir I, Curtius K, Cresswell G, *et al*. Low-coverage whole genome sequencing of low-grade dysplasia strongly predicts advanced neoplasia risk in ulcerative colitis. *Gut* 2025;74(5):740-751. doi:10.1136/gutjnl-2024-333353**

This study by Al-Bakir et al., evaluates the prognostic utility of low-pass whole genome sequencing (lpWGS) to stratify cancer risk in patients with ulcerative colitis (UC) who present with low-grade dysplasia (LGD). In a multicentre, retrospective case–control design, Al-Bakir et al., analysed 270 LGD lesions from 122 patients, classifying individuals as progressors (developing high-grade dysplasia [HGD] or colorectal cancer [CRC] within approximately 5 years) or non-progressors. Copy number alterations (CNAs) were quantified from archival formalin-fixed paraffin-embedded (FFPE) LGD biopsies using lpWGS

The study found that CNA burden was significantly higher in progressors than in non-progressors, and this genomic marker outperformed traditional clinical risk factors such as lesion size, shape, and resection status. A patient was deemed high risk based on high CNA burden (>14.5 segments), chromosome 17 loss, and presence of microsatellite instability (MSI). This score demonstrated high predictive performance in both discovery and validation cohorts, particularly when combined with clinical information (AUC (area under the curve) 0.85–0.95), with positive and negative predictive values exceeding 90% at 5 years.

Multivariate modelling incorporating the genomic score and incomplete LGD resection improved stratification of high-risk patients. Notably, CNA-based predictions were robust despite intralesional heterogeneity, supporting their use in routine samples. The findings also reinforce the concept of field cancerisation in UC, suggesting that CNA-bearing cells extend beyond morphologically dysplastic regions.

In conclusion, lpWGS-based CNA profiling is a powerful, cost-efficient, and clinically translatable biomarker for future cancer risk in UC, offering a path to more personalised and risk-informed management of dysplasia in inflammatory bowel disease.